# The CNCF Handbook for Parents of Children with Neuroblastoma





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# Acknowledgements

This handbook is an evolving work that we hope will be available to guide parents through their children's treatment for neuroblastoma until the day a cure is found. It has been "in the making" for many months, from its genesis in discussions over a bottle of wine, through telephone conferences and countless emails, to this on-line (and printable) document, which will continue to grow. Along the way, numerous members of the NB community have contributed their ideas, time, and talents to this project. Indeed, too many people have contributed for us to list their names here. We hope all the NB parents who find this resource will share their insights into how to cope with the daily challenges of NB treatment. Thank you from CNCF to all of those who have helped so far and all who will help in the future. We are very grateful to have you on our team!

Please contact editors@nbhope.org with any comments



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# Navigating Neuroblastoma and this Handbook (Read this First!)

Dear Parents in the NB Family,

This handbook has been prepared for you by parents of children who are or have been in treatment for neuroblastoma. We understand that there is no pain like hearing the word "cancer" used in connection with your child. Each of us has struggled to understand what it means to have our child diagnosed with a disease we had never heard of before, and to obtain the information we needed to manage our child's treatment. Having been there, we want to offer you hope and tools to make this journey easier.

Although at this time you may feel overwhelmed and even helpless, there **are** things you can do to help your child and your family weather this crisis. Parents almost always express a sense of empowerment when they learn as much as they can about neuroblastoma and its treatment. We have developed this parent handbook to share what we have learned through our experiences fighting neuroblastoma. We have worked together to pool our collective wisdom about things a parent or other primary caregiver needs to know, so you won't have to spend hours running down resources. We have assembled information that helped us cope and make informed decisions about our children's treatment--information we hope will help you as well. Our goal is to ease your learning and allow you to spend more time concentrating on what really matters—your child and family.

#### **About Neuroblastoma**

Neuroblastoma (NB or NBL) is the most common solid tumor cancer found in infants, but that does not make it a common disease. Although about 1.4 million cases of cancer are diagnosed in the U.S. each year, fewer than 1% are in children. Of approximately 13,000 new cases of childhood cancer in the U.S. each year, only about 650 are neuroblastoma. **See Chapter 1 "What is Neuroblastoma?"** 

Understanding that neuroblastoma is a rare disease is important. Some pediatric oncologists see very few neuroblastoma patients in an entire career. You are entitled to ask how many neuroblastoma patients your hospital treats, and to consult with pediatric oncologists and surgeons who specialize in neuroblastoma. You have the right to get all your questions and concerns answered to your satisfaction. **See Chapter 1 "Questions for Your Doctors"; "U.S. Neuroblastoma Specialists"; and "Patients' Rights and Responsibilities."** In addition to determining where and by whom your child should be treated, you may be faced with the decision of whether or not to enroll your child in a clinical trial. For many stages of this disease, the most promising treatments are available only through clinical trials. **See Chapter 1 "What is a Clinical Trial?"** 

Treatment for neuroblastoma is determined based on a number of indicators that, taken together, determine the degree of risk—low, intermediate or high. In addition, there is a special low-risk category that some infants fall into known as 4s. **See Chapter 1 "What is Neuroblastoma?"** Children with low or intermediate risk neuroblastoma generally have a good prognosis and can be treated successfully by most pediatric oncologists. Treatments for these stages of disease range from "wait-and-see"—monitoring the tumor with periodic scans to see if it regresses on its own—to

surgical resection and some chemotherapy. See Chapter 2 "Overview of Low- and Intermediate-Risk Treatment."

Half of all neuroblastoma diagnoses—about 350 cases per year in the U.S.—are classified as high risk. These children undergo aggressive, multi-agent therapy that includes chemotherapy, surgery, often some form of myeloablative therapy (transplant or targeted radiation treatments requiring stem cell rescue), radiation, differentiation therapy (e.g., Accutane), and often antibody treatments. **See Chapter 2 "Overview of High-Risk Treatment."** 

Neuroblastoma is most commonly diagnosed before age five. Diagnoses at later ages may present unique treatment challenges, because younger children can tolerate more aggressive treatment than teenagers and adults. Because of these differences, we have included a section on issues specific to teenagers and adults undergoing treatment. **See Chapter 3 "Special Issues for Teenagers and Adults."** 

At the current time, at least 20% of children diagnosed as high risk have "refractory" disease that is resistant to initial treatment, and over one third of those who reach remission—also referred to as NED, or "No Evidence of Disease"—will relapse and require additional treatments. Parents of a child with refractory or relapsed neuroblastoma may be faced with difficult and confusing choices. Because refractory or relapsed neuroblastoma tends to respond differently in each child, there is no agreed upon course of treatment, even among NB specialists, so parents must research available treatments and seek advice from many sources. **See Chapter 7 "Treating Refractory NB"; and Chapter 8 "Dealing with Relapse."** 

Because the risk of relapse remains significant after treatment for high-risk disease, additional treatment is important after children have reached NED. Some treatments are geared specifically toward eliminating microscopic disease, often called minimal residual disease (MRD), that standard testing may not be sensitive enough to detect. Some parents also consider the feasibility of alternative medicine. We have provided resources on this topic to help you explore the available options. See Chapter 5 "Reaching Remission"; and Chapter 11 "Utilizing Complimentary and Alternative Medicine."

Children treated successfully for neuroblastoma continue to require medical care and monitoring. We have included information on the more immediate concerns you may have once your child reaches NED, **see Chapter 5** "Reaching Remission," and a guide to resources addressing issues related to long-term follow-up care after treatment. **See Chapter 6** "Living with Long-Term Survivorship Issues."

# Your Role as Caregiver

As you have probably already discovered, the parent or primary caregiver of a child with cancer plays a critical role in the child's treatment. You are an integral part of the medical team. The doctors are the experts on medical issues, but **you** are the expert on **your child**.

You can help ensure that your child gets the best possible care by working closely with the medical team. How to do this appropriately is not always obvious. Cancer centers and hospitals with oncology departments are generally large institutions with complex, sometimes intimidating, bureaucracies. We have provided a brief overview of the typical hospital structure to introduce you to the different professionals you will meet and some common practices. **See Chapter 1 "The World of Hospitals."** 

Understanding the way hospitals work and the responsibilities of the various hospital professionals will help you cooperate better with your child's medical team. You will also be more effective if you can "speak the language" when you discuss your child's diagnosis, treatment, and daily well-being. The detailed information about neuroblastoma, its diagnosis and treatment in this handbook can help you do this. See Chapter 1 "What is Neuroblastoma?"; Chapter 2 "Understanding the Basics of Frontline Treatments"; Chapter 14 "Neuroblastoma Terminology."

You will also need to be familiar with the many different tests and scans used to diagnose your child and measure his or her response to treatment. These tests will be repeated about every 3 months during your child's treatment and periodically for several years thereafter. **See Chapter 4 "Getting Through Tests & Scans."** 

You are entitled to copies of test results and other reports for your child. It is important that you keep copies of all test and scan results, and the clinical summary of your child's diagnosis and protocol or clinical trial. See *Chapter 10* "Why Keep Records?" However, you do not need to keep copies of daily reports such as nursing notes, temperature charts or print outs of blood counts (which eventually may number hundreds of pages), if you maintain records sufficient to allow you to monitor your child's daily progress. Recordkeeping charts that you can download or print out and use for this purpose, along with explanations of common abbreviations and terms used by medical professionals, are included in the "Keeping Records" section of this handbook. *See Chapter 10* "Keeping Records." Because many different professionals will be responsible, often on a rotating basis, for your child's treatment, such records will be invaluable when updating doctors and nurses (as well as other family caretakers) on your child's status. You will be the medical team's most important source of information regarding your child's health.

A crucial part of your role will be finding ways to help your child cope with the rigors of cancer treatment, especially if your child is undergoing the aggressive treatment required for high-risk neuroblastoma. Chemotherapy, radiation, surgery, tests and scans, taking pills or liquid medicines, getting shots – these will be a part of your child's daily life. These invasive measures may cause nausea, fever, infections, hives, pain, or other side effects, as well as anxiety, anger, depression, or fear. Each child's reactions are different. We have drawn upon our collective experiences to provide you with information and tips that have helped parents not only manage their children's medical needs, but also keep their children feeling as safe, comfortable, and happy as possible. **See Chapter 3 "Coping with Treatment: Side Effects, Comfort, and Safety."** 

You may also need to help the medical staff perform the delicate balancing act of administering difficult treatments to your child without infringing on his or her dignity. The daily work of an oncology professional is understandably full of time pressure and emotional stress, and pediatric patients can be particularly challenging. Because maintaining your child's emotional well-being and sense of security is essential, we have included some guidance on ways to advocate for your child. **See Chapter 3 "Advocating for your Child."** 

Many have observed that when a child has cancer, the entire family has cancer, and we have found this to be true. The struggles of a child in treatment affect siblings, parents and even extended family members in many ways. The issues range from brothers and sisters having problems at school, to difficulties on the job or in the marriage, to insurance and other financial problems. We are not professional counselors, of course, but we have included some tips that helped our respective families weather full-time cancer treatment, **see Chapter 9 "Managing Emotions,"** as well as a list of support resources that have been useful to many of us. **See Chapter 13 "Support Resources."** Most of us have found that one of the most valuable resources for parents is – each other! You can join an on-line support group for parents of children with neuroblastoma by subscribing at http://www.acor.org/n-blastoma.html.

Finally, while it is our fervent hope that you will never need to turn to it, we have included information on hospice, pain management, and other end of life issues, as well as information on support groups for grieving parents and family members. See Chapter 12 "Turning to End of Life Care."

The path your family has embarked on is one that few have to travel. Like childbirth, there is no way out of it but through it. It will test your strength in ways you never imagined, and you will push yourself to do things you never dreamed you could. But along this path you will also find more companionship, understanding, and love than you ever thought possible. Your perspective on life, and its priorities, will never be the same. We know there are many things you must discover on your own, but we hope this handbook will be a useful source of information and support to you during your child's treatment for neuroblastoma. You are not alone!

Please contact <a href="mailto:editors@nbhope.org">editors@nbhope.org</a> with any comments



### WHAT IS NEUROBLASTOMA?

# Part 1: Description, Diagnosis and Staging

Upon learning their child has neuroblastoma (NB), many parents feel confused, frightened, and overwhelmed. Suddenly, obscure scientific terms are being used to describe their child's situation, his or her treatment, and even the possibility of cure. The best source of information about your child's cancer is *always* his or her oncology team. However, many of us have found that some additional background information about NB makes it easier to understand this new world.

Because NB is a complex disease, we have divided this explanation into three parts: Part 1 provides general information about NB, its diagnosis, and staging; Part 2 covers the factors used to determine risk assignment, including NB tumor pathology and genetic makeup. Finally, Part 3 summarizes the risk assignment categories and how they relate to a treatment plan.

# Description

### Neuroblastoma is a solid tumor cancer of the sympathetic nervous system.

Neuroblastoma is a solid tumor—a lump or mass—originating from neural crest tissue that is part of the sympathetic nervous system (SNS). This part of the nervous system is responsible for the "fight or flight" response when stress occurs. Nerves of the sympathetic nervous system run parallel along the outside of the spinal column and connect to organs. Since NB arises at the interface between the nervous system and the endocrine system (the hormone producing organs—NB is one of the few cancers that secrete hormones), it is also included in the class of neuroendocrine tumors.

The most common place for NB to originate is on the adrenal glands located above each kidney (40% of localized tumors and 60% of wide-spread disease). NB tumors can also develop in nerve tissues in the neck (1%), chest (19%), abdomen (30% non-adrenal), or pelvis (1%)—anywhere along the chain of the sympathetic nervous system. In rare cases, no primary tumor can be discerned. See visuals of the nervous system and the adrenal glands.

"Neuro-" indicates origin in nerve cells, and "blast" means immature cells. *Normal* "neuroblasts" (baby nerve cells) begin in embryonic tissue and grow and mature into functioning nerve cells. Neuroblast*oma* means the immature cells reproduce forming a mass and do not develop into functioning cells (the "-oma" ending denotes a tumor). NB is *not* a cancer of the central nervous system (CNS) and it is not a brain cancer, but occasionally NB metastasizes to the CNS. There are over 50 kinds of pediatric cancers that fall into 12 main categories, one of which is the sympathetic nervous system cancers. NB accounts for more than 97% of all sympathetic nervous system cancers.

#### NB is a very rare cancer.

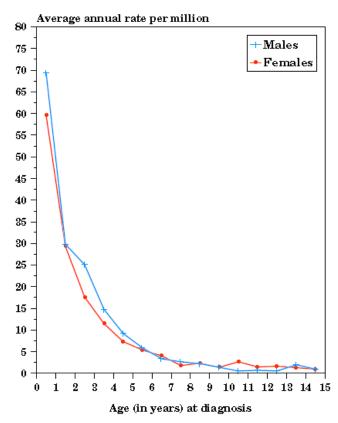
Of approximately 13,000 new cases of childhood cancer in the U.S. each year, only about 650-700 are neuroblastoma. There is similar incidence in other countries and no clear differences between ethnic groups.<sup>3</sup> About 55% of all NB patients are boys.

Understanding that NB is a rare disease is important. Many pediatric oncologists see few NB patients. You are entitled to ask how many NB patients your hospital treats, to consult with pediatric oncologists and surgeons who specialize in NB, and to get all your questions and concerns

answered to your satisfaction. See "Questions for Your Doctors"; "U.S. NB Specialists"; and "Patients' Rights and Responsibilities."

