

'Vanishing twin' explains increased risk of birth defects

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Australian researchers have made the significant discovery that loss of a twin during very early pregnancy explains the increased risk of birth defects seen in multiple pregnancies after infertility treatment.

Professor Michael Davies will tell the annual meeting of the European Society of [Human Reproduction](#) and Embryology today (Wednesday) that the "vanishing twin" phenomenon, in which only one child is born from a [pregnancy](#) that originally starts as a [multiple pregnancy](#), is linked to a nearly two-fold increased risk in any congenital malformation and to a nearly three-fold risk of multiple malformations.

Prof Davies, who is an Associate Professor and co-director of the Research Centre for the Early Origins of Health and Disease at the University of Adelaide, Australia, will say: "Our findings show that a 'vanishing twin' is a significant risk factor for congenital malformations in the surviving baby. This discovery means that we can now investigate what factors are occurring earlier in the process that could be influencing [embryo development](#) and loss. This has significant potential for advancing our understanding of the origins of congenital malformation, not just after [infertility treatment](#), but also in spontaneously conceived pregnancies."

It is difficult to study what factors in early pregnancy might be causing congenital malformations such as heart and skeletal defects and cerebral palsy. This is because, in the general population, the majority of pregnancy losses, including vanishing twins, occur in the early days and

weeks of pregnancy, often before the woman even knows that she is pregnant. The first [ultrasound scans](#) are usually carried out at around six to eight weeks. However, in women undergoing fertility treatment, [early pregnancy](#) is much easier to study because doctors know exactly when eggs were fertilised and transferred to the woman's womb, and this is followed by close monitoring with pregnancy tests and ultrasounds from the very beginning.

Prof Davies and his team studied data from all assisted reproductive technology (ART) cycles that took place in South Australia between January 1986 and December 2002, and linked them to registry data on birth defects and cerebral palsy. They identified cases in which a foetus had been lost by comparing routine six-week ultrasound data, which would show the presence of an empty foetal sac, and the number of babies actually delivered. These results were compared with pregnancies that had started off as single pregnancies and which had continued without loss of the foetus.

During this period 7,462 babies were delivered. In pregnancies where ultrasound had detected an empty foetal sac at six weeks, 14.6% of babies born had subsequent congenital malformations. The presence of an empty sac nearly doubled the risk of any malformation, and nearly trebled the risk of multiple malformations. [Multiple pregnancies](#) without any foetal loss were not associated with an increase in malformations when compared with single pregnancies without loss in the infertility group.

Prof Davies also looked at pregnancy loss after the first six weeks and he found that this was associated with birth defects in the surviving twin as well.

He will tell the conference: "To our knowledge, this appears to be the first report of the association of very early loss of a co-twin and a range

of congenital malformations. This result is important for several reasons. Firstly, it appears that the developmental competency, or 'quality' of embryos in twins is related. Where one fails to develop, it appears to be an important indicator of the health of the survivor. This is certainly a sensible interpretation within ART, where the embryos result from the same stimulation cycle and embryo culture conditions, and are returned together.

"However, it may be possible to generalise these results to birth defects seen in fraternal twins – twins created from two separate eggs – from spontaneous pregnancies in the general population. This is important from the point of reproductive biology. One interpretation is that twinning reflects a failure in the regulation of egg recruitment and early embryo selection to ensure that only a single best egg and embryo implant. From a clinical perspective, it also emphasises the importance of embryo quality – not just for pregnancy rates but also for the competency of the foetus to develop normally." Now he and his team will be trying to discover what mechanism is involved and whether it could be used to predict and improve embryo quality.

Prof Davies believes that the same mechanism may also be operating when babies with birth defects are born after spontaneously conceived single pregnancies, and that this could explain why a family history of miscarriage or a previous miscarriage is a risk factor for birth defects in a singleton pregnancy. "This interpretation may help us understand why both twinning and birth defects increase with maternal age, as there may be a common mechanism."

The results of the research to be presented today may have important implications for [fertility treatment](#), for instance when implementing a policy of single embryo transfer. "It may reinforce the importance of maximising embryo quality and factors that contribute to it," he will say. "Furthermore, creating and using multiple embryos of lower quality may

increase the risk of a developmentally compromised embryo both being selected for transfer and surviving to birth. However, it also appears that there may be predictable circumstances under which twin pregnancies do not carry a significant additional overall risk for [birth defects](#), although twinning would continue to be a high-risk pregnancy for mother and baby for numerous other reasons."

He will conclude: "It is particularly exciting to consider that in the near future we should be able to understand and influence the factors related to embryo quality in such a way as to drastically reduce the risk of [congenital malformations](#) in ART babies. Further, it appears plausible that these same factors will operate in the general population, and may, in principle, be modifiable."

Provided by European Society of Human Reproduction and Embryology

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