

# Letters to the Editor

## Society's contribution to assisted reproductive technology abuse

Sir,

Often the media seeks to portray assisted reproductive technology doctors as ruthless scientists eagerly pursuing absurd goals, with human cloning being the ultimate red flag. Public opinion so created led to strict regulatory actions, often at the expense of patients' interests and quality of care (see recent Italian assisted reproductive technology legislation). Bioethics in the field of assisted reproductive technology is a 'hot' subject, and a major source to many careers in academic institutions. In most cases, ethical considerations are taken to challenge assisted reproduction doctors.

However, it is often society itself that forces assisted reproduction doctors to create life in problematic ethical circumstances. The following case illustrates this point. A man aged 73 years was hospitalized with severe pneumonia after marrying a woman aged 36 years 10 months earlier. At the hospital he signed a will requesting that after his death sperm be retrieved from his body for the impregnation of the future widow. His lawyer secured a court order to execute the will. Immediately following his death, 3 days later, and under a court order, testicular biopsy was performed and 8 ampoules of frozen sperm were stored in liquid nitrogen. A month later the widow underwent an IVF cycle during which 18 oocytes were retrieved. One sperm ampoule was thawed and used in ICSI to fertilize the oocytes. Of the 14 embryos created, two were transferred to the widow's uterus resulting in the birth of a healthy girl. The other 12 embryos were frozen.

We doubt whether the above complies with acceptable ethical guidelines. Indeed, assisted reproduction doctors may be severely criticized should they conduct such treatment on their own initiative. Having said that, one cannot but wonder about the quick endorsement of assisted reproductive technology abuse by society, as represented by the legal system.

## Reference

Turone F (2004) Italy to pass new law on assisted reproduction. *BMJ* 328, (7430) 9-a.

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## Comment 1 on Staessen *et al.* (2004). Design and analysis of a randomized controlled trial studying preimplantation genetic screening

Sir,

We have read with great interest the manuscript by Staessen *et al.* (2004) reporting a randomized controlled trial (RCT) of preimplantation genetic screening (PGS) in couples with advanced maternal age (AMA). Several investigators, including Staessen *et al.* (2004), commonly use the term preimplantation genetic diagnosis for aneuploidies (PGD-AS) when referring to PGS. However, we will use the term PGS in this letter in agreement with recently adjusted nomenclature from the ESHRE PGD Consortium (Sermon *et al.*, 2005).

RCTs studying PGS for AMA have been awaited eagerly since PGS for AMA is applied more and more often in recent years (Sermon *et al.*, 2005) despite a lack of evidence of effectiveness. Only one other RCT has been published thus far (Werlin *et al.*, 2003), but that RCT included a very small number of patients (seven PGS for AMA versus 12 controls). Several non-randomized studies have been published (Gianaroli *et al.*, 1997, 1999; Munne *et al.*, 1999, 2003; Kahraman *et al.*, 2000; Obasaju *et al.*, 2001; Montag *et al.*, 2004). Despite deficiencies in the design and analysis of some of these comparative studies, the results seem to indicate that PGS for AMA leads to an improved implantation rate without an increase in clinical pregnancy rate. Only a few studies have reported on ongoing pregnancies and none on live birth, the ultimate outcome of interest to patients. The study by Staessen *et al.* (2004) is the first RCT to provide data on the effectiveness of PGS.

Its importance encouraged us to comment on some aspects of the design and analysis of this trial that, in our opinion, attenuate the conclusions that can be drawn.

Several investigators have stressed that the main outcome measure in subfertility trials should be live birth or, if not available, ongoing pregnancy rate (Barlow, 2003; Daya, 2003; Vail and Gardener, 2003). Live birth is the most important end result of any fertility treatment. By using implantation rate per embryo as the main outcome measure, Staessen and colleagues steer away from this recommendation. They also introduce a unit of analysis error.

Staessen and colleagues used the embryo implantation rate as their primary measure of effectiveness. The embryo implantation rate is the ratio between the number of gestational sacs with a fetal heartbeat and the total number of embryos transferred. This is an inappropriate measure since the denominator (number of embryos transferred) depends on the strategy, not on the design, as is shown in Table II of the paper. It is incorrect to calculate *P*-values, odds ratios and even a number needed to treat based on this ratio.