CANDLELIGHTERS

CHILDHOOD •CANCER •FOUNDATION™

The Quarterly Newsletter **SPRING 2001**

Included in the Next Edition of "The Quarterly"

- *Cognitive Late Effects*
- *Childhood Cancer Resources*

Now available on Candlelighters website:

- *Current list of COG treatment centers*
- *Current list of Long Term Follow-Up Clinics*
- *Video of Childhood Cancer Awareness Tree Lighting Ceremony*
- *Institution list for Enalapril Clinical Trial*

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Two Thousand Ribbons Adorn Nation's First Childhood Cancer Awareness Tree *by Ruth Hoffman*

December 15th, 2000 in the entrance to the Rayburn House Office Building in Washington DC, children with cancer, survivors of childhood cancer, their families, representatives from childhood cancer organizations and elected officials from across the country attended the lighting ceremony of the first annual Childhood Cancer Awareness Tree. The 16 foot Douglas Fir was adorned with over 2,000 gold ribbons, each bearing the name of a child who has or has had cancer.

All attending, gathered together to honor the lives of children who have or have had cancer, and to remember those children who had lost their battle to this horrid disease. Each year in the US, over 12,000 children and teens are diagnosed with cancer and one third of these children will die from it. In spite of improved treatment, childhood cancer remains the number one cause of death by disease, killing more children than asthma, diabetes, cystic fibrosis, congenital anomalies and AIDS combined! Candlelighters continues to embrace the lives of these children and their families, and lead the way in raising awareness of childhood cancer and its impact upon the entire family, through events such as the Childhood Cancer Awareness tree on Capitol Hill. Together, with **Gigi Thorsen** of *Gold Ribbons for Childhood Cancer* and **Pat Tallungan** of the *Children's Neuroblastoma Cancer Foundation*, the Childhood Cancer Awareness Tree quickly became a labor of love. I can't express the emotions that I experienced each and every day, as the mailman would deposit hundreds of envelopes into my mailbox,

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Treating High-Risk Neuroblastoma at the Turn of the Century

by C. Patrick Reynolds, MD PhD & Beth Hasenauer, RN MS

Neuroblastoma is a solid tumor of childhood that arises in the nervous system, outside of the brain. The goal of this article is to provide a guide to the initial treatment options available for children with high-risk neuroblastoma. Also reviewed, will be the design and conduct of clinical trials. This information will be of interest to parents dealing with other childhood cancers.

During the last part of the 20th century, clinical trials have shown that the basis for treating high-risk neuroblastoma should consist of induction chemotherapy, consolidation with high dose chemotherapy + stem cell transplant. The stem

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Childhood Cancer Awareness tree *continued...*

(continued from page 1)

each bearing the name of a child to be added to a gold ribbon. Daily, I would open these envelopes. Daily, tears were shed, as families shared their children's names and often letters of love describing their precious lives. There were the cousins who were both battling cancer, the babies who lost their battle at 10 months of age, multiple cases of siblings who were both fighting this disease, neighbor children, school classmates with cancer, and angels - so many, many angels!!!

There are also so many "thank-you's" to make. I'd like to thank Gigi and Pat for working tirelessly the entire eight weeks to pull this event together. Your vision and commitment to building awareness of the needs of childhood cancer across this country continues to make a difference!

Thank you to **Congresswoman Deborah Pryce** whose work on Capitol Hill made this event possible. You are truly a woman of integrity. Thank you to her assistants **Stephanie Christensen a**nd **Michele Apostolos** and to **Cynthia Duncan** of *Hope Street Kids*. Thank you to **Meg and Jim Crossett** who took on the huge task of delivering the tree while caring for their daughter **Rachel** as she continues her cancer battle, to **Holly Walker** and *Rhosymedre Design Group* who turned that 16 foot Douglas Fir and Rayburn entrance into a work of art. Thank you to **Kim Mehalick** of the *Childhood Cancer Awareness Project* for coordination of the quilts and their pictorial display of the courageous lives of our children. Thank you to **Bonnie Shoval** for her regular help in the office with the practicalities of making bank deposits and photocopying checks to keep our auditors happy. Thanks to Bonnie's husband **Jacob Shoval** who coordinated the sound system, to **David Azulay** of *Eminent Productions* who provided the sound system. A big thanks needs to be given to **Trevor Romain** who designed the tree logo with a 48 hour timeline and to **Geronimo** and **Marina Lee** for logo development. Thank you to national Board member **Lisa White**, who took care of so many details such as K-9 searches, off-site security check of the tree, transportation of posters, flowers, lights etc. Thank you to Board member **Steven Payne** who constantly updated our website and to **Patty Feist** who diligently placed all updates on her website as well. Thank you to Board member **Bryan Avery** for the special activity planning. Thank you to **Gina Peca** who connected us with *General Electric.* Thank you to **Beth McQuinn** and her children for their help in the office and with decorating. Thank you to **Diane Allen** and *El Paso Candlelighters* for their support and for bringing the poster children to the event. Thank you to **Deandra** and **Vanessa** and their families for being willing to be the poster children and-

provide "the face" of the cancer child to this cause! Thank you to speakers **Dr. Malcolm Smith** of the *NCI* and **Dr. Greg Reaman**, Chair of *C.O.G.*, to the grade eight choir of *Francis C. Hammond School,* to my son **Nathan Bartley** for his violin performance and to **Kira and Bill Small** for the composition and performance of "You Can Fly."

