

Pediatric Hodgkin's disease survivors face increased breast cancer risk

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Women who as children got radiation treatment for Hodgkin's disease are almost 40 times more likely than others to develop breast cancer, according to findings from five institutions, including the University of Florida.

The higher the radiation dose, the higher the risk, researchers report. These women are also likely to develop cancer in both breasts.

"Our first priority is always to get rid of the cancer. Our second priority is to do so in a way that preserves the best possible quality of life," said researcher Nancy Mendenhall, M.D., an oncologist with UF's College of Medicine who co-authored a paper detailing the results in the September issue of the *International Journal of Radiation Oncology Biology Physics*. "These findings tell us we're moving in the right direction with recent changes in treatment that lower radiation dose."

In the past, children with Hodgkin's disease were treated with radiation alone, in relatively high doses to large volumes of the body. Today, doses are half the levels used 20 years ago, smaller portions of the body are treated, and, in many cases, radiation has been replaced by chemotherapy.

"One of the hopes of that strategy is not only are there going to be better cure rates for Hodgkin's disease, but also fewer long-term side effects of therapy," said Kenneth B. Roberts, M.D., an associate professor of therapeutic radiology at Yale University who was not involved in the



study.

At the start of 2005, there were almost 76,000 women in the United States who had a history of Hodgkin's disease, according to the National Cancer Institute.

Death rates from Hodgkin's disease have plummeted by more than 70 percent in the last 40 years in the United States, and researchers now focus on reducing the so-called "late effects" of treatment that show up long afterward.

"We expect the future to be better than the past in terms of the likelihood of people developing breast cancer," said University of Rochester pediatric oncologist Louis S. Constine, M.D., who led the study. Still, he said, "it's important to understand the past because many people were treated like this."

Similar studies will be needed to measure the success of modern treatment strategies, Roberts said.

Hodgkin's disease is a cancer of unknown cause that affects tissue in the lymph nodes, spleen, liver and bone marrow. It can spread from one organ to another but can be cured with radiation, chemotherapy or a combination.

The American Cancer Society estimated that in 2008, about 8,220 people in the United States would be diagnosed with Hodgkin's disease and about 1,350 would die from it. Up to 15 percent of all cases occur in children and teenagers.

In the current study, 398 females younger than 19 who were treated for Hodgkin's were evaluated from 1960 until 1990. They had been seen at UF, the Rochester Medical Center, Boston Children's Hospital and Dana-



Farber Cancer Institute, St. Jude Children's Research Hospital or the Sidney Kimmel Cancer Center at Johns Hopkins University.

Researchers found that women who had been treated for childhood Hodgkin's disease were 37 times more likely than others to develop breast cancer — 29 developed breast cancer during the study's follow-up period.

On average, it took almost 19 years after treatment for cancer to develop. Guidelines call for Hodgkin's survivors to start being monitored for breast cancer 10 years after treatment or at age 30 — whichever comes first.

In the study, patients ages 12 to 19 at the time of treatment were at slightly higher breast cancer risk as adults than those who were younger than 12. And those diagnosed with early-stage Hodgkin's were at higher risk than those with more advanced disease.

Hodgkin's survivors who developed breast cancer were much more likely to have received higher radiation doses to the entire chest and neck — the so-called "mantle field" — which exposes both breasts to radiation.

About one-third of women who developed cancer in one breast also developed another cancer in the opposite breast. The time from the first to the second cancer ranged from one to three years.

"(That) means people need to be screened, if anything, even more intently after the development of the first cancer," Constine said.

Preventive mastectomies for certain patients at high risk for breast cancer might be worth considering, researchers said.

Surprisingly, radiation of the pelvis seemed to lower cancer risk.



"That finding challenges one of our basic beliefs, so I think we have to do a little more work to understand what is happening," Mendenhall said.

Researchers had thought that the greater the volume of tissue irradiated, the greater the cancer risk. But it is possible that radiation to the pelvis caused premature menopause or ovary failure, with an accompanying drop in the production of the hormone estrogen, a known risk factor for breast cancer.

Factors other than radiation treatment — such as biologic predisposition to cancer — could be at play in the observed rates of cancer development, the researchers said. A trait responsible for the development of breast cancer could also be responsible for Hodgkin's disease development in the first place.

Source: University of Florida

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