

LATE BREAKING news

from the **National Wilms Tumor Study**

Why Does the NWTs Request Medical Records for Pregnancies?

Over the years the questions we receive most frequently from you regard pregnancy and men's and women's fertility issues. Until eight years ago we did not have well documented information to use in answering your questions. We thus began to systematically collect information from mothers and fathers regarding their, or their partners', pregnancies and deliveries.

In order to provide you with accurate answers we must document all aspects of pregnancies with medical records. These enable us to document types and degrees of complications, the babies' birth weights, as well as the babies' health status. We quantify these in order to compare pregnancy events to the parent's treatment for Wilms tumor.

In 2001 we published our first findings relating pregnancies to treatment. In our Winter 2001 newsletter, we included an overview of this paper. If you did not receive a copy of this first newsletter and would like one please let us know. Some were quite surprised at the findings. Twenty-five or more years ago girls who received abdominal radiotherapy as part of their treatment were often told they would never have children. We found out this is not always true. Abdominal radiotherapy can affect the duration of pregnancy and

thus the baby's height and weight at birth. However, we found that only when the radiotherapy is given to a specific site in the abdomen is fertility affected.

Those early findings are still preliminary because we have not heard about all of our



NWTs participants' pregnancies. We are sure there is much more to understand about the relationship between treatment and pregnancy, and we need help from all of you. Please let us know about your pregnancies or if you have fathered a child, and please understand why we request your permission to obtain medical records. We want to provide you with the best answers

possible. You can pass these study findings along to the physicians and others caring for you during pregnancy to contribute to the safest possible pregnancies and deliveries.

If you or your partner have had a pregnancy and you do not think it has been reported to us, or if you are not sure, please call us at **206-667-4842** or email us at nwtsg@fhcrc.org.

National Wilms Tumor Study

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Signs of Wilms Tumor

by *Giulio J. D'Angio, MD*

Wilms tumor, also called “nephroblastoma,” is most common in boys and girls between one and four years of age. Black children, especially girls, seem to be more susceptible than white children of either sex. The most common sign by far is the presence in an otherwise healthy child of a painless lump in the side, not the middle, of the belly—that is, the flank.

Classically, it is first noted by a grandmother or aunt who comes to visit and while bathing the child first feels a mass. Mothers very often do not notice the gradual increase in size, and assume that this is just another part of a big belly, so often seen in healthy, chubby children. Abdominal pain, fever or bloody urine are less common first signs, or high blood pressure may be found during a routine well-baby visit to the pediatrician.

Very uncommon as the sole presenting sign is a varicocele in boys; that is, swelling of the veins near the testicle. It is due to pressure on the great vein of the abdomen (the vena cava) causing back-up of normal drainage.

Sometimes Wilms tumor occurs in children who have had other malformations or abnormality syndromes. Here are a few of the most common ones:

OVERGROWTH ABNORMALITIES

These in turn can be subdivided into **hemihypertrophy** and the **Beckwith-Wiedemann Syndrome (BWS)**. Hemihypertrophy means that one side of the body—in whole or in part—is larger than the other side. Thus, one whole leg or arm may be longer and bigger around than the other, but even smaller parts like one side of the face may be asymmetrical. The BWS is more complex. It is characterized by a large tongue that may protrude from the mouth, a hernial sac in the belly button (called an omphalocele), and low blood sugar levels. Children with the BWS may exhibit enlargement of other organs such as the liver and pancreas. Hemihypertrophy may also be seen. They can develop cancers other than Wilms tumor (for example malignant growths in the liver and the gland above the kidney which therefore is called the suprarenal gland).

THE WAGR SYNDROME

The W stands for **Wilms tumor**, the A for **Aniridia**, the G for abnormalities of the **Genito-urinary** organs, and the R for **Retardation**. Aniridia is the absence of the iris of the eye present at birth. The genito-urinary malformations include major anatomic maldevelopments. These include mixed development of the sexual organs making identification of sex uncertain, undescended testicle, or severe hypospadias. In this latter condition the urinary stream issues not at the tip of the urethra but from an abnormal orifice along the shaft of the penis or even higher than that; for instance, in the perineum. The R in mental Retardation completes the acronym.



DENYS-DRASH SYNDROME

This rare anomaly affects boys more than girls. It varies in complexity and severity, but abnormally developed kidneys that do not function normally are the principal feature. The children may be mentally retarded and may share other characteristics of the WAGR syndrome including ambiguous genitalia. They are also at higher risk than other children for developing Wilms tumors. Those with pronounced kidney problems rarely survive adolescence.

SUMMARY

Children with any of the rare syndromes described require careful follow-up in specialty clinics. This is needed not only for the other problems that make up these complicated anomalies, but also in order to detect a tumor when it is still small. Otherwise, parents need to be alert to any sign of a growing lump anywhere in the child's body; for instance, by feeling for one in the abdomen while changing a diaper or while bathing the child.



