NATIONAL CANCER INSTITUTE FactSheet

Childhood Cancers: Questions and Answers

Key Points

- Leukemias and cancers of the brain and central nervous system account for more than half of childhood cancers (see Question 1).
- The causes of childhood cancers are largely unknown (see Question 4).
- The National Cancer Institute is funding studies examining the causes of and the most effective treatments for childhood cancers (see Question 6).

1. What are the most common types of childhood cancer?

Among the 12 major types of childhood cancers, leukemias (blood cell cancers) and cancers of the brain and central nervous system account for more than half of the new cases. About one-third of childhood cancers are leukemias. The most common type of leukemia in children is acute lymphoblastic leukemia. The most common solid tumors are brain tumors (e.g., gliomas and medulloblastomas), with other solid tumors (e.g., neuroblastomas, Wilms tumors, and sarcomas such as rhabdomyosarcoma and osteosarcoma) being less common.

2. How many children are diagnosed with cancer in the United States annually?

In the United States in 2007, approximately 10,400 children under age 15 were diagnosed with cancer and about 1,545 children will die from the disease (1). Although this makes cancer the leading cause of death by disease among U.S. children 1 to 14 years of age, cancer is still relatively rare in this age group. On average, 1 to 2 children develop the disease each year for every 10,000 children in the United States (2).

3. How have childhood cancer incidence and survival rates changed over the years?

Over the past 20 years, there has been some increase in the incidence of children diagnosed with all forms of invasive cancer, from 11.5 cases per 100,000 children in 1975 to 14.8 per 100,000 children in 2004. During this same time, however, death rates

declined dramatically and 5-year survival rates increased for most childhood cancers. For example, the 5-year survival rates for all childhood cancers combined increased from 58.1 percent in 1975–77 to 79.6 percent in 1996–2003 (2). This improvement in survival rates is due to significant advances in treatment, resulting in a cure or long-term remission for a substantial proportion of children with cancer.

Long-term trends in incidence for leukemias and brain tumors, the most common childhood cancers, show patterns that are somewhat different from the others. Incidence of childhood leukemias appeared to rise in the early 1980s, with rates increasing from 3.3 cases per 100,000 in 1975 to 4.6 cases per 100,000 in 1985. Rates in the succeeding years have shown no consistent upward or downward trend and have ranged from 3.7 to 4.9 cases per 100,000 (2).

For childhood brain tumors, the overall incidence rose from 1975 through 2004, from 2.3 to 3.2 cases per 100,000 (2), with the greatest increase occurring from l983 through l986. An article in the September 2, 1998, issue of the *Journal of the National Cancer Institute* suggests that the rise in incidence from 1983 through 1986 may not have represented a true increase in the number of cases, but may have reflected new forms of imaging equipment (magnetic resonance imaging or MRI) that enabled visualization of brain tumors that could not be easily visualized with older equipment (3). Other important developments during this time period included the changing classification of brain tumors, which resulted in tumors previously designated as "benign" being reclassified as "malignant," and improvements in neurosurgical techniques for biopsying brain tumors. Regardless of the explanation for the increase in incidence that occurred from 1983 to 1986, childhood brain tumor incidence has been essentially stable since the mid-1980s.

A monograph based on data from the National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results (SEER) Program was published in 1999 on U.S. trends in incidence, mortality, and survival rates of childhood cancers. This monograph, *Cancer Incidence and Survival Among Children and Adolescents: United States SEER Program 1975–1995*, is available at http://seer.cancer.gov/publications/childhood/ on the Internet. In 2006, SEER published another monograph, *Cancer Epidemiology in Older Adolescents and Young Adults 15 to 29 Years of Age, Including SEER Incidence and Survival: 1975–2000.* This monograph is the first to collect detailed information about cancer incidence and outcomes in adolescents and young adults (AYA). It provides population-based incidence, mortality, and survival data specific to cancers that occur in the AYA population, along with epidemiological data and risk factors for the development of age-specific cancers. This resource is available at http://seer.cancer.gov/publications/aya/ on the Internet. More recent cancer statistics for children ages 0–14 and 0–19 are available in sections 28 and 29 of the *SEER Cancer Statistics Review, 1975–2004* at http://seer.cancer.gov/csr/1975_2004/sections.html on the Internet.

