TRANSITIONS AT NWTS

The National Wilms Tumor Study (NWTS) has been undergoing change, but we are still here and committed to providing you with information about Wilms tumor and will continue to gather important health data from you to be used to further Wilms tumor knowledge.

Shortly after the last newsletter in 2011, we learned that, due to national budget priority shifts, the National Cancer Institute (NCI) would most likely not renew our funding. In fact, we came within days of closing the study entirely. At the last minute, the NCI was able to provide funding at a reduced rate to keep the study going for the next five years.

Part of the transition is that two of our original staff members retired in 2012. Newsletter readers first met Pat Norkool and Janice Takashima via the Winter 2006 article "Patience, Persistence and Humor: Longtime DSC Colleagues’ History goes Back 27 Years." By the time they retired, each had logged over 30 years with the NWTS and had contributed data collection, project management, procedure continuity and help to individual participants and their families. We invite you to reread the 2006 newsletter article which is available online at www.nwtsg.org. Pat was Project Manager and Janice was Data Coordinator Supervisor. As a testimony to their strong bonds with the study, both Janice and Pat regularly return to the NWTS office to consult and share their project-long knowledge of the study.

The new Project Manager, Susan Peterson, is also known to LATE Breaking News readers (Winter 2005, Vol.4). Susan has served as the study’s Database Manager since 1998. As Database Manager she is responsible for storage and organization of all research data, maintenance of confidentiality of the data and retrieval of data for analysis by researchers. She continues in this capacity as well as more broadly leading the project as Manager.

Another major change in the National Wilms Tumor Study is a new Principal Investigator. After 45 years, Norman Breslow is semi-retired. He joined the NWTS in 1969, shortly after its inception, and was the first statistician. In addition to directing the NWTS Data and Statistical Center in Seattle, Washington, Dr. Breslow has also been a Professor of Biostatistics at the University of Washington School of Public Health. As of January 2, 2012, he is a Professor Emeritus. However, Dr. Breslow will continue his research at NWTS and remain involved with the study. Look for his latest publication on breast cancer in Wilms tumor survivors, soon to be published in Cancer. He fills his expanding free time with family and travel.
The new Principal Investigator is Dr. Wendy Leisenring, also a statistician. She is a member of the Cancer Prevention and Clinical Statistics programs at the Fred Hutchinson Cancer Research Center and leads the Statistical Center for the Childhood Cancer Survivor Study (CCSS), a multi-institutional collaborative study following more than 14,000 survivors of childhood and adolescent cancer. The CCSS includes some Wilms tumor survivors, so some of you may be familiar with CCSS and, in fact, may have completed their questionnaires as well as ours. In the future when you receive a letter from the National Wilms Tumor Study it might be from Dr. Breslow or Dr. Leisenring.

The study will continue to investigate late conditions that appear after completion of treatment for Wilms tumor. Over the coming years, areas of specific interest are heart and kidney conditions and subsequent malignancies. We will also follow pregnancies and related issues. In addition, investigators periodically target an area of special interest to study and publish about. For example, we have highlighted elsewhere in this newsletter, a recently published article about pulmonary complications after treatment for Wilms tumor as well as another on new trends in Wilms tumor treatments.

**Study Results Available Online from PubMed Central**

Participants often contact us about the latest results from the NWTS Late Effects Study, to which they contribute so much. Well, we have some good news! As a federally funded study through the National Institutes of Health (NIH), all our publications describing our research are subject to the NIH Public Access Policy. This means that they may be obtained online from PubMed Central (PMC), a free archive of medical research results maintained by the NIH National Library of Medicine. Since 2006, authors and publishers have been required by law to submit final copies of published manuscripts to PMC. There they are assigned a PMCID number and made available on the public website within one year of the date of publication.