Meet the Late Effects Study Staff

This year we are delighted to introduce you to two people at the DSC who support the efforts of everyone in our office. Deborah Box is our Administrative Assistant, and Susan Peterson is our Database Manager. They both make all of our work easier and more enjoyable.

Deborah Box has been working for the Fred Hutchinson Cancer Research Center (FHCRC) for nearly five years and in March 2002 joined the NWTs Data and Statistical Center (DSC). As Administrative Assistant she is responsible for facilitating our office's management. She works on a wide array of ongoing and special projects. Much of Deborah's work involves a tremendous amount of "keeping track of details." This includes being responsible for recording and distributing weekly staff meeting minutes and insuring that all procedures are updated and circulated among staff.

Deborah also handles all of our study's mailings, a crucial part of our research. Our study relies on the important information we receive daily about our participants. It is therefore necessary that our various mailings are carefully scheduled, prepared and sent accurately. Deborah also orders all of our supplies, updates our study's web site and makes sure that all of our office machines (phone, fax, copier) are working smoothly. She is also the person our staff consult with when we have questions involving office templates or need guidance with word processing.

Last year was a particularly busy year for Deborah as our office moved to a brand new building at the FHCRC campus. This move required extra attention from her in attending meetings, making decisions and sending out helpful reminders to staff. Deborah has also worked closely with our Project Manager, Pat Norkool, on a variety of routine regulatory issues as well as assisting with grant applications. Without Deborah's help we would all have much less time to devote to our

participants and our primary mission of gathering information about surviving Wilms tumor.

Deborah enjoys spending her free time cooking and venturing out along Washington's great hiking trails. She is also a great enthusiast of the theater and has attended local plays for the past 10 years. Currently Deborah is enrolled in biology and chemistry classes and is pursuing a medical degree in naturopathy. "What I like about naturopathy is that it is multi-faceted. It involves nutrition, science, counseling, and teaching. Participating in a cancer prevention study (Wellness Study) at FHCRC that was designed by a naturopath is what inspired me to learn more."



Susan Peterson has been the Database Manager for the NWTs Data and Statistical Center (DSC) for seven years. In past issues of **Late Breaking News**, you have been introduced to several of the data coordinators who write or call you to check on your health, on new pregnancies

and update news of major events in your life. The data coordinators collect important data and Susan manages those data so they can be used for research. Of course, one of her top priorities is to maintain the confidentiality of the data, at all times. Susan sets up and maintains the servers where the information resides and carries out all of the programming that allows the data coordinators to access, update, and summarize the material for analysis by researchers.

Susan's work often requires responding to multiple problems at one time. She works closely with Pat Norkool, the NWTs Project Manager, and with Dr. Norman Breslow, the study Statistician and Principal Investigator, in problem solving and communicating with staff and researchers. Keeping track of the data for the National Wilms Tumor Study is a big task as the study has been collecting it since 1969. It is one of the most extensive databases in cancer research that actively follows participants who have had childhood cancer!

Susan says, "The DSC is a wonderful place to work, because it is comprised of so many people who are dedicated to helping the participants and their families. It makes me proud to be part of a study that not only assesses the effects of childhood cancer treatment but also strives to inform and provide informational resources for continued good health of the participants and their offspring."

Outside of work Susan has recently completed her MBA in Technology Management. She is now looking forward to having more free time to enjoy the many recreational opportunities such as biking, hiking and skiing that Seattle and Washington State offer. While she keeps a close loving eye on her young adult children she still manages to enjoy the outdoors, movies and traveling to warm sunny places. This spring Susan got one more way to enjoy Seattle's beautiful weather and scenery; her husband Joe presented her with a shiny, bright red Miata convertible for her 40th birthday!

Keep in Contact with Your Institution

Many of you no longer return to the hospital or center where you were treated for Wilms tumor. We are contacting many of you directly, and you are not returning to your treatment center. However, we want to pass along a request from those hospitals and centers. They still want to hear how you are doing. When you receive our annual mailing, please take a few minutes to write a note to the cancer registry or to that doctor or nurse who was involved in your care. They very much want to know how you are. If you need the address, give us a call at **1-800-553-4878** or look it up on our [website](#).

Who Is Eligible for the Late Effects Study?

We have been asked by a number of Wilms tumor survivors who were not registered on our study at the time of diagnosis if they can be enrolled on or contribute information to our Late Effects Study. We appreciate the generosity of these offers and recognize that they are made with the motivation to share information that may lead to improved treatment and long-term outcome. Regretfully we cannot accept these offers.

The NWTS Late Effects Study is funded by the National Cancer Institute (NCI) and subject to their regulations. There are a number of elements that make someone eligible to participate in the NWTS Late Effects Study.

