

Ethics beyond ethics

C.B. Lambalk*, M. Van Wely, K. Kirkegaard, and C. De Geyter

*Correspondence. E-mail: editorial@humanreproduction.co.uk

In this issue of *Human Reproduction*, we publish a manuscript entitled “First PGT-A Using In vivo Blastocysts Recovered by Uterine Lavage: Comparison with Matched IVF Embryo Controls” by Munné and colleagues (Munné *et al.*, 2019). The authors of this contribution report a proof-of-concept study on genetic screening of embryos obtained after uterine flushing. The embryos were collected from the uterus of women that were treated with ovarian hyperstimulation and intrauterine insemination. Since uterine flushing does not require oocyte collection, *in vitro* fertilization and embryo culture, this technique could theoretically be less invasive and more cost-effective. The primary aim of the study was to demonstrate that this procedure is technically feasible.

The study has raised a considerable number of serious ethical concerns among reviewers and the journal's own Editorial Team, as addressed in the elegant, accompanying Editorial Commentary by Galia Oron (Oron, 2019). We anticipate that the readers of *Human Reproduction* are likely to share these concerns and thus speculate how such an ethically challenging manuscript nevertheless made it to publication. Consequently, as the journal's Editorial Team, we feel obliged to share our thoughts and actions with you.

At first submission, the manuscript immediately raised a number of ethical concerns: fertile women not wishing to become pregnant were exposed to ovarian hyperstimulation and were treated with intrauterine insemination with semen that did not necessarily come from their own partner. Despite uterine flushing, not all embryos were retrieved and some women accidentally became pregnant. For termination of pregnancy, those women were then treated with methotrexate (MTX), some even with a dilation & curettage (D&C). All of the above interventions are potentially harmful to the women who did not benefit directly from participation—other than through financial compensation.

The authors reported that IRB ethical approval was obtained and written informed consent was provided by the participants. Before sending the manuscript for review, we asked the authors to provide us with (i) the approvals, (ii) the patient information sheets and (iii) the amount of financial compensation paid to each participant.

We received all requested documents that verified IRB approval from both the USA-based Western Institutional Review Board (WIRB) and the Ministry of Health of the State of Nayarit in Mexico, where the interventions were carried out. Furthermore, we received fully informative patient information sheets both in English and in Spanish, which indeed detailed all the potential disadvantages for the study

participants including the risks of ovarian hyperstimulation syndrome and MTX and D&C treatment consequences, in case of an inadvertent pregnancy. The financial compensation amounted to \$1400 for each participant. This documentation convinced the Editorial Team that all necessary steps were truly taken for ethical approval.

During full, external peer review, several reviewers raised serious concerns with regard to the ethical aspects and some recommended outright rejection based on these concerns. Here is a study that in a well-documented way passed all the formal ethical approval steps to be taken, and yet it leaves us with a strong feeling of uneasiness, as voiced by Galia Oron.

So why have we not taken the easy way out and rejected the paper?

The scientific content of the study has been reviewed and the scientific merits accepted as significant. This study contributes with new knowledge on the biology of reproduction that is expected to be of interest among the scientific community.

We as researchers have obligations in regard to the publication and dissemination of the results of research carried out according to the Helsinki Declaration. Indeed, it could sensibly be argued that withholding publication of research that was carried out according to appropriate ethical principles and guidelines is unethical and unfair to the many patients and participants who, after providing their informed consent, took part in the study.

On the other hand, it is questionable whether it is ethically acceptable to offer individuals who participate in a study that offers no benefit to them (and indeed could potentially be harmful), substantial financial compensation. In Mexico, \$1400 is the equivalent to a 71-working-day wage. Under those conditions, were the participants still free enough to make a well-balanced choice?

The Helsinki Declaration states that the goal of new knowledge can never take precedence over the rights and interests of individual research subjects. Two ethical boards have evaluated the content and accepted the project under the guidance of this declaration. Are we entitled to overrule two Ethical boards (one American and one Mexican) that approved the study?

After much debate, and then more debate, we concluded that we should respect the decision and authority of the relevant ethical boards. Therefore, the results of the study are available in this issue of *Human Reproduction*, along with our concerns and considerations in order to underline the importance of maintaining high ethical standards and providing full editorial transparency.

References

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Oron G. How far should we go in the name of science. *Human Reprod* 2019.