

## Older fathers associated with increased birth risks, study reports

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A decade of data documenting live births in the United States links babies of older fathers with a variety of increased risks at birth, including low birth weight and seizures, according to a new study by researchers at the Stanford University School of Medicine.

The data even suggest that the age of the father can sway the health of the mother during pregnancy, specifically her risk for developing diabetes.

"We tend to look at maternal factors in evaluating associated birth risks, but this study shows that having a healthy baby is a team sport, and the father's age contributes to the baby's health, too," said Michael Eisenberg, MD, associate professor of urology.

Data from more than 40 million births showed that babies born to fathers of an "advanced paternal age," which roughly equates to older than 35, were at a higher risk for adverse birth outcomes, such as low birth weight, seizures and need for ventilation immediately after birth. Generally speaking, the

older a father's age, the greater the risk. For example, men who were 45 or older were 14 percent more likely to have a child born prematurely, and men 50 or older were 28 percent more likely to have a child that required admission to the neonatal intensive care unit.

Still, these numbers aren't reason to drastically change any life plans, as the risks are still relatively low, Eisenberg said. He compared the increased risks to buying lottery tickets. "If you buy two lottery tickets instead of one, your chances of winning double, so it's increased by 100 percent," he said. "But that's a relative increase. Because your chance of winning the lottery started very small, it's still unlikely that you're going to win the lottery. This is a very extreme example, but the same concept can be applied to how you think about these birth risks."

Instead, Eisenberg sees the findings as informational ammunition for people planning a family and hopes that they will serve to educate the public and health officials.

A paper describing the study will be published online Nov. 1 in the The *British Medical Journal*. Eisenberg is the senior author. Resident physician Yash Khandwala, MD, is the lead author.

## Increased risks at 35

Back in 2017, Eisenberg published a study showing that the number of older men fathering children was on the rise. Now, about 10 percent of infants are born to fathers over the age of 40, whereas four decades ago it was only 4 percent.

"We're seeing these shifts across the United States, across race strata, across education levels, geography—everywhere you look, the same patterns are being seen," Eisenberg said. "So I do think it's becoming more relevant for us to understand the health ramifications of advanced



paternal age on infant and maternal health."

Eisenberg and his colleagues used data from 40.5 million live births documented through a datasharing program run by the Centers for Disease Control and Prevention and the National Center for Health Statistics. The researchers organized the information based on the fathers' age—younger than and birth outcomes at a population level," said 25; 25 to 34; 35 to 44; 45 to 55; and older than 55—and controlled for a variety of parameters that might skew the association between the father's age and birth outcomes, such as race, education level, marital status, smoking history, access to care and the mother's age.

The data suggested that once a dad hits age 35, there's a slight increase in birth risks overall—with every year that a man ages, he accumulates on average two new mutations in the DNA of his sperm—but birth risks for infants born to fathers of the subsequent age tier showed sharper increases.

Compared with fathers between the ages of 25 and 34 (the average age of paternity in the United States), infants born to men 45 or older were 14 percent more likely to be admitted to the NICU, 14 percent more likely to be born prematurely, 18 percent more likely to have seizures and 14 percent more likely to have a low birth weight. If a father was 50 or older, the likelihood that their infant would need ventilation upon birth increased by 10 percent, and the odds that they would need assistance from the neonatal intensive care unit increased by 28 percent.

"What was really surprising was that there seemed to be an association between advanced paternal age and the chance that the mother would develop diabetes during pregnancy," said Eisenberg. For men age 45 and older, their partners were 28 percent more likely to develop gestational diabetes, compared with fathers between 25 and 34. Eisenberg points out that possible biological mechanisms at play here are still a bit murky, but he suspects that the mother's placenta has a role.

## **Beyond correlation**

Moving forward, Eisenberg wants to look into other population cohorts to confirm the associations

between age and birth risks, as well as begin to decode some of the possible biological mechanisms.

"Scientists have looked at these kinds of trends." before, but this is the most comprehensive study to look at the relationship between the father's age Eisenberg. "Having a better understanding of the father's biological role will be obviously important for the offspring, but also potentially for the mother."

More information: British Medical Journal (2018). www.bmj.com/content/363/bmj.k4372

British Medical Journal (2018). www.bmj.com/content/363/bmj.k4466

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