

Swedish National Council on Medical Ethics

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Statement of opinion on pre-implantation genetic diagnosis

In this opinion, the Swedish National Council on Medical Ethics presents its proposals concerning the regulation and use of pre-implantation genetic diagnosis (PGD).

The resolution was taken by Council members Daniel Tarschys (chairman), Ingrid Andersson, Leif Carlson, Kenneth Johansson, Tuulikki Koivunen Bylund, Elina Linna, Göran Sjönell and Conny Öhman. Chatrine Pålsson made a reservation against the decision.

Daniel Brattgård, Anne-Christine Centerstig, Göran Hermerén, Per-Christian Jersild, Lena Jonsson, Niels Lynöe, Lisbeth Löpare-Johansson, Christian Munthe, Elisabeth Rynning, Jan Wahlström and Kerstin Wigzell participated in the Council's discussions of the question. Special statements were made by Daniel Brattgård and Sture Gustafson.

Hans-Gunnar Axberger (head of the secretariate) and Lotta Eriksson (research secretary) have prepared the case.

Daniel Tarschys
Chairman

Summary

In this opinion, the Swedish National Council on Medical Ethics raises issues on pre-implantation genetic diagnosis (PGD). PGD is performed in connection with assisted reproduction. The diagnostic means that a fertilised ovum (egg) is submitted to genetic testing before being inserted into a woman's uterus, to develop into a foetus in due course.

PGD gives the possibility of obtaining complete information about the future child's genetic make-up. So far, the method has mainly been of interest for genetic information known to be associated with severe diseases or disabilities. When there is an increased risk of such a gene being inherited in an individual case, it can thus be located and screened out.

PGD can also be used as a standard procedure in the treatment of involuntary childlessness. In each individual treatment, all fertilised eggs then undergo genetic testing with the aim of using the egg providing the greatest chance of a successful outcome of the treatment. Since this method involves PGD testing of all fertilised eggs, it is known as 'pre-implantation genetic screening', PGS.

At present, PGD is not subject to any explicit statutory regulation. However, in 1995, the Swedish Parliament endorsed certain guidelines. These are highly restrictive, and mean that PGD should only be used to screen for grave, progressive, inherited disorders leading to premature death and for which there is no cure or treatment. These guidelines have been followed in Swedish healthcare, while also being criticised as inappropriate in various respects. The Committee on Genetic Integrity, a government commission, is currently entrusted with reviewing them.

In this opinion, the Swedish National Council on Medical Ethics discusses the medical and ethical conditions for PGD. The Council's deliberations have led to the conclusion that the use of the PGD technique should be allowed on a somewhat larger scale than what is permitted in the current guidelines. The Council also considers that all cases of PGD use should be reported to the National Board of Health and Welfare to facilitate monitoring and supervision.

According to the Council, pre-implantation genetic screening, PGS, should not be used as a standard procedure, given the current state of knowledge. Before a complete ethical assessment can be made, research and findings are needed that will identify possible advantages and disadvantages of this technique from medical, ethical and social points of view. However, the Council considers that PGS may, for the time being, be ethically acceptable within clearly defined research projects preceded by ethical assessment in a research ethics committee. Also in this case does the Council recommend an obligation to report to the National Board of Health and Welfare.

In conclusion, the Council finds that the PGD technique is under development and new areas of application will require further ethical standpoints. The technique can, for example, be used in situations where parents want a child who can become donor for a child they already have who suffers from a severe disease (so-called PGD/HLA typing). There are, however, several unresolved issues connected with this technology — issues that the Council intends to address in its future work.

Chatrine Pålsson (a Christian Democratic member of the Swedish Parliament) has entered a reservation. She considers that PGD should be regulated in a special framework law in accordance with the guidelines adopted by the Swedish Parliament in 1995. She does not consider that PGS should be introduced in research.

Daniel Brattgård, expert member, has issued a special statement of opinion that, in content, tallies with Chatrine Pålsson's reservation.

In a special statement of opinion, Sture Gustafsson, expert member, has entered a dissenting opinion with respect to PGD and PGS.

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Background to the opinion

The Swedish National Council on Medical Ethics has, at its own initiative, opted to give its opinion on pre-implantation genetic diagnosis (PGD). A written statement from Etisk Samrådsgrupp för Preimplantatorisk Genetisk Diagnostik, (ESPGD), (Ethical Consultation Group on Pre-implantation Genetic Diagnosis) to the Minister for/the Ministry of Health and Social Affairs was sent to the Council in May 2000. The issue was once more raised by the Council's experts when new forms of applying PGD were presented in the spring of 2002.

During the work on this opinion, the Council studied documents and facts about how PGD and its various applications are discussed and dealt with in Sweden and abroad, and also social and medical research on PGD. The Council has also consulted medical experts in the field.

The Council has consulted Kommitén om genetisk integritet (S 2001:01), (the Committee on Genetic Integrity) whose tasks include reviewing the Swedish Parliament's guidelines on PGD.

1 Pre-implantation genetic diagnosis — PGD

1.1 *What is PGD?*

Pre-implantation genetic diagnosis is carried out in connection with artificial fertilisation, i.e. in vitro fertilisation or the injection of sperm into an ovum. The testing is made possible by so-called biopsy, i.e. one or two cells are separated from a fertilised ovum (egg) at the stage when it consists of eight to ten cells. The diagnostics means that genetic testing is performed on a fertilised egg before it is inserted into a woman's uterus, to develop into a foetus in due course.

1.2 *Why is PGD performed?*

The aim of PGD is to obtain a genetic diagnosis. The fertilised egg has the same genetic make-up as the individual into which it can potentially develop. The genes of this future individual can be determined thanks to PGD.

If there is an elevated risk for the man and the woman wishing to have a child that their child will incur a grave genetically caused disease, this risk can be eliminated after PGD. Thus, only those fertilised eggs that are found to be free from the hereditary disposition in the testing are selected for implantation.

However, PGD can, in principle, be used for any form of genetically based selection. This is not necessarily related to hereditary dispositions; it can, for example, be used to select the sex of the future child.

1.3 *Various forms of PGD*

As we have seen, PGD makes it possible to obtain complete information about the genetic make-up of the future child and thus, it potentially contains a great deal of information. As in the case of all genetic information, it is difficult to interpret, however. So far, the method is of greatest interest for the kind of genetic information known to be associated with severe diseases or disabilities. When, in an individual case, there is an elevated risk of such a gene being inherited, this gene can thus be located and screened out. Used in this way, PGD is an alternative to prenatal diagnostics. Genetic prenatal diagnostics has long been used through tests of amniotic fluid (amniocentesis) or the placenta. These diagnostic results can guide the pregnant woman in her decision of whether to complete the pregnancy. By instead using PGD, the woman can obtain the corresponding information at a far earlier stage, before becoming pregnant. If the treatment is successful, she can almost be completely sure that the foetus she is carrying does not have the gene.

Moreover, PGD can be used as a standard procedure in the treatment of involuntary childlessness. All fertilised eggs are then subject to genetic testing with the purpose of using the egg with the best chance of resulting in a successful treatment in each individual case, since there is some knowledge of genetic factors influencing the success of the implantation and the risk of miscarriage. This knowledge can be used to select the most suitable fertilised eggs from these points of view. Since this method involves PGD testing of all fertilised eggs, it is known as 'pre-implantation genetic screening', PGS.

Genetic information is not confined to diseases and disabilities: it can also include traits or characteristics. In certain circumstances, it may be justified to seek such information through

PGD. This applies when a child suffers from a severe disease that could be cured by a transplant from someone with a similar genetic make-up. Potential donors for such a transplant may be sought among siblings. A possible means of treating the disease is for the parents to try to have another child with the required genetic make-up, by using IVF and PGD. The purpose of PGD is then for the future child to have the kinds of medical characteristics that will enable him/her to donate tissue to a gravely ill sibling. However, there is some uncertainty about this form of treatment, for example regarding the conditions for which it is suitable and in how many cases it could conceivably be used.

1.4 Medical background

1.4.1 PGD

Pre-implantation genetic diagnosis was developed more than a decade ago, as an alternative to prenatal diagnostics for couples with genes causing severe genetic diseases. In principle, all genetic tests that can be carried out on a foetus can also be carried out on a fertilised egg. Among other things, PGD can be used to diagnose monogenic inherited disorders, chromosomal abnormalities, sex determination and HLA typing. Currently, more than 100 conditions can be diagnosed, a number which is increasing every month.

Some 700–1000 children in the world are estimated to have been born due to PGD.¹ In Sweden, PGD is offered at two hospital departments, one at Huddinge University Hospital south of Stockholm and one at Sahlgrenska University Hospital in Gothenburg. Surveys at these two hospitals have shown that 75 couples have been treated and 17 children born after PGD. The number of PGD attempts (so-called ‘cycles’) initiated is 178.