- ◆ First, you must have been specifically **consented** to be treated on one of our five clinical trials. Informed consent is mandatory to be on our protocol studies, and without it candidates are immediately ineligible.
- ◆ Then you must have been **registered** on one of our clinical trials. All clinical trial data should have been submitted to the NWTS on forms designed by the NWTS for institutions to collect consistent data unique to the NWTS. If treatment was outside of a participating institution, the physician would not have access to these NWTS forms and could not provide the NWTS with complete data.
- ◆ Tissue from the tumor should have been sent to the NWTS Pathology Center for Central Pathology Review. This review by the NWTS Pathologist results in yet more data specific to the NWTS. The **reviewed diagnosis** must have been Wilms tumor, Clear Cell Sarcoma of the Kidney, or Rhabdoid Tumor of the Kidney.

The above is the summary picture of eligibility. Our clinical trial protocols must adhere to very strict guidelines in order to provide scientifically valid results. While we very much value offers to provide us data about Wilms tumor experiences from people not registered on the NWTS, we cannot currently include these in analyses because we are prohibited from using them in any way. Even in our newsletter, our information must be based upon eligible patient data. According to the rules that govern how we communicate about late effects, we cannot use anecdotal data.

However, if you were diagnosed with Wilms tumor after September of 1969, you might have been enrolled on one of our clinical trials and now be eligible for the Late Effects Study. If you would like to find out, please **contact us**.

Treatment Outcomes in Adults with Favorable Histology Wilms Tumor

Wilms tumor is rare in those 16 years of age or older, who for this discussion are considered adults. Adults with Wilms tumor treated in the past had very poor survival. Only one in four adults diagnosed with Wilms tumor in 1982 survived. However, the likelihood of recovery now is far better. In earlier years treatments were less consistent. Post-operative radiation and chemotherapy were used inconsistently, and the most effective drugs were not always employed. Reports from the National Wilms Tumor Study suggested better outcomes for these patients when they are treated by methods similar to those used with children.

A recent study by Dr. John Kalapurakal at Northwestern Memorial Hospital provides data on 45 adults with favorable histology (FH) Wilms tumor who received surgery, chemotherapy and radiation therapy (RT) similar to treatment for Wilms tumor in children. All 45 had stage and

histology-appropriate therapy after surgical removal of the tumor. Thus, they all received multi-agent chemotherapy with or without RT according to the extent of their disease. Their survival rates are similar to those reported for children, which is now very good.



Until now there have been no cooperative clinical trials of adult Wilms tumor patients. Such studies are done by nationwide groups of institutions called cooperative groups. The Children's Oncology Group (COG) currently oversees the development of clinical studies of Wilms tumor. The COG has raised the age limit for patient entry on future trials to include adolescents and young adults. Until the next generation of COG studies is completed, we recommend that adults be treated according to the guidelines in the NWTS-5 protocol. Adult patients and their physicians may contact us about these guidelines.

Thank You!

Thanks to many of you 2004 has been a busy and productive year for our office. You have permitted us to obtain medical records to document pulmonary problems, second tumors, many pregnancies (congratulations!), and some other health related issues. Thank you for this. You are helping us make strides in learning more about what conditions may be related to treatment, and thus to be able to provide all of you and your physicians with guidelines to improve your health care and your well being.

We very much appreciate your donations which support our research and supplement our funding from the National Cancer Institute (NCI).

Thank you to everyone who sent photographs. We have pictures of participants, their children, their families, and even a wonderful photo of a wedding party. Please keep sending these in. Seeing the faces of our participants helps us keep our mission in focus.

A final note of thanks to everyone who took time to write a personal note. We love to find out who is going to college, becoming a nurse or doctor, getting married and reports of everyday life. We also hear from some of you who are having health problems, and we try to provide what resources we know are available. And to those of you who write us words of appreciation and encouragement, we are grateful for the sentiment and the support.

Following Participants' Children

“Will My Diagnosis and Treatment of Wilms Tumor Affect My Children?”

We have no reason to believe that your children are at increased risk for any health problems, but we cannot make an authoritative statement about this until we have enough documentation. Therefore this is a question we are also currently researching. We are asking parents to permit us to follow their children's health each year. We will periodically assess the information to see if there are any trends developing.

We know it takes time to complete and return our forms, and we do not want to impose a new burdensome layer of questions to what we already ask. When you receive the form regarding your children we believe you will find it very brief and easy to complete. If you do not find this to be true, please let us know. Thanks in advance for helping with this important aspect of the study.

Adult Consents: A Question from a Participant

We received this question: *My parents consented for me to participate in the study when I was diagnosed. Why are you asking me to sign another consent?*

If you were under 18 when you were diagnosed, your parents signed a consent form as your guardians. Once you have reached your eighteenth birthday, you are legally an adult. As an adult you now are responsible for what information you share with us. We can receive your consent either verbally or in writing.

While we want your continued participation in the study, the consent form also gives you the opportunity to decline participation. Whatever you decide to do, we would appreciate receiving your decision verbally, via email or in writing.

Some young adults are busy with college or new careers and prefer that we continue to contact their parents. We certainly understand this, and can do this if we have your permission. If this is your preference, please let us know, and we will continue to contact your parents until you tell us to begin contacting you directly.

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