# NB is a pediatric cancer.

Neuroblastoma generally develops in young children—half of all cancers diagnosed in infants are neuroblastomas. The median age at diagnosis is about 2 years old. Numerous children are diagnosed after age 2, but the number of diagnoses decreases as age increases. Adult diagnoses of NB account for less than 2% of all cases.<sup>4</sup> The figure below shows the relationship between age and incidence:<sup>5</sup>



Age-specific incidence rate for sympathetic nervous system cancers (SEER)

#### No one knows the cause of NB.

Although the cause of NB is unknown, most physicians believe it is an accidental cell growth that occurs during normal development of the sympathetic nervous system. Only 1-2% of all cases are hereditary, and a particular genetic mutation (ALK) has been implicated in most of those cases.<sup>6</sup>

#### NB varies greatly in its behavior and prognosis.

NB exhibits a wide range of behavior. Some neuroblastomas with favorable characteristics may just go away without treatment (spontaneously regress) in infants. Other neuroblastomas with unfavorable characteristics may resist very intensive multimodal treatment, and in these cases, NB is known as one of the most aggressive and difficult to cure childhood cancers. While only 4% of all childhood cancers are the high-risk form of NB, it is responsible for 15% of all pediatric cancer deaths.

More than half of NB patients have disease at diagnosis that has already spread (metastasized) to other parts of the body. The most common locations of metastases at stage 4 diagnosis are bone (66%), bone marrow (87%), lymph nodes (19%), and liver (17%); less common are lung (5%) or brain

(9%) metastases. Stage 4S include bone marrow (61%), liver (76%) and skin (12%) metastases. <sup>7</sup> NB is just one of the tumors included in the class of "peripheral neuroblastic tumors" or pNTs. Although all pNT tumors arise from the same tissue, they range in character from highly malignant NB to benign "ganglioneuroma." Looking closely at the structure and form of the tumor under a microscope (its "pathology"), as well as determining certain genetic information inside the tumor cells, gives more information about the sub-type of neuroblastoma and its risk level (see following sections, "**Tumor Pathology and Genetics"** and "**Risk Assignment"**).

# NB differs fundamentally from adult cancers.

NB is fundamentally different from adult cancers – it arises in different tissues, has strikingly different characteristics, and its cause is unknown. This fact is helpful to remember when well-meaning people want to share their expertise from fighting breast, colon, lung, or prostate cancer—most of their experience simply does not apply to neuroblastoma.

#### **Diagnosis**

#### Symptoms of NB mimic common childhood illnesses.

Since NB is rare, most pediatricians have never seen a single case, and often the diagnosis is finally made only after a long trying period. Children may have a variety of symptoms such as irritability and low-grade fever that mimic common illnesses and viruses, or diseases such as juvenile rheumatoid arthritis that cause joint pain. Symptoms depend on where the tumor originates and if it has spread. For example, children with a tumor in the abdomen may have a swollen abdomen, constipation, vomiting, or diarrhea. A child with a tumor on the spine may stop crawling or walking, or may have weakness or paralysis. A tumor in the chest may cause breathing difficulties. A child whose disease has spread to bones may have black eyes, bone pain, bruises, fever, paleness, and may limp or stop crawling or walking. A tumor in the neck may cause different pupil size and sweating or redness on one side of the face ("Horner's syndrome"). In very rare cases, a child has an immune response known as opsoclonus myoclonus syndrome, or OMS, causing rapid eye movements and jerky muscle motions (2% of all NB cases).

#### NB can be difficult to diagnose.

Once the pediatrician or other doctor rules out other diseases and suspects cancer, the child is referred to a pediatric oncologist to determine the diagnosis.

NB can be difficult to diagnose because it is one of several small round blue cell tumors (such as acute leukemia, Ewing's sarcoma, Wilm's tumor, and rhabdomyosarcoma) that look identical under a microscope. To make a diagnosis, doctors look at a variety of scans and the results of blood and urine tests, as well as biopsies from the primary tumor or other sites of disease, such as the lymph nodes or bone marrow.

A biopsy of the primary tumor is preferred because certain information about the disease can only be derived from the primary tumor before chemotherapy treatments begin. The pathologist looks at the biopsy of the primary tumor under a microscope and grades the tumor as favorable or unfavorable by the structure and form of the cells (called histology or biology). See "Tumor Pathology and Genetics" for more on pathology of NB cells. Biopsy samples may be a prerequisite for some treatment protocols. If a biopsy of the primary tumor is not feasible, a definite diagnosis of NB can be made from a biopsy of tissue from metastases (such as lymph nodes or bone marrow) if certain "markers" in the urine known as "catecholamines" are also elevated.

Your child's doctor will likely want some or all of the following tests and scans:

Urine tests

- Blood tests
- X-rav
- Ultrasound
- CT scan
- PET scan
- MRI
- Bone scan
- MIBG scan
- Bone marrow aspiration and biopsy
- Lumbar puncture (LP) is NOT performed if NB is suspected

These tests and scans are required to determine the location and size of the primary tumor, the extent of spread (stage), and elevated disease markers that may be present in blood or urine. Lumbar puncture may cause spread of NB into the CNS (spinal canal or brain). Additional tests are required for baseline organ function. These tests are explained in more detail in the chapter "Getting Through Tests and Scans."

#### Staging

The treatment a child receives for neuroblastoma is dependent on placement in a risk group. Risk is determined by age, tumor characteristics (pathology and genetics), and stage--the extent to which the disease has spread. Disease stage is determined according to the International Neuroblastoma Staging System (INSS), developed in 1988 and last revised in 19938. The staging system is currently under revision by the International Neuroblastoma Risk Group (INRG) task force; see **Appendix** to Part 3. The diagnostic tests listed above help doctors assign the child's disease to one of the following INSS stages (percentages of each stage are taken from North America data on 1253 NB cases<sup>9</sup>):

#### ■ Stage 1 – 21%

The tumor is confined to one area of origin and can be completely removed through surgery. Although microscopic residual disease may remain after surgery, identifiable lymph nodes on both sides of the body are negative for NB.

#### Stage 2 - 15%

2A - The tumor is confined to one area but because of size, location, or proximity to other organs, cannot be completely removed. Identifiable lymph nodes on both sides of the body are negative for NB.

2B - The tumor is confined to one area and may or may not be completely removed. Identifiable lymph nodes on the side of the body where the tumor is located are positive for NB, but lymph nodes on the opposite side of the body are negative for NB.

# ■ Stage 3 – 17%

The tumor crosses the midline of the body (defined as the spine) and may or may not have spread to nearby lymph nodes; OR

the tumor is confined to one area of the body with disease in lymph nodes on the other side of the body; OR

the tumor is located crosses the midline with disease in lymph nodes on both sides of the body

# Stage 4 – 41%

Neuroblastoma is found in distant lymph nodes, bone marrow, bone, liver, or other organs (except in the special circumstances of Stage 4S, explained below). Indication of presence of NB cells by immunocytology alone (no visible tumor cells in bone marrow biopsy or aspirate) does not classify a child as stage 4.10

# ■ Stage 4S – 6%

Usually in infants, the tumor is confined to one area of the body, like a Stage 1 or 2 tumor, but disease has spread to only the liver, skin, or less than 10 percent of the bone marrow (no bone lesions).

# Summary

NB is a rare solid tumor cancer of the sympathetic nervous system. It has no known cause, primarily affects infants and young children, and is often difficult to diagnose. A variety of tests are needed to identify the disease and the extent of spread. Neuroblastoma varies greatly in its behavior and severity, and treatment is based on risk assignment, not stage. The next section, "Tumor Pathology and Genetics," discusses some of the very technical scientific information used to determine risk assignment. The final section, "Risk Assignment," sets forth the three risk assignment categories and their relation to treatment intensity and outcome.

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Please contact editors@nbhope.org with any comments

<sup>&</sup>lt;sup>1</sup> Friedman GK, Castleberry RP. <u>Changing Trends of Research and Treatment in Infant</u> Neuroblastoma Pediatr Blood Cancer 2007;49:1060–1065

<sup>&</sup>lt;sup>2</sup> SEER Pediatric Monograph, Introduction, NCI

<sup>&</sup>lt;sup>3</sup> Stiller CA, Parkin DM (October 1992). "International variations in the incidence of neuroblastoma". Int. J. Cancer 52 (4): 538–43. <a href="PMID 1399133">PMID 1399133</a>

<sup>&</sup>lt;sup>4</sup> Ladenstein R, Pötschger U, Hartman O, *et al.* (June 2008). "<u>28 years of high-dose therapy and SCT for neuroblastoma in Europe: lessons from more than 4000 procedures</u>". *Bone Marrow Transplant.* 41 Suppl 2: S118–27. <u>PMID 18545256</u>.

<sup>&</sup>lt;sup>5</sup> Sympathetic Nervous System Tumors, SEER

<sup>&</sup>lt;sup>6</sup> Mossé YP, Laudenslager M, Longo L, *et al.* (October 2008). <u>Identification of ALK as a major familial neuroblastoma predisposition gene</u>. *Nature* 455 (7215): 930–5. <u>PMID 18724359</u>.

<sup>&</sup>lt;sup>7</sup> Cheung & Cohn, *Neuroblastoma*, Springer (2005), p. 70

<sup>8</sup> Cheung & Cohn, Neuroblastoma, Springer (2005), p. 151

<sup>&</sup>lt;sup>9</sup> Cheung & Cohn, Neuroblastoma, Springer (2005), p. 74

<sup>&</sup>lt;sup>10</sup> Cheung & Cohn, Neuroblastoma, Springer (2005), p. 71



# WHAT IS NEUROBLASTOMA?

# Part 2: Tumor Pathology and Genetics

NB is sometimes referred to as a "heterogeneous" disease because of the wide range in its behavior in different children—some NB tumors with favorable characteristics go away on their own (regress), some mature into a benign growth (ganglioneuroma), and some with unfavorable characteristics grow and spread rapidly. The pathologist's job is to try to identify which type of NB tumor your child has. This information, together with the child's age and the stage of his or her disease, is used to determine the degree of risk for the child's specific situation. The resulting risk assignment enables the oncologist to prescribe the right treatment for your child's disease—not too much, but not too little.

The scientific information used to determine risk assignment for NB is very technical in nature; understandably, some parents are content just knowing their child's risk assignment and the resulting treatment required. The various categories of "risk assignment" are described in Section 3 following. For those who wish to know more, this section summarizes the various types of pathology and genetic information used to determine the risk category of specific disease profiles. Each term used in the criteria for risk assignment is explained in more detail as well.

NB risk assignment is dependent on four distinct factors:

- 1. age of the child;
- 2. stage of the disease;
- 3. pathology of the tumor; and
- 4. genetic make-up of the tumor.

Each factor has significance (favorable or unfavorable) but no factor alone can determine prognosis. The *combination* of this information dictates the risk group assigned and the treatment your child will receive.

Since it takes some time to get the pathology and genetic analysis (sometimes referred to as "cytogenetics") from the biopsy of the primary tumor, oncologists will often begin treating (surgery and/or chemo) very sick children before all of this information is obtained, rather than waiting for a final risk assignment, which can take a week or more.

### 1. Age of child.

Generally, the younger the patient is, the lower the risk assignment. For example, infants under 12 months with a certain pattern of metastasized disease are classified as low risk. Similarly, children aged 12-18 months with metastasized disease and other certain favorable tumor characteristics are classified as intermediate risk. In contrast, children over the age of 18 months with the same factors would be classified as high risk.

#### 2. Stage.

In children over 18 months old, the stage of the disease is one of the most important determinants of the child's risk group. Generally, localized disease is better, since getting rid of systemic disease can be more difficult.

# 3. Pathology of the tumor.

Another type of information used to determine risk classification is the pathology of the tumor after a sample (biopsy) is obtained. The pathologist determines whether the tumor has favorable or unfavorable "histology"--an analysis based on what the primary tumor cell structure looks like to the pathologist's eye and under a microscope. (Note that the "pathology," "histology" and "biology" of the tumor are often used as interchangeable terms.) Determination of histology as favorable or unfavorable is based on two factors: tumor grade and MKI.

**Tumor Grade.** NB is classified as one of the "peripheral neuroblastic tumors" or pNTs. Although they arise from the same tissue type, these tumors can behave very differently depending on the structure and genetics, and are graded accordingly. They range in character from highly malignant neuroblastoma to benign ganglioneuroma. Tumor grade is determined from a biopsy of the tumor obtained before treatment and based on the International Neuroblastoma Pathology Committee (INPC), also referred to as the "Shimada Classification," developed in 1999¹ and revised in 2003.² The pathologist looks for the proportion of non-cancerous structural cells called "stroma" (also known as "Schwannian" cells) and the degree of maturity (differentiation) of neuroblastic cells, and assigns one of the following tumor grades:

- NB (Neuroblastoma): stroma-poor, undifferentiated, poorly differentiated, or differentiating;
- GNBi (Ganglioneuroblastoma intermixed): stroma-rich, intermixed with Neuroblasts;
- GNBn (Ganglioneuroblastoma nodular): stroma-rich, nodules of neuroblasts; or
- GN (Ganglioneuroma): stroma-dominant, benign.

Ganglioneuroma (GN) is a benign tumor. Ganglioneuroblastoma (GNB) is essentially a benign tumor with less than half cancerous cells mixed in (GNBi) or nodules (GNBn) of cancerous cells visible--this tumor "mix" is considered malignant. NB is similar, but has less than half the proportion of benign stroma present in GNB, or none at all, and so is a malignant tumor.

**MKI.** In addition to tumor grade (NB, GNBi, GNBn, GN), information about cell division and activity is determined, referred to as the mitosis-karyorrhexis index (MKI). Dividing cells (mitosis) and cells with nuclear fragmentation (karyorrhexis) are counted and the MKI determined as follows:

- low MKI: Less than 2% (100 cells in a sample of 5000 tumor cells);
- intermediate MKI: 2-4% (100-200 cells per 5000 tumor cells); or
- high MKI: 4% or more (200 or more cells per 5000 tumor cells).

*Histology*. The above two factors--tumor grade and MKI--together with the child's age, allow INPC classification into two groups: favorable histology (FH) and unfavorable histology (UH):<sup>3</sup>

# Favorable Histology

- all ganglioneuroma (GN) and ganglioneuroblastoma intermixed (GNBi);
- ganglioneuroblastoma nodular (GNBn) with 50% or more Schwannian cells;
- neuroblastoma (NB), poorly differentiated or differentiating, intermediate MKI, under 18 months old; or
- neuroblastoma (NB), under 5 years old, differentiating, low MKI.