The PGD treatments carried out in Sweden to date have concerned structural chromosome changes, translocations and inversions and the hereditary monogenic diseases Duchenne, Wiskott Aldrich, Dystrofia myotonica, severe haemophilia and Fragile X.

A report on clinical activities by the European Society of Human Reproduction and Embryology (ESHRE) summarises the European experience in 1999–2001. The number of couples treated is not shown but 1318 cycles are said to have resulted in 215 pregnancies. In the latest reporting year (2001), nearly half (334 out of 772) of the PGD treatments consisted of screening for chromosome abnormalities (PGS). Particularly worth noting is that in 2001, 10 per cent (78) of the PGD cases reported concerned sex selection for social and psychological reasons, i.e. without any medical reasons.²

To date, no elevated risk of damage for the fertilised egg has been found in connection with the biopsy carried out in PGD, but there is limited experience.³ There might, for example, be a minor risk of malformations, and also of damage manifesting itself in later life or in a subsequent generation.

The PGD diagnosis has a margin of error of about a few percent.⁴ At present, foetal diagnostics is recommended in connection with all forms of PGD treatment.

¹ Nationaler Ethikrat, Germany, 2003, p 52.

² ESHRE, 2001. ESHRE’s studies do not cover all PGD performed in Europe, but only the cases of PGD reported to them. Twenty-four different centres are included in the reported material from 1999 to 2001. Material from 12 centres is included for the year 2001.

³ Ingerslev, H.J. et al., 2002, pp. 31 et seq. ESHRE, 2001. Munthe, C. 1999, p. 160.

⁴ The ESHRE report of 2001 gives a diagnostic error of 1.9–2.6%.

1.4.2. IVF (In Vitro Fertilisation)

The IVF method means that several eggs are taken from the woman's ovaries and brought into contact with the man's sperm in a nutrient solution. One of the eggs or more that are fertilised in this way, are selected for implantation in the woman's uterus. Nowadays, the egg might also be fertilised through a so-called 'microinjection', ICSI (intracytoplasmic sperm injection). When IVF is mentioned below, this also relates to ICSI.

The first 'test-tube baby' was born in Britain in 1978. At present, in the world, some 50 000 babies are estimated to be born each year due to IVF. The figure for Sweden is about 2000 (two per cent of the total number of births).

The question of whether IVF entails any risks for the children conceived in this way has been subject to numerous scientific studies.

IVF often leads to the birth of twins⁵ since, to improve the chances of a successful result, more than one fertilised egg is generally implanted. This, in turn, entails the complications associated with multiple births as such.

In a study from the Swedish Council on Technology Assessment in Health Care (SBU) compiling the accessible results from research on IVF, the data available indicated that IVF, as such, is not associated with any marked excess risks for the newborn baby. What was deemed to be the main problem in the context was the high incidence of multiple births, which creates a sharp increase in the need for neonatal hospital care and intensive care, thereby boosting the costs of paediatric departments. Under the heading 'Conclusions', it was stated that:⁶

The conclusions from this review of the literature are, above all, that much greater efforts must be made to follow up children born due to IVF, with a focus on physical as well as mental and social disabilities. The available literature is sparse and constitutes little scientific evidence, for example due to limited material and too short follow-up periods. In particular, the effects of the new techniques, such as ICSI, need to be studied in greater detail in sufficiently large amounts of material. The present literature review, however, gives no indications that the IVF technique, as such, would cause any large absolute increases in risk with respect to malformation frequency or neurological and psychological effects on children. However, it is evident that the high proportion of multiple births, with the ensuing elevated risks for premature birth and very low birth weight, represents marked risks of morbidity for the children, in the long as well as the short term.

The objective of future IVF activities must be that they should result in singleton pregnancies to the largest possible extent. The best way of reaching this objective is to only implant one egg at a time.

The results from a major Swedish register study conducted during the 1990s indicate that the risk of neurological disorders may be elevated when using IVF. In absolute figures, the risk is small, however. The elevated risk is mainly considered to be due to multiple births and maternal circumstances, rather than the IVF method as such. However, the group of

⁵ According to previous statistics, some 40 per cent of test-tube babies were twins. The present figure is probably lower.

⁶ SBU Report No. 147, 2000, *Barn födda efter konstgjord befruktning (IVF)* ('Children born due to in vitro fertilisation [IVF]'), p. 79

‘singleton’ IVF children also showed an elevated risk of developing neurological disorders as compared to other children.⁷

The largest longitudinal study to date of children born due to IVF was presented in the summer of 2003. The results show there to be no elevated risks for the child. However, the study shows the proportion of malformations in the urinary tract and genitals to be higher in the group of children born due to ICSI.⁸ Whether this statistical correlation is connected to ICSI or can be explained by other factors, such as heredity, is at present unclear.

In December 2002, the National Board of Health and Welfare issued new regulations concerning IVF treatment (*Socialstyrelsens föreskrifter och allmänna råd om assisterad befruktning* (NBHW Regulations and General Recommendations on Assisted Reproduction), SOSFS 2002:13 [M]). These include provisions on the number of eggs that may be implanted in a woman. The main rule is that one egg only may be reinserted. However, if the risk of a twin pregnancy is deemed to be low, taking scientific evidence and reliable experience into account, two eggs may be implanted. In such cases, the couple should be informed about the possible risks of a twin pregnancy, and be offered the opportunity of talking to a paediatrician. The reason for this limitation is the problems associated with multiple-birth pregnancies.

Thus, the risk does not seem to have been elucidated. However, current research may, with caution, be summarised as showing that there are certain elevations in risk that are small in absolute figures, and the causes of which are somewhat uncertain.

1.5 Regulations etc

1.5.1 Report and legislation

The issue of ‘pre-implantation genetic diagnostics’ was discussed in 1989 report *Utredningen om det ofödda barnet* (Report on the Unborn Child).⁹ As far as the commission knew, the technique had, at that time, not yet been used on humans; but experiments had shown that the method could probably be used for this purpose. The commission found it to be uncertain whether PGD could affect the development of the future child. Its conclusion was that as long as there was such remaining uncertainty, this type of diagnostics should not be performed at all. In other respects, the commission considered it too early to express any views on the extent to which the use of PGD should be allowed. The risk of the technique being used for selection of human beings was particularly emphasised as a reason for these doubts.

Several years later, PGD was also dealt with in a government bill on prenatal diagnostics etc.¹⁰ Enclosed with the bill was an opinion from the Swedish Medical Research Council where it appears that until 1991, some ten children had been born in the world as a result of the technique, but none in Sweden. In 1994, the method was still considered as a ‘clinical experiment’ in international contexts. In its bill, the Government expressed a restrictive view of PGD and proposed that the Swedish Parliament should adopt certain guidelines. An even more sceptical attitude to the method emerged in the debates on the bill in the Swedish

⁷ National Board of Health and Welfare Report 2000:4, Strömberg B., Dahlqvist G. et al., 2002, pp. 461–465.

⁸ ESHRE, 2003.

⁹ SOU 1989:51, pp. 107 et seq.

¹⁰ Swedish Government Bill 1994/95:142.

Parliament. The Standing Committee on Health and Welfare (SoU) proposed the following guidelines¹¹

(P)re-implantation diagnostics must be used very restrictively and only for couples carrying genes for grave, hereditary dispositions or chromosome abnormalities. The diagnostics should target grave, progressive, inherited disorders that result in premature death and for which there is no cure or treatment. Sex selection should only be permitted where it is medically justified.

These guidelines were adopted by the Swedish Parliament. In legal terms, the status of such guidelines is unclear. The established constitutional form of norm definition by the Swedish Parliament is law, but the guidelines do not include any real legal regulation of PGD. This lack of clarity has been one reason why the National Board of Health and Welfare has not considered itself to be able to issue any general recommendations on basis of the guidelines.

Given the Parliament resolution on the guidelines, the Government commissioned the National Board of Health and Welfare in November 1995 to monitor the PGD development. In the spring of 1996, the Board issued a brief reply, stating that PGD had been performed at Sahlgrenska University Hospital, but nowhere else in Sweden. There were, however, 'numerous parents' who were interested in PGD treatment for medical reasons. In this context, the National Board of Health and Welfare stated:

Those experts who have expressed their views to the National Board of Health and Welfare emphasise that a difficult educational situation arises when foetal diagnostics is routinely offered for certain diseases when these conditions, under the Bill (Council's note: i.e. the guidelines) cannot be subject to pre-implantation diagnostics. How to explain to a woman who has given birth to a child with cystic fibrosis that abortion-oriented foetal diagnostics must instead be carried out, since the disease is not sufficiently severe to qualify for pre-implantation analysis? There are countless examples of similar situations, where abortion-oriented foetal diagnostics has been a standard procedure for many years in this country and where the disease cannot, according to the Bill, be considered as a severe, progressive, hereditary disease resulting in premature death and that cannot be cured or treated. The latter definition only covers a small number of diseases; it does not, for example, cover the most common chromosome abnormalities that have been routinely detected by foetal diagnostics in Sweden for more than 25 years.

