

Polar body diagnosis Opinion of the German National Ethics Council

In its Opinion “Genetic diagnosis before and during pregnancy” (2003) the National Ethics Council has already discussed the possibilities and limits of polar body diagnosis and evaluated its ethical and legal aspects in the context of preimplantation genetic diagnosis.

Since polar body diagnosis is both permitted and actually practised in Germany, the National Ethics Council assembled a group of experts for a hearing¹ on 19 February 2004 in order to obtain information on advances in the technique, its application in the field of reproductive medical therapy and its use under the conditions laid down by the German Embryo Protection Law. The results of the consequent deliberations of the National Ethics Council are set out below.

1. Is polar body diagnosis consistent with the Embryo Protection Law?

Polar bodies can be retrieved before pronuclear membrane breakdown (“karyogamy”), a stage preceding the formation of an embryo as defined by the Embryo Protection Law.² The first polar body is expelled during oocyte maturation before sperm penetration and the second follows after the sperm has entered the oocyte. For this reason, the conduct of genetic diagnosis on polar bodies and the discarding of oocytes (including the pronuclear stage) is not considered to contravene the provisions of the Embryo Protection Law.

However, it is sometimes held that the second sentence of § 1(1) of the Embryo Protection Law, which provides for penal

¹ Both the Opinion and a verbatim record of the hearing can be accessed on the National Ethics Council website: www.ethikrat.org

² “The fertilized human ovum, being capable of development, from the time of karyogamy on, as well as any totipotent cell taken from an embryo, where such cell, provided that the further conditions necessary therefor are satisfied, is capable of dividing and developing into an individual, shall already be deemed to be an embryo within the meaning of this law.” (§ 8(1) of the Embryo Protection Law)

sanctions against any person who “undertakes the fertilization of an oocyte for a purpose other than to bring about a pregnancy in the woman from whom the oocyte originates”, prohibits preimplantation genetic diagnosis; according to this view, polar body diagnosis would also be banned, as § 1(2) already relates to the penetration of the sperm into the oocyte.

2. Is polar body diagnosis an established method of proven practical value?

Polar body diagnosis is a procedure applied to the oocyte in which inferences are made from the genetic or chromosomal endowment of the first – and if possible also the second – polar body as to the genetic material that remains in the oocyte during the process of maturation and is passed on to the embryo. The diagnosis thus covers only maternally transmitted predispositions.

A fundamental distinction must be drawn between the diagnosis of a predisposition to a monogenic disease, of structural chromosomal alterations (translocations) and of numerical chromosomal aberrations (aneuploidies). In the first two cases a diagnosis is undertaken if a specific risk has been identified in a couple and the nature of the alteration is known. Regardless of the presence or absence of sterility, this risk may constitute an additional indication of the desirability of assisted reproduction techniques for the purposes of a polar body diagnosis. In the third case, on the other hand, there is only the possibility of an unspecified increase in risk, due, for example, to the advanced age of the woman, multiple miscarriages or the repeated failure of reproductive-medicine procedures; polar body diagnosis is then carried out in the context of sterility-related assisted-reproduction treatments.

In the first two cases polar body diagnosis is useful because there is a high probability of successfully identifying oocytes affected by the relevant genetic alterations and of excluding them from transfer. In the third case (the diagnosis of aneuploidy), however, the procedure has not yet been demonstrated to have the desired effect – i.e. an increase in birth rate. The discarding of

aneuploid oocytes is expected to lead to an increase in the pregnancy rate, a fall in the abortion rate and, at the same time, a reduction in the rate of multiple pregnancies because of the smaller number of embryos transferred. Only large-scale scientific studies can determine whether these results can actually be obtained in the risk situations mentioned.

Polar body diagnosis can be regarded as an alternative to preimplantation genetic diagnosis on blastomeres retrieved from an embryo only in certain cases, because, as stated earlier, it can detect only maternally transmitted genetic or chromosomal abnormalities.

A significant disadvantage of polar body diagnosis as compared with the blastomere procedure is that in the case of X-linked or autosomal recessive disorders the discarded oocytes include those that could have developed into a child unaffected by the disease. This is the case if the fertilizing spermatozoon bears an X chromosome or does not carry the pathogenic mutation.

For these reasons, in view of the substantial technical difficulties and of the Embryo Protection Law’s time limits for the conduct of polar body diagnosis, the procedure is regarded solely as a fallback for couples who, given the same medical indication, would opt for blastomere-based preimplantation genetic diagnosis if this technique were permitted in Germany. Internationally, polar body diagnosis is performed at a small number of centres only, and then as a rule in combination with a blastomere diagnosis.

Since polar body diagnosis, like all genetic diagnostic techniques, carries a risk of error, in the event of pregnancy couples are recommended to undergo a confirmatory prenatal diagnosis to verify the findings.

3. What should be the scope of regulation to guarantee quality standards?

Polar body diagnosis is a highly sophisticated, currently still experimental technique, whose actual value for the detection of aneuploidies, moreover, is not yet proven. The National Ethics

Council therefore welcomes the initiative of the centres that use it in conducting the procedure only in the context of a joint scientific study. From the point of view of children’s welfare, a particularly desirable additional measure would be ongoing monitoring of the health of children born following the application of the procedure.

Although not conducted on embryos as defined in the Embryo Protection Law, polar body diagnosis is carried out in the context of the selection of oocytes suitable for reproduction before and during fertilization, so that, if the technique is applied indiscriminately, the ethical issues of possible undesirable social consequences, risks to the woman’s (or the couple’s) physical and mental health, and the deliberate selection of characteristics in the unborn child must receive attention in the same way as with blastomere-based diagnosis. For this reason, consistent medical quality standards should preferably be introduced, specifying both the indications for polar body diagnosis and conditions for its application. Particular attention should be devoted in this connection to the provision of comprehensive information, education and advice to couples.

4. Is there a need for legislation?

The National Ethics Council does not at present see any need for specific legislation to regulate polar body diagnosis. However, it repeats its recommendation to the German legislature to draw up and pass a Reproductive Medicine Law for the regulation of all aspects of this field.

Berlin, 16 June 2004

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