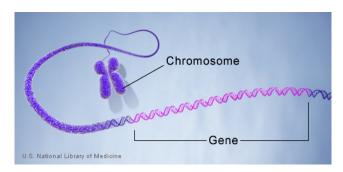
# Unfavorable Histology

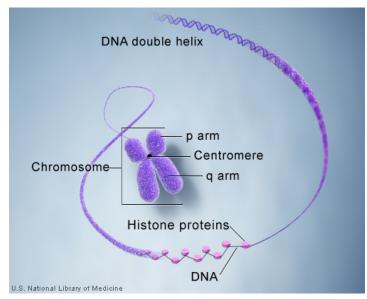
- ganglioneuroblastoma nodular (GNBn) with less than 50% Schwannian cells:
- neuroblastoma (NB), undifferentiated;
- neuroblastoma (NB), high MKI;
- neuroblastoma (NB), poorly differentiated or differentiating, intermediate MKI, over 18 months; or
- neuroblastoma (NB), differentiating, low MKI, over 5 years old.

This complex scheme enables pathologists to decide if the tumor has favorable or unfavorable characteristics, but this information *alone* does not determine prognosis or treatment intensity. It is used along with age, stage, and genetics to assign risk for treatment purposes. The next section, **"Risk Assignment,"** shows that favorable or unfavorable histology makes a difference in risk assignment in some situations, such as stage 3 or 4 disease, but not in others, such as stage 1 or 2.

# 4. Genetic Make-up of the Tumor.

NB tumors act differently depending on genetic information coded inside the nucleus of the tumor cell. A cell has very long chains (about 5 feet) of compacted DNA within its nucleus. The DNA is wound up into strands like coiled rope and packaged in the chromosomes. Each chromosome has two short "p arms" and two longer "q arms," and hence is shaped like an X. Each place on a chromosome holds genetic information that pertains to the expression of a trait, and each piece of information on a chromosome is a gene. *See* illustrations below.





The presence or absence of certain genetic information in an NB tumor cell is another factor used to determine risk category. Two types of genetic information currently considered relevant are "ploidy" and "MYCN."

**Ploidy.** As noted, all dividing cells share genetic information through chromosomes, the "package" for DNA. Two copies of the DNA is normal in healthy cells and is called "diploidy" or a DNA index of 1.0. Diploidy is a poor prognostic factor for neuroblastoma and indicates higher risk disease. Three copies of DNA (DNA index 1.5 or DNA index > 1) in an NB cell is favorable, and is called triploidy (or hyperdiploidy).

**MYCN.** Another genetic factor considered in risk assignment is MYCN (also written N-myc). MYCN is a type of oncogene--a gene with a DNA sequence that causes cancer. MYCN is unfavorable factor—when there are more than 10 copies present, the NB tumor is referred to as MYCN amplified. MYCN is commonly multiplied, by 100 times, and has been found as high as 700 times in an NB cell. About 20% of all NB cases have MYCN amplification. It is more common in widespread disease than localized tumors. MYCN amplification is found in less than 10% of stage 1 & 2 cases, in about 10% of stage 4s, and in about 30% of stage 3 & 4 cases.<sup>4</sup> (Note: MYCN amplification is often found in other cancers such as retinoblastoma, medulloblastoma, and small-cell lung cancer.<sup>5</sup>)

MYCN is an important prognostic factor. Younger children and children with lower stage disease will be treated as high-risk (see the following section on risk assignment) if their tumor is MYCN amplified, but MYCN does not necessarily contribute to a poorer prognosis in high-risk cases because one or more unfavorable characteristics are present in all high-risk cases.<sup>6</sup>

**Other genetic and molecular factors.** Other genetic variables believed to have prognostic value for NB have been identified, but not all are currently used in risk assignment. For example, tumor suppressor genes are believed to be associated with 1p and 3p chromosomes, and deletion of either in the NB is considered an unfavorable prognostic factor, as well as loss of 11q or gain of 17q.<sup>7</sup> Currently 1p and 11q are used to further define treatment for intermediate risk.<sup>8</sup> The INRG (International Neuroblastoma Risk Group) will include 11q status in the new risk assignment schema.<sup>9,10</sup>

A host of potential prognostic factors have been studied over the past 25 years, and current consensus is that none add anything significant to current use of age, stage, pathology, ploidy, and MYCN amplification. For example, lack of "trkA" and "CD44" expression on the NB cell surface are also considered unfavorable, but not independently prognostic. <sup>11</sup> TrkA is a high-affinity nerve growth factor receptor, and CD44 is a cell surface glycoprotein (antigen) involved in cellular interactions and homing to bone marrow. Overexpression of CD44 has been noted in the growth and spread in different types of malignancies, such as lymphomas. In neuroblastoma, however, unfavorable tumors often have low CD44 expression. <sup>12</sup>

#### Summary

The information involved in the diagnosis, staging, and prognosis of a rare disease like NB can be overwhelming This section identifies and introduces important factors used to determine the most critical treatment issue: risk assignment, which dictates treatment intensity. The next section, "Risk Assignment," explains how these pieces fit together to determine whether a child receives treatment for low, intermediate, or high risk NB. However your child's oncologist is the definitive source for learning how all of this information relates to his or her particular case.

#### Please contact editors@nbhope.org with any comments

<sup>1</sup> Shimada H, Ambros IM, Dehner LP, *et al* (July 1999). "<u>The International Neuroblastoma Pathology Classification (the Shimada system)</u>". *Cancer* 86 (2): 364–72. <u>PMID 10421273</u>.

Journal of Clinical Oncology, 2007 ASCO Annual Meeting Proceedings Part I. Vol 25, No. 18S (June 20 Supplement), 2007: 9503

<sup>&</sup>lt;sup>2</sup> Peuchmaur M, d'Amore ES, Joshi VV, *et al* (November 2003). "Revision of the International Neuroblastoma Pathology Classification: confirmation of favorable and unfavorable prognostic subsets in ganglioneuroblastoma, nodular". *Cancer* 98 (10): 2274–81.

<sup>&</sup>lt;sup>3</sup> Peuchmaur M, d'Amore ES, Joshi VV, *et al* (November 2003). "<u>Revision of the International Neuroblastoma Pathology Classification: confirmation of favorable and unfavorable prognostic subsets in ganglioneuroblastoma, nodular". *Cancer* 98 (10): 2274–81.</u>

<sup>&</sup>lt;sup>4</sup> Cheung & Cohn, Neuroblastoma, Springer (2005), p. 79

<sup>&</sup>lt;sup>5</sup> Williamson,D et al "<u>Relationship Between MYCN Copy Number and Expression in Rhabdomyosarcomas and Correlation With Adverse Prognosis in the Alveolar Subtype</u>" *Journal of Clinical Oncology*, Vol 23, No 4 (February 1), 2005: pp. 880-888

<sup>&</sup>lt;sup>6</sup> Cheung & Cohn, Neuroblastoma, Springer (2005), p. 80

<sup>&</sup>lt;sup>7</sup> Stallings RL. <u>Origin and functional significance of large-scale chromosomal imbalances in neuroblastoma</u>. *Cytogenet Genome Res.* 2007;118(2-4):110-5.

<sup>&</sup>lt;sup>8</sup> National Cancer Institute, <u>Phase III Study of Response- and Biology-Based Combination</u> <u>Chemotherapy and Surgery With or Without Isotretinoin in Young Patients With Intermediate-Risk Neuroblastoma</u>, COG-ANBL053, opened 2007

<sup>&</sup>lt;sup>9</sup> Friedman GK, Castleberry RP. <u>Changing Trends of Research and Treatment in Infant Neuroblastoma</u> *Pediatr Blood Cancer* 2007;49:1060–1065

<sup>&</sup>lt;sup>10</sup> S. L. Cohn, W. B. London, T. Monclair, K. K. Matthay, P. F. Ambros, A. D. Pearson, for the INRG Working Group. "<u>Update on the development of the international neuroblastoma risk group (INRG)</u> classification schema"

<sup>&</sup>lt;sup>11</sup> Vasudevan SA, Nuchtern JG, Shohet JM. <u>Gene profiling of high risk neuroblastoma</u>. *World J Surg*. 2005 Mar;29(3):317-24. Review.

<sup>&</sup>lt;sup>12</sup> Kramer K, Cheung NK, Gerald WL, LaQuaglia M, Kushner BH, LeClerc JM, LeSauter L, Saragovi HU. <u>Correlation of MYCN amplification, Trk-A and CD44 expression with clinical stage in 250 patients with neuroblastoma.</u> *Eur J Cancer.* 1997 Oct;33(12):2098-100.



#### WHAT IS NEUROBLASTOMA?

# Part 3: Risk Assignment

"Risk assignment" groups children with NB into "good" and "poor" prognostic categories; this is crucial information because different treatment plans are used for each risk group. This section discusses how risk groups are assigned. For more specific information describing the treatment plans for each risk group, see "Understanding the Basics of Frontline Treatments."

NBs range significantly in behavior, from tumors that grow smaller or disappear on their own without treatment (usually in infants), to widespread disease that is difficult to cure in preschoolers and older children and that requires aggressive treatment. The risk assignment systems were developed to group together the children with similar prognoses. The previous sections "**Description**, **Diagnosis and Staging**" and "**Tumor Pathology and Genetics**" cover staging and tumor characteristics. These factors (age, stage, pathology, and genetics) taken together determine the risk assignment (low, intermediate, or high risk), and this ultimately dictates the prognosis and treatment plan.

It is important to note that various study groups have assigned risk differently (as well as having devised different treatment protocols). Currently an international task force is working on a revision to the international staging system (INSS) and devising a new risk assignment system, the "International Neuroblastoma Risk Group" or INRG. *See* more on this revision in the "**Appendix**" to this section as well as the current 2007 COG risk schema.

The discussion here utilizes the Children's Oncology Group risk assignment schema (COG: US, Canada, Australia, New Zealand, Netherlands, Switzerland). This schema refers to stage, age, MYCN status, Shimada Classification (i.e., favorable or unfavorable histology), and DNA ploidy (or DNA index) used by COG to assign risk.<sup>1</sup>

Of all NB cases diagnosed:

- 37% of all NBs are low risk (good prognosis, minimal treatment);
- 18% of all NBs are intermediate risk (good prognosis, moderate treatment); and
- 45% of all NBs are high-risk (poor prognosis, intensive treatment).<sup>2</sup>

This means that in the U.S. every year approximately 260 low-risk cases are diagnosed, 130 intermediate-risk, and 315 high-risk cases (with about 700 total for all groups). A brief overview of each NB risk group follows, with prognosis and treatment intensity compared. (Terms used in the criteria below are discussed in the prior section, "**Tumor Pathology and Genetics**.")

# COG Low Risk (2007 revision)

| INSS<br>Stage | Age           | MYCN amp > 10 copies | DNA ploidy<br>(DNA index)     | Histology<br>(Shimada) | Other           |
|---------------|---------------|----------------------|-------------------------------|------------------------|-----------------|
| 1             | any           | any                  | any                           | any                    |                 |
| 2A or 2B      | any           | no                   | any                           | any                    | > 50% resection |
| 4S            | <12<br>months | no                   | hyperdiploidy<br>DNA index >1 | favorable              | asymptomatic    |

Prognosis and treatment for Low Risk Patients. About 37 percent of all NBs are classified as "low

risk." Many of these tumors are discovered by chance and treatment requires only surgery. Occasionally a "wait and see" approach is recommended because some types of low-risk NB are known to go away on their own. Emergency treatment (surgery, chemotherapy, or radiation) is very individualized if critical symptoms are caused by the tumor, such as compromised breathing or spinal compression. *See* "Overview of Treatment for Low and Intermediate Risk NB." Children diagnosed with low-risk NB have a survival rate as high as 95 percent.

#### COG Intermediate Risk (2007 revision)

| INSS<br>Stage | Age      | MYCN amp > 10 copies | DNA ploidy<br>(DNA index)     | Histology<br>(Shimada) | Other                      |
|---------------|----------|----------------------|-------------------------------|------------------------|----------------------------|
| 2A or 2B      | any      | no                   | any                           | any                    | < 50% resection            |
| 2A or 2B      | any      | no                   | any                           | any                    | bone marrow<br>biopsy only |
| 3             | <12 mo   | no                   | any                           | any                    |                            |
| 3             | ≥ 12 mo  | no                   | any                           | favorable              |                            |
| 4             | <12 mo   | no                   | any                           | any                    |                            |
| 4             | 12-18 mo | no                   | hyperdiploidy<br>DNA index >1 | favorable              |                            |
| 4S            | <12 mo   | no                   | diploidy<br>DNA index = 1     |                        |                            |
| 4S            | <12 mo   | missing              | missing                       | missing                |                            |
| 4S            | <12 mo   | no                   |                               |                        | Symptomatic                |
| 4S            | <12 mo   | no                   | any                           | unfavorable            |                            |

**Prognosis and treatment for Intermediate Risk Patients.** About 18 percent of all NB cases are deemed "intermediate risk." Children with intermediate-risk disease generally require surgery and four to eight rounds of moderate-dose outpatient chemotherapy, but have a very good prognosis, with overall 90 percent of children surviving.<sup>3</sup> **See "Overview of Treatment for Low and Intermediate Risk NB."** 

# COG High Risk (2007 revision)

| INSS<br>Stage | Age      | MYCN amp > 10 copies | DNA ploidy<br>(DNA index) | Histology<br>(Shimada) | Other |
|---------------|----------|----------------------|---------------------------|------------------------|-------|
| 2A or 2B      | any      | yes                  | any                       | any                    |       |
| 3             | any      | yes                  | any                       | any                    |       |
| 3             | ≥ 18 mo  | no                   | any                       | unfavorable            |       |
| 4             | any      | yes                  | any                       | any                    |       |
| 4             | 12-18 mo | no                   | diploidy                  | any                    |       |
|               |          |                      | DNA index = 1             |                        |       |
| 4             | 12-18 mo | no                   | any                       | unfavorable            |       |
| 4             | >18 mo   | any                  | any                       | any                    |       |
| 4S            | <12 mo   | yes                  | any                       | any                    |       |

**Prognosis and treatment for High Risk Patients.** The remaining 45 percent of NB cases are considered "high risk." Children with high-risk disease receive aggressive multi-modal treatment that includes high-dose induction chemotherapy, surgery, radiation, consolidative therapy (single or double stem cell transplant and/or antibody therapy), and differentiation therapy with retinoids in

an effort to eradicate minimal residual disease. Although the percent of children surviving has increased with this aggressive treatment, relapse remains a significant hurdle. The high number of relapses contributes to a poor long-term survival rate in past years of only about 35 percent for children diagnosed with high-risk disease, although recent studies by some institutions indicate an increasing survival rate of 50% or more for high-risk disease.<sup>4,5</sup> **See "Overview of Treatment for High Risk NB."** 

#### Summary

This and the previous two sections of **"What is Neuroblastoma?"** describe the general features, diagnosis, staging, tumor pathology and genetics, and risk group assignment for NB. This description has been prepared by laymen and is intended only as a brief general introduction of these matters for parents. More detailed information can be found in the sources listed at the end of Part 1 and in the various footnotes. Another valuable source of the most up-to-date research findings are the respective lists provided by major cancer centers of publications by the NB doctors and researchers affiliated with them.