Today, PGD has been established as a method of preventing the transmission of such genes as those described. The 1995 guidelines stand firm. So far, they seem to have been complied with in medical practice, thereby leading to a restrictive use of PGD.

As we have seen, the status of the Parliament guidelines is unclear. When a physician wrote to the National Board of Health and Welfare to say that, contrary to current accepted practice, he intended to offer parents PGD for Fragile X, the Board replied that PGD activities as such are not subject to statutory regulation. Instead, the Board referred the decision on whom should be offered PGD to the head of department, who is responsible for ensuring that the activities are carried out in accordance with science and reliable experience.¹²

In 2001, a parliamentary committee was appointed with the objective of reviewing various issues concerning genetic diagnosis, for example.¹³ One of the commissions of this

¹¹ 1994/95: SoU 18, p. 13.

¹² Letter from the National Board of Health and Welfare to Magnus Nordenskjöld, Head of Department at Karolinska University Hospital, Reg. No. 11570/2001.

¹³ S 2001:01.

committee, which adopted the title of *Kommittén om genetisk integritet* (the Committee on Genetic Integrity), is to review the Parliament guidelines on PGD. The Committee's directives state that it shall consult the Swedish National Council on Medical Ethics. As we have seen, such consultation has taken place on PGD, for example.

1.5.2 Regulations abroad

PGD is permitted to a certain extent in the following countries: Denmark, France, Norway, Spain and the United Kingdom. However, the regulations are differently designed and vary in terms of restrictiveness and forms of supervision. PGD is prohibited in Ireland, Switzerland, Germany and Austria. In the absence of specific regulations, PGD is permitted in Belgium, Finland, Greece, Italy and the Netherlands.

The US have no special regulations. There are private reproduction clinics urging prospective clients to get in touch with any possible wishes, if these are not found among the options presented.¹⁴ However, a future legal regulation of PGD might be likely in the US, in order to prevent 'designer babies'.¹⁵

Proposals from Etiska Samrådsgruppen för PGD, (Ethical Consultation Group on Pre-implantation Genetic Diagnosis)

An independent ethical consultation group has drawn up a proposal for ethical guidelines for PGD.¹⁶ This group was formed to consider the problems that physicians in clinical practice, and others, perceived as being due to the prevailing situation regarding PGD. Participants in the group have had detailed discussions on the ethical conditions for carrying out PGD. The group's considerations are, in principle, based on the description of problems issued by the National Board of Health and Welfare in the cited paragraph above, in its 1996 reply to the Government. After reporting the factual background, the group drew the following conclusions:

1. It may be ethically acceptable to offer PGD.
2. It may be ethically well-justified for a couple to opt for PGD.
3. The question of whether offering PGD is ethically acceptable must be answered on basis of an overall assessment in each individual case.
4. Single diagnoses, disease characteristics or other isolated factors can never in themselves constitute sufficient grounds for deeming it ethically acceptable to offer PGD.

The conclusions resulted in a proposal for specific guidelines intended to serve as support for physicians providing treatment, who take decisions on PGD and are responsible for the care thus offered. In these guidelines, the ethical consultation group both defines the preconditions ('prerequisites') for the application of PGD to be acceptable and a number of factors that should always be considered in the context ('relevant factors in needs assessment').

¹⁴ 'Diseases not listed may be available or may involve mutation analysis workup, so please inquire if the disease of interest is not listed' (http://www.jonesinstitute.org/assist_pgd.html).

¹⁵ 15 Kahn, J.P. 2002. Adams, K.E. 2002

¹⁶ Blennow, E., Munthe, C., Wahlström, J. et al., 2002

Prerequisites

1. The couple must carry a specific monogenic or chromosomal hereditary disease that entails a high risk of giving birth to a child with a genetic disease or damage that can be diagnosed by PGD.
2. IVF is sufficiently reliable for the couple concerned.
3. The couple must have received detailed written and oral information about the nature (prognosis, treatment options, etc) of the disease in question, the extent of the hereditary risk, how PGD is performed, and the advantages and disadvantages of PGD as compared to alternative methods.
4. The couple continues to require PGD in a well-considered way.
5. In the event of pregnancy, conventional foetal diagnostics must be offered.

Relevant factors in needs assessment

1. The couple's general motives for requiring PGD.
2. The couple's attitudes to the alternatives.
3. The couple's life situation, experiences and general mental state.
4. The degree of voluntariness in the couple's wish for PGD in relation to their social circle and factors in society.
5. The degree of severity of the disease.
6. The size of the hereditary risk.
7. The reliability of the diagnosis.

According to the consultation group, these proposals deviate from the Parliament guidelines in two ways. First, the demarcation is not absolute: that is, the application could be more flexible. Second, its guidelines would entail a more restrictive application due to the requirement that the method should only be applied in the case of strongly inherited disorders. The group's assessment was that this would give 'at least the same degree of restriction of activities' as in the guidelines of the Swedish Parliament, 'but with greater clarity and responsiveness to the needs and the particular situation of individual couples'. The group estimated that roughly 50 couples a year would be treated with PGD if its guidelines were implemented.

1.6. General observations on the issues of medical ethics

1.6.1 Starting points

The Swedish National Council on Medical Ethics takes the view of all humans being of equal value and a humanist view of humans as its starting point. The Council's standpoints are based on an assessment based on available knowledge of, first, the possible advantages of the technique in question for various parties concerned and, second, the risks it may be deemed to be associated with, on the same grounds. The Council's task is to devote particular attention to the social aspects.

PGD brings a number of ethical principles and some additional issues that will be generally elucidated below, to the fore.

1.6.2 *The principle of human dignity*

In its earlier publication, *Det svårfångade människovärdet* ('Human Dignity — an Elusive Concept', 1993), the Council claimed that:

- Human dignity is connected to the existence of human beings, not to their functions or characteristics.
- Human dignity is an axiom that cannot be proved by empirical studies or assessments.
- Human dignity means that all human beings have certain fundamental rights that must be respected and that, in these respects, no person is superior to another.
- Human dignity does not exclude the possibility of evaluating people's characteristics, suitability or qualifications in a particular, defined context.

The fundamental requirement that no one is superior to anyone else — the equal value of all human beings — has constituted the basis of the Council's discussion of PGD. The principle of human value also means that there may be limits to what we may subject people to, even in those cases where the intentions and consequences may seem good. Two issues arise from this view: whether the destruction of fertilised eggs that PGD entails means that such a boundary is transgressed; and also whether a systematic screening of eggs with genes for grave diseases and chromosome aberrations (mutations) can create a shift in the view of human dignity that, in the long term, might result in a reduced tolerance of people with disabilities.

In previous opinions, the Council has dealt with the issue of the moral status of the fertilised egg, for example *Assisterad befruktning* ('Assisted Reproduction', 1995), *Om livets början – en debattskrift* ('When Life Begins', Ethical Landmark 10, 2000) and the statement of opinion on *Embryonal stamcellsforskning* (On Embryonic Stem Cell Research) (2002).

There are various views in society of the moral status of a fertilised egg. Three different views can be distinguished:

1. Human life begins at the time of fertilisation and the fertilised egg has full human dignity, i.e. it is entitled to protection and has an unconditional right to life.
2. The creation of human life is a process where the fertilised egg is a life in the making, with a certain value that deserves protection. This value steadily increases with the development of the foetus. At the time when the foetus may be viable outside the mother's body, the value deserving protecting becomes human dignity.
3. The fertilised egg has development potential but possesses no value deserving protection in itself.

The Council has expressed its support for the second view in previous opinions.

One reason for the restrictive use of PGD in Sweden so far is the risk of the technique being applied to systematically screen certain types of people. Based on the principle of human dignity, it is evident that the technology must not be used for such purposes. People with a genetic disposition towards a grave hereditary disease or chromosome aberrations may still perceive the use of this technique as disagreeable and stigmatising, since fertilised eggs with genes corresponding to those they carry themselves are removed.

In the disability movement, there are both opponents to PGD and people in favour of certain forms of PGD for the purpose of avoiding severe diseases (the Swedish Cystic Fibrosis Association). *De Handikappades Riksförbund* (DHR, the Swedish Association for the Disabled) rejects all foetal diagnostics performed with the aim of detecting fetuses with disabilities, on the grounds that it contradicts the idea of the equal value of all human beings. In DHR's view, human dignity must not be graded on a scale laid down by the present predominant attitudes and notions of what is a good life. For the same reasons, they also reject PGD.¹⁷

A central problem discussed in connection with both PGD and prenatal diagnostics is what is commonly known as the 'list problem', i.e. the fact that sensitive issues of demarcation are resolved by listing diseases and disease genes for which treatment or diagnostics is offered. Thus, it has been discussed whether disease genes for which PGD is to be permitted should be listed. One counter-argument that is usually put forward by the disability movement, for example, is that such lists indirectly become descriptions of people considered to be of inferior value, and thereby discriminate against people living with the particular diseases included on such a list.

