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# Incidence of Second Cancers in Patients Treated for Hodgkin's Disease

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Abstract

*Background:* Numerous studies of treatment for Hodgkin's disease have demonstrated large increases in the incidence of leukemia in the early years following chemotherapy, although the duration of effect and the specific agents involved are not well understood. Also, some, but not all, studies have indicated that the incidence of certain solid tumors increases following treatment for Hodgkin's disease. *Purpose:* We studied the association between treatment for Hodgkin's disease and the incidence of second cancers. *Methods:* We conducted a study within a cohort that included 10 472 patients from 14 cancer centers in the United States and Canada who were first diagnosed as having Hodgkin's disease at some point from 1940 through 1987. Discounting the 1st year after diagnosis, the average length of follow-up was 7.1 years per subject. *Results:* We observed 122 leukemias and 438 solid tumors. The relative risk (RR) of leukemia following chemotherapy, compared with no chemotherapy, was 14 (95% confidence interval [CI] = 5.6–35). Increased risks of leukemia were observed after treatment with chlorambucil (RR = 2.0; 95% CI = 1.1–3.6), procarbazine (RR = 4.9; 95% CI = 2.6–9.1), vinblastine (RR = 1.7; 95% CI = 1.1–2.8), and a group of rarely used drugs that included methotrexate, vindesine, etoposide, and 22 others (RR = 3.8; 95% CI = 1.9–7.4). RRs were also estimated for various combinations of drugs, including MOPP (mechlorethamine, vincristine, procarbazine, and prednisone) (RR = 5.9; 95% CI = 2.9–12) and ABVD (doxorubicin, bleomycin, vinblastine, and dacar-bazine) (RR = 1.5; 95% CI = 0.7–3.4). The RR of leukemia associated with splenectomy was 1.6 (95% CI = 1.0–2.5). The RR of solid

tumors following chemotherapy was 1.4 (95%CI = 1.1–1.8). For the group of rarely used drugs, the RR of solid tumors was 3.1 (95% CI = 1.7–5.8). Chemotherapy was associated with an increased risk of cancers of the bones, joints, articular cartilage, and soft tissues (RR = 6.0; 95% CI = 1.7–20), and cancers of the female genital system (RR = 1.8; 95% CI = 1.1–3.2). In patients followed for 10 or more years after radiotherapy, increased risks were found for cancers of the respiratory system and intrathoracic organs (RR = 2.7; 95% CI = 1.1–6.8) and for cancers of the female genital system (RR = 2.4; 95% CI = 1.1–5.4).*Conclusions:* Procarbazine, chlorambucil, and vinblastine are associated with increased leukemia risk. Combination drug regimens have leukemogenic effects estimated as the product of RRs for individual drugs. Chemotherapy and radiotherapy increase the risk of selected solid tumors, and the effect of chemotherapy on solid tumor risk is weaker than the leukemogenic effect. *Implications:* Without doubt, the benefits of treatment of Hodgkin's disease outweigh the risk of a subsequent malignancy, but data on the carcinogenic effects of radiation and drugs beyond 10 years after treatment continue to be sparse, and future analyses should be directed at long-term survivors. [J Natl Cancer Inst 87:732–741, 1995]