

### Lack of clinical and scientific evidence to justify the systematic use of ICSI in HIV-serodiscordant couples wishing to conceive where the male partner is infected

To the Editor:

Sauer et al. (1) reported, in a recent *Fertility and Sterility* issue, ten years' experience of an intracytoplasmic sperm injection (ICSI) program in 181 human immunodeficiency virus (HIV)-serodiscordant couples. One hundred three deliveries were reported. It is noteworthy that the multiple pregnancy (MP) rate was 41%, and that 43% of infants were born preterm. Twenty-one infants weighed <1,500 g. No female HIV-seroconversions occurred.

The authors affirm that their work provides "evidence that IVF-ICSI is indeed reasonable, safe, and effective alternative for managing the fertility needs of HIV-serodiscordant couples."

We cannot agree with these conclusions.

1. The choice of ICSI method was not "reasonable." In this context, one must remember that the majority of serodiscordant couples, with HIV-infected males using condoms to avoid female contamination, were fertile. In our opinion, there is no justification for systematic use of ICSI in these couples. Since the pioneering study by Semprini et al. (2), several teams have developed intrauterine insemination (IUI) programs with efficiency and no female contamination (3). Although the debate on HIV presence in spermatozoa is not definitively closed, the safety of assisted reproductive technology (ART) methods was clearly demonstrated in a published European multicenter study (4). The sperm abnormalities sometimes reported in the literature cannot justify ICSI for all serodiscordant couples.
2. The choice of ICSI method in this context cannot be regarded as "safe." Regarding the HIV transmission risk, the current literature supports ICSI as being safe, but no safer than IUI. Compared with IUI, superovulation and oocyte retrieval in IVF-ICSI carry risks to the women. However, the main concern with IVF-ICSI is the significantly increased MP rate and resulting complications, such as increased rate of preterm delivery and increased risk of maternal morbidity and mortality. Multiple birth infants have significantly increased risks of adverse health outcomes, predominantly as a result of preterm delivery, such as low birth weight, infant death, and physical and neurologic disabilities. The literature on ART has clearly established that practitioners should strive to avoid MP. Because of that, performing IVF or ICSI in serodiscordant couples when there is no sound medical basis for it cannot be justified.

3. ICSI did not prove to be an "effective" treatment. The live birth rate (56.9%) in the ICSI group was similar to the cumulative live birth rate reported in IUI programs. From a public health perspective, if we integrate the cost of ICSI on the effectiveness, ICSI was less effective than IUI programs for HIV-serodiscordant couples, even when the cost of viral testing of semen is taken into account. Moreover, if we add the huge financial burden associated with MP and prematurity, ICSI then becomes a very costly treatment.

In countries where health insurance companies often do not cover infertility treatment, the cost of ICSI may prohibit ART to reduce transmission risk during reproduction for many serodiscordant couples, which may in turn lead to such couples attempting to conceive through unprotected intercourse. From this aspect, we believe systematic use of ICSI in such couples carries ethical implications.

In conclusion, we believe that the systematic use of ICSI in serodiscordant couples, where the male partner is HIV infected, is not reasonable, safe, effective, or ethical. We believe that patients should be informed about all of the options for reducing the risk of HIV transmission and that the choice of ART methods should be related only to the fertility status (5).

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#### *Reply of the Author:*

I was disappointed to read the response of CREAThE to the detailed report of our ten years of work. Columbia University has labored to provide a reproductive “alternative” for Americans with human immunodeficiency virus (HIV) since 1997, within an environment very different from that existing in Europe and the U.K. We have never advocated for a “systematic” approach using either IVF or IUI therapy, and in fact I have published on the value of using both methods (1). However, in providing an alternative to no care at all, we chose to allow open access to HIV-infected patients despite recommendations against the practice by the Centers for Disease Control, when few, if any, U.S. centers offered services, and accepting the fact that it might be considered to be illegal in various parts of this country, the U.S., to treat them. We chose intracytoplasmic sperm injection (ICSI) to avoid prohibitions against “insemination” and to negate the need to test individual samples for HIV with assays that are expensive and/or not licensed or commercially approved to be used on semen.

Our patients elect to come here. They are fully informed of the risks and the benefits. Their risks are no different from other patients who also choose IVF, many of whom could also have consented to less invasive approaches but may prefer the enhanced success rates, expedited approach, and ability to cryopreserve embryos that remain advantages of IVF over IUI therapies.

We have been transparent in our attempts to advocate treatment of HIV-infected patients, publishing our protocols and updating our experience regularly along the way. This includes reports of complications of the use of IVF for this purpose (2). More than any other American program, and with numbers that rival any of the individual centers within the CREAThE network, Columbia University has gained an experience that is large and deep in both its clinical aspects and cultural importance. To question our method is one thing; to question our ethics is quite another.

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