1.6.3 The principle of doing good

One fundamental aim of treatment in healthcare is that the form of treatment provided must do some good. A technique can never be justified without its having clear advantages. The beneficial aspects of PGD vary among its forms, and are most appropriately discussed in connection with each of these forms.

What is good is not always unambiguous. What benefits one person does not always benefit another. Cultural and social background can influence what is regarded as useful and how various factors should be ranked in relation to one another, from a utility point of view.

In general, it may be said that PGD for diagnostics of genes for severe inherited disorders may be of great value for those concerned. The international studies of PGS carried out so far are not entirely reliable, but there is a great deal to suggest that using fertilised eggs without chromosome abnormalities increases the chances of successful implantation and pregnancy in IVF treatment. ESHRE, for example, emphasises the importance of research in the field to increase the knowledge of the possible advantages of this technique before it is applied on a larger scale.¹⁸

1.6.3 The principle of respect for self-determination and integrity

So far, few couples in Sweden have been treated with PGD. If there were a change in established practice in a somewhat liberalised direction, the number of treatments would be considerably larger. Making it possible to perform PGS for diagnosing chromosome aberrations in women with fertility problems would greatly increase the use of the technique.

If there is such a trend, it is important that those treated will be given guidance and information about the implications and risks of the technique. From an ethical point of view, it is crucial that the patients understand that they can decline, and are not given the impression that this would have negative consequences, e.g. that a couple would miss their chance of getting IVF if they did not allow genetic testing of their eggs.

¹⁷ De Handikappades Riksförbund, 1999.

¹⁸ ESHRE, 2002, pp. 4–5.

If the technique is offered within clinical research, information and consent must naturally comply with the standards of research ethics.

1.6.4 The principle of not doing harm

Treatment must not entail unjustified risks of injury to the treated person. PGD involves several stages that should be considered from that point of view. These include the actual IVF treatment that is a precondition for PGD (see below) and the biopsy carried out in PGD. So far, no risk of damage to the egg has been found in this context, but there is limited experience. It is possible that there is a minor risk of malformations, for example, and also of damage manifesting itself later in life or in a later generation.¹⁹

Mild damage may prompt refinement of the technique, but severe damage is an argument against its use. Since the risks remain difficult to assess, there is much in favour of a restrictive application.

A larger number of the woman's eggs are usually extracted for PGD than in 'ordinary' IVF, since the number of healthy embryos is smaller and the actual biopsy stage may be unsuccessful. The hormone treatment carried out to generate more eggs for fertilisation might constitute a further strain on the woman. Given the potential advantages of the technique for couples with fertility problems, the suffering in connection with hormone treatments may be considered as relatively minor.

The treatment may also fail, thus resulting in great disappointment for the couple. It is thus important to prepare the individuals involved for this possible outcome.

1.6.6 The principle of fairness

There are several different requirements and principles of fairness. In this context, the demand for fairness mainly applies to how people are treated and how resources are distributed.

The basic idea of the fairness requirement is that equal treatment should be provided for equal individuals. From this viewpoint, it is immoral to give special treatment to certain groups unless there are ethically relevant differences between them. This is a formal requirement that needs to be supplemented with criteria for determining relevant similarities and differences.

If one person out of two is selected for treatment and there is good reason to believe that the treatment will benefit that patient only, while the other risks injuries or side-effects, these constitute relevant differences between the patients. Naturally, there is then no injustice in only one of the patients receiving the treatment. However, exactly defining what ethically relevant differences are is not always that simple, and the views may change over time.

Distinguishing between ideals and reality is important. 'Equal pay for equal work' and 'the right to the same treatment, regardless of residential area' are examples of fairness requirements of the type discussed here. There may be broad consensus on these principles but divergent opinions on their application in practice.

The idea of fairness is an essential starting point for all discussions on priorities. Section 2 of the Health and Medical Services Act lays down that the objective of health and medical

¹⁹ Ingerslev H.J. et al., 2002, pp. 31 et seq. ESHRE, 2001. Munthe, C. 1999, p. 160.

services is good health and care on equal terms for the whole population, and also that care should be provided with respect for the equal value of all human beings and the dignity of each individual. The person with the greatest need should be given precedence in access to care.

Priority arguments of importance for the assessment of whether new treatment methods should be offered. *Prioriteringsdelegationen* (The ‘Priority Delegation’) has discussed various principles as a basis for deciding how to assign priorities.²⁰

As concerns PGD, this new form of treatment can be discussed from several points of view. As compared to an initial pregnancy followed by foetal diagnostics and then abortion, PGD spares the people involved from trials. In terms of costs, PGD for grave inherited disorders also means that — besides the cost of the technique itself — IVF resources are used.

With the principles of human dignity, needs and solidarity as starting points, there is also ample reason to allow clinical research to explore the potential of this form of treatment for the involuntary childless. If the treatment then turns out to work, the method may be economically defensible since it makes IVF treatment more effective. Within the framework of IVF, PGS may therefore seem well justified in terms of priorities. But given that, at present, involuntary childlessness and IVF are supposed to be a low-priority area in Swedish healthcare, according to a statement from the Swedish Parliament, devoting additional resources to this sector is hardly warranted when there are healthcare sectors enjoying higher priority.²¹

1.6.7 Sex selection

The use of PGD raises the issue of sex selection. PGS generally involves an analysis of the sex chromosomes and the sex of the fertilised eggs analysed is thus revealed. Already today, some fertility clinics in the US offer PGS with sex selection included in the price.²² Also in Europe has the technique begun to be used to determine the sex of the foetus without any medical reasons.²³

When the Council dealt with information issues in connection with foetal diagnostics in 1996, the question was discussed of whether information about the sex of the foetus should be disclosed when this question is of no medical importance. The Council then deemed that information about the sex of the foetus could be disclosed in connection with foetal

²⁰ Swedish Government Official Reports (SOU) 2001:8, *Prioriteringar i vården. Perspektiv för politiker, profession och medborgare* (‘Priorities in Healthcare. Perspectives for Politicians, Professionals and the Public’), final report from *Prioriteringsdelegationen* (2001), Chapter 2. Definitions in accordance with the ethical platform of *Prioriteringsdelegationen*:

‘The principle of human dignity: all human beings are of equal value and have equal rights, irrespective of personal characteristics and functions in society.’

‘The principle of needs and solidarity: Resources should be distributed according to needs.’

‘The cost-effectiveness principle: In the choice between different activities or measures, the aim should be a fair relationship between cost and effect, in terms of improved health and enhanced quality of life.’

²¹ In 1997, the Swedish Parliament endorsed the proposal made in Government Bill 1996/97:60 on priorities in healthcare. This Bill stated that treatment of involuntary childlessness should belong to priority category III, i.e. the category of second lowest priority.

²² ‘Sex selection with a 99.9% guarantee of chosen gender including genetic “normalcy” aneuploidy studies’, (http://www.fertility-docs.com/fertility_fees.phtml, http://www.fertility-docs.com/fertility_gender.phtml).

²³ 23 ESHRE, 2001.

diagnostics. However, this information should not be offered automatically, but must be provided if asked for. The Council based this standpoint on the right of self-determination. The public should be able to trust that medical service does not withhold essential information from those concerned.²⁴ Under the current law, patients are entitled to full information about the findings of an examination.²⁵

Accordingly, if asked, a physician is not entitled to refuse parents information about the results. In this situation, does the physician have the right to allow the couple to choose the sex of the fertilised egg to be implanted? Or may the physician refuse? Today, in reinserting a fertilised egg into the woman's uterus, the physician should, in practice, make a random choice between seemingly potentially viable eggs.

Some people defend sex selection not due to medical considerations. The main argument in favour is the prospective parents' right of self-determination.²⁶ One of the main arguments against this is that a clear limit is transgressed, since sex selection means choice of a characteristic. If sex selection is permitted, there is a risk of further 'sliding criteria' in PGD, for example when/if it becomes possible to choose other characteristics. Another counter-argument is that sex selection would mean gender discrimination.

1.6.8 So-called 'Sliding criteria'

The attitudes to reproduction have changed over time. PGD further reinforces a technologically oriented view of, and control of, human reproduction that may, in the long run, change our view of parenthood and human dignity.

