

Proposal No: 98-06
Topic: Thyroid Disease

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98-06

CHILDHOOD CANCER SURVIVOR STUDY
Analysis Concept Proposal

Submitted: February 3, 1998

1. **Title:** Thyroid Disease in Survivors of Childhood and Adolescent Hodgkin's Disease
2. **Working Group and Investigators:** This proposed publication will be within the Chronic Diseases Working Group. Proposed investigators will include:

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3. **Background and Rationale:** External irradiation to the region of the neck is associated with a variety of diseases of the thyroid gland. Primary hypothyroidism is the most common disorder of the thyroid following neck/mantle irradiation for Hodgkin's disease. Risk factors for hypothyroidism include dose of radiation, age at irradiation (<20 years vs >20 years), and length of follow-up. Female sex, use of combination chemotherapy, and prior exposure to iodine-containing contrast (e.g., lymphangiograms) have been implicated as risk factors in some but not all studies. Although less prevalent, an increased incidence of thyroid neoplasms, both benign and malignant, and hyperthyroidism have also been reported following treatment for Hodgkin's disease. Evaluation of thyroid diseases in this large cohort of survivors of Hodgkin's disease will permit more precise determination of the treatment variables (i.e., dose of irradiation, type/dose of chemotherapy) and patient characteristics (i.e., age, sex) which predispose to thyroid disease after treatment of childhood and adolescent Hodgkin's disease.
4. **Specific Aims/Objectives/Research Hypotheses:** This publication is designed to investigate the prevalence of and risk factors for hypothyroidism, tumors of the thyroid, and hyperthyroidism in long-term survivors of childhood/adolescent Hodgkin's disease.

Hypotheses:

1. The incidence of hypothyroidism, thyroid neoplasms, and hyperthyroidism in survivors of Hodgkin's disease will be increased compared to the general population.
2. The risk of hypothyroidism will increase with younger age at diagnosis, higher dose of radiation to the thyroid, and longer duration of follow-up.
3. The risk of thyroid neoplasms will increase with female sex, younger age at treatment, and longer duration of follow-up.

5. **Analysis Framework:**

- a. Outcomes of interest: thyroid medication (B.8-5), thyroid disease (E.1-E.4), thyroid surgery (I.15), thyroid cancer (K.1-K.8).
- b. Subject population: all CCSS cases with diagnosis of Hodgkin's disease.
- c. Explanatory variables: sex, age at diagnosis, age at follow-up, time since diagnosis, recurrence, type of treatment, dose of radiation to the thyroid, doses of chemotherapy.
- d. Specific tables:
 - 1) Characteristics of all Hodgkin's disease cases by hypothyroid status:
 - sex
 - age at diagnosis (0-5, 6-10, 11-15, 16-21)
 - age at follow-up (10-15, 16-21, 22-30, 31-35, 36-40, 41-45, >45)
 - time since diagnosis (5 yrs, 6-10 yrs, 11-15 yrs, 16-20 yrs, >20 yrs)
 - type of treatment
 - chemotherapy only
 - neck/mantle irradiation only
 - chemotherapy + neck/mantle irradiation
 - dose of radiation to the thyroid (<200, 201-500, 501-1000, 1001-1500, 1501-2000, 2001-2500, 2501-3000, 3001-3500, >3500)
 - use of each chemotherapy drug (y/n)
 - dose of each chemotherapy drug (the 28 major drugs)
 - 2) Repeat 1) for hyperthyroidism, thyroid cancer, benign thyroid tumors
 - 3) Standardized incidence rates for hypothyroidism by:
 - sex
 - age
 - 4) Repeat 3) for hyperthyroidism, differentiated thyroid carcinoma, thyroid adenomas

6. Special considerations: Thyroid neoplasms will need to be verified from path reports obtained from the institution where the thyroid diagnosis was made.