4. What are the known or suspected causes of childhood cancer?

The causes of childhood cancers are largely unknown. A few conditions, such as Down syndrome, other specific chromosomal and genetic abnormalities, and ionizing radiation exposures, explain a small percentage of cases.

Environmental causes of childhood cancer have long been suspected by many scientists but have been difficult to pin down, partly because cancer in children is rare and because it is difficult to identify past exposure levels in children, particularly during potentially important periods such as pregnancy or even prior to conception. In addition, each of the distinctive types of childhood cancers develops differently—with a potentially wide variety of causes and a unique clinical course in terms of age, race, gender, and many other factors. Possible risk factors for specific childhood cancers are discussed in the SEER monograph mentioned above. It can be found at http://seer.cancer.gov/publications/childhood/ on the Internet.

A number of studies are examining suspected or possible risk factors for childhood cancers, including early-life exposures to infectious agents; parental, fetal, or childhood exposures to environmental toxins such as pesticides, solvents, or other household chemicals; parental occupational exposures to radiation or chemicals; parental medical conditions during pregnancy or before conception; maternal diet during pregnancy; early postnatal feeding patterns and diet; and maternal reproductive history. Researchers are also studying the risks associated with maternal exposures to oral contraceptives, fertility drugs, and other medications; familial and genetic susceptibility; and risk associated with exposure to the human immunodeficiency virus (HIV).

5. What have studies shown about the possible causes of childhood cancer?

For several decades, the NCI, a part of the National Institutes of Health (NIH), has supported national and international collaborations devoted to studying the causes of cancer in children. Key findings from this research include the following:

- High levels of ionizing radiation from accidents or from radiotherapy have been linked with increased risk of some childhood cancers.

- Children with cancer treated with chemotherapy and/or radiation therapy may be at increased risk for developing a second primary cancer. For example, certain types of chemotherapy, including alkylating agents or topoisomerase II inhibitors (e.g., epipodophyllotoxins), can cause an increased risk of leukemia.

- Recent research has shown that children with AIDS (acquired immunodeficiency syndrome), like adults with AIDS, have an increased risk of developing certain cancers, predominantly non-Hodgkin lymphoma and Kaposi sarcoma. These children also have an additional risk of developing leiomyosarcoma (a type of muscle cancer).

- Certain genetic syndromes (e.g., Li-Fraumeni syndrome, neurofibromatosis, and Gorlin syndrome) have been linked to an increased risk of specific childhood cancers.

- Children with Down syndrome have an increased risk of developing leukemia.

- Low levels of radiation exposure from indoor radon have not been significantly associated with childhood leukemias.

- Ultrasound use during pregnancy has not been linked with childhood cancer in numerous large studies.

- Residential magnetic field exposure from power lines has not been significantly associated with childhood leukemias.

- Pesticides have been suspected to be involved in the development of certain forms of childhood cancer based on interview data. However, interview results have been inconsistent and have not yet been validated by physical evidence of pesticides in the child's body or environment.

- No consistent findings have been observed linking specific occupational exposures of parents to the development of childhood cancers.

- Several studies have found no link between maternal cigarette smoking before pregnancy and childhood cancers, but increased risks have been related to the father's smoking habits in studies in the United Kingdom and China.

- Little evidence has been found to link specific viruses or other infectious agents to the development of most types of childhood cancers, though investigators worldwide are exploring the role of exposures of very young children to some common infectious agents that may protect children from, or put them at risk for, developing certain leukemias.