The use of this technique may, in the long run, come to affect reproductive choices. In particular, it may induce older women to opt for IVF, even if they do not really need it, to gain access to PGD. They can then go through their pregnancy with reduced risk and less anxiety about chromosome aberrations, and also avoid amniocentesis. The existence of this option may also conceivably encourage postponement of pregnancy. The potentially large-scale and routine nature of PGS (i.e. PGD used for screening purposes) could be a factor making the step to positive selection, i.e. choice of characteristics, smaller.

2. PGD for diagnosing severe inherited disorders

2.1 Regulations etc

The existing regulation of PGD for grave inherited disorders has been described above.

2.2 Previous opinion of the Swedish National Council on Medical Ethics

The Council dealt with PGD in a preliminary opinion and a subsequent memorandum in 1992 where PGD is not recommended as a clinical routine, in particular since the medical risks of

²⁴ Swedish National Council on Medical Ethics, *Ang information i samband med fosterdiagnostik* (On Information Provided in Connection with Foetal Diagnostics) 1996.

²⁵ Section 2, paragraph 2a of the Health and Medical Services Act (1982:763):

'Health and medical services shall be conducted so as to meet the requirements for good care. In particular, this means that they must build on respect for the self-determination and privacy of the patient.'

Under the Secrecy Act (1980:100), health and medical services are only entitled to withhold information about an individual from that person under very special and specific circumstances. Chapter 2, Section 1, paragraph 2 of the Constitution Act guarantees individuals freedom of information vis-à-vis the public sector.

²⁶ McCarthy, D. 2001, pp. 302–307.

the analysis for the future child were unknown at that point in time. However, the Council considered that — with reference to the potential of the method for meeting strong needs among parents — it was ethically defensible to offer PGD within clinical research programmes, after approval by the relevant committee of research ethics. But it should only be offered to couples being treated for involuntary childlessness and whose future child ran the risk of incurring a grave hereditary disease.

2.3 Considerations

General

PGD brings to the fore the conflict between

on the one hand

- parents' interest in having healthy children

and, on the other,

- the requirement of respect for human dignity
- concern about the possible repercussions on society of using PGD in the long term
- uncertainty about possible medical risks to the future child.

As we have seen, PGD is now used clinically within the framework of the guidelines of the Swedish Parliament. The Council considers this use to be ethically acceptable in principle, when the parents' needs are sufficiently strong. Moreover, the Council wishes to stress the advantages of PGD as compared to traditional foetal diagnostics:

- PGD can spare the couple and the woman from suffering, since they will avoid a possible future selective abortion.
- A couple with a grave genetic disease can embark on pregnancy with reduced risk and less anxiety.
- Assuming that the foetus is deemed more worthy of protection than a fertilised egg, PGD has clear advantages, in terms of the ethics of abortion, as compared to traditional foetal diagnostics.

The strongest argument against PGD is ultimately based on the fact that the method is so efficient that it can be pushed too far. Since fertilised eggs are selected before implantation, undesirable characteristics and diseases can be eliminated with greater precision than in traditional foetal diagnostics — both because more eggs are available each time and because PGD may be easier to accept than foetal diagnostics followed by abortion.

In the case of a grave hereditary disease, there may be a risk of PGD being used for eugenic purposes, as opposed to foetal diagnostics possibly followed by abortion, since PGD may be perceived as a less serious intervention. In this context, however, it should be emphasised that PGD presupposes IVF, which is a relatively complicated treatment. It involves several courses of hormone treatment and often several IVF attempts before resulting in pregnancy.

Another factor to consider is the risk of commercialisation. As the PGD technique develops, it will probably become increasingly available and may very well be included as a standard procedure in connection with IVF. (Today, PGD is already offered as a standard procedure at many private IVF clinics in the US.)

The selective features of the PGD method, together with the commercialisation of reproduction, thus create misgivings. Today, sex selection and so-called HLA typing are options; soon, it might be possible to predict other characteristics. All these considerations may be given as reasons for a strict regulation of how this technique is applied.

The guidelines adopted by the Swedish Parliament, which have so far governed the use of PGD in Sweden, have turned out not to have a satisfactory effect, as has emerged in the above account. Consequently, the ESPGD group's proposals have been put forward. Their guidelines are more flexible, in that the gravity of individual diseases is not expected to be the sole criterion when deciding whether PGD should be offered or not. The group's proposals also include a continued restriction in the activities.

The Council largely agrees with the group's general conclusions on PGD. However, the technique should be reserved for diagnostics of grave hereditary genetic diseases.

Against this background, the Council considers that the requirements in the guidelines of the Swedish Parliament that PGD should only be used to screen for diseases resulting in premature death and for which there is no cure or treatment should be modified and clarified. Overall, the following general conditions should apply:

- PGD can be used for couples
 - who are carriers of a specific, severe monogenic or chromosomal hereditary disease
 - that entails a high risk of giving birth to a child with a genetically caused disease or damage.
- PGD must only aim at ensuring that the child does not inherit the genes for the disease or damage in question.
- PGD must not be allowed for the purpose of selecting characteristics.

Regarding the conditions that should be allowed as grounds for PGD, it is thus the Council's view that, contrary to the current guidelines, it should also be possible to consider the method for conditions that do not necessarily result in premature death, and also for grave conditions for which some treatment, but of only limited palliative value, is available.

PGD treatment presupposes that the couple concerned is most familiar with the disease/malformation in question, the risk of its being inherited, the treatment options and other support available for a child born with this gene, and what the treatment means. Couples having understood this information and continuing to ask for PGD may then be considered for the treatment.

Treatment should only be allowed to focus on preventing the condition to which it is due. Sex determination shall, for example, only be allowed on medical grounds. PGD should not be permitted other than when the diagnosis can be considered as certain.

The activities should be subject to continuous supervision. To satisfy the need for carefully monitoring the development in this area, all cases where PGD is used should be reported to the National Board of Health and Welfare.

In summary, the Council considers that a special legal regulation for PGD is required. It should be based on the principles specified above. Given that the legal regulation is subject to special investigation in the Committee on Genetic Integrity, it is not the Council's responsibility to define the design of such a regulation in detail. A procedure that may be considered, however, is that the National Board of Health and Welfare is given legal authorisation to draw up regulations for the activities, and is also given the responsibility for supervision.

3. Pre-implantation genetic screening (PGS)

3.1 General information

Pre-implantation genetic screening, PGS, is a method of diagnosing chromosome aberrations in fertilised eggs before these are implanted in the uterus. The method has been launched to enhance the possibilities of success in IVF treatment, in those cases where the chances of pregnancy are much reduced, for example owing to the woman's advanced age or previous repeated miscarriages. The primary aim is a higher rate of implantation, i.e. more pregnancies. The secondary aim is fewer miscarriages. A third aim may be to avoid chromosome aberrations in the baby that is born.

The European Society of Human Genetics and Embryology (ESHRE) has made a summary of the European experience in 1999–2001. According to its latest annual report, almost half the PGD treatments constitute screening for chromosome aberrations, i.e. PGS.²⁷

3.2 Medical background

IVF is the most efficient method of treatment for helping involuntarily childless couples to have children, regardless of the cause of their infertility. Between 1994 and 1999, 17–25% of all IVF treatments (including ICSI) culminated in childbirth.²⁸ The number of births per egg implantation falls markedly with the woman's rising age.²⁹

Implanting more than one egg increases the chances of pregnancy, while also increasing the risk of multiple births — i.e. the woman giving birth to twins, triplets, etc. A multiple birth represents a major risk for the children and an elevated risk for the mother. The National Board of Health and Welfare's Regulations and General Recommendations concerning assisted reproduction therefore now prescribe, as mentioned above, that one egg only should be implanted.³⁰ Consequently, if only a single egg is implanted, the chance of pregnancy decreases.

²⁷ ESHRE, 2001. ESHRE's studies do not comprise all cases of PGD use in Europe, but only those reported to them. Twenty-four centres are included in the material reported for 1999–2001. For 2001, material from 12 centres is included.

²⁸ National Board of Health and Welfare, Centre for Epidemiology, *Assisterad befruktning (Assisted Reproduction)* 1999, p. 24.

²⁹ According to the statistics of the National Board of Health and Welfare for 1999 on the number of births per implantation, some 30% of the implantations in women aged 20–35 resulted in childbirth. The average figures for women in the 35–39 age group and women aged 40 and over were approximately 24% and 10%, respectively.

³⁰ SOSFS 2002:13 (M), *Assisterad befruktning (Assisted Reproduction)*, Chapter 9, 'The number of eggs that may be implanted in a woman', §1.

3.3 PGD to improve the chances of successfully treating involuntary childlessness

Chromosome aberrations are regarded as one of the main reasons why a fertilised egg is not viable. Using PGD, it is possible to check whether the number of chromosomes deviates from the norm. Changes consisting of damage or mutations (aberrations) to parts of chromosomes can also be detected. Recent Scandinavian studies have shown that if eggs seem damaged, this is very likely to be due to chromosome aberrations.³¹ The trend probably means that it will eventually be possible to analyse all chromosome pairs.

