

Proposal No: 98-02
Topic: Pregnancy Outcomes

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Submitted to Publications Committee: 2/4/98

Approved by Publications Committee: 9/23/98

Priority Rating: 2.5

98-02

TITLE: Pregnancy Outcome of Survivors of Diagnosed During Childhood and Adolescence

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BACKGROUND AND RATIONALE:

The prognosis for children and adolescents with childhood cancer has improved dramatically during the past 20 years. As a result, many former patients have completed their education, entered the workplace, and have made or are presently making decisions regarding marriage and reproduction. While obtaining employment appropriate to ones education and interests and forming close interpersonal relationships are important and challenging life goals for any individual, widely held beliefs regarding cancer survivors' continued vulnerability and diminished capacity can be expected to influence both the survivor's opportunity and ability to achieve these goals.

Successful therapy for children and adolescents with childhood cancer includes the use of ionizing irradiation and/or chemotherapeutic agents. These may produce DNA damage, resulting in cell death or the damage may be sublethal. These effects may be expressed in the gonads as sterilization or germ cell DNA damage. Sterilization may be acute, or identified by the occurrence of premature menopause. DNA damage may be identified by an increased risk for chromosomal syndromes, single gene defects or major congenital malformations in the offspring.

Previous studies have demonstrated that birthweight is significantly lower among the offspring of women who have received pelvic irradiation. This outcome has been investigated primarily in patients successfully treated for Wilms tumor.

The present cohort includes patients with diverse treatment exposures, and will allow more accurate estimation of this effect of treatment on pregnancy outcome and offspring birthweight. These data will facilitate pregnancy management by obstetricians who care for female

survivors of childhood cancer.

SPECIFIC AIMS/OBJECTIVES/RESEARCH HYPOTHESES:

This publication is designed to investigate the effect of disease and treatment on: 1. The birthweight of offspring, stratified by gender of childhood cancer survivor, and treatment (pelvic irradiation, alkylating agent therapy, cumulative alkylating agent dose, non-alkylating agent therapy, cumulative non-alkylating agent dose for drugs of interest such as doxorubicin, bleomycin)

The specific hypotheses are:

1. The frequency of intrauterine death after 20 weeks gestation and stillbirth will be higher among the female childhood cancer survivors who received pelvic irradiation than among the gender-matched siblings or the female childhood cancer survivors who were not treated with pelvic irradiation;
2. The frequency of intrauterine death after 20 weeks gestation and stillbirth birthweight will not be higher among the spouses of male childhood cancer survivors who received pelvic irradiation than among the gender-matched siblings or the spouses of male childhood cancer survivors who were not treated with pelvic irradiation;
3. The frequency of intrauterine death after 20 weeks gestation and stillbirth will be higher among the female childhood cancer survivors who received alkylating agent therapy than among the gender-matched siblings or the female childhood cancer survivors who were not treated with alkylating agent therapy;
4. The frequency of intrauterine death after 20 weeks gestation and stillbirth birthweight will be higher among the spouses of male childhood cancer survivors who received alkylating agent therapy than among the gender-matched siblings or the spouses of male childhood cancer survivors who were not treated with alkylating agent therapy;
5. The birthweight of the offspring of female childhood cancer survivors who received pelvic irradiation will be lower than the birthweights of the offspring of gender-matched siblings or the birthweights of the offspring of female childhood cancer survivors who were not treated with pelvic irradiation, after considering the effects of alcohol consumption and tobacco use during pregnancy;
6. The birthweight of the offspring of the spouses of male childhood cancer survivors who received pelvic irradiation will not be lower than the birthweights of the offspring of gender-matched siblings or the birthweights of the offspring of the spouses of male childhood cancer survivors who were not treated with pelvic irradiation, after considering the effects of alcohol consumption and tobacco use during pregnancy;

ANALYSIS FRAMEWORK:

- a. Outcomes of interest: Intrauterine death after 20 weeks gestation, stillbirth, birthweight.
- b. Subject population - all CCSS cases, all CCSS gender-matched sibling controls, US population
- c. Explanatory variables - gender, age at diagnosis, age at first pregnancy, age at follow-up, gonadal radiation dose, pelvic radiation dose, alkylating agent treatment, cumulative alkylating agent dose, non-alkylating agent therapy (doxorubicin, bleomycin), cumulative non-alkylating agent dose, tobacco use during pregnancy, alcohol consumption during pregnancy.

D. Specific tables:

Population

CCSS males - Number, number reporting one or more pregnancies, number reporting definite azoospermia, number reporting androgen hormone replacement therapy.

CCSS females - Number, number reporting one or more pregnancies, number reporting definite amenorrhea, number reporting sterilizing operation (bilateral salpingo-oophorectomy, and/or hysterectomy), number reporting hormone replacement therapy

Birthweight

Sex ratio of liveborn offspring by gender of treated parent, by pelvic irradiation status, by alkylating agent treatment status, by non-alkylating agent treatment status

Intrauterine death - By gender of survivor, by gender of gender-matched sibling

Stillbirth - By gender of survivor, by gender of gender-matched sibling

Birthweight - By gender of survivor, by gender of gender-matched control

 separate for gender of offspring, by gender of treated parent

 By pelvic irradiation status, by alkylating agent treatment status, by non-alkylating agent treatment status, by smoking status of mother of offspring (female survivor or spouse of male survivor), by alcohol consumption of mother of offspring (female survivor or spouse of male survivor)

SPECIAL CONSIDERATIONS:

REFERENCES:

Birthweight

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