Reply: Mirror exchange of donor gametes should also accommodate scientific research

Sir,

The letter by Heng and Tong raises a very interesting point: should patients entering the mirror donation system have the option to donate their gametes for scientific research? This question could be extended to all present donor systems, such as embryo sharing, in which some remuneration is given. My answer is focused on two points: the internal logic of the mirror gamete donation system and the balance between benefits and risks for women who donate oocytes.

Mirror gamete donation will only work to a satisfying extent if the discrepancy between the number of oocyte donors and the number of sperm donors is not too large. Every additional donor obviously helps to diminish the shortage, but if donors have to wait too long before receiving gametes in return, the benefit (i.e. reduction of waiting time) is lost. It might indeed be expected that a number of patients will prefer to direct their gametes to research or, in the future, stem cell therapy because such use would not generate a genetic link. I mentioned in my article that people who refuse to be identified in a country where donor identifiability is imposed by law cannot participate (Pennings, 2005). This group could theoretically be included if the option of research were offered. However, the benefit in the mirror donation system is the reduction of waiting time. This reduction is the result of the fact that more people become contributors. If they donate for research, there are no extra gametes available for the pool and, consequently, no reduction of waiting time.

Beside the argument that the system will only function properly if there is a reasonable balance between oocyte and sperm donors, there is the psychological advantage of direct reciprocity. The partner knows what he or she has to give and what he/she will get in return. Heng and Tong correctly state that donation to scientific research can also be seen as a reciprocal contribution to society. However, this also applies to blood donation. Should we then allow blood donors to receive priority for oocytes or sperm? The mirror donation system is designed the way it is because we do not want body material but gametes, and we do not want gametes for research but gametes for reproduction.

The second point concerns the question whether progress in scientific research is sufficient to justify the risk and effort involved in oocyte donation. The difference in investment between embryo and sperm donors also plays in this context. Few people will object when men donate sperm for research. However, donation of embryos for research is a lot more contentious. Some authors object to this idea, especially when this is considered in the context of somatic cell nuclear transfer (SCNT). They would like to see much more caution in approaching women for altruistic donation for stem cell research (Magnus and Cho, 2005). One main concern is linked to the risk of exploitation, especially of poor women, when payment is provided (Dickenson, 2004). This is not applicable in this system, since there is no payment involved. A second reason is that the effort (health risk, discomfort, time investment, psychological burden, etc.) of the oocyte donation is not compensated by benefits. Stem cell research is a long-term project of which the results in terms of therapeutic applications in humans remain uncertain. The oocytes donated by one woman would at best contribute to a small increase in knowledge. From the experiment to therapy is still a long way to go. It is reasonable not to subject women to the risk of ovarian hyperstimulation syndrome purely for research purposes. As Heng and Tong themselves suggest, oocyte donation for research should be restricted to women who need IVF for infertility and donate surplus oocytes for research. However, this option is not applicable here, since women in mirror gamete donation are not infertile. In short, reproduction (for themselves or for others) justifies the risks for the health of the woman but scientific research does not.

In the long run, it would be more useful and efficient if other sources of oocytes are explored to obtain oocytes for research. These alternatives (such as fetal oocytes, cadaveric oocytes and stem cell-derived gametes) all presuppose *in vitro* maturation, but since the clinical trials on SCNT are still a long way off, we can use this time to improve this technique. If indeed many oocytes are needed for research (although nobody really knows at the moment), these other sources would moreover immediately give a large amount of starting material.

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Adenomyosis in endometriosis – prevalence and impact on fertility. Evidence from magnetic resonance imaging

Sir,

We read with great interest the paper by Kunz *et al*. entitled 'Adenomyosis in endometriosis – prevalence and impact on fertility. Evidence from magnetic resonance imaging' (Kunz *et al*., 2005). The authors found a higher incidence of uterine adenomyosis in women with endometriosis than in women without endometriosis and suggested that adenomyosis could be a determinant of infertility (Kunz *et al*., 2005). However, this article raises issues concerning the magnetic resonance (MR) imaging protocol used to diagnose adenomyosis.