Thank you to our sponsors: the *Alex Salisbury Foundation* and *NCCR* for their financial assistance, to *General Electric* for providing the many thousands of lights, to *3M* for the donation of their new product that made the hanging of the quilts on the marble walls possible, to *Starlight Children's Foundation* (Mid Atlantic Division) for providing the "Bears" for the kids attending, to *NCCF* for providing gold ribbon lapel pins for those attending, to *Airlifeline* pilots and Director **Richard Love** for arranging the transportation of a cancer child to the lighting event.

Most importantly, I wish to thank everyone who shared their children with us in this first annual awareness event, by honoring their lives on the thousands of gold ribbons!! ***What started out as a "Tree of Hope, truly became a "Tree of Love!"***

To view this national awareness event, a nine-minute video "Light up the Holidays with Hope" has been created. The video, can be purchased from Candlelighters web site store at http://www.candlelighters.org. The childhood cancer awareness CD 'You Can Fly', along with Candlelighters logo apparel are also now available.

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Ruth Hoffman, *Executive Director & Newsletter Editor*

Late Effects to the Thyroid Gland

By Nancy Keene and Kevin Oeffinger MD

Treatment for childhood cancer sometimes damages the thyroid gland. Fortunately, late effects to the thyroid are usually very easy to treat. It is therefore important to find out if you are at risk and ensure that you get the appropriate tests so that any problems are identified early and treated appropriately.

What is the thyroid gland?

The thyroid is a small butterfly-shaped gland located in front of the trachea in the lower part of the neck. An exquisitely sensitive gland, it enlarges and becomes more active during puberty, pregnancy, or times of great stress. It also alters its size and shape during women's menstrual cycles.

Some glands produce substances called hormones, a term derived from the Greek word *"hormaein"* which means "to excite." Hormones are released in tiny amounts but they travel throughout the body to orchestrate complicated processes like growth, puberty, reaction to stress, temperature regulation, and urine output. Disruptions in the balance of these chemical messengers can profoundly affect both health and quality of life.

Two hormones secreted by the thyroid gland, thyroxine (T_4) and triiodothyronine (T_3), have far-reaching effects on almost all tissues in the body and are intimately involved in physical growth, metabolism, and mental development. Simplistically, the thyroid hormones, T_3 and T_4, can be thought of as regulators of our metabolism. Thus, when the thyroid hormones are low, the body's metabolism slows, resulting in fatigue, a lowered heart rate and blood pressure, slowing of the intestines leading to constipation, and a constant feeling of being cold. Conversely, when one or both of the thyroid hormones is high, the body's metabolism is increased, resulting in an increased heart rate and blood pressure, increased activity of the intestines leading to diarrhea, and a constant feeling of being hot.

The pituitary, a gland in the brain, makes a chemical called thyroid-stimulating hormone (TSH) which travels in the blood stream to the thyroid. As you might guess from the name, thyroid-stimulating hormone stimulates the thyroid gland to make the thyroid hormones, T_3 and T_4. When levels of T_3 and T_4 are low, then the brain increases the production of TSH which in turn tries to make the thyroid gland produce more T_3 and T_4. Conversely, if the level of either T_3 or T_4 is too high, the brain senses this and decreases the production of TSH which leads to less production of T_3 and T_4.

Treatment for childhood cancer sometimes damages the thyroid gland. Fortunately, late effects to the thyroid are usually very easy to treat.

The possible late effects

The thyroid is generally not affected by chemotherapy. If damage occurs, radiation is usually the culprit. Several types of thyroid problems can develop after radiation.

Primary hypothyroidism (primary = damage at the thyroid gland; hypo = low; thyroidism = disease of the thyroid) can occur from damage to the thyroid gland caused by radiation. In this type of hypothyroidism, the TSH is elevated because the brain is trying to make the thyroid produce more T_3 and T_4. If you received more than 1500 cGy of radiation to the neck or more than 750 cGy total body irradiation (TBI), you are at risk. This includes survivors of Hodgkin's disease, non-Hodgkin's lymphoma, head and neck tumors, or those who had TBI prior to a bone marrow transplant. Hypothyroidism sometimes occurs in patients treated with cranial or craniospinal radiation for leukemia.

While less than one percent of children with leukemia treated with 1800 cGy of cranial radiation develop hypothyroidism, 40 to 90 percent of Hodgkin's patients who receive mantle radiation and up to 50 percent of bone marrow transplant patients do. Treatment at a young age may also increase the likelihood of developing a thyroid problem. Thyroid dysfunction (dys = abnormal) can occur soon after radiation, but generally does not occur until several years later.

Secondary hypothyroidism (secondary = damage in the pituitary gland/brain) is an uncommon late effect caused by radiation damage to the pituitary gland which results in a decreased production of TSH. Thus, in this type of hypo-thyroidism, the TSH and T_4 levels are low.