To date, no elevated risk has been found to be connected with the actual PGD technique. However, knowledge is limited and a marginally elevated risk of malformations, for example, cannot be excluded.

Turner's syndrome, an aberration in the sex chromosomes, is one of the most common chromosome aberrations. It also entails a substantial risk of miscarriage, which makes it interesting to include in the analysis, although it also provides information about the sex of the future child.

3.4 PGD as an alternative/supplement to foetal diagnostics

In foetal diagnostics with chromosome analysis, Down's syndrome (Trisomy 21) is the predominant diagnosis and it is also the prevalent reason why pregnant women opt for abortions in this context.³²

As shown by statistics from the National Board of Health and Welfare's Congenital Malformation Register, there is an increase in abortions of fetuses with Down's syndrome. This increase also takes place among women aged 30–35 — a group not routinely offered amniocentesis. However, this increase is due to the growing number of births among women of this age; it is thus not an indication of the probability of having a baby with Down's syndrome having increased in this age span.³³

In the Swedish discussion, it has been emphasised that the main purpose of PGS is to find normal fertilised eggs so as to enhance the prospects of pregnancy. Nevertheless, PGS may also be seen as an alternative to foetal diagnostics, with the aim of avoiding a future selective abortion of fetuses with, for example, Down's syndrome, Trisomy 13 and Trisomy 18. This is also the emerging view from international studies and from the European Parliament's Report on the ethical, legal, economic and social implications of human genetics.³⁴

³¹ Hardarson et al., 2001, pp. 313–318.

³² *Genetik och Genteknik i hälso- och sjukvården* ('Genetics and Genetic Engineering in Healthcare'), National Board of Health and Welfare Report 1999:12, p. 27.

³³ National Board of Health and Welfare's Congenital Malformation Register, 2000.

³⁴ European Parliament 2001. Temporary Committee on Human Genetics and other new technologies of modern medicine, Report on the ethical, legal, economic and social implications of human genetics. pp. 52–53.

3.5 *International studies etc concerning PGS*

The studies carried out so far (mainly in the US) provide no unequivocal answers to the question of whether PGS genuinely improves the pregnancy outcome, i.e. whether it boosts the implantation rate and reduces the number of miscarriages.

However, there are indications that the more chromosomes that are investigated effectiveness is improved.³⁵ Deviations in the number of chromosomes increase with advancing age in the woman.³⁶ The group of older women with a fairly small chance of successful IVF treatment can thus improve their chances through PGS. The trend seems to be towards increasingly advanced PGD-based screening. PGS may be assumed to only be an initial step on the path towards increasingly effective methods. Researchers are engaged in developing techniques for carrying out a complete determination of the number of chromosomes and their aberrations, if any.³⁷ One such technique, CGH (Comparative Genomic Hybridisation), is already being used in research.³⁸

In a report on assisted reproduction, an expert group in WHO recommended further clinical research concerning the possibilities for detecting chromosome aberrations through PGD.³⁹

The ESHRE Ethics Task Force has issued an opinion on PGD and has briefly mentioned PGS. The purpose of PGS is described as increasing the reproductive efficiency in IVF. It is pointed out that this technique has not yet been implemented on any large scale, and further knowledge should therefore be obtained before its use becomes more extensive.⁴⁰

3.6 *Regulations etc*

Using PGD to increase the chances of pregnancy among involuntarily childless people was not an option when the guidelines now applying to PGD were adopted by the Swedish Parliament in 1994. The Parliament only took a stand on PGD as an alternative to foetal diagnostics. It is clearly stated in the guidelines that PGD may only be used very restrictively, and only for couples with genes for grave hereditary dispositions or chromosome aberrations and that the diagnosis should target grave, progressive, inherited disorders leading to premature death, for which there are no cure or treatment. PGS, which is equivalent to routine PGD for certain purposes, is hardly compatible with the basic view of the guidelines.

The Council of Europe Convention on Human Rights and Biomedicine (1997) prohibits sex selection in reproduction technology, except in cases where grave inherited disorders can thus

³⁵ Gianaroli et al. obtained a significantly better implantation rate when investigating eight pairs of chromosomes instead of five (1999).

³⁶ Munné (2002) deems that there is, in particular, good reason for recommending PGS to women over 37, then using eight or nine pairs of chromosomes. It is also reported that the proportion of babies born with chromosome aberrations after PGS is only 0.8%, against 3.2% in an age-matched control group. The clearest outcome of PGS for women over 37 thus appears to be that the number of babies born with chromosome aberrations falls by 75 %.

³⁷ According to Munné, 2002.

³⁸ At Sahlgrenska University Hospital, for example.

³⁹ Current Practices and Controversies in Assisted Reproduction, WHO, October 2002, p. 378.

⁴⁰ ESHRE, 2002, pp. 4–5.

be avoided.⁴¹ Analysing sex chromosomes for other motives may thus contravene the Council of Europe Convention.

In Sweden, sex selection is not regulated by law. However, under Government Bill 1994/95:142 and the guidelines of the National Board of Health and Welfare, sex selection may only be performed as part of the diagnostics of sex-linked inherited disorders, for which there is no cure or treatment.⁴²

3.7 Previous standpoint of the Swedish National Council on Medical Ethics

In its opinion *Assisterad befruktning* (Assisted Reproduction) (1995), the Council deemed it ethically defensible to use medical measures in an attempt to eliminate obstacles to fertilisation and pregnancy, with reference to the principle of doing good and the principle of reducing suffering. But this does not necessarily mean that any method that could be used for this purpose would be ethically acceptable. In this context, the Council emphasised that every new application of a reproduction technique must undergo ethical scrutiny.

3.8 Considerations

General

The basic ethical problem of PGS is the contradiction between

on the one hand

- the interest in successful treatment of involuntary childlessness,

and, on the other,

- the requirements of respect for human dignity and
- concern about the social repercussions that the use of this technique might create in the long run.

The experience of being unable to have a desired child may result in crises in the marital relationship and give rise to unfavourable social and psychological consequences that, in some cases, may require treatment. In Sweden, the estimate is that 250 000 couples suffer from infertility problems.

At present, there is a tendency for the number of involuntarily childless people to rise since building a family comes later in the life cycle. Given that successful IVF-treatment becomes increasingly difficult with the increasing age of the woman, PGS may conceivably come to play a major role in connection with assisted reproduction in the future.

As we have seen, the chances of successful IVF increase if several fertilised eggs are implanted. At the same time, this means the risk of multiple births — which, as such, entails considerable risks for both mother and child. There is thus a clear conflict of objectives with ethical dimensions. It is therefore vital to try out every technical progress in medicine that can

⁴¹ Convention on Human Rights and Biomedicine, 4, IV 1997, Chapter IV, Article 14.

⁴² National Board of Health and Welfare, 1999, *Genetik och Genteknik i hälso- och sjukvården* ('Genetics and Genetic Engineering in Healthcare'), pp. 29–30.

reduce this conflicting situation. The hope is that, using PGS, it will be possible to enhance women's prospects of becoming pregnant when one fertilised egg only is implanted.

Besides the possibility of increasing the chances of pregnancy, offering PGS to couples with IVF indications would also have other advantages. Women over 35, among whom the risk of chromosome aberrations is elevated, are today offered amniocentesis to detect whether there is any chromosome damage in the foetus. When such damage is found, preventive selection through abortion is an option. With PGS, the woman could embark on her pregnancy with less risk and anxiety, and there would be no need for amniocentesis or any future selective abortion. If couples with infertility problems undergo IVF and have access to PGS, the need for foetal diagnostics and possible selective abortion can therefore be assumed to decrease, although the significance of such an effect is uncertain.

The principle of doing good and the principle of reducing suffering are thus both arguments for PGS in these forms.

In connection with IVF, several eggs are fertilised to increase the chances of producing an egg suitable for implantation. At present, the fertilised eggs are assessed in morphological terms, i.e. they are studied under a light microscope for the purpose of selecting the eggs visually appearing to have a normal development. With PGS, the fertilised eggs are instead genetically examined. In this way, the eggs with the greatest potential for survival are obtained, while those with chromosome aberrations are discarded. Accordingly, the technique as such does not mean that any further limit is exceeded with respect to the destruction of fertilised eggs, as compared to current IVF practice. The difference is that the selection becomes more reliable.

The purpose of PGS as part of the treatment of involuntary childlessness, is under no circumstances to 'weed out' a certain kind of people but, rather, to improve the chances of a baby being born at all. Seen in this way, selection does not constitute a threat to human dignity.