However, as emphasized above, NB exhibits widely disparate characteristics and seems unique in every child. The specific nature of your child's NB disease and his or her treatment must always be determined by an experienced pediatric oncologist. Although many parents find that the information in secondary sources and research papers about NB increases their understanding of their child's illness, there is no substitute for an informed discussion of these matters with your child's oncologist.

# Addendum on Revised Staging and Risk Assignment

# Revision to INSS Staging and Risk Assignment (INRG)

Until recently, there has been no international agreement on criteria for risk assignment, so study groups in addition to COG, such as those in Japan, Germany (GPOH), and Europe (SIOP) have developed their own risk classification systems. This lack of agreement makes it difficult to compare results of treatments used in international studies.

The stage and risk assignment system discussed above is under revision by an international task force with the goal of developing a standardized international risk group classification called International Neuroblastoma Risk Group (INRG), and will include a new staging system as well (INRGSS—International Neuroblastoma Risk Group Staging System). The INRGSS proposed will take in account "image-defined risk factors" (IDRFs) at diagnosis, distinguishing between tumors that can be safely removed and those that cannot be surgically removed at diagnosis. In Europe surgical risk factors (determined by imaging) have long been used as a criteria included in risk assignment.<sup>6</sup>

The proposed INRGSS staging system can be summarized as follows:

Stage L1 – localized tumor (without image-defined risk factors);

Stage L2 – locoregional tumor (with image-defined risk factors);

Stage M - metastatic disease, except for MS;

*Stage MS* – metastatic disease under 18 months with spread to only skin, liver, under 10% of bone marrow, or same as 4S.<sup>7</sup>

To standardize risk assignment worldwide, the INRG task force has proposed a new schema. The proposed system will determine INRG risk according to the INRGSS (stage L1, L2, M, MS), age (under or over 18 months), tumor grade, presence or absence of *MYCN* amplification, unbalanced 11q aberration, and DNA ploidy, which will assign all NB cases into *four* risk groups: very-low, low,

intermediate, and high.

# COG Neuroblastoma Risk Groups (2007)

| Stage | Age        | MYCN    | Ploidy  | Histology | Other          | Risk<br>Group |
|-------|------------|---------|---------|-----------|----------------|---------------|
| 1     |            |         |         |           |                | Low           |
| 2A/2B |            | NA      |         |           | > 50 % resect. | Low           |
|       |            | NA      |         |           | <50% resect.   | Inter.        |
|       |            | NA      |         |           | Bx only        | Inter.        |
|       |            | Amp     |         |           |                | High          |
| 3     | < 547 d    | NA      |         |           |                | Inter.        |
|       | ≥ 547 d    | NA      |         | FH        |                | Inter.        |
|       |            | Amp     |         |           |                | High          |
|       | ≥ 547      | NA      |         | UH        |                | High          |
| 4     | <365 d     | Amp     |         |           |                | High          |
|       | < 365 d    | NA      |         |           |                | Inter.        |
|       | 365.<547 d | Amp     |         |           |                | High          |
|       | 365.<547 d |         | DI=1    |           |                | High          |
|       | 365<547 d  |         |         | UH        |                | High          |
|       | 365<547 d  | NA      | DI>1    | FH        |                | Inter.        |
|       | ≥547 d     |         |         |           |                | High          |
| 48    | <365 d     | NA      | DI> 1   | FH        | Asymptomatic   | Low           |
|       | <365 d     | NA      | DI=1    |           |                | Inter.        |
|       | <365 d     | Missing | Missing | Missing   |                | Inter.        |
|       | <365 d     | NA      |         |           | Symptomatic    | Inter.        |
|       | <365 d     | NA      |         | UH        |                | Inter.        |
|       | <365 d     | Amp     |         |           |                | High          |

Recent Changes to COG Risk Assignment Schema

Please contact editors@nbhope.org with any comments

<sup>&</sup>lt;sup>1</sup> <u>Children's Oncology Group Neuroblastoma Risk Grouping</u>, National Cancer Institute (last modified 11/2007)

<sup>&</sup>lt;sup>2</sup> Maris, John. <u>Translating Neuroblastoma Genomics to the Clinic</u>, ASCO 2007 Education Session, ASCO Annual Meeting presentation

<sup>&</sup>lt;sup>3</sup> Baker, DL et al <u>A phase III trial of biologically-based therapy reduction for intermediate risk neuroblastoma</u>, *Journal of Clinical Oncology*, 2007 ASCO Annual Meeting Proceedings Part I. Vol 25, No. 18S (June 20 Supplement), 2007: 9504.

<sup>&</sup>lt;sup>4</sup> Cheung, NK "<u>Reducing Therapy for Low-risk and Advancing Immunotherapy for High-risk Neuroblastoma</u>" <u>Embryonal Cancers I: Neuroblastoma---Recent Advances in Biology and Therapy</u>, Education Session, 2007 Educational Book, 2007 ASCO Annual Meeting presentation

<sup>&</sup>lt;sup>5</sup> George RE, Li S, Medeiros-Nancarrow C, *et al* (June 2006). "<u>High-risk neuroblastoma treated with tandem autologous peripheral-blood stem cell-supported transplantation: long-term survival update</u>". *J. Clin. Oncol.* 24 (18): 2891–6. <u>PMID 16782928</u>.

<sup>&</sup>lt;sup>6</sup> Monclair, T "<u>The new international neuroblastoma risk group</u> staging system – implications for surgeons" SIOP Education Book 2006, International Society of Paediatric Oncology, p.64

<sup>&</sup>lt;sup>7</sup> Maris, J et al. "Neuroblastoma." *The Lancet*, Volume 369, Issue 9579, pages 2106-2120 (June 2007)



# **Questions for Your Child's Doctors**

You have the right to have all questions about your child's diagnosis, treatment, prognosis, and other available treatments answered to your satisfaction, keeping in mind that many questions about neuroblastoma have no definitive answer. The questions below are some that we *wish* we had asked at the time of our child's diagnosis, so that we would have been better informed in facing the situation. We hope these questions will help you get the information you need to understand better your child's diagnosis and the treatment options.

#### **Understanding Your Child's Diagnosis**

How long will it take you to determine my child's diagnosis?

What tests will be done to diagnose my child?

Will all tests be performed at this facility?

Are there tests to determine neuroblastoma diagnosis and prognosis that are not available at this center?

What are the results of my child's tests and scans?

Where is my child's cancer? Has my child's cancer metastasized? To what extent?

What stage of disease does my child have and what risk assignment?

How do I get copies of my child's test results?

#### **Understanding Your Child's Prognosis**

What is the survival rate for children with my child's stage of disease and risk assignment?

What are the prognostic factors for NB and how are they determined?

Which prognostic factors affect my child and what is their significance?

What is my child's chance of surviving cancer-free for five years? For ten years?

# Exploring Your Hospital's Experience with Neuroblastoma

How many children have you/this hospital treated with my child's stage of disease and risk

assignment in the past year? In the past five years?

What cancer does each doctor in the department specialize in? What other cancers besides NB do they treat?

Which specific doctors at this center will treat my child? Which doctor is primarily responsible for my child's care?

Do the same doctors care for my child in both the day clinic and the hospital?

Who will perform my child's surgery? What types of surgery does this doctor perform? How many NB surgeries does this doctor perform per year?

#### Getting a Second Opinion

Are there NB experts in the country that I might consult? Who would you recommend?

Which centers in the country treat the most patients with NB?

Who are the leading NB surgeons in the country?

# **Exploring Treatment Options**

What is the treatment for my child's disease stage and risk assignment?

What are the realistic goals of this treatment?

How many children have been treated on this protocol?

How long has this treatment protocol been in use?

Is this treatment a clinical trial (open or closed)? What are the purposes of this trial? Is randomization involved? What specific rules or limitations do I need to know about this trial?

What is the survival rate of children treated on this protocol?

Are there other treatment options for neuroblastoma and where are they available?

How do the survival rates vary for the different treatments?

Will my child undergo a stem cell transplant? What type?

What transplant alternatives are offered elsewhere?

Will my child be eligible to receive antibodies after transplant at this institution?

How does the regimen offered here differ from regimens at other centers? What are the risks and benefits of each?

Will stem cells be collected? When?

When will surgery be performed? How does this compare with other centers?

Do we have any choices about the treatment?

If this were your own child, what would you do and why?

## **Understanding the Demands of NB Treatment**

How long does this treatment regimen generally take to complete?

Can you give me a detailed outline and schedule for my child's treatment?

Realistically speaking, what are the caretaking demands of this treatment on parents?

How often will my child be hospitalized? How many days per week will we be in clinic?

Can we do any parts of this treatment at our local hospital? What are the risks of doing so?

How will my child feel during treatment?

Which treatments are done on an out-patient basis, and which on an in-patient basis?

How do I keep my child safe during treatment?

#### Learning About the Risks of Treatment

What are the risks and short-term side effects of this treatment?

What are the long-term side effects of this treatment?

# **Understanding Tests to Determine Response to Treatment**

How often will my child's response to treatment be evaluated?

Which tests will be used?

Where will these tests be done?

Do other cancer centers use different tests to determine a child's response to NB treatment?

# Finding Information and Support

Where can I find information to learn about NB?

Where can I find the results of studies about this treatment?

Have you published any studies about this treatment?

Where can I find studies about other available NB treatments?

What support services are available at this center for my child? For my family?

Who do I contact about insurance and payment issues?

Could I speak with the parent of a child who has completed this treatment?

Please contact <a href="mailto:editors@nbhope.org">editors@nbhope.org</a> with any comments



# U.S. Neuroblastoma Specialists

Listed below are institutions and medical professionals who specialize in the treatment of neuroblastoma. This is not an exhaustive list, and is subject to change. Medical literature searches may reveal additional neuroblastoma specialists and researchers. Some of the researchers do not see patients. Please help us keep an up-to-date list by sending additions or corrections to editors@nbhope.org

#### **EASTCOAST**

BOSTON, MA Dana Farber Cancer Institute/Children's Hospital of Boston 300 Longwood Avenue, Boston, MA 02115 www.childrenshospital.org

| Suzanne Shusterman          | (617) 632-4901 |
|-----------------------------|----------------|
| Robert Shamberger (surgeon) | (617) 355-8326 |

#### BURLINGTON, VT

Vermont Cancer Center/Fletcher Allen Health Care E-213 Given Building, 89 Beaumont Avenue, Burlington, VT 05405 http://vermontcancer.org

Giselle Sholler (802) 847-2850

NEW YORK, NY Memorial Sloan-Kettering Cancer Center 1275 York Avenue, New York, NY 10021 www.mskcc.org

| Nai-Kong V. Cheung                | (212) 639-8401 |
|-----------------------------------|----------------|
| Brian H. Kushner                  | (212) 639-6793 |
| Kim Kramer                        | (212) 639-6410 |
| Michael La Quaglia (surgeon)      | (212) 639-7002 |
| Shakeel Modak                     | (212) 639-7623 |
| Mark M. Souweidane (neurosurgeon) | (212) 639-7057 |

# NEW YORK, NY

Morgan Stanley Children's Hospital of New York-Presbyterian/Columbia 161 Fort Washington Ave IP-7, New York, NY 10032 <a href="https://www.childrensnyp.org">www.childrensnyp.org</a>

Darrell J. Yamashiro (212) 305-3379

PHILADELPHIA, PA Children's Hospital of Philadelphia 324 South 34th Street, ARC 902A, Philadelphia, PA 19104 www.chop.edu

> Rochelle Bagatell Garret M. Brodeur (215) 590-2817 Stephen Grupp (215) 590-5475 Yael Mosse (215) 590-0965 John M. Maris (215) 590-5242

#### SOUTHEAST

DURHAM, NC **Duke Medical Center** 2301 Erwin Road Durham, NC 27710 www.dukehealth.org

> Susan Kreissman (919) 684-3401

ATLANTA, GA Children's Healthcare of Atlanta Aflac Cancer Center & Blood Disorders Service 2015 Uppergate Drive, 4th Floor, Atlanta, GA 30322 www.choa.org

> Howard Katzenstein (404) 785-0908

MEMPHIS, TN St. Jude's Children's Research Hospital 332 N. Lauderdale, Memphis, TN 38105 www.stjude.org

> Wayne L. Furman (901) 495-2403 Victor M. Santana (901) 495-2424 Andrew M. Davidoff (surgeon) (901) 595-4060

#### **MIDWEST**

ANN ARBOR, MI University of Michigan /C.S. Mott Children's Hospital 1500 E. Medical Center Drive, Ann Arbor, Michigan 48109-0253 www.med.umich.edu/mott

| Michael B. Armstrong | (734) 936-9814 |
|----------------------|----------------|
| Rajen J. Mody        | (734) 936-9814 |
| Gregory A. Yanik     | (734) 936-9814 |

CINCINNATI, OH

Cincinnati Children's Hospital Medical Center 3333 Burnet Avenue, Cincinnati, Ohio 45229 www.cincinnatichildrens.org

| John Perentesis | (513) 636-6090 |
|-----------------|----------------|
| Lars Wagner     | (513) 636-4266 |

CHICAGO, IL

University of Chicago/Comer Children's Hospital 5721 S. Maryland Avenue, Chicago, IL 60637 www.uchicagokidshospital.org

> Susan L. Cohn (773) 702-2571

MADISON, WI

University of Wisconsin Comprehensive Cancer Center 600 Highland Ave., K5/601, Madison, WI 53792 www.cancer.wisc.edu

> Paul Sondel (608) 263-9069

FORT WORTH, TX Cook Children's Medical Center 801 Seventh Avenue Fort Worth, Texas 76104 www.cookchildrens.org

> Meaghan Granger (682) 885-4007

HOUSTON, TX

Baylor College of Medicine /Texas Children's Cancer Center 6701 Fannin Street, Houston, Texas 77030 www.texaschildrenshospital.org

> (832) 822-4277 Heidi Russell (832) 822-3135 Jed Nuchtern (surgeon)

#### WESTCOAST

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> Judith G. Villablanca (323) 669-5654 Robert C. Seeger (323) 669-5618

PALO ALTO, CA Lucile Packard Children's Hospital 300 Pasteur Drive, Palo Alto, CA 94305-5208 www.lpch.org

> Clare J. Twist (650) 723-5535

SAN FRANCISCO, CA University of California, San Francisco 505 Parnassus Ave, San Francisco, CA 94143-0106 www.ucsfhealth.org/childrens

> Katherine K. Matthay (415) 476-3831

SEATTLE, WA Children's Hospital and Regional Medical Center 4800 Sand Point Way NE, Seattle, WA 98105 www.seattlechildrens.org

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#### What is a Clinical Trial?