The best way to access NWTS study results is via the NWTS website: [http://nwtsg.org](http://nwtsg.org). Click on Bibliography at the top of the page and you will find a complete listing of our publications ordered by year of publication. For most publications that are a year or more old, you will find a PMCID number at the end of the bibliographic entry. This is linked to the official copy of the article in the PMC archive. All you need do is click on the ID number and you will be directed to the publication. For example, to access the report published in late 2010 on secondary tumors in NWTS patients, you would click on [PMC2878923](http://ncbi.nlm.nih.gov/pmc/articles/PMC2878923).

As many of you know already, the NWTS website contains a lot of other valuable information about Wilms tumor and our study. Copies of all our previous Newsletters are available there, in PDF format. Also, there is a link to Survey Monkey where you can easily submit your Annual Status Reports. We urge you to explore it in depth!

**Pulmonary Disease After Lung Radiation**

In a recent article we published, we describe some of the pulmonary problems that Wilms tumor survivors can have. Some patients with Wilms tumor receive radiation treatments to their lungs to treat clumps of cancer cells (pulmonary metastases) that have spread there. Little is known about the long-term effects of radiation therapy to the lungs. We studied the occurrence of lung disease among 6,449 patients treated on National Wilms Tumor Studies -1, -2, -3, and -4 whose flow sheets or annual status reports
indicated the participant had a relationship between radiation total radiation therapy dose, and Eighty participants reported lung of lung disease fifteen years after was 4.8% among those who for pulmonary metastases that original diagnosis of Wilms tumor. was approximately thirty times treated at some time with lung metastases than among those who never received lung radiation therapy. Our results suggest that patients who received radiation therapy to their lungs for Wilms tumor may have problems with the function of their lungs in the future. Such individuals should avoid other factors that may impair their lung function, such as smoking or obesity. In addition, their physicians need to be aware of their past medical history since acute illnesses, such as bronchitis or pneumonia, may be more severe among patients who have decreased lung function due to their past lung radiation therapy. Other important preventive health practices include routine immunization for protection against influenza and immunization to protect against pneumococcal pneumonia. As the result of this study and the risks for lung disease that were reported, doctors now know with greater accuracy the risk of giving radiation therapy to the lungs and will try in the future to give such treatment to a more select group of patients whose pulmonary metastases cannot be successfully treated with only chemotherapy. Further information may be found in the recent NWTS publication listed in the Biography section of our website (http://www.nwtsg.org/bibliography/bibliography.html).


A Second Cancer?

Cancer survivors, unfortunately, are not immune to development of another cancer. When this happens it is termed a secondary malignant neoplasm or SMN. Even though the risk of a second cancer is low, it is often higher than the risk of a first cancer for members of the general population. Wilms tumor is no exception. In some cases the second cancer is caused by the same genetic characteristic that led to the first cancer. More often, however, it is due to the treatment that resulted in cure of the first cancer. Radiation is a known carcinogen, for example, as are some types of chemotherapy. The goal of the NWTS Late Effects Study is to quantify the occurrence of SMNs and other serious medical conditions so that treatments are designed to cure the Wilms tumor while minimizing their side effects. This is the rationale behind our motto: “Cure is not enough”!

A recent NWTS publication\(^1\) reported on the largest number of Wilms tumor patients to date to develop a second cancer. The results are freely available online via the NWTS website: http://nwtsg.org in the Bibliography section. See the companion article in this newsletter on how to access them via links to PubMed Central.

The study was an international collaborative effort. The NWTS and the Childhood Cancer Survivor Study contributed information on 8,884 patients from the US and Canada. There were 2,893 patients from Great Britain and 1,574 from the Nordic countries. Among these 13,351 patients diagnosed with Wilms tumor between 1960 and 2004, 195 developed an SMN. Some later developed a third (5 patients) or even a fourth (2) cancer. Common skin cancers were not counted.

The type of second cancer depended on the time since diagnosis of Wilms tumor, with leukemia occurring first (mostly within the first 5-10 years), thyroid tumors in the intermediate range (10-19 years) and breast tumors last (20-30+) years), for example. The cumulative risk of developing a solid SMN by age 40 was 7% and the
total number (174) of such cancers was 5 times that expected from general population cancer rates, regardless of country. The rates of leukemia were likewise elevated, with 24 cases observed vs. 3.9 expected in the US and Canada, 4 observed vs. 1.1 expected in Britain but none in the Nordic countries (only 0.7 expected).