Compensated hypothyroidism. A mildly elevated TSH and normal T_4 may occur if your thyroid is working too hard. There are usually no symptoms. An overstimulated gland is at increased risk for developing tumors, both benign and malignant. Survivors with compensated hypothyroidism are sometimes given supplemental thyroid hormone to allow the gland to rest.

Hyperthyroidism (hyper = high) occurs when too much T_3 or T_4 are produced causing the body to use energy faster than it should. This late effect is not well understood but

Late Effects to the Thyroid Gland *continued ...*

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has been found in very small numbers of survivors who were treated with neck radiation.

Thyroid cancer. Radiation to the neck can result in thyroid cancer later in life so all survivors at risk need life-long evaluation of thyroid function.

What are the symptoms of thyroid damage?

Signs and symptoms of an underactive thyroid hypothyroidism) can include:

Fatigue or lethargy
Hoarseness
Difficulty concentrating
Depression or mood changes
Constipation
Weakness
Intolerance to cold
Swelling around the eyes
Poor growth
Delayed puberty
Puffy face and hands
Weight gain
Dry or rough skin
Brittle hair
Joint or muscle aches
Slow heart rate
Low blood pressure
High cholesterol
Decreased tolerance for exercise

The signs and symptoms of an overactive thyroid hyperthyroidism) can include:

Nervousness or anxiety
Difficulty concentrating
Fatigue
Muscle weakness or tremor
Rapid or irregular heartbeat
Excessive perspiration
Heat intolerance
Diarrhea
Weight loss
Menstrual irregularities
Protruding eyes
Tenderness in the neck
Decreased tolerance for exercise

Signs and symptoms of thyroid cancer:

Thyroid cancer is generally a slow growing cancer without a lot of signs or symptoms. Usually, a painless, hard mass (lump) in the thyroid gland can be felt. One might also experience hoarseness, problems with swallowing, enlarged lymph nodes in the neck and difficulty breathing.

Thyroid problems can occur years or decades after treatment for cancer, so a yearly check is necessary for the rest of your life if you are at risk.

What follow up is needed for those at risk?

Your T_4 and TSH levels should be checked every year after radiation to the chest, neck, or head and any time symptoms develop. These are simple blood tests. At your yearly follow-up appointment, your thyroid should be palpated (felt by hand) and your growth (if you are a child or teen) should be plotted on a chart.

In some facilities, radioactive iodine uptake by the thyroid is measured. The benefit of screening with periodic ultrasound of the thyroid every 1 to 3 years is controversial and is currently being studied. Thyroid problems can occur years or decades after treatment for cancer, so a yearly check is necessary for the rest of your life if you are at risk. If any abnormalities are detected during an examination, referral and follow-up by an endocrinologist or surgeon may be necessary.

How is damage to the thyroid treated?

Your healthcare provider should talk to you about the signs and symptoms of thyroid problems so that you will recognize them if they develop. Although thyroid problems are common in survivors who had radiation to the head and neck, treatment generally is easy and effective.

- Primary hypothyroidism (high TSH, low or normal T_4): To make one euthyroid (normal thyroid level), a daily pill of levothyroxine, a synthetic form of thyroxine, is used to replace what the thyroid gland is not making. Common brand names of this medication include Synthroid, Levoxyl, Levothyroid, and L-thyroxine. Treatment is for life!!! Some survivors to want to avoid taking medications, and so get tired of taking a daily pill. Stopping the medication will result in redeveloping the symptoms of hypothyroidism.
- Compensated hypothyroidism (mildly elevated TSH, normal T_4): Daily pill of levothyroxine may be used to suppress excessive gland activity.
- Thyroid-stimulating hormone deficiency (low TSH, low T4): Daily levothyroxine.
- Hyperthyroidism (low TSH, high T_3 or T_4): The overproduction of the thyroid hormones, T_3 or T_4, can cause life threatening changes to the body, so more aggressive therapies are required to make the thyroid produce less or no thyroid hormone. There are three options to treat hyperthyroidism: (1) surgery to remove most of the thyroid gland; (2) a medication to cause the thyroid to be unable to make as much thyroid hormone (generally only a temporary treatment); and (3) drinking a radioactive liquid called I^{131} which is taken up

(*Continued on next page*)

Treating High-Risk Neuroblastoma *continued...*

(Continued from page 1)
cell transplants use the patient's own previously stored stem cells obtained from either the bone marrow or peripheral blood (PBSC) to replace the bone marrow, which is destroyed by the high-dose chemotherapy. Patients also receive local radiation to tumor sites, followed by post-transplant maintenance treatment with 13-cis-retinoic acid (Accutane). 13-cis-retinoic acid is aimed at eliminating any remaining tumor cells that are possibly left after the transplant. These established principles apply to "up-front" therapy of high-risk neuroblastoma.

To date, a single large clinical study with long-term survival data (the Childrens Cancer Group CCG-3891 study) has employed all of these therapeutic principles uniformly in a large group of patients beginning at diagnosis. Based on the CCG data, a child diagnosed with high-risk neuroblastoma when treated with the above approaches, can expect an estimated 40% probability of disease-free survival four years from diagnosis. Potential improvements in all components of therapy (induction chemotherapy, intensive consolidation with stem cell transplant, and post-transplant therapy) have occurred since the CCG-3891 study. Thus, it is reasonable to expect the potential for a higher disease-free survival for high-risk neuroblastoma in ongoing and future clinical trials.