Clinical trials are scientific studies conducted to learn more about a disease and find new or better treatments. Clinical trials are the standard of care for children with neuroblastoma: virtually all children treated for intermediate- and high-risk disease as well as many low-risk NB patients are enrolled on a clinical trial or treated "per" a clinical trial. The treatment is the same in either case, but only the outcomes of those enrolled are included in the final trial results.

Since neuroblastoma is a rare disease, clinical trials are planned and carried out either by large single institutions, small groups of institutions, or large, international cooperative groups such as the Children's Oncology Group (COG). See the Appendix "What are Study (Cooperative) Groups?" at the end of this section for more on study groups. Clinical trials may study therapeutic results of patient treatment or examine non-therapeutic issues such as what causes a type of cancer, similarities and differences between tumors, or what late effects patients may experience as a result of cancer treatment.

The current focus of clinical trials for low- and intermediate-risk neuroblastoma is to reduce treatment toxicity while maintaining high survival rates, as well as to determine how to identify at diagnosis the small subset of those with higher risk of treatment failure or relapse. By contrast, the focus of trials for high-risk neuroblastoma is primarily to increase the survival rate.

There are different types, or phases, of therapeutic clinical trials: Phase I, II, III, and IV.

# **Phase I Clinical Trials**

Phase I pediatric clinical trials are the initial attempt to use a drug or drug combination in children, and often enroll small numbers of patients (e.g., 10 to 30). Phase I trials are open only to children who have "refractory" disease that has not responded to other treatments or children who have relapsed. In addition to measurable or detectable disease, eligibility criteria usually include adequate organ function such as specified blood cell counts, and liver, kidney, and heart test values. Some trials do not allow brain metastases or other condition. Prior treatments may affect eligibility, such as particular drugs used, radiation to bone marrow, allogeneic transplants, etc.

Phase I trials are not intended to cure a child of disease, but to learn more about potentially effective new agents. A child enrolled on a Phase I study often does not benefit directly from the drug (although individual beneficial results are hoped for and do happen), but other children may benefit from what researchers learn about the drug, its administration, and side effects.

The goals of a Phase I clinical trial will usually include one or more of the following:

- **Pediatric use:** To determine whether a drug or drug combination can be used in children. Drugs or drug combinations in a Phase I trial have been shown to be effective against neuroblastoma cell lines in the laboratory and usually have been previously studied in adults— but have not been tried in children.
- **Toxicity**: To determine what side effects and toxicities the drug causes when used in children. Toxicity is quantified (grades 1, 2, 3, and 4) and reported according to NCI's

What is a Clinical Trial?

Common Toxicity Criteria.

• **Dosage:** To determine the highest tolerated dose of the drug or drugs in children. You may hear such studies referred to as "dose escalation studies." In these studies, a small number of children (usually three) are given the same dose and their response to the drug, including any adverse effects, are observed. If the first group of children tolerates the treatment well, the next group of children enrolled on the study will receive an increased dose, until the doctors determine the maximum tolerated dose (MTD) that can be given without serious side-effects. "Intrapatient dose escalation" design allows for the dose to be increased in each patient as tolerated.

• **Absorption ("pharmacokinetics"):** To determine how well a new drug or a new method or formulation for delivering an old drug or combination of drugs is absorbed in the child's system, and how long before it is eliminated.

The extent of a child's disease is monitored periodically during the clinical trial and is reported commonly as reduced (response to treatment), stable, or progressive (disease is growing). Children who have progressive disease are removed from the trial and other treatment options are explored. Children who have severe adverse reactions will also be removed from the study. In some cases, studies have been closed when several children experienced very serious side effects.

#### **Phase II Clinical Trials**

Like Phase I trials, Phase II clinical trials are generally open to refractory or relapsed patients who have not responded to more conventional treatments. Drugs or drug combinations in a Phase II trial have undergone Phase I testing, so the recommended maximum tolerated dose has been established and toxicities are known.

The primary goal of Phase II trials is to determine if the drug or drug combination is active against neuroblastoma—whether the drug will shrink tumors or, in some cases, prevent the cancer from recurring. In addition, researchers may learn more

about side effects and toxicities associated with taking the drug. Phase II trials typically enroll more patients than Phase I, often 30-60 in the case of neuroblastoma.

Some Phase II trials are designed specifically to test new frontline treatment regimens on newly diagnosed patients. Such Phase II trials are available only at certain large institutions and are often referred to as "pilot" studies or protocols. These studies determine toxicity and survival rates for new treatment regimens for frontline therapy. If the results are promising, future Phase III trials may incorporate the new regimens to be verified as more effective.

#### **Phase III Clinical Trials**

Children newly diagnosed with high-risk neuroblastoma usually are enrolled on the current or recently completed COG Phase III clinical trial, unless their hospital runs single-institution trials, which may be a Phase II trial. If your child is not either enrolled on a trial, or being treated "per" a trial, you should ask your doctor why your child is not receiving the newest treatments. It is worth noting that children are often treated on *closed* trials (Phase II or III protocols), so their data is not included in the results of the study.

Although they utilize some of the most effective treatments against neuroblastoma, enrollment on a

Phase III trial does not guarantee a cure. Because the prognosis for high-risk disease is so poor, doctors and researchers are constantly working to find more effective treatments that pose fewer long-term risks to children.

Phase III clinical trials require enrollment of a large number of patients for increased statistical significance, usually in the 300-500 patient range. These studies compare two or more treatments that are specific to neuroblastoma and try to determine which one is more effective. Most Phase III studies are randomized—children in the "control group" receive the "standard" treatment, while other children receive a different drug or treatment designed to answer a specific research question. A computer is used to randomly select which children receive the experimental treatment and which receive the standard treatment.

For a history of recent Phase III trials for high-risk neuroblastoma, see **Appendix to "Overview of High-Risk Treatment."** 

#### **Phase IV Clinical Trials**

These trials are to verify the safety of a newly approved treatment or drug. None of these "Post Marketing Surveillance Trials" are currently designed for neuroblastoma.

# Single or Limited Institution Trials

Some institutions, such as St. Jude's Children's Research Hospital and Memorial Sloan-Kettering Cancer Center, conduct trials limited to patients at their facility. Other trials are conducted at only a few institutions. Single institution and limited institution trials may take the form of pilot studies or individual drug studies—i.e., the initial study examining a new method or treatment. These smaller trials allow researchers to answer critical questions before a drug or treatment is made available to more patients through a larger study.

# Non-therapeutic Clinical Trials

Non-therapeutic clinical trials generally fall into one of four categories:

- Biological studies—studies that examine the biology of tumor samples and identify prognostic variables;
- Epidemiological studies—studies that look for the causes of a type of cancer and the frequency with which it occurs;
- Cancer control studies—studies designed to find the best methods for dealing with side effects; and
- Late effects studies—studies designed to identify and deal with the after-effects of treatment.

# **Patient Safety**

Clinical trials are carefully planned and rigorously monitored. Each hospital must elect to open a study and enroll patients, which requires approval from the hospital's Institutional Review Board (IRB). Because patient safety is such a concern with experimental treatments, there are strict

What is a Clinical Trial?

guidelines for carrying out clinical trials. For example, there is no flexibility in eligibility criteria. If the study requires patients to have a platelet count of at least 100,000 no patient can be enrolled with less. Similarly, there are strict monitoring requirements for disease status and reporting toxicity.

#### Compassionate Use

Occasionally parents pursue "compassionate use" of "investigational new drugs" (INDs) from the FDA and manufacturers. Reasons for this may be that the drug is offered in an open study but the child does not meet eligibility criteria, or no study is currently open. The child's oncologist, the principal investigator of the new drug, the manufacturer of the drug, and the FDA are all involved in obtaining approval for use on a case-by-case basis. Approval is highly variable based on many factors.

### **Enrolling Your Child on a Clinical Trial**

Before your child can be enrolled in a clinical trial, you must give your informed consent to treatment. As part of the informed consent process, you should receive a document that provides a summary of the clinical trial—its purpose, procedures and schedule, and potential risks and benefits—and that explains your rights (and your child's rights) as a participant in the trial. **See Patients' Rights & Responsibilities.** 

The National Cancer Institute—a part of the U.S. National Institutes of Health—has issued recommendations for research institutions and clinical centers to use in writing informed consent documents. Although documents may vary by institution, all informed consent documents should include the following:

- Title of the trial:
- Purpose (Why the trial is being conducted);
- Description of procedures involved in the trial;
- Estimated duration of the trial:
- Risks of the trial;
- Benefits of participating in the trial;
- Alternatives to participation;
- A statement explaining the extent to which information about the patient will be kept confidential;
- Explanation of costs or additional expenses;
- Statement of the patient's rights as a participant;
- Information for whom to contact with questions or problems;
- A list of additional sources of information, such as websites, community organizations, etc.;
   and
- Signature line representing the patient's (or the parent's) legal consent to participation in the trial.

If you decide to enroll your child on a trial, you must sign the document indicating your consent. After you sign the document, you should receive a copy to keep for yourself and to use as a source of information throughout the course of the trial.

After you have read the trial document, but before you sign and give your consent, you should have an opportunity to discuss the trial and the information in the document with your doctor. During this conversation, your doctor should review all of the information in the consent document, such as

the purpose of the trial, potential risks and benefits, and your child's rights as a participant, and give you the opportunity to ask any questions you may have.

Even after you have given your informed consent to enroll your child in a clinical trial, you should feel free to ask questions and raise concerns about the treatment at any time. You are also free to take your child off of the trial at any time—for any reason, or no reason at all—without giving up the ability to receive other treatments for your child.

**Informed assent.** Children under 18 cannot legally consent to participate in a clinical trial; consent must be given by the parents or legal guardian. However, if your child is over the age of 7, he or she may be asked to agree to participate in the trial in a process known as informed assent.

Your child will not be asked to give informed assent to a treatment unless you have already given informed consent to his or her participation. Once you have done so, the child can be provided with a form that explains in age-appropriate terms the purpose of the research, what your child will be asked to do, and procedures that may be performed. For teenagers over 16, this form may be very similar to the informed consent document parents are asked to sign. Forms used with younger children use simpler language. All forms should be clear that the child has the right to leave the trial at any time, for any reason, without penalty and that information will be kept confidential.

There are two exceptions to the requirement for informed assent by the child:

- If the child is incapable of participating in the process, or
- If the trial "holds out a prospect of direct benefit that is important to the health or well-being of the child and is available only in the context of the research." This exception applies when the treatment offered in the study is believed to be a better option than other currently available treatments, or when the treatment is the only alternative available. This exception often applies to patients with stage 4 neuroblastoma and those who have relapsed, because most of the treatments for these types of disease are clinical trials.

Even in situations where one of the exceptions applies, the research team is still expected and encouraged to obtain the child's assent. Many medical professionals believe that involving the child in these decisions is empowering, giving the child a feeling of control and a sense of ownership in what happens during the trial.

## Sources:

CureSearch/National Childhood Cancer Foundation, <a href="www.curesearch.org">www.curesearch.org</a>. National Cancer Institutes, <a href="www.cancer.gov">www.cancer.gov</a>. ACOR Ped-Onc Resource Center, <a href="www.acor.org/ped-onc">www.acor.org/ped-onc</a>. NCI Clinical Trials, <a href="www.cancer.gov/clinicaltrials">www.cancer.gov/clinicaltrials</a>.

What is a Clinical Trial?

### **Appendix**

## What are Study (Cooperative) Groups?

In an effort to improve survival rates and therapies for neuroblastoma, various clinical trials are planned and carried out by cooperative pediatric oncology groups. Individual and small groups of institutions also carry out smaller "pilot" studies to test new therapies. Many patients are needed for phase III (randomized) trials to discern the effectiveness of new therapies. Since incidence of neuroblastoma is small, cooperative groups are often international.

