CASE STUDY  Children born after cryopreservation of embryos or oocytes

With an estimated 3.5 million children born to date using ART, of which up to half a million have been estimated from slow freezing, researcher Dr Ulla Britt. Dept. Obstetrics and Gynaecology, Institute for Clinical Sciences, Gotteborg, Sweden reviewed data for outcomes for IVF/ICSI children born after cryopreservation.

Synopsis: A systematic review was performed. We searched the PubMed, Cochrane and Embase databases from 1984 to September 2008. Inclusion criteria for slow freezing of early cleavage stage embryos were controlled studies reporting perinatal or child outcomes. For slow freezing and vitrification of blastocysts and oocytes, and vitrification of early cleavage stage embryos, case reports on perinatal or child outcomes were also included. Three reviewers independently read and evaluated all selected studies. Results: For early cleavage embryos, data from controlled studies indicated a better or at least as good obstetric outcome, measured as preterm birth and low birthweight for children born after cryopreservation, as compared with children born after fresh cycles. Most studies found comparable malformation rates between frozen and fresh IVF/ICSI. For slow freezing of blastocysts and for vitrification of early cleavage stage embryos, blastocysts and oocytes, limited neonatal data was reported. We found no long-term child follow-up data for any cryopreservation technique. Conclusion: Data concerning infant outcome after slow freezing of embryos was reassuring. Properly controlled follow-up studies of neonatal outcome are needed after slow freezing of blastocysts and after vitrification of early cleavage stage embryos, blastocysts and oocytes. In addition, child long-term follow-up studies for all cryopreservation techniques are essential.

Discussion: The reason for better outcome for children born after cryopreservation as compared with children born after fresh transfer in most studies is not known. Mechanisms that have been discussed include adverse effect of hormone stimulation in fresh cycles and selection of women as well as embryos. Embryos surviving freezing and thawing might be of better quality than fresh embryos, and this may have a positive influence on child outcome. Vitrification as a method for freezing has increased greatly in use in recent years, particularly for freezing of blastocysts and oocytes. Better post-thawing survival rates and encouraging pregnancy rates as compared with slow freezing of embryos have been demonstrated (Loutradi et al., 2008). Most studies after vitrification of blastocysts are case reports or small case series without data on infant outcome. We identified only four retrospective studies and four case reports, which included information on 252 children. The largest study (Takahashi et al., 2005) showed no differences in obstetric outcomes for children born after vitrified blastocysts compared with children born after fresh blastocysts but a preterm birth rate of 18.5% and low birthweight rate of 43.5% among all children in the vitrified group is worth noting. Data on children born after freezing of oocytes, both slow freezing and vitrification, is also sparse. We found some neonatal information on a total of 148 children born after slow freezing of oocytes and 221 children born after vitrification of oocytes. The very limited data published about the children showed birthweights within the normal range. The largest study on vitrified oocytes (Chian et al., 2008) including 200 children found a preterm birth rate of 26% among singletons, which is two to three times higher than that reported for slow freezing of embryos. In conclusion, cryopreservation of oocytes and spare embryos has gained increased importance in recent years, concomitant with the introduction of single embryo transfer and the increased demand to preserve oocytes for future use. Slow freezing of embryos has been used for 25 years and data concerning infant outcome seems reassuring with even higher birthweights and lower rates of preterm and low birthweights than children born after fresh IVF/ICSI. For the newly introduced technique of vitrification of blastocysts and oocytes, very limited data have been reported on obstetric and neonatal outcomes.