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Male infertility linked to mortality

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Men who are infertile because of defects in their semen appear to be at increased risk of dying sooner than men with normal semen, according to a study led by a researcher at the Stanford University School of Medicine.

Men with two or more abnormalities in their semen were more than twice as likely to die over a roughly eight-year period as men who had normal semen, the study found.

Smoking and diabetes—either of which doubles mortality risk—both get a lot of attention, noted the study's lead author, Michael Eisenberg, MD, PhD, assistant professor of urology and Stanford's director of male reproductive medicine and surgery. "But here we're seeing the same doubled risk with male infertility, which is relatively understudied."

Infertility is a widespread medical complaint in developed countries, where about one in seven couples is affected at some point. But this is only the third study worldwide, and the first in the United States, to address the question of a connection between male infertility and mortality, said Eisenberg.

Results from the two earlier studies, one in postwar Germany and another of more recent vintage in Denmark, were conflicting.

In the new study titled "Semen quality, infertility and mortality in the USA," to be published online May 16 in *Human Reproduction*, Eisenberg and his colleagues examined records of men ages 20 to 50 who had

visited one of two centers to be evaluated for possible infertility. In all, about 12,000 men fitting this description were seen between 1994 and 2011 at Stanford Hospital & Clinics or between 1989 and 2009 at the Baylor College of Medicine in Houston. At both clinics, data were available for several aspects of a patient's semen quality, such as total semen volume and sperm counts, motility and shape. (Dolores Lamb, PhD, and Larry Lipshultz, MD, of Baylor were senior authors of the study.)

By keying identifiers for the patients to data in the National Death Index and the Social Security Death index, the investigators were able to monitor these men's mortality for a median of about eight years. "We were able to determine with better than 90 percent accuracy who died during that follow-up time," Eisenberg said. "There was an inverse relationship. In the years following their evaluation, men with poor semen quality had more than double the mortality rate of those who didn't."

While no single semen abnormality in itself predicted mortality, men with two or more such abnormalities had more than double the risk of death over the eight-year period following their initial fertility examination compared with those with no semen abnormalities. The greater the number of abnormalities, the higher the mortality rate, the study found.

"Eisenberg and colleagues provide empirical evidence in support of the evolving literature suggesting that human fecundity influences health and disease across the life span," Germaine Buck Louis, PhD, director of the division of intramural population health research at the Eunice Kennedy Shriver National Institute of Child Health and Human Development, wrote in an accompanying editorial, "Male fecundity and its implications of health and disease across the lifespan," in Human Reproduction. "Human fecundity may be both informative and predictive about

continual health status and later-onset disease."

Of the 11,935 men who were followed, 69 died during the follow-up period—a seemingly small number. This reflects, first and foremost, the patients' relative youth: Their median age was 36.6 years. But it also reflects the fact that men who get evaluated for infertility tend to have a higher-than-average socio-economic status and have accordingly better diets, education and access to health care.

Moreover, men who are concerned about infertility are men who want to have children. "If you're trying to have a child, you're probably reasonably healthy at the moment and in mental shape to be planning for your future," Eisenberg said. In fact, the men seen at the two medical centers—both those with and those without semen abnormalities—tended to die at slower rates than the general U.S. male population.

Nevertheless, within this select group, the difference in death rates between those who had semen abnormalities and those who didn't was statistically significant. Those with two or more semen abnormalities were more than twice as likely to die during the follow-up period as those without any. This difference remained despite the investigators' efforts to control, where possible, for baseline health differences between the two sets of patients. They corrected for age and known diseases.

"It's plausible that, even though we didn't detect it, infertility may be caused by pre-existing general health problems," Eisenberg said. The true cause of increased mortality risk, then, would be not infertility per se, but those health problems.

"But we controlled for this factor as best we could, and while that did attenuate the measured risk somewhat, there seems to be something else

going on. Could it be genetic, developmental or hormonal factors? Or could it be that something about the experience of having and raising kids—even though you may sometimes feel like they're killing you—actually lowers mortality?"

Eisenberg and his associates are trying to figure out why this is happening. "Is their blood pressure rising? What about their blood sugar, or other measures? We are starting to do prospective data collections now, through a collaboration involving several centers in the United States and Canada," he said.

Provided by Stanford University Medical Center

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