Pediatric oncology study groups are found around the globe and some conduct significant studies on neuroblastoma. Some have been limited within one or more countries such as Japan's Study Group, and Germany's GPOH (Gesellschaft für Pädiatrische Onkologie und Hämatologie), a German language study group including institutions in Germany and Switzerland. The Société Internationale d'Oncologie Pédiatrique or SIOP conducts large studies on neuroblastoma in 17 countries including UK and Israel. It is also known as "International Society of Paediatric Oncology." The first annual general meeting was held in Madrid in 1969 and began with a distinct focus on neuroblastoma among other pediatric cancers.

Annual meetings of cooperative study groups and professional societies are important occasions for researchers to present results of studies. Hundreds of researchers interested in neuroblastoma also have an opportunity to present findings every two years at "Advances in Neuroblastoma Research" or ANR. ANR does not conduct cooperative studies.

In North America Children's Oncology Group (COG) was the result of a merger in 1999 with Children's Cancer Group (CCG) and Pediatric Oncology Group (POG), and currently has over 230 member institutions in the US, Canada, Australia, New Zealand, Netherlands, and Switzerland. Not all member COG institutions participate in every trial run by the COG. For example, your hospital may be a COG institution but not enrolling patients in a particular COG trial. Each hospital's Institutional Review Board (IRB) must approve *each* trial.

COG is the largest pediatric cancer group, and <u>40,000</u> children with all types of pediatric cancers are currently treated on approximately 150 COG protocols. <u>Requirements</u> for membership as a COG institution and principal investigator include treating a minimum annual average of twelve newly diagnosed pediatric cancer cases. COG investigators must also enroll a minimum annual average of six children on COG therapeutic trials and a minimum of two children on non-therapeutic trials. Specific <u>support</u> specialists and facilities must also be provided in COG institutions. **Every pediatric oncology patient treated at COG hospitals must be registered in the COG database, even if they are not treated on a COG protocol.** 

A smaller group of investigators specializing in neuroblastoma at 14 institutions comprise the <u>New Approaches to Neuroblastoma Therapy</u> (NANT) consortium. This group plans and offers phase I and phase II trials for refractory and relapsed neuroblastoma.

Please contact editors@nbhope.org with any comments



# The World of Hospitals

For people with no medical background, the hospital environment can be both bewildering and intimidating. This primer will help you learn the ropes.

## Who are all these people?

There is a hierarchy in hospitals and it can be mystifying at first. Just as the military is organized by rank, with corresponding authority and responsibilities, the hospital has its own ranking system. In large hospitals there will be a team of people responsible for your child's well-being during treatment.

In teaching hospitals, the hierarchy looks like this:

# Attending Physician

Attending physicians are the doctors in charge of choosing an overall treatment plan for your child. "Attendings" are usually also professors; they teach residents and fellows in the hospital and students in any affiliated medical school. Attending physicians have spent four years in college, four years in medical school, and three years as a resident, although in pediatrics, the first year of residency is also the internship year. To specialize in pediatric oncology, a doctor must then be selected for a fellowship in pediatric oncology. After several years of treating children with cancer and doing research, the doctor may seek a position as attending physician. Attending physicians are the top dogs.

In some hospitals attending physicians treat all pediatric cancers, although at large cancer centers each attending physician is generally a specialist in one or more cancers, such as leukemias, brain tumors, bone cancers, neuroblastoma, and so on. Some attending physicians at research hospitals also oversee labs, where they do research with a team of researchers in their respective fields.

The attending physicians usually rotate the responsibility of being in charge of the daily well-being of patients who are hospitalized. This attending doctor (who does not necessarily treat patients with your child's particular cancer) will oversee your child's daily recovery while he or she is an in-patient, although your child's specialist or surgeon will also check on your child. During hospitalizations, a team (often including the fellow, resident, interns and students) supervised by the attending may visit your child on "rounds," the daily check-up on each patient's condition.

# Fellow

Fellows are doctors who are working on becoming a specialist in pediatric oncology. Depending on the way your hospital works, a fellow may follow your child's case throughout treatment, or the fellows may rotate. Pediatric fellows have completed four years of college, four years of medical school, and three years as a resident.

The extent of a fellow's pediatric oncology experience is determined by the number of years he or she has been working directly with pediatric cancer patients. Many have a great amount of knowledge in the daily work of caring for children undergoing cancer treatment. Like the attendings, the fellows may rotate the responsibility for children who are currently hospitalized, and they will be an important source of information and support for daily issues when your child is in-patient.

Because the number of cases of neuroblastoma per institution per year is usually very small (most institutions see fewer than four new NB cases per year), a fellow may work many years in a large institution before becoming an expert in the disease. At research hospitals, fellows generally divide their time between clinical and research responsibilities, and are assigned to a specific research lab. A fellow specializing in neuroblastoma will probably be very knowledgeable about your child's treatment.

#### Resident

Residents are "junior" doctors who are receiving "hands-on" training. Residents are on duty on nights and weekends, and can handle most urgent items and prescribe medications, but big decisions are always made by an attending physician, or perhaps by a fellow in consultation with an attending.

Residents have spent four years in college and four years in medical school. When you see pediatric residents in the hospital, they are completing their three years of residency. At the end of their residency, they are eligible to pass a test and become board certified pediatricians, but they are not experts in pediatric oncology. They can be helpful, however. For example, if you have a concern on a Saturday night, a resident can probably get the right specialist on the case.

#### Intern

Pediatric interns are first-year residents usually not left in charge on their own, but who work with more experienced doctors and do not make treatment decisions. Interns have spent four years in college and four years in medical school. They are beginning their residency by learning about the practical aspects of medical practice. They are not specialists in pediatric oncology, so their knowledge is more general. They will rely on more experienced doctors for important issues.

#### Student

A medical student has not yet finished four years of medical school. They are not doctors yet (and are not addressed as "doctor"), and do not make treatment decisions. They are present in the hospital to learn, not to treat patients, which is why they accompany the attendings, fellows, and residents on "rounds" in hospitals affiliated with a medical school.

#### Physician Assistant (PA)

Physician's Assistants are exactly what the name implies—they assist physicians in the diagnosis and treatment of patients. Physician assistants usually earn a bachelor's or master's degree in an accredited PA program. They are able to prescribe medications and perform procedures such as bone marrow biopsies under the supervision of a doctor. PAs in oncology clinics have additional training in oncology.

PAs in your hospital or clinic may wear white lab coats like doctors, so knowing what to call them can be confusing. If your PAs do not tell you how they want to be addressed, ask them. Some hospitals are very formal and refer to PAs as Mr. or Ms., but other institutions are less formal and PAs are referred to by their first names.

#### Nurse Practitioner (NP)

Pediatric nurse practitioners are registered nurses who have completed additional training and hold a master's degree. Most hospitals have either PAs or NPs, but not both, as they are roughly equivalent.

NPs can examine and assess patients and determine whether they need to be seen by an attending or are able to proceed with treatment. NPs perform some duties that physicians usually perform, such as prescribing drugs, writing orders, and performing bone marrow aspirations.

In some hospitals NPs may be assigned to specific attendings. If NPs are assigned to the attending who treats neuroblastoma, they will probably be an important member of your medical team, providing you with invaluable support. For example, a neuroblastoma NP will likely know much more about neuroblastoma than a resident or intern.

### Registered Nurse (RN)

Registered Nurses have a two or four year college degree and must pass an exam and be licensed by the state. RNs administer medication. Some oncology wards have dedicated "chemo nurses" who have special training and administer all of the chemotherapy treatments for patients on that floor.

#### **Charge Nurse** (or similar title)

The Charge Nurse is the nursing supervisor for a particular shift on a particular floor of the hospital. The Charge Nurse is the person to see if you have a problem with a nurse, LPN, or nursing assistant, or with a specific nursing rule or practice. There may also be a separate charge nurse who supervises the nurses in the day clinic.

### Licensed Practical Nurse (LPN)

Licensed Practical Nurses have a one or two year degree and perform bedside care. LPNs can change bandages, draw blood, remove IV's, and administer some medications.

## Certified Nurse Assistant (CNA)

CNAs check vital signs (blood pressure, pulse, etc) and change bedding, but they cannot administer medications. CNAs are good people to become friends with—for example, they can get extra linens and supplies when you need them.

# Social Worker (LSW or LCSW)

Licensed social workers usually have a master's degree in social work and are valuable resource people. Your social worker will help you with parking discounts and meal tickets for the cafeteria, and will suggest support groups if they are available at your hospital or clinic. They work closely with child psychologists to help support the well-being of the "whole" person. Social workers also can tell you about wish organizations, cancer camps, free flights for treatment, the Ronald McDonald House, and other financial resources including your state's programs for children with disabilities.

# Patient Advocate or Patient Representative

Most problems that you have in the hospital can be resolved simply, either by speaking directly with the offending party or the charge nurse. If you encounter problems that cannot be resolved through these channels, there are third parties you can contact to help. Many hospitals have a patient advocate or patient representative who can help resolve complaints if you cannot handle them yourself. The complaints can be anything from consistently poor service to hygiene concerns to billing errors. If your hospital does not have a patient advocate, you should speak to the social worker about your concerns. A social worker that cannot help may be able to provide information on independent patient advocacy organizations that can assist you. **See "Patients' Rights & Responsibilities."** 

# Child Life Therapist

Child life specialists have a bachelor's or master's degree in child development or some type of therapy. They use play therapy, arts and crafts, and other techniques to provide emotional and developmental support to children and families and help minimize the stress and anxiety of the health care experience.

Child life therapists can help you explain to your child the need for surgery, help your child learn about caring for a central line, and prepare your child for scans, test and other medical procedures. Child life professionals work to create "family centered care" in health care facilities. Some hospitals have volunteers who are supervised by the child life specialists. Individual volunteers may well become significant members of your support network by providing diversion for your child, time out for parents, a sympathetic ear, and in many cases, warm friendship.

In addition to these key players, there are a host of other support staff and specialists, such as psychologists, physical therapists, audiologists, radiologists, billing coordinators, secretaries, and other people working behind the scenes. Knowing "Who's Who" can help you pose your particular question to the right person. For example, if you ask the nurse how to get parking discounts or a referral for the Ronald McDonald House, she's not likely to know, but the social worker will.

# **Hospital and Clinic Routines**

The amount of time required to treat high-risk neuroblastoma is staggering. Between inpatient (hospital) stays and outpatient visits to the clinic, it is not unusual to spend over 200 days in the course of the first year of treatment—and treatment often continues for two years or longer. You will quickly learn that hospitals and clinics have their own routines developed with the goal to provide consistent high-quality care. Learning the routines and preparing your child as well as you can, depending on the child's age, will reduce the stress of the "unknown" every time your child faces treatment and supportive care.

#### One more thing...

Hospitals are complex institutions and you will interact with many different professionals doing demanding work in an array of departments. You will be trying to find your way and understand the daunting science of cancer treatment at the same time that you may feel traumatized or angry about your child's diagnosis. While most of the medical professionals you meet will be among the most dedicated and compassionate people you know, it's likely you will also encounter some who are brisk, arrogant, thoughtless, or even downright rude.

Building a good relationship with medical staff and professionals is a necessary part of the treatment process. Naturally, and especially at first, you are under great stress and may not process information the way you normally would. You should feel free to ask questions and if something does not make sense, ask for further explanation. An important part of your job as a parent is to be an advocate for your child, and the most effective advocates are positive, determined, and respectful. An extra "thank you" or a smile often works magic.

As obvious as this all is, most of us can remember too many times when we were so offended, frustrated, or outraged with our child's illness that we just wanted to punch the first person we saw in a white coat. As challenging as such times will be, try to be as calm and controlled as you can. Working with sick children every day is a very difficult job, and a seemingly rude or distracted medical profession may instead be affected by what happened in the sick room he or she just left.

However, if you do determine that someone has been unprofessional or incompetent, then don't hesitate to tell the patient representative or appropriate supervisor. Sometimes, on further quiet reflection, you may realize that *you* were the one who crossed the line. In that case, a sincere "I'm sorry" will go a long way toward resolving the situation. Most pediatric professionals understand that you are coping with every parent's worst nightmare. You are only human. Do your best to treat everyone in the hospital and clinic the way you would like to be treated, but be forgiving and kind to yourself as well!

Please contact <a href="mailto:editors@nbhope.org">editors@nbhope.org</a> with any comments

| Health Care Team Modify this chart and add appropriate contacts |      |                     |  |  |  |
|---|------|---------------------|--|--|--|
| Position  | Name | Contact Information |  |  |  |
| Attending   |      |                     |  |  |  |
|   |      |                     |  |  |  |
| Fellow  |      |                     |  |  |  |
|   |      |                     |  |  |  |
| Resident  |      |                     |  |  |  |
|   |      |                     |  |  |  |
| PA or NP  |      |                     |  |  |  |
| Nurse   |      |                     |  |  |  |
| Nurse   |      |                     |  |  |  |
| Nurse   |      |                     |  |  |  |
|   |      |                     |  |  |  |
| Audiologist   |      |                     |  |  |  |
|   |      |                     |  |  |  |
| Social Worker   |      |                     |  |  |  |
| Psychologist  |      |                     |  |  |  |
| Child Life  |      |                     |  |  |  |
| Patient   |      |                     |  |  |  |
| Advocate  |      |                     |  |  |  |
| Hospital  |      |                     |  |  |  |
| Billing   |      |                     |  |  |  |
| Insurance   |      |                     |  |  |  |
|   |      |                     |  |  |  |
|   |      |                     |  |  |  |



# **Reaching Out and Accepting Help**

When a child is diagnosed when cancer, people instinctively want to help. Many families have found it useful to appoint a close friend or family member to coordinate offers of assistance. The lists below are based on the experiences of an Aunt who assisted a large family over the three-year course of her niece's illness. Although each of these items may not apply to your situation, they may help you think of other specific ways those who offer to help can assist your family.

