OPINION

Fertility factor

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More than 5 million children worldwide have been born through assisted reproductive technologies such as *in vitro* fertilization (IVF). The proportion of women in the U.S. who experience fertility problems **exceeds 10 percent**. In some countries, such as Denmark, as much as **9 percent** of children are born with the help of fertility treatments.

Still, the verdict on whether children conceived through these methods are **at greater risk** for disorders such as autism has **see-sawed** in the past several years.

In spite of some **evidence to the contrary**, the mainstream press periodically sounds the klaxons warning that children conceived via IVF are in danger of developing autism, cerebral palsy and other disorders.

Two new studies indicate that for most IVF procedures, the risk, where it exists at all, is extremely low. These studies, based on **Swedish** and **Danish** populations, suggest that the simplest form of IVF does not increase the risk for autism and intellectual disability, although the effect of other fertility treatments is still unclear.

It seems obvious that the same factors that increase the likelihood of infertility might also hike the risk of having a child with a disorder — which complicates how well we can interpret any study seeking a relationship between fertility treatments and the disorder.

For example, **fathers** and **mothers** older than 40 are both thought to be at higher-than-average risk of having a child with autism. And some causes of **mild infertility** in women stem from mutations that can lead to disorders such as **fragile X syndrome** in their children.

What’s more, most studies that have examined the effect of fertility treatments on brain

development are relatively small, including fewer than 500 children, with medical follow-up ending in preschool or earlier.

Subtle risk:

One of the new studies, published 2 July in *The Journal of the American Medical Association,* examined data from more than 2.5 million children born between 1982 and 2007 in Sweden. About 31,000 of the children had been born following an IVF procedure.

The researchers considered both the traditional form of IVF, in which sperm and egg cells are fertilized outside the body, and intracytoplasmic sperm injection (ICSI), a treatment for male infertility that involves the injection of sperm directly into the egg. ICSI is the most common type of fertility treatment in the U.S.

As a whole, IVF techniques **do not significantly increase the risk for autism or intellectual disability.** Even for the most complicated procedures, the low risk that exists seems to be related to the higher rate of multiple births from IVF rather than to the techniques themselves.

Children conceived through ICSI with surgically extracted sperm have nearly five times the risk of autism and more than double the risk of intellectual disability compared with those conceived through simpler IVF techniques, the study found.

The manipulation of sperm and egg for this technique may be risky, but the high-risk figure may have nothing to do with that. Doctors surgically extract sperm when a man's sperm counts are extremely low, the motility is subpar, or a malformation or scar tissue blocks their exit from the reproductive tract. Any of these might signal a mutation load in the man or his sperm that is heavy enough to also affect his children.

The second study, published 5 July in the *British Medical Journal*, tracked the 588,967 children born in Denmark from 1995 to 2003. Of these, nearly 15,000 children were born after IVF or ICSI, and more than 18,000 after hormone treatment to induce ovulation or after insemination directly into the uterus.

The study found that **IVF procedures do not increase the risk for disorders** such as autism, but ICSI slightly elevates the risk of a child developing a tic — the compulsion to repeatedly make a particular movement or sound.