We anticipate that rates of secondary solid tumors observed in future survivors of Wilms tumor will decline because of the decreasing use of radiation therapy. Indeed, a trend in this direction was observed in the international study, although it was not statistically significant. The rates of secondary leukemia relative to rates among persons of like age in the general population may increase somewhat due to the substitution of chemotherapy for radiation in modern treatment protocols, but the overall risk of their occurrence should remain very low.


**The Future of Wilms Tumor Research**

Between 1969 and 2002 the National Wilms Tumor Group (NWTSG) conducted 5 clinical studies. You or your child most likely participated in one of these studies. The goal of each study was to improve survival and decrease the late effects of treatment. The survival rate increased significantly during the 5 clinical studies. The 4-year survival noted in the 5th study was greater than 90% for many people with Wilms tumor, although certain types of Wilms tumor (e.g. anaplastic) and other forms of childhood kidney tumors (e.g. clear cell sarcoma, rhabdoid tumor, renal cell carcinoma) still often have survival rates below 80%. Even among those cured of their Wilms tumor or kidney cancer, late complications of treatment have not been uncommon, with up to a quarter of long-term survivors reporting some serious health condition 25 years after their diagnosis. These conditions have included new cancers (see “A Second Cancer?” in this newsletter), lung disease (see the article “Pulmonary Disease After Lung Radiation”) and heart disease. As a result, there has been a growing focus on modifying treatment, particularly among those tumor types with excellent cure rates, in ways that could reduce the likelihood that the cancer treatments will cause these later health problems.

To accomplish this, much of the current work has focused on using genetic information from individual tumors to help make better treatment choices for any given child. For example, depending on tumor genetics, some children may now be successfully treated with surgery alone without needing chemotherapy and radiation treatment, while others can expect high cure rates with surgery and limited chemotherapy, but not require both stronger chemotherapy and radiation treatment. In contrast, tumor genetics can also help identify which patients may still need both stronger chemotherapy and radiation treatments following surgery. A variety of new chemotherapy drugs also are continually being tested, many of which may offer the promise of fewer long-term side effects. These are first being tested among those children whose kidney tumors have recurred after initial treatment, and if promising, may then also be introduced among children with newly diagnosed Wilms/kidney tumors.

Since 2002, the Wilms tumor clinical studies in much of North America have been led by the Children’s Oncology Group (COG), which was formed by the merger of the NWTSG with several other children’s oncology research groups. The leadership of COG’s Wilms/kidney tumor studies includes many investigators who have been active with the NWTSG. The NWTSG’s Late Effects of Treatment Study
also continues to this day, providing important long-term health information that helps inform the current generation of children being treated. This Late Effects Study would certainly not be possible without the active participation of people like you from the original five clinical studies.


Do you have a Late Effects Clinic?

Getting medical care that is targeted to the needs of childhood cancer survivors is an important step in maintaining a healthy and happy life after surviving cancer.

- Your personal health needs and concerns can be addressed
- Tailored screening programs can be prescribed relevant to your treatment and cancer history

The number of Late Effects clinics has dramatically increased, and even if you have moved away from the institution at which you were originally treated, there are many clinics throughout the country where you could be seen. To find one near you, visit the Children's Oncology Group’s Late Effects directory of services: http://www.childrensoncologygroup.org (bottom of page) or if you don’t have internet access, please contact us and we’ll help 800-553-4878.
A big thank you to everyone who has made a donation! 100% of all money donated to the NWTS goes directly to research.

For those wishing to make a donation in the future, we are located at the Fred Hutchinson Cancer Research Center in Seattle, WA, which is a tax exempt 501c3 organization.

Donations by check should be made payable to the National Wilms Tumor Study and mailed to:

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