

Parental infertility and cerebral palsy in children born spontaneously or after IVF/ICSI

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Doctors have known for some time that children born after fertility treatments such as in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI) are at increased risk of cerebral palsy. However, it was not known whether this risk was due to the treatment itself, the higher frequency of preterm or multiple births, or a mechanism associated with couples' underlying infertility.

Now, new research published online in Europe's leading [reproductive medicine](#) journal *Human Reproduction* [1] today (Wednesday 3 November) indicates that underlying infertility is not the main reason for the increased risk seen in IVF/ICSI children.

The study led by Dr. Jin Liang Zhu, an epidemiologist at the Danish Epidemiology Science Centre at the University of Aarhus, Denmark, is the first to examine the association between the time it takes a couple to achieve a pregnancy and the risk of cerebral palsy. The researchers used the Danish National Birth Cohort to compare children born after 0-2 months of waiting time to pregnancy with those born after a time to pregnancy of 3-5 months, 6-12 months, and longer than 12 months, as well as those born after IVF/ICSI, ovulation induction with or without intrauterine insemination, and unplanned pregnancies. Parents who conceive quickly are likely to be normally fertile, while a waiting time of a year or more is likely to indicate some degree of subfertility.

After adjusting for factors that could influence the health of the baby, such as the mother's age, parity, whether or not she smoked, her education, the sex of the child, whether the birth was preterm, and whether it was a multiple birth (e.g. twins or triplets), the researchers found there was no significant association between the time to pregnancy and the risk of cerebral palsy in children born as a result of a spontaneous pregnancy, even after a waiting time to pregnancy of a year or more.

Dr. Zhu said: "Our research enabled us to examine whether untreated subfertility, measured by time to pregnancy, might be the reason for the higher risk of cerebral palsy after IVF/ICSI. Our results showed that this was not the case because, even for couples who took a year or longer to conceive, there was no statistically significant increased risk if they conceived spontaneously."

The researchers did find that, even after adjusting for the risks associated with preterm births and multiple pregnancies (both of which are more common during [fertility treatment](#)), children born after IVF/ICSI treatment had double the risk of cerebral palsy compared with children born after spontaneous conception. However, this was only when they were compared with children conceived spontaneously within two months – a group in which fertility treatments would never be used. When the IVF/ICSI children were compared with children conceived spontaneously after a waiting time to pregnancy of more than a year, the risk decreased.

Dr. Zhu said: "It is important to stress that the risks of cerebral palsy after IVF/ICSI are low. Out of more than 90,000 children in the Danish National Birth Cohort, born between 1997 and 2003, only 165 (0.18%) were diagnosed with cerebral palsy. Of the 3,000 children in this cohort born after IVF/ICSI, only 17 (0.57%) had cerebral palsy. This means that the absolute risk of having a child with cerebral palsy after IVF/ICSI

treatment is still low – approximately one in 176 babies – and this risk is even lower if the children are born as a result of a single embryo being transferred to the mother's womb, thus avoiding the risks of a multiple pregnancy. Further analysis of the data showed that, when children born after IVF/ICSI were compared with children conceived spontaneously after a waiting time of more than 12 months, the elevated risk of cerebral palsy reduced and was no longer statistically significant."

Dr. Zhu concluded: "More research is needed into why there might be an increased risk of cerebral palsy associated with IVF/ICSI, besides the pathway of multiple pregnancies and preterm births. It is also important to remember that IVF/ICSI techniques have developed and improved considerably since 2003 when the youngest children in our study were born."

Another study [3] of a much larger group of children in Sweden (2,623,517 babies born between 1982-2007, of which 31,587 babies were born after IVF) has found no statistically significant increase in cerebral palsy in children born after IVF/ICSI, after adjusting for confounding factors. For the period 2004-2007 when the rate of [multiple births](#) fell to less than 10% in Sweden, the risk of cerebral palsy after IVF was the same as for babies conceived spontaneously. The authors concluded that any slight increase in cerebral palsy was "most likely a consequence of an increased risk of neonatal morbidity, notably associated with multiple births".

Professor Karl Nygren, one of the authors of the Swedish study and deputy co-ordinator of the European Society of [Human Reproduction and Embryology's](#) special interest group on safety and quality in ART (assisted reproduction technology) said: "It seems to us that the previously noted increased risk of cerebral palsy after IVF is certainly decreasing and may actually have disappeared in recent years in countries that only transfer a single embryo at one time. This is good

news."

More information: [1] Parental infertility and cerebral palsy in children. Human Reproduction journal. [doi:10.1093/humrep/deq206](https://doi.org/10.1093/humrep/deq206)

[2] The work was supported by grants from the Danish Medical Research Council and the Intramural program of the National Institute of Environmental Health Sciences, National Institutes of Health in the USA.

[3] "Cerebral palsy in children born after in vitro fertilization. Is the risk decreasing?" European Journal of Paediatric Neurology, published online on May 5, 2010.

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