For those patients in whom the tumor progressively grows during or after therapy, the chances of survival are reduced. Because there are no established effective treatments for such patients, therapies listed above and/or highly experimental therapies with unknown risks may be appropriate for such patients.

What is high-risk neuroblastoma?

The clinical behavior of neuroblastoma is highly variable, with some tumors being easily treatable, but the majority being very aggressive. This article will only address therapy of high-risk neuroblastoma. The treatment of low or intermediate risk tumors is very different from treating high-risk disease. All patients with stage 4 disease diagnosed after one year of age are classified in the high-risk category. In stage 4 disease, the neuroblastoma tumor cells have already spread (or metastasized) to other sites in the body, such as the bone or bone marrow. Essentially all patients who have tumors with many copies (or amplification) of the *MYCN* oncogene also have high-risk disease, even if they do not have evidence of the tumor having spread. Given the aggressiveness of the tumor type, it is accepted practice to treat high-risk neuroblastoma patients with intensive therapy, to increase the probability of cure. Most

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Late Effects to the Thyroid Gland *continued...*

(*Continued from page 4*) by the thyroid gland and causes it to 'scar' over. The goal of treatment of hyperthyroidism is to make the patient either euthyroid (normal thyroid level) or hypothyroid, which can then simply be treated with a daily pill of levothyroxine.

- Thyroid nodules: Patients with nodules detected by palpation should be further tested. This is generally done with a special type of needle biopsy called a fine needle aspiration (FNA). A thyroid scan and/or an ultrasound of the thyroid is sometimes done as part of the evaluation.
- Thyroid cancer: Thyroid cancer is usually very treatable. Depending upon the type and stage of thyroid cancer, treatment generally includes a subtotal thyroidectomy (surgery to remove almost all of the thyroid) followed by taking a large dose of I^{131} intended to ablate (destroy) any of the remaining thyroid tissue and cancer cells. The patient is then placed on levothyroxine and followed on a regular basis.

If you are risk for thyroid problems, and are planning to become pregnant, you should have a blood test done to evaluate your thyroid function.

Both the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology recommend that all women planning to become pregnant be screened before they conceive because mothers with thyroid disease have a higher risk of having children with neurological defects.

Thyroid problems are common in survivors who had head or neck radiation. However, treatment is generally easy and effective. Make sure to discuss your thyroid gland with your health care provider at your yearly follow up visits.

Dr. Kevin Oeffinger MD directs a multi disciplinary program for young adult survivors of childhood cancer at UT Southwestern at Dallas TX and is partially supported as a Robert Wood Johnson Foundation Generalist Physician Faculty Scholar. He enjoys backpacking, running and hiking with his wife Patty, 16-year-old son Daniel and 13-year-old daughter Ashley.

Nancy Keene is the author of Childhood Leukemia, Childhood Cancer (with co-author Honna Janes-Hodder), Your Child in the Hospital, Working with Your Doctor and Childhood Cancer Surivors (co-authored with Wendy Hobbie RN and Kathy Ruccione). She is Chair of the Patient Advocacy Committee of COG (Children's Oncology Group) and mother of 12-year-old Kathyrn who is a survivor of high risk ALL and 10-year-old daughter Alison.

Treating High-Risk Neuroblastoma : continued

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pediatric oncologists agree that even with optimal current intensive therapy, the aggressive nature of this disease warrants entering as many of these children as possible on clinical trials that may identify improved forms of treatment.

Clinical trials. Clinical trials are research studies that test a new approach to therapy. Phase III clinical trials focus on a particular disease and ask specific scientific questions, with the long-term goal of defining the best approach to treatment by comparing one therapy to another. These large studies test a new treatment/procedure in comparison to the current standard treatment by using randomized assignment to determine which of these approaches offer an improvement in terms of outcome and patient safety as compared to the current standard. Those patients who cannot participate in a clinical trial should receive therapy that has been proven in previous clinical trials to be safe and to deliver the best-proven probability of achieving long-term survival.

Participation in clinical trials allows patients access to state-of-the-art treatment for that disease and to also have the chance of being among the first to benefit from a new treatment that may be more effective.

An advantage to participating in a clinical trial is that the patient receives a therapeutic approach that has been mapped out and reviewed by a team of investigators who specialize in the disease being studied.

Participation in clinical trials allows patients access to state-of-the-art treatment for that disease and also the chance of being among the first to benefit from a new treatment that may be more effective.

All clinical trials are reviewed by the committee for protection of human subjects (also known as Institutional Review Board or IRB), at the institution where the patient is treated. This review ensures that the rights of the patient will be upheld and protected and that the patient will not be exposed to any unnecessary or extreme risk if he/she agrees to participate in the clinical trial.

The larger the organization carrying out the trial, the greater the review of the plan of therapy. For example, a phase III cooperative group trial (in pediatric oncology, a nationwide trial) would be reviewed by many pediatric oncologists, surgeons, pathologists, radiation oncologists, nurses, statisticians, etc in the cooperative group, by the National Cancer Institute's Cancer Treatment Evaluation Program (CTEP), and by the IRB's of many dozens of institutions.

