

Men who can't produce sperm face increased cancer risk, study finds

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Men who are diagnosed as azoospermic—infertile because of an absence of sperm in their ejaculate—are more prone to developing cancer than the general population, a study led by a Stanford University School of Medicine urologist has found. And a diagnosis of azoospermia before age 30 carries an eight-fold cancer risk, the study says.

"An azoospermic man's risk for developing [cancer](#) is similar to that for a typical man 10 years older," said Michael Eisenberg, MD, PhD, assistant professor of [urology](#) at the medical school and director of male reproductive medicine and surgery at Stanford Hospital & Clinics. Eisenberg is lead author of the study, which will be published online June 20 in *Fertility and Sterility*.

Diagnoses of male infertility and azoospermia are surprisingly common in the United States. About 4 million American [men](#)—15 percent of those ages 15-45—are infertile. Of these, some 600,000—about 1 percent of those of reproductive age—are azoospermic. "There is evidence that infertility may be a barometer for men's overall health," Eisenberg said, "and a few studies have found an association of male infertility with testicular cancer." The new study, he said, not only assigns the bulk of [infertile men](#)'s increased cancer risk to those with azoospermia, but also suggests that this risk extends beyond testicular cancer.

Eisenberg conducted most of the analysis for the study at Stanford, using data gathered from the Texas Cancer Registry and the Baylor College of

Medicine in Houston, where he completed his medical training. The study's senior authors are Larry Lipshultz, MD, and Dolores Lamb, PhD, professors of urology at Baylor.

The study population consisted of 2,238 infertile men who were seen at a Baylor andrology clinic from 1989 to 2009. Their median age was 35.7 when they were first evaluated for the cause of their infertility. Of those men, 451 had azoospermia, and 1,787 did not. There were otherwise no apparent initial differences between the two groups.

Azoospermia can arise for two reasons. Obstructive azoospermia is caused by a blockage that prevents otherwise plentiful, fit sperm produced in the testes from reaching the ejaculate. But a screen of about one-fourth of the azoospermic men in the study population indicated that the vast majority suffered from the non-obstructive variety: Their testes didn't produce enough sperm for any to reach their ejaculate, most likely because of genetic deficiencies of one sort or another. Fully one-fourth of all the genes in the human genome play some role in reproduction, Eisenberg noted, so there are a lot of ways for the capacity to sire offspring to go astray.

After undergoing a semen analysis, the men were followed for an average of 6.7 years to see which of them turned up in the Texas Cancer Registry. (Fortunately for the analysis, most people tend to stay in the state where they've grown up, said Eisenberg.) Their rates of diagnosed cancer incidence were then compared with age-adjusted cancer-diagnosis statistics of Texas men in general.

In all, a total of 29 of the 2,238 infertile men developed cancer over a 5.8-year average period from their semen analysis to their cancer diagnosis. This contrasted with an expected 16.7 cases, on an age-adjusted basis, for the male Texas population in general (which, Eisenberg said, closely reflects cancer incidence rates for the entire U.S.

population). This meant that infertile men were 1.7 times as likely to develop cancer as men in the general population. This is considered a moderately increased risk.

But comparing the cancer risk of azoospermic and nonazoospermic infertile men revealed a major disparity: The azoospermic men were at a substantially elevated risk—nearly three times as likely to receive a diagnosis of cancer as men in the overall population. Infertile men who weren't azoospermic, in contrast, exhibited a statistically insignificant increased cancer risk of only 1.4 times that of men in the overall population.

By excluding men whose cancer [diagnosis](#) came within two or three years of their infertility evaluation, the researchers were able to rule out the possibility that azoospermia caused by an undiagnosed cancer had affected the statistics.

While the study wasn't large enough to delineate which specific types of cancer pushed azoospermic men's incidence rates up, the diagnoses they received covered a wide range of cancers: brain, prostate and stomach tumors, as well as melanoma, lymphoma, testicular cancer and cancer of the small intestine. The findings suggest that genetic defects that result in azoospermia may also broadly increase a man's vulnerability to cancer, Eisenberg said, supporting the notion that azoospermia and cancer vulnerability may share common genetic causes.

The study, which was funded by the National Institute for Child Health and Human Development, is the first to examine the cancer risk of azoospermia in particular, or to link it to non-germ-cell cancers. Previous studies have failed to consistently identify any increased risk for nontesticular cancers in infertile men, whether azoospermic or otherwise. In those previous studies, however, azoospermic men couldn't be separately examined because [sperm](#) analyses weren't available.

Most striking of all, said Eisenberg, was the cancer risk among azoospermic men who first had their semen analyzed before age 30. They were more than eight times as likely to subsequently develop cancer than Texas males in the general population of the same age. In contrast, there was no relationship between age of semen analysis and risk of cancer for nonazoospermic men.

The good news, Eisenberg said, is that while the [cancer risk](#) among young azoospermic men was quite large compared to their same-age peers, their relative youth means that their absolute risk of contracting cancer during the follow-up period remained small. The bad news, he said, is that men in their 30s often don't have a primary health-care provider. He advised that young men who are diagnosed as azoospermic should be aware of their heightened risk and make sure to get periodic checkups with that in mind.

Provided by Stanford University Medical Center

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