TITLE: The University of Chicago Childhood Cancer Survivors Project

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ABSTRACT:
The long term goal of the proposed work is to characterize the clinical characteristics of a population of childhood cancer survivors in order to develop intervention strategies for individuals at high risk of second malignant neoplasms and end stage organ damage due to their previous cancer therapies.

To meet these objectives, we propose:

To develop a local registry of retrospective and prospective cases and to build a prospective biobank of childhood cancer and stem cell transplant survivors as a resource for research studies that explore identification, screening and management of the late effects of childhood cancer therapy.

BACKGROUND AND SIGNIFICANCE:
Until recently, the main focus in Pediatric Oncology was in the research and development of novel treatments to cure disease. As this work has become increasingly successful with overall cure rates approaching 80%, we find ourselves now in the midst of a paradigm shift (1, 2). There is a large, growing population of childhood cancer survivors who are at significant risks for early death, development of second cancers and may have damage to many vital organ systems with increased risk of early onset organ dysfunction (3-10). In order to maintain their health into adulthood, it is imperative to characterize these often devastating long-term toxicities. Further, we must investigate which subjects are at the greatest risk for these issues. This will be accomplished by examining both past and present clinical information. Lastly, we must develop novel clinical strategies to screen for and treat late effects so that cancer therapy morbidities are minimized and survivors go on to lead long, productive lives. We propose to initiate a project to collect clinical data, blood and DNA from childhood cancer survivors seen in the University of Chicago Childhood Cancer Survivors Center, as well as collect retrospective data from pediatric cancer survivors (diagnosed between January 1, 1987 and December 31, 1999) no longer followed by pediatrics.

PURPOSE:
The major goal of this proposal is to facilitate research in subjects who survived childhood cancer in order to develop new preventive and therapeutic strategies for the late effects of cancer therapy.

To achieve this goal, the objectives include:

1. Collect and store data in the University of Chicago Childhood Cancer Survivor database, which will contain profiles of study subjects
2. Identify subjects who may be eligible for enrollment in future research studies.
3. Access subjects’ medical record for current and future updates of the database and use for potential studies. WHAT IS THE END DATE THAT WE WOULD LIKE TO USE?

4. Collect and bank blood (DNA and serum) for future studies to identify the molecular basis of late effects of cancer therapy (Prospective Cases Only)

METHODS:

Inclusion Criteria:

Prospective Cases:
Subjects of any age (pediatric and adult) with a history of a childhood cancer diagnosis or stem cell transplantation who:

a. Are at least 2 years from completion of therapy for their childhood cancer diagnosis or stem cell transplantation

b. Were less than 21 years at the time of their primary cancer diagnosis or stem cell transplantation

Retrospective Cases:
Cancer Survivors diagnosed between January 1, 1987 and December 31, 1999, who have survived five years from date of diagnosis. For those patients who are not currently being followed, a waiver of consent will be utilized to collect their data.

Exclusion Criteria:
Subjects who are being treated for a relapse of their primary cancer diagnosis.

Procedures

Prospective cases:
Subjects will be recruited to the study when they are in clinic at the University of Chicago Childhood Cancer Survivors Center. Eligible subjects will be offered enrollment.

A. If a subject or parent/legal guardian (in subjects less than 18 years of age) responds “yes”, he/she will be asked to sign the consent form allowing access to their medical records. Care will be taken to instruct the subject on their right to confidentiality and our inability to randomly screen anyone’s medical history without their permission. Subjects/parents or legal guardians will be given the option to participate in the data collection but decline participation in the biobank. In signing consent, they will check “yes” or “no” as to participating in collection of biological specimens and as to future contact for additional research studies.

B. If a subject or parent/legal guardian responds “no”, the subject or family member will be thanked. The subject’s disinterest will not affect the care they receive at this institution nor will it involve penalty or loss of benefits to which they would otherwise be entitled.
Dr. Henderson or her Research Staff will review the consent form with the eligible individuals or in the case of subjects under age 18, with their parent or legal guardian. Of note, for individuals less than 18 years of age at initial entry into the study, the individuals will be asked to re-consent after they reach the age of majority in order to stay on study.