## 25 Ways to Help ANY Family Fighting for their Child's Life

- 1) Bring Food Take prepared food in containers that do not need to be returned.
- **2) Serve a Meal** Serve a meal and clean up afterward—it may give parents the only half-hour of spare time they get that day.
- **3) Make a Donation** Donate to an expense fund for the child's non-reimbursed medical expenses, such as co-pays, home-care medications, and travel expenses.
- **4) Organize Fund-Raisers.** Organize a fund-raiser, so the parents aren't forced to leave the child's side to raise money to pay for care and medications. Remember, insurance covers only about 80% of associated costs, and cancer bills often top \$1,000,000 after 3 years, depending on treatment.
- 5) Organize People. Organize a small revolving group to do meals or grocery shopping, etc.
- **6) Check on Necessary Supplies.** Call from the grocery store and say, "I'm at the store...look in the fridge and tell me if you have (a) milk (b) bread (c) apples/bananas (d) lunch meat (e) butter (f) eggs (g) cereal. Then have them check reserves on (h) pet food (i) toilet paper (j) paper towels (k) laundry detergent (l) soap (m) diapers. Ask if there are specific brands they prefer or package sizes they need. Do this without expecting repayment, and consider it part of philanthropic giving or tithes and gifts.
- **7)** Little Gifts Mean a Lot. Presents are sweet and thoughtful, but daily necessities are also greatly appreciated. Consider a simple bag of apples and paper towels.
- **8)** Do a Household Chore. Clean the bathrooms or kitchen, change the sheets, or do a load of laundry. Bring the supplies you'll need with you, and be aware that it's often best to do noisy or disruptive tasks when the family is out.
- **9) Take on a Regular Task.** Offer to do a weekly task like drive a sibling to a lesson, picking kids up from school, packing lunches, or helping with homework one night a week. Knowing that they can rely on you doing something consistently gives the family a little predictability. Still, you should always confirm the routine, because their lives are always "up in the air" and a medical crisis may necessitate a change in plans.
- **10) Help Them Think (no kidding!).** Help one or both parents think through the week and obligations for the other children, such as soccer games and parent-teacher conferences. Ask if there are insurance forms to fill out, bills to be paid, and gas tanks to be filled. Going through a list like this can help them focus and organize thoughts that may otherwise be a jumble.

- **11) Take the Kids Out.** Take the siblings to dinner, the movies, or another event they'd enjoy. Or if the sick child is able, take him/her to the park, or for a slurpee or ice cream cone. This gives everyone a break and is usually great quality time.
- **12) Pay a Bill Anonymously**. Call the electric/gas/phone company—anonymously if you wish—and tell them you want to pay the current bill for the family.
- 13) Gift Certificates. Give them gift cards for the grocery store, McDonald's, Starbucks, etc.
- **14) Give Them Supplies to Simplify Their Lives**. Stop by the house with a bag of paper cups, paper plates, and trash bags to make life easier.
- **15) Give the Parents a Short Break**. Offer to sit and read or play games with the sick child—either in the hospital or at home. An hour break from the stress of constant-care can be reviving.
- **16) Help Research Treatment Options, Medications, Alternative Medicine, etc.** Do the Internet research that is so critical in pro-active education and care, and provide them with printed pages in a file or notebook. Highlight the pertinent information so they don't have to read the entire report.
- **17) Give the Parents a Date Night.** Babysit one night a month so the parents can go out for a walk, go to dinner, or see a movie.
- **18) Thank-You's.** Provide stamped thank-you notes and offer to write some for them.
- 19) Help with Pet Care. Take the family pets to the groomer or to the vet for checkup/shots
- **20) Help with Car Care.** Take their car to the shop for inspections and repairs, or fill up the gas tank and run it through the car wash.
- **21) Help with Kid Care Needs.** Take the kids for haircuts, medical checkups, and shopping for clothes, shoes, school or camp supplies they need.
- **22) Help with Holidays.** Help pick up holiday gifts and wrap them, or offer to put up their decorations.
- **23) Support the Mom and the Dad**. Determine the best way to emotionally support each parent separately. Mothers may want to talk, bake, rest, or shop; fathers may prefer to a chance to play golf or go to a ball game.
- **24) Help with Financial Chores**. Offer to come balance the checkbook, make deposits, pay bills, or just organize the medical bills.
- **25) Help with Seasonal Household Chores**. Make sure the walks and drives are plowed in winter, grass is cut in the summer, and leaves are raked in the fall.

# Things to Avoid Saying or Doing When a Family is Dealing with a Child's Life-threatening Illness

- 1) **DON'T be judgmental.** Everyone differs in the way they run their family and handle stress. Never judge a parent with a sick child. Negative judgments are incredibly destructive and can forever damage relationships.
- **2) DON'T let your interest or involvement dwindle.** People tend to surround a family at the time of diagnosis then, understandably, go on with their lives. But the sick child and family continue the battle for years, and need ongoing support.
- 3) DON'T talk too much about new purchases, vacations, other volunteer or philanthropic causes, or how great your life is. It's only a reminder of how horrid their lives are at the moment. While they want and need to share happy things in your life, be sensitive to their changed priorities and values.
- **4) DO be judicious about talking about your own, or other family, problems.** Learning of others' problems when they cannot help will tend to depress them and add to their stress.
- **5) DO take your cue from the parents regarding topics of conversation.** Sometimes they need a break from thinking about their problems, so talk about other light subjects with them. Don't be afraid to laugh with them or talk about funny things.
- **6) DON'T try to take over.** Parents need to feel they have control over something, since there is so much in their lives that they cannot control. Leave ultimate decisions to them and support them in those decisions, even if you do not agree.
- 7) DON'T yell at them or have cross words unless a situation is life-threatening. Now is the time to exercise restraint and control over your own emotions. If you need to cry or scream, do it to someone who isn't consumed with fighting for his or her child's life.
- 8) DON'T try to help if you yourself are physically or emotionally weak or ill. Find a way to help within your own abilities and limitations. If you cannot be there for the family physically, you can still help with less demanding (but equally critical) areas like financially, spiritually, or writing thank-you's.
- **9) DON'T avoid the family if you're close to them.** It's a sad fact that some people cannot deal with unpleasant events. More than any other time in your life, NOW is the time to let people know you care about them. It is inevitable that one day we will all need the same kind consideration. There are many ways to support a family and still "protect" yourself. (see "How to Help" list )
- **10) DON'T knowingly expose the child or family to a virus or other illness.** Children in cancer treatment have no immune system, so don't take a chance exposing anyone in the family to illness. The parents, too, are more prone to illness because it is unlikely they are getting sufficient sleep or eating nutritious meals.
- 11) DON'T EVER tell a parent that he or she is "lucky to have other children."

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Please contact editors@nbhope.org with any comments



# Overview of High-Risk Treatment

All treatments for newly diagnosed high-risk NB share many components, but differences in protocols do exist, due to continued efforts to increase survival rates using various approaches. Currently, each of the national and international cooperative pediatric oncology groups, such as the Children's Oncology Group (COG), the International Society of Paediatric Oncology (SIOP), and the German Society for Paediatric Oncology and Haematology (GPOH), have clinical trials for newly diagnosed NB cases. In addition, some institutions treating a large number of NB cases, such as Memorial Sloan-Kettering Cancer Center (MSKCC), Baylor/Texas Children's, and St. Jude's Children's Research Hospital, have their own single-institution or multi-institution frontline protocol. The chemotherapy agents (and their administration and dose), number of induction cycles, timing of stem cell collection, timing of surgery, type of radiation therapy, use (or not) of transplant, conditioning regimen for transplant, timing of Accutane, and use (or not) of antibodies – all of these components differ somewhat in the various frontline protocols.

The focus of this chapter is to provide some general background information on the common components of treatment for high-risk disease. Side effects of these treatments, and ways to cope with them, are discussed in Chapter 3, "Coping with Treatment: Side Effects, Comfort Measures and Safety Precautions." Treatments for refractory and relapsed NB are discussed in the respective chapters Chapter 7, "Treating Refractory NB" and Chapter 8, "Dealing with Relapse." Information about clinical trials, contacting NB specialists for second opinions, and other matters that arise at diagnosis may be found in Chapter 1, "Confronting the Diagnosis."

The following summary has been prepared by NB parents in the hope it will help you have a more meaningful dialogue with your NB team – who is always the ultimate source of information about NB treatments and their relevance to your child's specific case.

#### **Induction Phase**

The induction phase is the initial phase of treatment aimed at ridding the body of all detectable NB using chemotherapy and surgery. During induction the child will have a central venous line placed, then undergo chemotherapy, surgery to remove the primary tumor and affected lymph nodes, stem cell harvest, and tests, scans, and bone marrow biopsies to monitor response to treatment. If the child responds with a "complete response" (CR) or in some cases "very good partial response" (VGPR), he or she moves on to next phase called "consolidation."

#### Central venous line (CVL)

Children undergoing chemotherapy have some type of central venous access device placed before chemotherapy begins. Usually a single or double Broviac™ or Hickman™ central line will be placed, although some children receive a single or double "port"—a device implanted under the skin that is accessed by a special needle. Some type of venous access is necessary because in addition to chemotherapy treatments, the child will need blood and platelet transfusions, IV medications, and fluids for hydration. Double lines are required for stem cell transplant. In addition, blood samples are needed quite frequently, and these can be easily obtained through a central line or port with minimal trauma to the child. For additional information, see Chapter 3, "Central Venous Lines: Broviacs, Hickmans, & Ports."

### Chemotherapy

Various combinations of high-dose chemotherapy are administered intravenously for a few days out of approximately every 21 days (or 10 days in Europe), for five to eight cycles, usually inpatient. The table below lists the agents used in various protocols, but the dosages are not all the same. (This is *not* an exhaustive list of current protocols.)

| Chemotherapy Agents used in Selected High-Risk Induction Protocols |      |                   |                   |                  |                    |  |  |
|--|------|-------------------|-------------------|------------------|--------------------|--|--|
| Study group  | COG1 | SIOP <sup>2</sup> | GPOH <sup>3</sup> | MSK <sup>4</sup> | TXCCC <sup>5</sup> |  |  |
| phase  | III  | III               | III               | II (pilot)       | II (pilot)         |  |  |
| accrual  | 495  | 1000              | 360               | <100             | 30                 |  |  |
| cycles   | 6    | 8                 | 6/8*              | 5                | 5                  |  |  |
| length of cycle, days  | 21   | 10                | 21                | 21               | 21                 |  |  |
| CHEMOTHERAPY AGENTS  |      |                   |                   |                  |                    |  |  |
| cisplatin  | X    | x                 | X                 | X                | X                  |  |  |
| carboplatin  |      | X                 |                   |                  |                    |  |  |
| cyclophosphamide/Cytoxan   | X    | x                 | X                 | X                | X                  |  |  |
| doxorubicin/Adriamyacin  | X    |                   | X                 | X                | X                  |  |  |
| etoposide/VP-16  | x    | x                 | X                 | X                | x**                |  |  |
| vincristine  | X    | x                 | X                 | X                |                    |  |  |
| topotecan  | X    |                   | x*                |                  |                    |  |  |
| vindesine  |      |                   | х                 |                  |                    |  |  |
| dacarbazine  |      |                   | x                 |                  |                    |  |  |
| ifosfamide   |      |                   | x                 |                  |                    |  |  |

<sup>\*</sup>GPOH randomizes half enrolled to extra two cycles containing topotecan.

For example, the COG protocol uses six cycles, the German protocol uses either six or eight cycles (half are randomized to two extra cycles of topotecan), and the European SIOP protocol uses eight 10-day cycles of a rapid chemotherapy administration (termed "Rapid COJEC"). MSKCC's protocol uses five cycles of induction chemo. Baylor/Texas Children's pilot protocol also uses five cycles, but includes low-dose etoposide and high-dose cisplatin in the first two cycles to determine if an improved response rate will result from a high-dose/low-dose mix (called "chemo-switching").

**Growth Factor.** A growth factor (granulocyte colony stimulating factor or G-CSF) is administered in most protocols after each cycle of chemotherapy to boost white cell count recovery. G-CSF is usually given as daily injections until the white cell count reaches a prescribed level. The use of G-CSF is randomized in the current SIOP protocol in Europe (see appendix below).

Coping with the impact of chemotherapy on your child is discussed in Chapter 3, "Coping with Treatment: Side Effects, Comfort Measures and Safety Precautions – Getting Through Chemotherapy and Surviving Neutropenia."

#### Stem Cell Harvest

All high-risk NB treatment protocols currently include a collection of peripheral blood stem cells, *ideally* as soon as the bone marrow is clear of NB. Early collection minimizes the stem cell exposure to chemotherapy and clear bone marrow minimizes the chance for contamination with NB tumor cells. Whether or not the collected stem cells should be "purged" (i.e., subjected to a laboratory process to remove any NB cells) was answered by the recent (2000-2006) randomized study COG-

<sup>\*\*</sup>Both low dose oral and high dose IV etoposide used.

COG Children's Oncology Group; SIOP International Society of Pediatric Oncology; GPOH German Pediatric Hematology Oncology Group; MSK Memorial Sloan-Kettering Cancer Center, New York; TXCCC Texas Children's Cancer Center, Houston/Baylor

A3973, which showed purging stem cells did not increase survival rates.<sup>6</sup> The advantage to *not* purging is that some of the stem cells could be damaged or lost in the expensive purging process.

The harvest may be done as early as after the second round of induction chemotherapy (COG, MSKCC, and GPOH) or as late as after the last round (SIOP). Stem cells are boosted after a cycle of chemotherapy by administering daily G-CSF shots for a week or more, until white blood count is high enough to begin collection. This stimulates the bone marrow to push stem cells out into the peripheral blood.

The collection is performed through a process known as "apheresis." Blood is drawn and passed into a machine that spins the blood to remove certain stem cells (those identified as "CD34+"), and then the blood is returned to the child. Apheresis may be scheduled on an outpatient basis in the blood bank, or your child may be admitted to the hospital, depending on the institution's practice. Your child may or may not require placement of a special apheresis line or catheter to collect stem cells. This process is usually done over a few consecutive days to collect enough stem cells. At least 2 million cells per kilogram (child's weight) are required for one rescue. The stem cells are tested for the presence of NB cells with very sensitive methods (RT-PCR immunocytohistochemistry) and used only if no NB cells are detected (i.e., no NB cells detected per 500,000 stem cells). The stem cells are divided into "rescue" doses and frozen with a preservative called DMSO (dimethyl sulfoxide; this causes the distinct smell of "creamed corn" when thawed and reinfused in the child during "rescue"). The cells will be tested for viability before use, and have been used successfully as long as 8 to 10 years after collection.8

Most protocols use the collected stem cells for autologous stem cell transplant (ASCT) in the consolidation phase of treatment. However, even children that do not undergo ASCT may have need for stem cells later, as some NB treatments may be damaging to the bone marrow and a stem cell "boost" may be given to help rejuvenate bone marrow.