There are currently several different clinical trials in the United States for newly diagnosed high-risk neuroblastoma. Most of the these trials utilize initial therapy (induction chemotherapy and perhaps surgery), followed by high-dose chemotherapy with stem cell transplant using the patient's own stem cells. Most studies also employ local radiation, and after completion of all cytotoxic therapy (including stem cell transplant and radiation), Accutane is given for six months. Phase III trials conducted by the national cooperative group (The Childrens Oncology Group, or COG) occur without change over more then 3 years, so we will review those trials in detail. Table 1 summarizes most of the modalities of therapy currently being tested in clinical trials for high-risk neuroblastoma, including phase I and phase II studies.

Childrens Oncology Group (COG) Phase III Studies.

The Childrens Oncology Group is a national group of physicians, nurses, and other specialists devoted to the study of childhood cancer. Phase III trials run by cooperative groups such as the COG help to establish state of the art cancer therapy. There are currently 2 planned COG phase III trials for high-risk neuroblastoma. Both of these trials will enroll the same group of patients because the treatments being tested are sequential in nature. This means that a patient enrolled on the first study (known as A3973) may, but is not required to, enroll on the study that comes later in therapy, which is known as ANBL0032. However, patients who do not enroll on the A3973 study beginning at diagnosis are not eligible to participate in the ANBL0032 study. This requirement is to insure the statistical validity of the studies.

The A3973 study, which opened on February 10, 2001 employs very aggressive multi-drug induction chemotherapy, during which patient's PBSC are harvested, ideally after 2 cycles of chemotherapy. The major research question being asked in this study is: Does selective removal (purging) of tumor cells from PBSC improve the tumor-free survival of patients given a stem cell transplant? To address this question, half of the patients are randomized to have their stem cells treated with antibodies attached to magnetic beads, which are then used to remove any residual tumor cells that might be remaining in the PBSC. The other half have their untreated stem cells stored for subsequent use. After successfully storing purged or un-purged PBSC, patients will complete 4 additional cycles of chemotherapy (for a total of 6 cycles), followed by intensive myeloablative chemotherapy and the PBSC reinfusion. The myeloablative therapy used in A3973 is known as CEM-LI (carobplatin, etoposide, melphalan, local irradiation). Patients receive the local radiation after the stem cell transplant to the primary tumor site and other sites of known

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Founding CCCF Board Member Julie Sullivan Retires

by Barb Rennhoff, Secretary

December 2000

Dear Julie,

The Board of Directors of Candlelighters Childhood Cancer Foundation would like to express our deep appreciation for the many gifts and talents that you have shared so generously with Candlelighters families. The sadness that touches us as you retire from the Board is mellowed by the gratitude that we feel remembering your invaluable contributions.

Along with Dick, your beloved husband, and a small nucleus of other parents, you worked long and hard to establish Candlelighters in 1970 as a national resource for families of children with cancer who felt so alone and hungry for education, information, and support. It has been our continued good fortune that you have been willing to persist in nurturing your network of families by serving their needs in any and every aspect of Candlelighters activities.

For more than thirty years the first reassuring contact that many parents of newly-diagnosed children had with another caring parent was when they met you. Whether on the telephone, through meetings, or in the newsletter, your voice, your patient ear, empowered parents to cope with the challenges that they faced. No one can begin to measure the hours that you have devoted to establishing and maintaining our foundation. The eternal paperwork, the ringing telephones, the bills to pay, the ruffled feathers to soothe, the brainstorming, the travel, the late nights and early mornings, the challenge of good decision-making, the heart-breaking stories, the piles of thank you notes, the detailed planning, the special events, the advocacy, the knocking on doors, the confidences kept, the hands held, the setbacks and the triumphs…belonged for thirty years to you. You have conducted yourself with dignity and have served as a model for the rest of us in kindness, dedication, and common sense.

We speak for all of the families who have been touched by the good work of our foundation in saying thank you, Julia, for embracing all of us in your own grief, and in doing so, easing some of ours. We will all miss you. You have carried the candle for Candlelighters families so that the darkness of childhood cancer is held at bay like the wolf at the door. We thank you for the mission that you chose and know deeply in our hearts that:

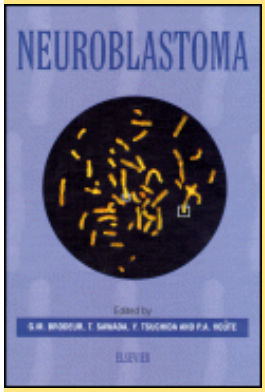
"It is better to light one candle than to curse the darkness."

Sincerely,
The 2000-2001 Board of Directors
Candlelighters Childhood Cancer Foundation

"I am only one, but still I am one. I cannot do everything, but still I can do something, and because I cannot do everything I will not refuse to do the something that I can do." --Helen Keller

New Resource: Neuroblastoma (Text Book)

Edited by G.M. Brodeur MD, T. Sawada MD, Y. Tsuchida MD,P.A. Voûte MD



This book summarizes the current state-of-the-art of neuroblastoma biology and therapy. The international authorship of this book illustrates the global interest in neuroblastomas by pediatric oncologists, surgeons, radiologists, biologists, pathologists and others. As it addresses all major areas from basic science to late effects of treatment, it will be a useful resource to a wide range of individuals in basic research, clinical investigation and treatment, as well as parents who are seeking an in-depth analysis of neuroblastoma.