*Retrospective Cases:*
1. A list of cancer survivors will be generated by cancer registrar.
2. Chart reviews will be completed
3. A notification of chart review will be placed in patient’s Medical Record

*Data Collection:*
Data regarding the subject’s medical history, including detailed primary cancer treatment information will be obtained from the subject in UCCCS clinic (Prospective cases only) as well as the subject’s medical record. This data will be entered by Research staff into the Childhood Cancer Survivor Center database [Microsoft ACCESS].

*Biological Specimen Collection (Prospective Cases Only):*
If subject consented to participation in the biobank, 1 lavender top (EDTA) tube containing 4 mL peripheral blood and one red top tube containing 4 mL peripheral blood will be obtained for DNA and plasma. Blood will be obtained at the visit the subject is enrolled in the study.

*Procedure for serum separation, aliquoting and freezing (serum separator tube):*
The serum separator tube drawn above should be kept at room temperature and processed within 1 hour as specified below.

a. **Label Cryotubes.** Pre-label the screw cap cryovials. All specimens will be labeled with the study number, subjects’ birthday and medical record number.

b. **Allow Blood To Clot.** Allow the blood to clot upright at room temperature for 1 hour. It is critical that this period is as accurate as possible.

c. **Centrifuge Blood.** The blood must be processed rapidly after step b. Please centrifuge to separate the serum (yellowish liquid) from the fibrin clot and the blood cells. Centrifuge the blood at 1100-1300 x g for 15 min at room temperature.

d. **Aliquot Serum.** Remove the caps from the blood tube and the cryovials. Draw the serum into a sterile syringe or transfer pipette, transfer the serum into cryovials. Cap the cryovials securely. Leave remaining pellet in the blood tube.

e. **Freeze Serum and Pellet.** Store in a -80 degrees Celsius freezer in the laboratory of Dr. Kenan Onel of the Department of Pediatrics, Section of Pediatric Hematology, Oncology and Stem Cell Transplantation.
**Procedure for Blood Storage:** Store in a -80 degrees Celsius freezer in the laboratory of Dr. Kenan Onel of the Department of Pediatrics, Section of Pediatric Hematology, Oncology and Stem Cell Transplantation.

The collection and storage of data will be ongoing. The subjects will be followed by Dr. Henderson in the University of Chicago Childhood Cancer Survivors Center located in the Duchossois Center for Advanced Medicine (DCAM).

**Subsequent Studies:**
All subsequent studies involving the data and/or samples collected for this project will be submitted to the University of Chicago’s IRB for review.

**STATISTICAL ANALYSIS**
Once the dataset is of sufficient size, research studies will be planned and submitted for IRB approval. Appropriate statistical methods will be performed based on the future design of each research study.

**COMPENSATION:**
Subjects or their families will not be compensated for their participation.

**HUMAN SUBJECTS RESEARCH AND PROTECTION FROM RISK:**

1. **Subject Population.** The population to be studied are individuals are children or adults who are at least 2 years off therapy for a childhood cancer or least 2 years status post a bone marrow transplant before the age of 21 years through the University of Chicago Childhood Cancer Survivors Center. Clinical data and biological specimens are to be collected on subjects who are cared for in the Survivors Center who agree to the study and those patients considered lost to follow-up will be included in the registry via a waiver of consent. We plan to recruit participants of all race and gender.

2. **Research Materials.** All materials are to be collected for research purposes. Medical records will be used to obtain a patient’s history for retrospective cases. For prospective cases, the materials will include peripheral blood to provide a source of DNA. Other information will be collected from direct subject interview.

3. **Consent and Waiver Procedures.** The consent procedure is described above under the “procedures” section.

4. **Potential Risks.** The potential risks for Prospective Cases are those associated those of a blood draw (discomfort, bruising). There is minimal risk for either Prospective or Retrospective cases with respect to breach of confidentiality. Steps will be taken to avoid inappropriate access to the registry, as only research team personnel will have access to the patient identifying information.

5. **Confidentiality.** Confidentiality of the information will be maintained utilizing coded identification numbers and locked storage of raw data. The blood samples will be obtained by a registered nurse or trained phlebotomist under standard conditions of sanitation and stored in a locked laboratory.
6. **Benefits.** There are minimal risks associated with the projected studies. We anticipate far-reaching benefits with respect to improving our understanding of the epidemiology and etiology of the late effects of childhood cancer and stem cell transplant survivors.

**REFERENCES**