
To the Editor: Bhatia et al. found that 17 of 483 girls in whom Hodgkin's disease was diagnosed before the age of 16 years subsequently had breast cancer (ratio of observed to expected cases, 75.3; 95 percent confidence interval, 44.9 to 118.4). Radiotherapy was implicated in the development of many of the cases of breast cancer. Another recent study, involving 1641 patients treated for Hodgkin's disease as children in five Nordic countries, reported a relative risk that was 17 times higher than that in the general population, on the basis of 16 cases of breast cancer.¹

We evaluated data on 3869 women in population-based registries participating in the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Pro-

TABLE 1. CASES OF BREAST CANCER AFTER RADIOTHERAPY FOR HODGKIN'S DISEASE, ACCORDING TO AGE AT TREATMENT AND TIME SINCE DIAGNOSIS.*

AGE AT TREATMENT†	TIME SINCE DIAGNOSIS OF HODGKIN'S DISEASE								Excess Risk‡
	2 MO-4 YR		5-9 YR		≥10 YR		ALL INTERVALS		
	Observed Cases	Observed: Expected Cases	Observed Cases	Observed: Expected Cases	Observed Cases	Observed: Expected Cases	Observed Cases	Observed: Expected Cases (95% CI)	
All women	14	1.47	9	1.36	32	3.81§	55	2.24 (1.7-2.9)§	10.6
<16 Years	0	0	1	146.80§	5	54.97§	6	60.57 (22.1-132)§	23.3
16-29 Years	0	0	1	0.98	19	7.21§	20	4.74 (2.9-7.3)§	10.4
≥30 Years	14	1.56	7	1.25	8	1.41	29	1.43 (1.0-2.1)	8.0
No. of women	3,869		2187		1200		3,869		
No. of person-years	14,024		8267		6417		28,707		

*Data are for cases of Hodgkin's disease diagnosed as a first primary cancer during the period from 1935 to 1972 (674 cases in the Connecticut Tumor Registry) or 1973 to 1992 (3195 cases in the Surveillance, Epidemiology, and End Results Program), among patients who survived two or more months. The follow-up period ended December 31, 1992, for both cohorts. CI denotes confidence interval.

†At the time of treatment, 275 women were less than 16 years old, 1831 were 16 to 29 years old, and 1763 were 30 or older.

‡The excess (absolute) risk of breast cancer was estimated by subtracting the expected number of cases from the observed number, dividing the difference by the number of person-years of follow-up, and multiplying the quotient by 10^4 to yield the excess number of cancers expected per 10,000 women per year.

§ $P < 0.05$ for the comparison between the observed and expected number of cases.

gram (for the period from 1973 to 1992) or in the Connecticut Tumor Registry (CTR) (for the period from 1935 to 1972). These registries account for approximately 10 percent of the U.S. population. All the women had received a diagnosis of Hodgkin's disease as a first primary cancer, had survived for two or more months, and had received radiotherapy as the initial treatment. The SEER and CTR files were examined to identify all invasive second primary breast cancers among these patients, and standard methods were used to quantify risk. Cases reported to the SEER Program between 1973 and 1985 and those reported to the CTR (1935 to 1972) were included in an earlier survey.² We have extended the follow-up through 1992 for the current analysis.

Breast cancer developed in a total of 55 patients (ratio of observed to expected cases, 2.24), and the risk increased with the time since the diagnosis of Hodgkin's disease (P for trend < 0.01) (Table 1). The risk of breast cancer was 60.57 (95 percent confidence interval, 22.1 to 132) among the women in whom Hodgkin's disease was diagnosed before the age of 16 years, with most tumors occurring 10 or more years after treatment. The risk of breast cancer decreased with increasing age at the time of therapy and was only slightly elevated among the women who were 30 years old or older when treated (ratio of observed to expected cases, 1.43). The excess risk of breast cancer among girls less than 16 years of age at the time of treatment (23.3 excess cases of cancer per 10,000 patients per year) was approximately two to three times that among the older women.

Our results indicate that in the general population of the United States, substantial numbers of excess cases of breast cancer can be identified after radiotherapy for Hodgkin's disease during childhood. Prior studies³ have shown that in the young, the breast is especially sensitive to the carcinogenic effects of ionizing radiation, with excess cancers typically developing after a latent period of 10 or more years. Since the increased risk of cancer may persist

for decades after irradiation,³ survivors of Hodgkin's disease should be monitored carefully throughout their lives. The influences of well-established risk factors for breast cancer (e.g., a family history of breast cancer and a younger age at menarche) and possibly others⁴ on the development of radiation-associated tumors should be considered in future studies.

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