Hardcover ISBN: 0 444 50222 $196.50 (U.S.) 610 Pages Illustrations Throughout

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Children's Oncology Group elects its first Group Chair

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Gregory H. Reaman, MD has been elected as the first Group Chair of the Children's Oncology Group (C.O.G.), the new National Cancer Institute-supported clinical trials cooperative group formed by the merger of the Children's Cancer Group (CCG), the Intergroup Rhabdomyosarcoma Study Group (IRSG), the National Wilms' Tumor Study Group (NWTSG), and the Pediatric Oncology Group (POG). Dr. Reaman is Professor of Pediatrics at the George Washington University School of Medicine and Health Sciences in Washington, DC, the Executive Director of the Center for Cancer and Blood Disorders, and Chair of the Division of Hematology-Oncology at the Children's National Medical Center.

"My vision for C.O.G. is that our unity of membership, purpose, and mission will result in an environment that will enable our new unified cooperative research enterprise to effect even greater and more immediate benefits for children with cancer," says Dr. Reaman. Collaboration at every level is essential for the scientific discovery, which originates from the best, validated concepts and will translate into advances in care."

C.O.G. develops and coordinates cancer clinical trials conducted at the 238 member institutions, which include cancer centers of all major children's hospitals and university teaching hospitals throughout the U.S. and Canada, as well as sites in Europe and Australia. Member institutions register all patients entering C.O.G. studies through a web-based remote data entry system, through which patient responses to therapy are centrally collected and analyzed.

With unified resources, increased efficiency and more patients on trials, C.O.G. will be able to complete studies faster and make better cancer treatments more readily available. In future research, C.O.G. also intends to conduct more extensive survivor follow-up, to address health care economics, enroll more adolescents on clinical trials, and to create the national childhood cancer registry.

Dr. Reaman will soon identify the Group Vice-Chair, who will work with him to activate the Group's decentralized scientific committee structure and develop an internal peer review process for C.O.G. The Group is preparing to submit its first competing grant application to the National Cancer Institute in February 2002.

"There is much work to be done," says Dr. Reaman. "I am confident that together we can and will face this challenge in the new millennium."

A National Cancer Institute supported clinical cooperative group

Participants Needed For Afterload Reduction Therapy for Late Anthracycline Cardiotoxicity Study

As a follow-up to Candlelighter's Fall 2000 newsletter and its article on "Anthracyclines and the Heart", Candlelighters would like to inform its readers of a new clinical trial, currently enrolling survivors. **Trial "A9480"** is the first cardiac study within C.O.G. that focuses upon therapeutic intervention. This randomized, placebo controlled, double-blinded clinical trial will analyze the possible benefits of the drug enalapril for patients with asymptomatic heart dysfunction, who have been previously treated with an anthracycline drug for childhood cancer. The trial is geared towards entering patients into study who are at least eight years of age, and less than 22 years of age at the time of their cancer diagnosis. Presently, more than half of childhood cancer survivors received one or more anthracycline drugs during their cancer treatment. These include: adriamycin, doxorubicin; cerubidine, daunorubicin; Idamycin, idarubicin. Years later, some survivors are faced with decreased cardiac function that may compromise their quality of life.

Primary Objectives of COG Study A9480:

1. To determine whether enalapril therapy will minimize damage to the heart by reducing the effects of progressive cardiotoxicity to heart muscle abnormalities more than one year after completion of anthracycline therapy.
2. To study the long-term effects of enalapril treatment Enalapril has shown potential in treating other forms of heart disease by helping to lower blood pressure and thus reduce the stress on the heart. However, the full long-term effects of enalapril therapy are not known. A9480 will determine whether improvement in cardiac function, achieved by enalapril is sustained.
3. To assess the impact of enalapril on quality of life measures.

For further information about A9480, including a list of participating institutions with contact names and phone numbers, visit our website at: www.candlelighters.org (click on Children's Oncology Group) or call COG Cardiology Coordinator, Seema Shaikh at: 716-275-1712.

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metastases, followed by 6 months of Accutane. Patients on A3973 are eligible to enter the ANBL0032 study.

The ANBL0032 study is testing a monoclonal antibody (ch14.18) that attaches to neuroblastoma cells which have a molecule called G_{D2} on their surface. Once the antibody attaches to the G_{D2} it helps the tumor cells to be destroyed. This antibody does not attach to most normal cells because they do not have G_{D2} on their surface. Laboratory experiments and small clinical trials suggest that ch14.18 can help the body's own immune cells to destroy neuroblastoma cells. These immune cells include cells that are activated by GM-CSF (monocytes and neutrophils) and cells that are activated by IL-2 (lymphocytes). The antibody ch14.18 + GM-CSF or IL-2 will be given after completion of intensive therapy supported by PBSC infusion (A3973 therapy). In addition, 13-cis-retinoic acid (Accutane) will also be given in between cycles of therapy with ch14.18 + GM-CSF or IL-2. The purpose of giving antibody therapy and 13-cis-retinoic acid is to maximize the chances of eliminating any residual neuroblastoma tumor cells (known as minimal residual disease) that may be left after intensive therapy, such as that given in A3973.