When the technology is used as an alternative to foetal diagnostics, i.e. to trace chromosome aberrations that could culminate in an abortion decision later in the process, on the other hand, the purpose is to permit possible selective removal that may be said to have an impact on human dignity. However, it must then be borne in mind that this selection is possible at the foetal stage, and that it is not intended to be used for any other purpose than as a means of treating involuntary childlessness. An overall ethical assessment based on the situation of the individual couple, based on the problem of childlessness, therefore tends to lead to the conclusion that PGS may be justified for this purpose.

Obviously, if this method is to be permitted, its application must be subject to strict requirements in order to counteract discriminatory effects. If PGS is only offered to and performed for couples undergoing IVF due to involuntary childlessness, there is less danger of and concern for discrimination and eugenics, since the technique is then not used to screen out a certain kind of people. If the Government authorities also explicitly emphasise that such screening is not an acceptable reason for extending the use of that technology, the risk that approval of the technique would signal eugenic values is probably very small. However, this does not exclude the risk that certain individuals with disabilities may nonetheless find it repugnant that, de facto, PGS means screening out embryos with chromosome aberrations.

As previously, the Council finds that it is ethically defensible to use medical measures in an attempt to remedy physiological obstacles to reproduction and pregnancy, with reference to the principle of doing good and the principle of reducing suffering. This does not mean that all means or methods that might be used are ethically acceptable. Since there is a risk of 'sliding criteria', it is important that the practice can be stopped at every stage through official scrutiny. Every new application of reproduction techniques should therefore be reviewed in terms of ethics, so that they are not solely determined by new medical and technical possibilities. Thus, it is important to ensure a judicial regulation of PGD and its various forms of application, and also that there are clear rules for continuous scrutiny in clinical research projects of this kind.

With the current state of knowledge, the Council does not consider it appropriate for PGS to become standard procedure. Before a complete ethical assessment can be made, there is a need for research and findings that show the possible advantages and disadvantages of this technique from medical, ethical and social points of view. Besides medical research, there should also be social and ethical research which clarifies all aspects of PGS.

Given these considerations, the Council considers that PGS may be ethically acceptable for the time being within clearly defined research projects that have been ethically assessed in advance in a research ethics committee. A precondition for approval is that PGS is solely offered to involuntarily childless women, to increase their chances of having children. Clinical research should focus on groups of women with especially poor prospects of pregnancy, where there is particular reason to believe that the treatment would increase their chances. To meet the need for careful monitoring of the development in this area, cases of this kind should be reported to the National Board of Health and Welfare.

4. Other areas of application

The PGD technique is relatively new. It is likely to become more relevant than what has been discussed above. The development will require further ethical standpoints. So-called PGD/HLA is already a topic of discussion, i.e. efforts to use PGD technique to help parents of a gravely ill child to try to have a sibling with such genetic make-up that he/she can become a donor. There have been occasional such cases of PGD in the world.⁴³

The Council has held in-depth discussions on this matter and found there to be reason for caution. Admittedly, PGD/HLA provides treatment options in very deserving cases, and the idea of using the method should therefore not be rejected. Nevertheless, there is considerable uncertainty about the technique, for example with respect to the risks it may entail and its prospects of success. The method raises issues that are difficult to assess in ethical terms. The Council will therefore continue its discussion of this subject.

⁴³ HLA typing of eggs through PGD has been carried out in the US. The first 'donor child', Adam Nash, was born in the year 2000. Adam Nash came into being after PGD, partly for the purpose of becoming a bone-marrow donor for his sister. The sister suffered from Fanconi Anaemia, a rare hereditary genetic blood disorder with fatal outcome; to survive, she needed bone-marrow transplantation. This was carried out, with bone marrow donated by her new brother, and she was cured (Verlinsky, Y., Rechitsky, S., Schoolcraft, W., Strom, C., Kuliev, A. 2000, Vol. 1, No. 2: 31).

5. Reservation and special statements

5.1 *Chartrine Pålsson (Christian Democratic member of the Swedish Parliament) and Daniel Brattgård, expert*

1. *Pre-implantation genetic diagnosis (PGD)*

In line with the Council majority, we consider that judicial regulation of PGD should be introduced. Unlike the Council, we consider that a framework law should be passed for PGD, in accordance with the guidelines adopted by a unanimous Swedish Parliament in 1995 (Report, 1994/95: Swedish Government Official Reports [SOU] 18):

Pre-implantation diagnostics must be used very restrictively and only for couples carrying genes for grave hereditary dispositions or chromosome abnormalities. The diagnostics should focus on severe, progressive, inherited disorders that result in premature death and that cannot be cured or treated. Sex selection should be permitted only if it is medically justified.

2. *Pre-implantation genetic screening (PGS)*

Unlike the Council majority, we consider that pre-implantation genetic screening (PGS) should not be introduced in research. PGS is a method of diagnosing chromosome aberrations in fertilised eggs before these are implanted in the uterus. The purpose of the method is to increase the chances of pregnancy in IVF treatment, since chromosome aberrations are deemed to be a major reason why a fertilised egg does not become viable. It would be strange, to say the least, to introduce this new technique that, de facto, is solely intended to be used for fertility reasons.

Reasons for our opinion

The main reason for our standpoints is the principle of human dignity. The inviolability of human life should be an overarching standard for all work in society. As such, it should also characterise the frameworks and regulations in the area of medical ethics.

Genetic engineering forces us to take fundamental and difficult ethical stances that both depend on and will influence our view of humankind and life. In face of this development, it is important for all citizens to be able to, in democratic forms, join in the attempt to shape the framework for ways of using this knowledge. This cannot be left to a few experts.

Discussing and adopting standpoints on these issues is therefore necessary. The main task, in our view, is to protect human dignity and ensure that the integrity of individuals is not violated.

Striving for perfection — the perfect society, the perfect human being — is always highly risky. We must be concerned about safeguarding a society of diversity and pluralism. If the state were to sanction the screening of human beings with reference to their characteristics or diseases/disabilities, this would be a hazardous route, just like screening due to sex and race, for example.

5.2 *Sture Gustafson, expert*

Due to SMER's standpoint regarding pre-implantation genetic diagnosis (PGD), I wish to make the following statement:

PGD may be seen as a complex of distinct issues: PGD in general, PGS and PGD-HLA. Different standpoints can be reached on various subsidiary issues; thus, saying yes to extended indications for PGD does not mean that one must also accept PGS and/or PGD-HLA. Since SMER has not reached a final standpoint concerning PGD-HLA, I shall exclude this from my special statement.

1. PGD for diagnosis of grave inherited disorders

In the deliberations of the Council, the contradiction becomes obvious between on the one hand, *the wish for healthy children among parents who have previously had children with grave inherited disorders*

and, on the other hand, *respect for fundamental values, such as human dignity, concern for where the technique might lead, and uncertainty about the medical risks for the future child.*

There is also a conflict within the disability movement. Associations representing people with hereditary and grave medical disabilities have long maintained that the guidelines for PGD adopted by the Swedish Parliament are too restrictive. For example, would-be parents who carry the genes for cystic fibrosis are denied PGD, which means that foetal diagnostics with selective abortion has become their only option.

Other associations that have clearly taken a distance to screening foetal diagnostics are of the opposite view. Whether selection takes place at the embryonic or foetal stage is, in principle, of no importance.

The Council's conclusions are based on previous standpoints concerning the moral status of the fertilised eggs. As reported in the Council's memorandum reports, these are based on the assumption that the fertilised egg has a certain value worth protecting, which gradually increases in the course of pregnancy. When the foetus may be viable outside the mother's body, this protection value turns into human dignity.

I have strong objections to this conclusion. Human dignity cannot be graded in this way. From the very first stage of development, a human being is a person. *Human dignity is not obtained because of something, but by virtue of being someone.* If human value were linked to 'viability', the value of a human being would also be reduced to protection value in the final stage of life, since there is no longer any 'viability'.

The fertilised egg is undoubtedly part of the human family. It has the potential to develop into a unique human individual. Also from this viewpoint does the embryo have human dignity and an unconditional right to protection.

The selective feature in PGD is obvious. From my viewpoint of the embryo as the starting point, any selection is clearly impossible. We are not entitled to select individuals or deny certain defined groups the right to life.

For the above-mentioned reasons, I do not support the Council's conclusions.

At the same time, I understand how families with a child suffering from a grave hereditary disease wish for a healthy child next time. For these people, SMER's deliberations and standpoints are of value.

2. Pre-implantation genetic screening (PGS)

The selection stage is even more striking when it comes to PGS. Also in this case does SMER point to the conflict between

on the one hand, *the interest of involuntarily childless couples in successful IVF*

and, on the other hand, *the risk of eroding the respect for human dignity, and the possible long-run consequences of the use of the PGS technique to society.*

In its deliberations, the Council mentions the selective aspect; but it does not allow this to become a main argument in the conclusions.