Concerning the imaging technique itself, the authors directly adopted a protocol used in a study published five years previously (Kunz *et al*., 2000) that may not be optimal for the diagnosis of adenomyosis. First, a 1.5-T pelvic phased-array coil with a 256 × 512 matrix offers better spatial resolution than a 1-T body coil with a matrix of 154 × 256, particularly for the

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detection of hyperintense myometrial spots, which are the findings most specific to adenomyosis. Second, the usefulness of fat-saturated turbo-spin echo sequences for the detection of adenomyosis has never been demonstrated. Third, breath-hold T2-weighted sequences (true fast imaging with steady-state precession and turbo-inversion-recovery sequences) offer better differentiation between focal adenomyosis and uterine contraction, optimize the accuracy of MR imaging for the diagnosis of adenomyosis and reduce interobserver variability, while fast spin-echo T2-weighted images and breath-hold T2-weighted sequences appear to have similar accuracy (Bazot *et al*., 2003).

Concerning the MR imaging criteria, Kunz *et al*. considered that a junctional zone maximum of >11 mm (JZ_{max}) was alone sufficient for the diagnosis of adenomyosis (Reinhold *et al*., 1996). In our experience, however, isolated JZ_{max} >11 mm has a sensitivity and specificity of, respectively, 62% and 96% for the diagnosis of adenomyosis (Bazot *et al*., 2001). The combination of JZ thickness with high-signal-intensity myometrial spots, JZ_{max}/entire myometrium >40% and regular homogeneous uterine enlargement increases the accuracy of MR imaging in women with adenomyosis who do not have associated leiomyomas, raising the sensitivity and specificity to 87% and 100%, respectively (Bazot *et al*., 2001). Regarding clinical implications, using a JZ_{max} threshold of 10 mm as a criterion of adenomyosis, Kunz *et al*. found a very high prevalence of adenomyosis in the 'total endometriotic' group (79%) compared to both 'healthy controls' (9%) and 'total controls' (28%) (Kunz *et al*., 2005). These results contrast with those of a recent study in which only 44 (27%) of 163 women with pelvic endometriosis proven by laparoscopy and histology had adenomyosis on pre-operative MR imaging (Bazot *et al*., 2004).

Finally, like Kunz *et al*. we also found that uterine adenomyosis was the main determinant of infertility in a series of 34 women undergoing laparoscopic segmental colorectal resection for endometriosis, 22 of whom wished to conceive (Darai *et al*., 2005).

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Reply: Adenomyosis in endometriosis – prevalence and impact on fertility. Evidence from magnetic resonance imaging

Sir,

We thank the authors for their interest in our work. The bulk of the MR imaging scans of our study was obtained during 1999 through 2001. That is why we used the same MRI method as described in our publication of 2000 (Kunz *et al*., 2000). With this method, high quality scans were obtained (Figures 1 and 4 of our paper) (Kunz *et al*., 2005) which allowed us to identify alterations of the junctional zone that were interpreted as signs of focal and diffuse adenomyosis, respectively, according to the data of Reinhold *et al*. (1999). We were even more cautious in that a threshold value of more than 10 mm was chosen above which, with additional signs up to 12 mm, diffuse adenomyosis was assumed.

The authors report a lower prevalence of adenomyosis in endometriosis but confirm our finding of a significant impact of adenomyosis on subfertility and infertility in endometriosis. The discrepancy with respect to prevalence might be a matter of interpretation and the methods used. But it has also to be kept in mind that patient selection plays a key role in this respect.

According to our understanding of the disease process, minimal and mild endometriosis of the fertile woman, endometriosis in association with adenomyosis of the infertile woman and pre- and perimenopausal adenomyosis, respectively, constitute a pathophysiological continuum that could be summarized with the term 'syndrome of dislocated basal endometrium' and is characterized in its clinically most important form by pain, infertility and bleeding disorders. Circumstantial evidence suggests a causal relationship with uterine peristalsis and its dysfunctions. In women with normoperistalsis, minimal and mild endometriosis might develop without affecting fertility. Chronic uterine peristaltic activity throughout the reproductive period of life might result in pre- and perimenopausal adenomyosis. In our study, the prevalence of adenomyosis in the 'total control group' is largely due to the inclusion of women older than 35 years of age. This 'functional ageing' of the uterus might, in the general population, be further enforced by additional trauma such as pregnancy and delivery, as well as abortion curettage.

In infertile women, due to an abnormal stimulation of archimetral estrogen receptors that results in hyperperistalsis (Leyendecker *et al*., 2004), the process of the development of endometriosis and adenomyosis, respectively, is intensified and advanced. On a temporal scale, however, the development of the two disease varieties might not take place simultaneously

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