

Do eggs matured in the laboratory result in babies with Large Offspring syndrome?

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A review of studies of babies born after in vitro maturation (IVM) fertility treatment has suggested that they are more likely to be born larger than normal and to have more difficult births requiring more obstetric interventions such as caesareans.

Authors of the literature review to be presented to the 26th annual meeting of the European Society of [Human Reproduction](#) and Embryology in Rome today (Wednesday) believe that this may be a problem associated with the IVM process in which immature eggs are retrieved from a woman's ovaries and matured in the lab before being fertilised and any resulting embryos transferred to the woman's uterus. They have urged caution in the use of IVM until further studies can clarify their findings.

Dr Peter Sjöblom, unit manager of Nurture, the Nottingham University IVF clinic at Queen's Medical Centre (Nottingham, UK), said: "We looked at four different data sets from four different countries and, although the numbers were small and differences modest, we saw a consistent pattern that cannot be ignored. We strongly believe that these findings must be explored further."

Dr Sjöblom and his colleagues analysed data from studies of babies born after IVM, in vitro [fertilisation](#) (IVF) and [intracytoplasmic sperm injection](#) (ICSI) in Denmark, Finland, Canada and Korea. They found that the [birth weight](#) of the 165 babies born after IVM was between 0.3% and 6% higher than the national average for singleton births and

6%-9% higher than babies conceived after IVF and/or ICSI. Caesarean rates were consistently higher after IVM as well: for singleton IVM births they were 30-60% versus 27-44% for IVF/ICSI births. IVM pregnancies had high miscarriage rates (25-37%) and the average period of gestation was 3-11 days longer than for IVF/ICSI. Although there were no firm data on other obstetric interventions, the authors thought it was probable that there was also a higher number of procedures such as inductions, vacuum extractions and forceps deliveries compared to IVF/ICSI births and births after natural conception.

"These findings suggest a significant impact of the IVM procedure on early development," said Dr Sjöblom. "The pattern of increased birth weight, more obstetric interventions and possibly a longer gestation period are consistent with Large Offspring Syndrome. It cannot be explained by there being a higher proportion of women with polycystic ovarian syndrome in the IVM group*, since the birth weight of their offspring was not significantly different from babies born after natural conception.

"We urge IVM practitioners and clinics to pool their data on obstetric and neonatal outcomes after fertility treatments because, at present, only limited data on small numbers of births are available. This should enable us to look more closely at the health and physiology of babies born after [fertility treatment](#) so that we can make a more detailed assessment of infant health. If the observed pattern still holds as the number of observations increases, then in-depth studies of mechanisms must be initiated. Caution is called for before proceeding with IVM on a large scale."

He said the possible mechanisms involved were unclear. "It has been described in the literature that gene expression is altered in IVM eggs compared to those matured naturally in the body; it may be the case that the final stages of egg development before ovulation involves events that

are crucial to development and that this is not happening when they are matured in the lab. Another explanation could be that the preparation of the lining of the womb (the endometrium) is different and this may influence development, as has been shown in animal studies."

The long-term consequences to the health of babies born after IVM are also unknown. "For the sake of the health and safety of the babies and their mothers, we need to be following IVM babies from the moment the eggs are matured in the laboratory through to their birth and into adulthood. We also need to look in detail into possible physiological effects, like alterations in blood pressure. However, we must make it clear to the public that, at the moment, no major health problems have been observed in children born after IVM. Nevertheless, all fertility clinics should share their detailed data, so that we can, hopefully, conclude that there is no reason for concern," concluded Dr Sjöblom.

Provided by European Society of Human Reproduction and Embryology

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