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# Prevention of multiple pregnancies in infertility treatment

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### Keywords:

assisted reproductive treatment cryopreservation elective single embryo transfer multiple pregnancy ovulation induction ovulation stimulation The most important outcome of infertility treatment is a birth of a healthy baby. In many countries, in-vitro fertilisation treatments carry a high risk of twin pregnancy, which brings a higher risk to the mother and child than singleton pregnancies. Preterm delivery and low birth weight are the main factors accounting for the excess in neonatal morbidity. The use of elective single embryo transfer combined with cryopreservation can minimise the twin rate. Recent studies have shown that repeat single-embryo transfer can produce more live births per oocyte retrieval than doubleembryo transfer. Ovulation-induction treatment protocols can also be improved and optimised. Correct counselling is important, as many infertile couples may desire twin pregnancies. Good counselling should include realistic information on the risks of twin gestation and also on later burdens with a multiple birth. © 2012 Elsevier Ltd. All rights reserved.

### Background

The use of infertility treatments has expanded, and the increased success of these methods has been accompanied by concerns about rising rates of multiple pregnancies. Assisted reproductive techniques (ART), including the use of ovulation-inducing drugs, in-vitro fertilisation (IVF) and intracytoplasmic sperm injection (ICSI), have been criticised for producing high rates of multiple pregnancies, including twins. This criticism is well deserved. The increased efficiency of IVF and ICSI programmes in many centres has produced overall pregnancy rates of 30–35% per cycle, with multiple rates of 25–30%. This means that even one-half of children born after ART may have originated from multiple pregnancies. The most important perinatal risk linked to multiple-order pregnancies is prematurity, which occurs in

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1521-6934/\$ – see front matter @ 2012 Elsevier Ltd. All rights reserved. http://dx.doi.org/10.1016/j.bpobgyn.2012.05.011 more than one-half of twin pregnancies, and often results in a number of complications, including low birth weight (low birth weight <2500 g).

The contribution of IVF and ICSI to multiple pregnancies is better known than that of ovulation stimulation alone or combined intrauterine insemination. This is because several countries have established national registries for ART. Some prospective cohort studies on this subject, however, have been published; one of them was undertaken in a large training hospital in the Netherlands to evaluate the contribution of different fertility treatments to the number of multiple pregnancies.<sup>1</sup> Of all pregnancies, 46% were conceived spontaneously, 16% were induced by clomiphene citrate, 2.4% by follicle stimulating hormone and 14% by intrauterine insemination combined with controlled hyperstimulation. In-vitro fertilisation and its related techniques resulted in about one-fifth of all continuing pregnancies, but were responsible for more than one-half of multiple pregnancies. Furthermore, 18% of multiple pregnancies were induced by ovulation-induction protocols, whereas about 11% were conceived spontaneously.

Births resulting from infertility treatment account for around 1–3% of singletons, 30–50% of twins and more that 75% of higher-order multiple births in many European countries.<sup>2</sup> Another reason for the higher rate of multiples is older maternal age, which accounts for 25–30% of the rise in multiple birth rates since 1970. Data from the latest report from the European Society of Human Reproduction and Embryology on ART results in Europe<sup>3</sup> showed a multiple birth rate of 22.3% (21.3% twin and 1.0% triplet) in 2007. The proportion of multiple deliveries had not decreased compared with 2006 (20.8%) and 2005 (21.8%). The clinical pregnancy rates per aspiration and per transfer were 29.1 and 32.8% for IVF, and 28.6 and 33.0% for ICSI. Delivery rate after intrauterine insemination with the husband's sperm cells was 10.2% in women younger than 40 years with twin deliveries in 11.7% and triplets in 0.5%.

In many European countries, the number of multiple pregnancies has increased considerably during the past 20 years (Fig. 1).<sup>4</sup> In Finland, the same trend has been true; furthermore the effect of IVF practices on this change has been analysed (Fig. 2). In the USA between 1998 and 2003, the number of twin births increased by 17%, whereas the number of higher-order multiple births was unchanged. According to the same report, since 1998, total births resulting from ART increased by 65%, triplet births deceased by 8%, and quadruplet births decreased by 35%. In 2003, the estimated percentages of multiple births resulting from ART and ovulation induction were twins 16% and 21%, triplets 45% and 37%, and quadruplets 30% and 62%, respectively. After publication of the Society for Assisted Reproductive Technologies and the American Society for Reproductive Medicine recommended limits on number of embryos transferred, the ratio of higher-order multiple births to total ART births decreased substantially.<sup>5</sup>



Fig. 1. The proportion of multiple births in six countries (per 1000 births). Published with permission.<sup>4</sup>

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