6. What research is NCI currently doing on childhood cancer?

The NCI is funding a large portfolio of studies (http://researchportfolio.cancer.gov/) looking at the causes of and the most effective treatments for childhood cancers. Ongoing investigations include:

- **Studies to identify causes of the cancers that develop in children:** The Children's Oncology Group (COG) (http://www.childrensoncologygroup.org) is evaluating potential risk factors for a variety of childhood cancers. Very large studies have been completed of childhood acute lymphoblastic leukemia, acute myeloid leukemia, non-Hodgkin lymphoma, primitive neuroectodermal tumors of the brain, astrocytoma, neuroblastoma, and germ cell tumors. One large study, the Childhood Cancer Survivor Study, is evaluating the risks of second cancers related to radiation therapy

and chemotherapy received by survivors of childhood cancer as part of treatment for their primary cancer (see below).

COG has also established a Childhood Cancer Research Network that creates a national registry of children with cancer. This initiative builds upon the unique NCI-supported national clinical trials system for treating children with cancer.

- **Monitoring of U.S. and international trends in incidence and mortality rates for childhood cancers:** By identifying places where high or low cancer rates occur, researchers can uncover patterns of cancer that provide important clues for further in-depth studies into the causes and control of cancer.

- **Studies to better understand the biology of childhood cancer, with the hope that this understanding will lead to new treatment approaches that target critical cellular processes required for cancer cell growth and survival:** The Childhood Cancer Therapeutically Applicable Research to Generate Effective Treatments (TARGET) Initiative was established by the NCI and the Foundation for the National Institutes of Health to identify and validate therapeutic targets in childhood cancers. The first TARGET project focuses on targets for high-risk acute lymphoblastic leukemia and the second TARGET project focuses on neuroblastoma. More information about the TARGET Initiative can be found in the article "Initiative TARGETs Childhood Cancer" at http://www.cancer.gov/NCICancerBulletin/NCI_Cancer_Bulletin_112106 on the Internet.

- **Preclinical studies (animal studies) of new agents to identify promising anticancer drugs that can be evaluated in clinical trials:** The NCI-supported Pediatric Preclinical Testing Program (PPTP) systematically evaluates new drugs and substances using animal models (animals with a cancer similar to or the same as a cancer found in children) to find the drugs most likely to have significant anticancer effects in clinical trials. The program is based on a large amount of research showing that animal models imitate the effects of proven anticancer drugs and can be used to prospectively identify new drugs that are effective against childhood cancers in subsequent patient studies. More information about the PPTP is available at http://pptp.stjude.org/ on the Internet. Questions concerning the PPTP can be addressed to the PPTP Project Officer, Dr. Malcolm Smith (smithm@ctep.nci.nih.gov).

- **Projects designed to improve the health status of survivors of childhood cancers:** The NCI funds the Childhood Cancer Survivor Study (CCSS), a study coordinated by St. Jude Children's Research Hospital. The CCSS has over 25 sites across the country at medical institutions with doctors specializing in long-term care for children and young adults. This study was created to gain new knowledge and to educate cancer survivors about the long-term effects of cancer and cancer treatment. Information about the study, including access to a list of participating institutions, is available at http://www.stjude.org/stjude/v/index.jsp?vgnextoid=0d5dd3ce38e70110VgnVCM100

001e0215acRCRD&vgnextchannel=448d0817933fe010VgnVCM1000005f2015acRCRD on the Internet.

- **Clinical trials to identify superior treatments for childhood cancers, thereby leading to improved survival rates for children with cancer:** Each year about 4,000 children enter 1 of approximately 100 ongoing clinical trials sponsored by the NCI. The following groups are conducting these trials:

  The COG, with support from the NCI, conducts clinical trials devoted exclusively to children and adolescents with cancer at more than 200 member institutions, including cancer centers of all major universities, teaching hospitals throughout the United States and Canada, and sites in Europe and Australia. COG was formed in 2000 by the merger of four children's cancer cooperative groups to accelerate the search for a cure for childhood cancers and to make it possible for children with cancer, regardless of where they live, to have access to state-of-the-art therapies and the collective expertise of world-renowned pediatric specialists.