Recurrent or Progressive Neuroblastoma: High-risk neuroblastoma patients who develop progressively growing tumors during therapy, or have tumor recurrence after chemotherapy, are encouraged to enter into phase I or II clinical trials that test new approaches to therapy. Some of these studies are carried out within the COG, some within a multi-institutional consortium funded by the National Cancer Institute known as the New Approaches to Neuroblastoma Therapy (NANT) Consortium, and some within individual institutions. Examples of such studies are included in Table 1 below. Because the toxicity (especially the long term toxicities) of these new therapies are not fully known, and because the ability of these therapies to improve outcome for patients is not proven, many of these new approaches are limited to testing in patients with recurrent disease.

Table 1: Modalities of Therapy Currently in Clinical Trials for High-Risk Neuroblastoma.

Induction chemotherapy. Chemotherapy that doesn't require marrow or PBSC support. Examples of drugs used include cyclophosphamide, cisplatin, carboplatin, vincristine, doxorubicin, etoposide, ifosfamide, and topotecan.

Surgery: Partial or total surgical removal of the tumor.

Local Radiation: Radiation given to a localized area that includes the tumor.

Myeloablative Therapy: Very intensive chemotherapy or chemotherapy + total body irradiation that destroys the marrow cells, requiring the infusion of marrow or PBSC to restore marrow function. Myeloablative therapy approaches currently being tested include those with intensive chemotherapy, those with intensive chemotherapy + local irradiation, and multiple rounds of myeloablative therapy (tandem transplants).

Antibody Therapy: Administration of a monoclonal antibody that attaches to tumor cells, often together with factors called cytokines that stimulate white blood cells (attached to the tumor via the antibody) to kill the tumor cell. Examples of antibody therapy include the ch14.18 antibody, the 3F8 antibody, and a new designer molecule (called an immunocytokine) in which the hu14.18 antibody (an anti-GD_2-antibody) is fused together with the IL-2 cytokine.

Retinoid Therapy: Administration of high doses of a drug that is derived from vitamin-"A", which has an anti-tumor effect. Retinoids usually have very little or no marrow cytotoxicity and so they are employed soon after myeloablative therapy. Accutane (13-cis-retinoic acid) is a retinoid that causes the neuroblastoma cells to stop growing and differentiate (mature) into more normal appearing cells. Fenretinide is a newer retinoid that, rather then inducing tumor cell differentiation, kills neuroblastoma cells.

MIBG: Administration of high doses of a radioactive chemical selectively taken up by neuroblastoma cells. The MIBG molecule is made with radioactive iodine (^{131}I), which is why the thyroid has to be protected during such therapy. The concentration of the MIBG at the tumor results from the tumor pulling in the MIBG, concentrating the radiation into the tumor. This provides very high doses of radiation to the tumor cells.

Vaccine Therapy: Injection of substances into patients that are designed to stimulate the immunological system to attack the tumor. Examples of such vaccines include tumor cells that have been engineered to make cytokines (those molecules that stimulate the immune system) or antibodies that are designed to elicit an antibody response that will attack the tumor. Antibodies produced by the patient in response to the vaccine could be effective in attacking neuroblastoma cells. Such antibodies are known as "anti-idiotypic antibodies". Another approach being tested involves genetically engineering neuroblastoma cells so that the tumor cells make a cytokine, irradiating those cells to prevent them from forming tumors, and injecting those cells into the patient to stimulate the immune system.

Resources for Further Information. The internet provides a medium for rapid exchange of information. The following are just some of the information resources available to parents of children with neuroblastoma on "the net":

The NBLASTOMA mailing list is an automated email mailing list where parents of children with neuroblastoma can communicate with one another. In addition to being able to join the list, one can find the archives of the list (which contains a lot of information and discussion in previous posts to the list). The list web site is: **www.acor.org/n-blastoma.html**

National Cancer Institute (NCI) site devoted to cancer clinical trials: **www.cancertrials.nci.nih.gov**

The COG web site: **www.members.childrensoncologygroup.org**

The NANT web site: **www.nant.org**

The Neuroblastoma Hope Foundation has a web site which contains a lot of information on neuroblastoma and links to other sites: **www.acor.org/nbl/**

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The "Crown" We Wear

by Jocelyn Brent

A crown, of sorts, is placed upon our heads when we enter this world of cancer. A crown for all to see. Tarnished, dinged, bent - yet, it must be worn with grace and dignity. All who know us will see us with it.

Each member of our family had this crown bestowed upon them in the spring of 1995. Our youngest son, Jon, was diagnosed with standard risk leukemia at three years of age. Our older son, Clayton, became the brother of a child with cancer. What a role that was to be! He began this role at six years of age. And, at just seven years into our marriage, my husband Tom and I became the parents of a child with cancer.

