

IVF: Safe method of conception for those with infertility or 'evolutionary experiment'

It may be time to add another risk factor for cancers, diabetes and high blood pressure to the list: mode of conception. Evolutionary biologist Pascal Gagneux reignited the public controversy over long term effects of assisted reproduction at a panel discussion at the American Association for the Advancement of Science annual meeting earlier this month.

"We're engaging in an evolutionary experiment... The jury is out about whether these children are going to be healthy 80 years down the line," [Gagneux said](#).

Gagneux went on to compared assisted reproduction to high fructose corn syrup in how it took us decades to discover high fructose corn syrup was linked to negative health effects. Today, the oldest child born of in vitro fertilization, Louise Brown, is 39. Is her, and many others, future health at risk because of their location of a fertilization event or is Gagneux simply promoting the precautionary principle?

[Five million children](#) have been born using assisted reproduction. And according to many studies, these kids, teenagers and mid-life adults are as healthy as their conventionally conceived counterparts. But a couple of studies have shown differences. Gagneux highlighted two in his comments: a study of 60 assisted reproduction children and a study documenting cardiovascular changes and aging in mice. Both were done by the same Swiss research group.

In the first study, [65 children](#) whose parents used IVF were taken up a Swiss mountain to see how their hearts would perform in a low-oxygen, high altitude environment. The physicians who did the study say the mountain environment mimics aging because it causes stress on the heart and circulatory system. The Swiss team found that assisted-reproduction children had 30 percent higher blood pressure in the artery that runs from their heart to their lungs (called the pulmonary artery). And, relatedly, their blood vessels didn't dilate as much as control children throughout their cardiovascular system.

But the study was very small — only 65 kids and all from Switzerland. And while having high blood pressure in your [pulmonary artery](#) is a risk factor for cardiovascular disease, and something that seems to occur naturally as people age, it doesn't mean that the assisted-reproduction kids are all going to have heart attacks. Moreover, the cardiovascular risks might not be a factor of IVF, but rather because assisted-reproduction babies are more likely to be born prematurely, at a low birthweight, or be a multiple birth as [cardiologist David Celermajer](#) wrote in an editorial that accompanied the study. All three of those scenarios also increase the risk of cardiovascular deficits.

The other study Gagneux mentioned looked at the [aging of mice](#) conceived using assisted reproductive technologies. These mice also had stiffer arteries that didn't dilate as well. As did their offspring. And when they were fed a high-fat diet, in order to mimic a western diet, the mice lived a 25 percent shorter life than control mice who were fertilized in vivo and also ate the high fat diet. Interestingly, mice who ate a normal laboratory diet had similar lifespans no matter how they were conceived.

This study also documented gene expression in the assisted reproduction mice. They found substantial

changes in gene expression — what genes are being turned into proteins that do the business of the body — in tissues in the mice's hearts. Adding to a potential mechanism for how this 'vascular dysfunction' could arise. They also studied the chemicals used to support the embryos after they are created in the lab, but before they are implanted into a uterus. By changing those chemicals, the scientists could reverse the atypical pattern of gene expression. This is further evidence, they say, that it might be the chemical cocktails used to support embryos before transferring them that might be causing the cardiovascular effects.

But neither of these studies could pinpoint the exact cause of the cardiovascular defect. In fact, in humans, the effect is still under debate. With 5 million kids out there now, it seems like we could end up with some good data, but there is not a national reporting system for children who were conceived with technological assistance. It's going to be hard to pull that data together. And [headlines](#) like "IVF children face time bomb of poor health and short lives" that appear at the *Daily Mail* don't do justice to either the research or the children and parents who are needlessly alarmed.

The [New Scientist](#) did take the chance to look at what is incontrovertibly a potentially risky side effect of assisted-reproduction technologies like IVF: multiple births. During these procedures, parents and their physicians decide how many embryos to introduce to the uterus in hopes they develop into pregnancies. More embryos can lead to higher success rates, but also to having twins and triplets. Multiple births mean multiple risk factors to a pregnancy. So much so that the standard recommendation now is to only use one. [New Scientist](#) explains:

Many would-be parents see twins as a bonus. But multiple births are more dangerous for the mother, and the children are more likely to be born prematurely or have a low birthweight, and to suffer from lifelong physical and mental issues such as deafness, blindness or cognitive impairment.

And being born early, before 37 weeks, is also emerging as a [major risk factor](#) for cardiovascular disease. So now we are back to what seems like a chicken and a technologically-assisted egg problem. Multiple births, prematurity, IVF and adult cardiovascular disease are all associated. What we don't know is how many of those are directly linked and how those causal links work together. Many IVF specialists and scientists spoke out to [disagree](#) with Gagneux, Allan Pacey, a professor of andrology at the University of Sheffield, spoke out saying:

Where some differences have been observed, these are largely explained by genetic defects in the sperm of the father rather than the fact that fertilisation and embryo development occurred outside of the body. I don't share the concerns raised by Dr Gagneux. If we were always led by the precautionary principle, medicine would never make any advances.

[Gagneux studies](#) the interactions of sperm and egg and the importance of the molecules lining their surfaces in normal conception. His hypotheses and comments are based on his knowledge that these molecular signals help eggs meet with the healthiest, most fit sperm a process which is still poorly

understood and is a process that is totally bypassed in IVF. Learning more about the cellular and molecular processes involved in conception could make IVF better. So could furthering our understanding of the cellular mediums used to foster IVF embryos before they head to the uterus for implantation.

These are fascinating ideas and under-researched. Calling them out as 'evolutionary experiment' is a great way to draw attention, and potential funding. But it could also make millions of parents worried about a phenomenon that we won't be able to measure for a few more decades and could turn many people away from their only opportunity to have biological offspring.

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