  The Pediatric Brain Tumor Consortium (PBTC) (http://www.pbtc.org) includes 10 leading academic institutions with extensive experience in the design and conduct of clinical trials for children with brain tumors. The group's primary objective is to rapidly conduct phase I and II clinical evaluations of new therapeutic drugs, treatment delivery technologies, new biological therapies, and radiation treatment strategies in children up to age 21 with primary central nervous system (CNS) tumors. Another objective of the PBTC is to develop and coordinate innovative neuroimaging techniques. Results from PBTC studies are made available to large international collaborative groups for confirmatory phase II and multiagent phase III clinical trials.

  New Approaches to Neuroblastoma Therapy (NANT) (http://www.nant.org) is a consortium of university and children's hospitals funded by the NCI to test promising new therapies for neuroblastoma. NANT members constitute a group of closely collaborating investigators linked with laboratory programs where novel therapies for high-risk neuroblastoma are being developed. The group conducts early clinical trials to test new drugs and new combinations of drugs so promising therapies can be tested nationally.

  The Pediatric Oncology Branch (POB) (http://home.ccr.cancer.gov/oncology/pediatric/) of the NCI's Center for Cancer Research conducts basic, preclinical, and clinical studies of childhood cancer at the NIH Clinical Center in Bethesda, MD. Basic studies include analyses of genetic and biological characteristics of childhood cancers, as well as the study of immune system interactions with these cancers and the effects of chemotherapy on the immune system. Preclinical studies by the POB identify new drugs and types of immunotherapy (treatment to boost the immune system's ability to fight cancer), as well as agents to control infectious diseases that occur in childhood cancer patients. An active clinical trial program includes phase I and phase II studies of new agents to treat childhood cancers, with a focus on molecularly targeted therapy and immunotherapy, as well as bone marrow transplantation and the development of immunotoxins (antibodies linked to a toxic substance that bind to cancer cells and kill

them) to treat childhood leukemia. The POB also develops and tests new treatments for tumors associated with genetic predisposition syndromes such as neurofibromatosis type 1 and multiple endocrine neoplasia.

- **Evaluations of new drugs that may be more effective against childhood cancers and that may have less toxicity for children:** The COG Phase I/Pilot Consortium is a major component of the NCI's pediatric drug development program. The primary objective of the consortium is to develop and implement pediatric phase I and pilot studies to promote the integration of advances in cancer biology and therapy into the treatment of childhood cancer. The consortium includes approximately 20 institutions that carefully monitor the drugs for toxicity and safety. After their initial evaluation for safety in children by the consortium, the agents and regimens can then be studied within the larger group of COG institutions to determine their role in the treatment of specific childhood cancers.

Selected References

1. American Cancer Society. *Cancer Facts and Figures 2007*. Atlanta, GA: American Cancer Society. Retrieved December 26, 2007, from http://www.cancer.org/downloads/STT/CAFF2007PWSecured.pdf.

2. Ries LAG, Melbert D, Krapcho M, et al. *SEER Cancer Statistics Review, 1975–2004*. Bethesda, MD: National Cancer Institute. Retrieved December 26, 2007, from http://seer.cancer.gov/csr/1975_2004.

3. Smith MA, Freidlin B, Ries LA, Simon R. Trends in reported incidence of primary malignant brain tumors in children in the United States. *Journal of the National Cancer Institute* 1998; 90(17):1269–1277.

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Related NCI materials and Web pages:

- National Cancer Institute Fact Sheet 1.21, *Care for Children and Adolescents With Cancer: Questions and Answers* (http://www.cancer.gov/cancertopics/factsheet/NCI/children-adolescents)
- National Cancer Institute Fact Sheet 2.11, *Clinical Trials: Questions and Answers* (http://www.cancer.gov/cancertopics/factsheet/Information/clinical-trials)
- Childhood Cancers Home Page (http://www.cancer.gov/cancertopics/types/childhoodcancers)

For more help, contact:

NCI's Cancer Information Service
Telephone (toll-free): 1–800–4–CANCER (1–800–422–6237)

TTY (toll-free): 1–800–332–8615
LiveHelp® online chat: https://cissecure.nci.nih.gov/livehelp/welcome.asp

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