

Marijuana use linked to increased risk of testicular cancer

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Frequent and/or long-term marijuana use may significantly increase a man's risk of developing the most aggressive type of testicular cancer, according to a study by researchers at Fred Hutchinson Cancer Research Center. The study results were published online Feb. 9 in the journal *Cancer*.

The researchers found that being a marijuana smoker at the time of diagnosis was associated with a 70 percent increased risk of testicular cancer. The risk was particularly elevated (about twice that of those who never smoked marijuana) for those who used marijuana at least weekly and/or who had long-term exposure to the substance beginning in adolescence.

The results also suggested that the association with marijuana use might be limited to nonseminoma, a fast-growing testicular malignancy that tends to strike early, between ages 20 and 35, and accounts for about 40 percent of all testicular-cancer cases.

Since the 1950s, the incidence of the two main cellular subtypes of testicular cancer, nonseminoma and seminoma - the more common, slower growing kind that strikes men in their 30s and 40s - has increased by 3 percent to 6 percent per year in the U.S., Canada, Europe, Australia and New Zealand. During the same time period, marijuana use in North America, Europe and Australia has risen accordingly, which is one of several factors that led the researchers to hypothesize a potential association.

"Our study is not the first to suggest that some aspect of a man's lifestyle or environment is a risk factor for testicular cancer, but it is the first that has looked at marijuana use," said author Stephen M. Schwartz, M.P.H., Ph.D., an epidemiologist and member of the Public Health Sciences Division at the Hutchinson Center.

Established risk factors for testicular cancer include a family history of the disease, undescended testes and abnormal testicular development. The disease is thought to begin in the womb, when some fetal germ cells (those that eventually make sperm in adulthood) fail to develop properly and become vulnerable to malignancy. Later, during adolescence and adulthood, it is thought that exposure to male sex hormones coaxes these cells to become cancerous.

"Just as the changing hormonal environment of adolescence and adulthood can trigger undifferentiated fetal germ cells to become cancerous, it has been suggested that puberty is a 'window of opportunity' during which lifestyle or environmental factors also can increase the risk of testicular cancer," said senior author Janet R. Daling, Ph.D., an epidemiologist who is also a member of the Center's Public Health Sciences Division. "This is consistent with the study's findings that the elevated risk of nonseminoma-type testicular cancer in particular was associated with marijuana use prior to age 18."

Chronic marijuana exposure has multiple adverse effects on the endocrine and reproductive systems, primarily decreased sperm quality. Other possible effects include decreased testosterone and male impotency. Because male infertility and poor semen quality also have been linked to an increased risk of testicular cancer, this further reinforced the researchers' hypothesis that marijuana use may be a risk factor for the disease.

Daling first got the idea to explore a possible association between

marijuana use and testicular cancer about eight years ago, when she attended a talk by a physician at the University of Washington who presented findings that only two organs, the brain and the testes, had receptors for tetrahydrocannabinol, or THC, the main psychoactive component of marijuana. Since then, a number of other sites have been found to contain THC receptors, including the heart, uterus, spleen and immune-system cells.

The male reproductive system also naturally produces a cannabinoid-like chemical that is thought to have a protective effect against cancer. The authors speculate that marijuana use may disrupt this anti-tumor effect, which could be another explanation for the possible link between marijuana and increased risk of testicular cancer.

For the population-based, case-control study, Daling, Schwartz and colleagues interviewed 369 Seattle-Puget Sound-area men, ages 18 to 44, who had been diagnosed with testicular cancer about their history of marijuana use. For comparison purposes they also assessed marijuana use among 979 randomly selected age- and geography-matched healthy controls. (More than 90 percent of the cases and 80 percent of the controls in the study were Hispanic or non-Hispanic white men, due to the fact that testicular cancer is very rare in African-Americans, and because the Seattle-Puget Sound region has a relatively small African-American population.)

Study participants were also asked about other habits that may be correlated with marijuana use, including smoking and alcohol consumption. Even after statistically controlling for these lifestyle factors, as well as other risk factors, such as first-degree family history of testicular cancer and a history of undescended testes, marijuana use emerged as a significant, independent risk factor for testicular cancer.

The researchers emphasize that their results are not definitive, but rather

open a door to more research questions.

"Our study is the first inkling that marijuana use may be associated with testicular cancer, and we still have a lot of unanswered questions," Schwartz said, such as why marijuana appears to be associated with only one type of testicular cancer. "We need to conduct additional research to see whether the association can be observed in other populations, and whether measurement of molecular markers connected to the pathways through which marijuana could influence testicular cancer development helps clarify any association that exists," he said.

In future studies the researchers plan to measure the expression of cannabinoid receptors in both seminomatous and nonseminomatous tumor tissue from the cases in the study, and to see whether variation in the genes for the receptors and other molecules involved in cannabinoid signaling influences the risk of testicular cancer.

In the meantime, Schwartz said, "What young men should know is that first, we know very little about the long-term health consequences of marijuana smoking, especially heavy marijuana smoking; and second, our study provides some evidence that testicular cancer could be one adverse consequence," he said. "So, in the absence of more certain information, a decision to smoke marijuana recreationally means that one is taking a chance on one's future health."

Source: Fred Hutchinson Cancer Research Center

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