Without knowing exactly where the disability movement as an entity stands on this matter, my impression has been that there is great doubt — and in any case circumspection — among leading people in the disability movement. Naturally, this in particular applies to the associations that are clearly opposed to prenatal diagnosis, such as DHR.

Screening of embryos takes place in all IVF treatment. Here, a further step is taken: the embryo undergoes genetic testing. The manner and methods whereby an embryo is screened out are not important in principle. However, PGS entails a screening-out of a certain group of people: those with chromosome aberrations, including Down's syndrome, Turner's syndrome, etc. This may, on good grounds, be regarded as manifesting — or resulting in — a questioning of the human dignity among people with chromosome aberrations. This, then, is entirely in contrast with the view of the equal value of all human beings, which is the cornerstone of the disability movement's objectives.

The Council's attitude, that PGS should not become routine procedure, is justified by lack of knowledge. Admittedly, this is true; but the main reason should be the element of selection that is a salient aspect of PGS. This starting point does not constitute any support for the experimental activity proposed by SMER either. Moreover, experience shows that pilot projects tend to result in the activities in question becoming permanent.

Given the above considerations, I do not subscribe to the Council's conclusions.

6. List of sources

Adams K. E. (2002), 'Ethical considerations of applications of pre-implantation genetic diagnosis in the U.S,' *World Congress on Medical Law, Book of Proceedings II*.

Auerbach A.D. (1994), 'Umbilical Cord Blood Transplants for Genetic Disease: Diagnostic and Ethical Issues in Foetal Studies', *Blood Cells* 20, pp. 303–309.

Blennow, E.; Munthe, C., Wahlström, J. et al. (2002), 'Förslag till etiska riktlinjer för preimplantatorisk genetisk diagnostik', *Läkartidningen*, No. 14, Vol. 99.

Comité Consultatif National d'Ethique pour les sciences de la vie et de la santé (2002), 'Reflections concerning an extension of Pre-implantation Genetic Diagnosis', No. 72.

Convention on Human Rights and Biomedicine, 4, IV (1997), Chapter IV, Article 14.

Dagens Forskning, March 2003.

Danish Centre for Evaluation and Health Technology Assessment (DACEHTA), National Board of Health, *Præimplantationsdiagnostik – en medicinsk teknologivurdering*. Health Technology Assessment 2002: 2 (1).

Danish Council of Ethics (2003), *Etiske problemer vedrørende kunstig befrugtning, 3. del: Mikroinsemination og præimplantationsdiagnostik*.

De Handikappades Riksförbund (1999). *Remissyttrande över genetik inom hälso- och sjukvården. En kunskapsöversikt och vägledning vid etiska bedömningar, 1998, SoS*.

ESHRE PGD Consortium Steering Committee (2001), ESHRE Preimplantation Genetic Diagnosis (PGD) Consortium: Data Collection III (May 2001). *Human Reproduction* Vol. 17, No 1.

ESHRE Ethics Task Force 5 (2002), *Pre-implantation genetic diagnosis*.

ESHRE (2003). 'ICSI and IVF are safe — results from the world's largest, longest-running study', Press release, 2 July 2003.

European Parliament (2001), Temporary Committee on Human Genetics and other new technologies of modern medicine: *Report on the ethical, legal, economic and social implications of human genetics*.

German National Ethics Council (2003), Opinion: *Genetic diagnosis before and during pregnancy*.

Gianroli L., Magli, M-C., Feraretti, A. & Munné, S. (1999), 'Pre-implantation diagnosis for aneuploidies in patients undergoing in vitro fertilization with a poor prognosis: identification of the categories for which it should be proposed', *Fertil. Steril.*, 72, 837–844.

Hardarson et al. (2001), *Human Reproduction*, Vol. 16: 313–318.

Human Fertilisation and Embryology Authority (2001), Opinion of the Ethics Committee of the Human Fertilisation and Embryology Authority, *Ethical issues in the creation and selection of pre-implantation embryos to produce tissue donors*. 22 November 2001.

Ingerslev H.J. et al. (2002), *Præimplantationsdiagnostik – en medicinsk teknologivurdering*. Health Technology Assessment 2002: 2 (1).

International Working Group on Pre-implantation Genetics. Tenth anniversary of pre-implantation genetic diagnosis. *J Assoc Reproductive Genetics* 2001; 18: 64–70.

Kahn, J. P. (2002), 'Should we be able to choose our kids?' <http://www.cnn.com/2002/HEALTH/08/19/ethics.matters/index.html>.

Kant, Immanuel (1785), *Introduction to the Metaphysic of Morals*.

King, D. S. (1999), 'Pre-implantation genetic diagnosis and the "new" eugenic', *Journal of Medical Ethics* 25: 176–182.

Lundin, S. (1997) *Guldägget – Föräldraskap i biomedicinens tid*.

McCarthy, D. (2001), Why sex selection should be legal, *Journal of Medical Ethics*, 27: 302–307.

Melle, M.V. (2002), 'Prenatal diagnosis and embryo selection — Do we need more restrictions on reproductive freedom?' *World Congress on Medical Law, Book of Proceedings II*.

Munné, S. (2002), 'Pre-implantation genetic diagnosis of numerical and structural chromosome abnormalities', *Reproductive BioMedicine Online* Vol. 4, No. 2: 183–196.

Munthe, C. (1999), Pure Selection: The ethics of Pre-implantation Genetic Diagnosis and Choosing Children without Abortion, *Acta Universitatis Gothoburgensis*.

Nationalencyklopedin, Volume 14.

Nuffield Council on Bioethics (2002), *Genetics and Human Behaviour — the Ethical Context*.

Shakespeare, T. (1999), 'Losing the plot? Medical and activist discourses of contemporary genetics and disability', *Sociological Perspectives on the New Genetics*, eds. Conrad P. & Gabe J., Blackwell Publishers.

Staessen C., Van Assche E., Joris H., et al. (1999), 'Clinical experience of sex determination by fluorescent in situ hybridisation for pre-implantation genetic diagnosis.' *Mol. Hum. Reprod.*, 5, 382–389.

Strömberg et al. (2002), 'Neurological sequelae in children born after in-vitro fertilisation: a population-based study', *Lancet*, 359: 461–465.

Swedish Council on Technology Assessment in Health Care (SBU) Report No. 147 (2000), *Barn födda efter konstgjord befruktning (IVF) [IVF]*'.

Swedish Government Bill 1994/95:142, *Fosterdiagnostik och abort*.

Swedish Government Official Reports (SOU), *Den gravida kvinnan och fostret – två individer. Om fosterdiagnostik. Om sena aborter*, SOU 1989:51.

Swedish Government Official Reports (SOU), 'Priority Delegation' (2001): *Prioriteringar i vården. Perspektiv för politiker, profession och medborgare*, SOU 2001:8.

Swedish National Board of Health and Welfare (1999), *Genetik och Genteknik i hälso- och sjukvården*, Report 1999:12.

Swedish National Board of Health and Welfare (1999), Centre for Epidemiology, Assisted Reproduction Register.

Swedish National Board of Health and Welfare (2000), Congenital Malformation Register.

Swedish National Board of Health and Welfare (2000), *Neurologiska funktionshinder hos barn födda efter provrörsbefruktning 1982–1995*, Report 2000:4.

Swedish National Board of Health and Welfare (2002), *Regulations and General Recommendations on Assisted Reproduction (SOSFS 2002:13)*.

Swedish National Council on Medical Ethics (1995), *Assisterad befruktning – synpunkter på vissa frågor i samband med befruktning utanför kroppen*.

Swedish National Council on Medical Ethics (1996), information relating to foetal diagnostics.

Swedish National Infertility Patient Association (*Infertilas Riksförening i Sverige, IRIS*), <http://www.iris.y.se/>.

Tranöy, K.E. (1993), *Medicinsk etik i vår tid* ('Medical Ethics in Our Time'). Studentlitteratur, Lund.

Verlinsky, Y., Rechitsky, S., Schoolcraft, W., Strom, C., Kuliev, A. (2000), 'Designer babies — are they a reality yet? Case report: Simultaneous pre-implantation genetic diagnosis for Fanconi anaemia and HLA typing for cord blood transplantation'. *Reproductive BioMedicine*, Vol. 1, No. 2.

Wertz, D.C. & Knoppers, B.M. (2002), 'Serious Genetic Disorders: Can or Should They Be Defined?' *American Journal of Medical Genetics* 108.

World Health Organization (2002), *Current Practices and Controversies in Assisted Reproduction*, Report of a meeting on Medical, Ethical and Social Aspects of Assisted Reproduction held at WHO Headquarters in Geneva, Switzerland, 17–21 September 2001 (<http://www.who.int/reproductivehealth/infertility/index.htm>).

German National Ethics Council (2003), *Genetic diagnosis before and during pregnancy*.