Our crown garnered many reactions like... "Oh look at how strong they are wearing that crown." "I know you are wearing that crown, but, can you get that report out this afternoon?" "That's one big crown for a kid, but, let's see if he can behave a little more appropriately." We concern ourselves about its weight, about how it looks on us, about how we look with it, about its appearance, about our appearance, about how we want to take it off. Once it is placed on our heads, so many lives changed.

Yet, when we take a look at this crown, really look, we see jewels. After all, they shine brighter than the tarnish. Each struggle, each angel in our path, each neighbor who has cut a lawn, each repairman who has "forgotten a bill', each anonymous phone card, every lesson we teach, every lesson we learn, the jewels that our crowns are adorned with are its beauty.

Jon relapsed and needed a bone marrow transplant. He needed a bone marrow donor, and his brother was not a match. This meant that Jon's only chance for survival was to find a matched unrelated donor on the bone marrow donor registry. We received a miracle when we were told that there was a perfect match. Jon received his bone marrow transplant in November 1998, on his fathers 40th birthday. After an ongoing struggle with graft vs. host disease which was finally brought under control this past December, we enjoyed our best holiday season ever! Visiting with family and friends had me seeing even more clearly the many jewels we wear on our crowns.

No masks, no "immune-compromised" isolation from those we hold dear. Waking up and feeling great, we were finally able to travel, and travel we did. After a year and a half, we re-visited Jon's transplant center. We were able to see the many smiles and a few tears from those who cared for our family in the most dire of circumstances. How brightly those "jewels" who have helped to care for us shine - those who have helped us in Jon's beginning years, and those who have come to our aid during these past years of complications. These are the people who have seen our suffering at its worst. They know so intimately the burden of the crown we wear. At all times, their caring was constant and steadfast. These are the jewels that glowed with compassion, kindness, wisdom and support. They are so very precious, and they help us to wear our crown with dignity.

How wonderful it was for them to see Jon and all of our family. They saw a young boy with hair, wearing regular clothes, jumping about, spouting off jokes to his favorite nurses, with a glorious twinkle in his eye. They saw a growing family (Clayton at 5' now!). They saw joyful parents. They saw the lives that they affected. How gracious they were to have thanked us for coming by; for showing them the reason why they do what they do every day.

And, we met our most brilliant jewel – Melissa. She donated her bone marrow to my son Jon. She is bright and vibrant. She has a quick smile and a loving heart. Melissa joined the unrelated donor registry at age 18, for a drive for a young girl in her area. It was the first time she had ever given blood. She's a "Big Sister," and a volunteer in a Grade 3 classroom (the same grade Jon is in). She is 22 now, and just finishing college. She is training to be a teacher, but in so many ways, she already is one. She teaches faith and hope in the future, by her living example of selfless generosity.

The whole meeting was wrought with coincidences. Tom's aunt teaches at a college near where Melissa lives. Melissa has a friend who Tom's aunt taught. This friend brought in a newspaper article to Tom's aunt, knowing that her nephews son had just had a bone marrow transplant. The article was about her friend, Melissa, who had just donated her bone marrow to a stranger. They knew that the recipient was a six year old boy. Jon was six at the time of his transplant! The article was printed on December 1. My birthday. The name of the street Melissa lives on - John Street!

Seeing Jon and Melissa together helped me to once again see the enormity of her gift. There are so many shining moments of joy we have lived these past years. Of course, there has been struggle beyond anything I could convey. There has been suffering beyond anything I could have fathomed, but, there is such profound joy in our every day. Every path of every life we each have crossed, while wearing our crowns - bear witness to these past days…

We haven't found a way to take our crowns off. They are just there now. Somewhat askew. At times banged up and dingy. So very heavy, so much so that their weight has been unbearable some days...
But brilliant … brilliant with jewels.

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Gold Ribbons for Childhood Cancer

Order on the web at: www.goldribbons.org
Or contact Gigi at:
(801) 944-2464 Fax: (801) 944-0209
Email: gigi@lgcy.com
8814 Oak Valley Dr., Sandy, UT 84093
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This gold ribbon pin is the symbol of Childhood Cancer Awareness representing our children:

- ♥ It is a precious metal, as are our children;
- ♥ it is the flame of hope;
- ♥ it is the purity of our children's hearts.

The childhood cancer awareness gold ribbon campaign was started in 1997 by Gigi Thorsen in memory of her daughter Kelsey's battle with cancer. Since 1998 she has distributed over 50,000 gold ribbon pins. The campaign has been embraced by Candlelighters Childhood Cancer Foundation, parents of children with cancer, pediatric oncology treatment facilities, affiliated foundations and friends of children with cancer worldwide. Please wear the gold ribbon and support Childhood Cancer Awareness.

We welcome letters to the editor: poetry, photos, short stories, and other material from readers.
Articles are selected for space and may be edited. Please write your name and address on the back of any photo that you would like returned to you.

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We're on the Web www.candlelighters.org

Link to Candlelighters Childhood Cancer Foundation Website at: http://www.candlelighters.org to find the latest copy of our quarterly newsletter, our mission statement, publications list, local group information and membership sign up form.

Email us at: info@candlelighters.org

We encourage you to continue to visit the site regularly as new links to affiliated organizations and other health-related websites are added regularly.

"Dream as if you'll live forever. Live as if you'll die today."
James Dean