In the event a child's disease is deemed refractory (resistant to treatment) or relapses (recurs), having stem cells on hand can make the difference between qualifying for a promising new treatment or being ineligible. For this reason, it is advisable to discuss with your doctor the quantity of stem cells that will be collected, with an eye toward any necessary long-term treatment. Most neuroblastoma patients are small at diagnosis (average age of 2), so it is also important to consider the potential growth of a child who might double or triple in size, thus requiring a much larger amount of cells for a future rescue.

### Surgery

All high-risk NB patients undergo tumor resection, usually after receiving at least 3 cycles of chemotherapy. In some cases, a surgeon may be able to remove the primary NB tumor at biopsy, but this is rarely the case, because high-risk NB tumors are invasive and notorious for growing around major blood networks and organs. The surgeon carefully plans the surgery to remove the primary tumor as well as all suspicious lymph nodes while aiming to spare organs. Chemotherapy helps shrink the tumor and makes removal less difficult, although resection of a high-risk NB is still considered a difficult and major surgery. Parents should expect their children to be in the operating room at least five hours and sometimes as long as 12 hours or more.

The timing varies according to different protocols. Surgery may be done after the second (TXCCC), third (MSKCC), fourth (GPOH), fifth (COG), or eighth cycle (SIOP) of induction chemotherapy.

The necessity of full removal (gross total resection) in high-risk cases remains a subject of controversy among some NB specialists. Some oncologists believe that total removal of the primary tumor, though desirable, is not a necessity because chemotherapy and radiation given subsequent to surgery will destroy any remaining disease, and cite complications in difficult surgeries. Others have

concluded that complete resection is related to increased survival. 10,11,12 For example, referring to this controversy, Dr. Michael LaQuaglia, author of "The Role of Surgery in the Treatment of Neuroblastoma" in the 2005 pediatric oncology text *Neuroblastoma* (Cheung & Cohn, eds.), says:

"Despite doubts as to the feasibility, safety, and efficacy of surgical resection in high-risk neuroblastoma, the present consensus in the Children's Oncology Group (COG), and European and Japanese cooperative groups is that an aggressive resection of loco-regional disease should be attempted. Surgery has an even more important role in low- and intermediate-risk disease." <sup>13</sup>

Parents with children who have tumors deemed to be unresectable often decide to seek another opinion from an experienced NB surgeon who routinely removes difficult tumors, such as Dr. Michael LaQuaglia in New York City, Dr. Robert Shamberger in Boston, Dr. Andrew Davidoff in Memphis, or Dr. Jed Nuchtern in Houston, among others. *See* Chapter 1, **U.S. Neuroblastoma Specialists**.

See Chapter 3, "Coping with Treatment: Side Effects, Comfort Measures and Safety Precautions - Surgery" for information about caring for your child after surgery.

#### **Consolidation Phase**

Consolidation therapy is anti-cancer treatment given when a child is in complete remission (CR) or very good partial remission (VGPR), aimed at killing any remaining cancer cells. Consolidation therapy varies according to different protocols.

### Stem Cell Transplant: 1, 2, 3 or 0?

Stem cell transplant (also referred to as *myeloblative* therapy) is currently the most frequently used form of consolidation. Terminology surrounding stem cell transplant can be confusing, as many terms used are synonymous. *Autologous* means the stem cells are one's *own*, and *allogeneic* means the source of stem cells is a *donor*. Most NB treatments use autologous stem cells collected from the patient's peripheral blood. Peripheral blood stem cells engraft much faster than cells surgically removed from the bone marrow, so "bone marrow transplants" are much less common in NB treatment today. You will see the synonymous terms *peripheral blood stem cell transplant* (PBSCT), *stem cell transplant* (SCT), *autologous stem cell transplant* (ASCT), *hematopoietic stem cell transplant* (HSCT), and *high-dose chemotherapy with stem cell rescue* (HDC/SCR) all used interchangeably.

Stem cell transplant is high-dose chemotherapy or other treatment so severely suppressing the bone marrow that a subsequent "transplant" or "rescue" infusion of stem cells is required. Transplant has been frequently used since the 1980s for consolidation for high-risk NB. Three randomized studies of patients accrued since the 1980s -- most notably the phase III study CCG-3891 conducted by the Children's Cancer Group and published in 1999 -- have suggested that survival is improved with transplant. 15,16,17,18

Subsequently, autologous stem cell transplant has been widely adopted for treatment of high-risk NB. Double 19 and triple 20 autologous tandem transplants have also been tested in pilot studies, as well as allogeneic transplants. 21

The recent phase III study COG-A3973, as noted above, showed no need for purging stem cells used for rescue at transplant, and other important changes in treatment adopted for that study included the use of higher dose induction chemotherapy, using stem cells from peripheral blood rather than bone marrow, and local radiation rather than TBI. The current COG phase III transplant study, ANBL0532, began accruing patients in December 2007 and randomizes them to either a single or double (tandem) autologous stem cell transplant with local radiation (no TBI).

Some institutions offer their own unique regimens for transplant, such as using donor or cord blood for the source of stem cells, or using a new combination of chemotherapy, or using triple tandem transplants, and some institutions use protocols from closed trials. Most conditioning regimens use mega-doses of chemotherapeutic agents—usually drugs not used in the induction phase—while less common regimens use chemo with total body irradiation (TBI) or MIBG radiation therapy. In the current European SIOP trial children are randomized to one of two different chemo combinations (See "Appendix" below).

See Chapter 3, "Coping with Treatment: Side Effects, Comfort Measures and Safety Precautions - Special Issues of Transplant" for information to help you get your child through the transplant treatment.

A notable exception to the use of transplant for high-risk NB cases is MSKCC, whose frontline protocols have not included stem cell transplant since 2004 and instead use antibody treatment for consolidation. Doctors at MSKCC say they have not observed myeloablative consolidation treatments to have a significant impact on survival rates in their studies over the past 15 years.<sup>22</sup> After successful response to induction chemotherapy and surgery, patients on MSKCC's current protocol move on to local radiation, 3F8 antibodies, and Accutane.

#### Radiation

Children diagnosed with high-risk disease routinely undergo radiation therapy after induction chemotherapy and surgery. In protocols that include stem cell transplant, radiation therapy usually begins after the patient is released from the hospital.

Even children whose tumors have been completely removed receive radiation to the primary site of disease. Some institutions also radiate bone sites where NB was present at diagnosis, even if those tumors have completely responded to chemotherapy; other places radiate only the spots still showing before transplant. At least one protocol includes MIBG radiation therapy if remaining disease is detected by MIBG scan before transplant.<sup>23</sup>

NB is generally responsive to radiation, but because intensive radiation treatment poses a significant risk of causing secondary cancers and other health issues, doctors try to use the minimum effective dose. Also, radiation beams must be carefully pinpointed to avoid damaging nearby organs, so children undergo a planning session with three-dimensional CT scan simulation before treatment starts. They may receive tiny pinpoint tattoos that are used to align the radiation beams. For children receiving radiation to the head or orbits, a mask is made that can be fastened to the radiation table, so the child does not move during the treatments. Similar "forms" may be made to hold a child's arm or leg in position, if treatment to those areas is necessary.

External beam, MIBG radiation therapy, total marrow irradiation (TMI or TomoTherapy), proton beam, radiosurgery (Gamma knife), intraoperative radiation therapy (IORT), and intensity-modulated radiation therapy (IMRT) are various ways radiation can be delivered, depending on the protocol and the patient's circumstances.

For information on helping your child cope with radiation therapy, see Chapter 3, "Coping with Treatment: Side Effects, Comfort, and Safety – Radiation: From Tattoos to Side Effects."

#### **Treating Minimal Residual Disease**

One of the things that makes NB so difficult to cure is the fact that even when it cannot be found through scans, lab tests, or bone marrow biopsies, the disease can still be present in very small amounts in the body. Doctors believe that this undetectable disease can sometimes smolder and

grow, eventually coming back as relapsed NB, which is much harder to cure. Accutane and antibodies are two strategies that have been developed to help eradicate undetectable disease, but the two work in very different ways. Much research on vaccines against NB has been accomplished, but use after frontline therapy is a new development.

#### Accutane

Accutane, or 13-cis retinoic acid, is a synthetic vitamin A derivative that has been shown to stop the growth of NB cells. Accutane can cause some NB cells to mature (differentiate) into non-cancerous cells. A five-year (1991-1996) randomized study (CCG-3891) concluded that high doses of Accutane improved the event-free survival for children in remission.<sup>24</sup> Since those findings were published in 1999, the use of Accutane has become widely accepted for high-risk NB.

Accutane is given by mouth in capsule form in two-week on/off cycles—the medicine is taken twice a day for two weeks, then children take no medication for two weeks. Typically, children receive Accutane over six months. In the German NB2004 protocol it is given for six months with a three-month break, and then three more months.

Accutane has many side effects, but they are mostly an annoyance, such as dry skin, moodiness, and sun sensitivity. Because some of Accutane's side effects can be more serious, children are monitored during their Accutane treatment with regular check-ups and blood draws (particularly for calcium levels and triglycerides).

It is **extremely** important that pregnant women, and those who may become pregnant, follow strict safety precautions when handling Accutane, because ingestion of the drug (which can be absorbed through the skin) poses a risk of serious birth defects and deformities.

For more information on administering Accutane and coping with its side effects, see Chapter 3, "Coping with Treatment: Side Effects, Comfort Measures and Safety Precautions - Accutane."

#### **Monoclonal Antibodies**

Our bodies manufacture antibodies that create an immune response to bacteria, viruses, and other foreign substances to help keep us healthy. Ordinarily, a child's immune system will not attack NB because the cancer is a part of the child's body. Monoclonal antibody therapy (*monoclonal* refers to development from *one clone*) uses mouse antibodies produced in the laboratory from plasma (myeloma) cells. The antibodies used in NB treatment attach to a ganglioside (a fat-sugar complex molecule) on the NB cell called GD2. Because the antibody alerts the child's own immune system to attack the NB cell the antibody is attached to, the cancer cell is destroyed. Long-term immune response may be initiated by antibody treatments in some cases.

COG currently offers a phase III study (COG-ANBL0032) of the monoclonal antibody ch14.18 (administered with "cytokines" to augment the immune response to the antibody) to patients following completion of frontline treatment protocols that include stem cell transplant. After an early review of 226 children enrolled determined significantly higher survival with antibodies, the study was amended in April 2009 to stop randomization and allow all patients subsequently enrolled to receive the antibody. The study will continue until final accrual goal of 423 is met, and it is anticipated that ch14.18 will be part of standard treatment for all COG protocols. <sup>25</sup> <sup>26</sup> The *ch* prefix indicates the antibody is "chimeric" or part human (75%) and part mouse (25%) in its formulation. In the current European SIOP trial the use of the same antibody ch14.18 is randomized (but without the use of cytokines). Note that the similar protocol number of COG-ANBL0322 using a different but similarly named antibody, hu14.18-IL2, is a closed phase II study which was open only to children with relapsed or refractory NB. The *hu* prefix means the antibody is completely humanized. *See* Chapter 3, "Coping with ch14.18 Antibodies"

MSKCC uses a 100% mouse-derived 3F8 antibody treatment for high-risk patients who complete induction therapy with a good response. GM-CSF (granulocyte-macrophage colony-stimulating factor—a "cytokine" that stimulates the immune system) is usually given with 3F8. This antibody has been in use for two decades. MSKCC reports that their studies have shown improved survival among their patients who successfully complete at least four cycles of 3F8 antibody therapy.<sup>27</sup> For more information on the administration and side effects of 3F8 antibodies, see Chapter 3, "Coping with Treatment: Side Effects, Comfort Measures and Safety Precautions - 3F8 Antibodies."

#### **Vaccines**

Various vaccines against NB have been created and tried in relapsed and refractory children, but recently the CHESAT vaccine became available in a trial In Houston TX for children who have successfully completed frontline therapy with a single transplant.<sup>28</sup>

### **Summary**

The above discussion provides a *very* general introduction to the common components of frontline treatment for children with high-risk NB. Parents interested in learning more about any of the trials mentioned are advised to contact the doctor or institution in charge of the specific trial. Questions about the rationale, specific components and impact of your child's particular treatment should of course be directed to your child's oncologist.

Please contact editors@nbhope.org with any comments

### **APPENDIX**

# A brief history of phase III studies for high-risk neuroblastoma

Treatment randomized in bold.

1982-1985: European Neuroblastoma Study Group (ENSG1) enrolled 167 children and randomized to melphalan autologous **bone marrow transplant or no further therapy** (no radiation therapy given to any). Transplant and no-transplant arms each had 65 patients, and recent long-term follow-up report revealed better 5 year event-free survival for stage 4 over 1 year old in melphalan-transplant group versus no further treatment.<sup>29</sup>

1990-1999: European study (EU-20592 or CCLGNB-1990-11) randomized 262 high-risk children over 1 year old and revealed higher survival rate for **rapid sequence induction** (10-day cycle) versus **standard induction** (21-day cycle) with same total dose. Ten-year event free survival was 27% and 18% respectively with non-aggressive surgical approach, no radiotherapy, and melphalan-only autologous bone marrow or stem cell transplant for both groups.<sup>30</sup>

1991-1996: Phase III trial with two sequential randomizations for 379 high-risk NB patients was carried out by the Children's Cancer Group (CCG-3891) which demonstrated improved survival with **myeloablative therapy** (with total body irradiation) and **13-cis-retinoic acid** (Accutane) with 50 patients in each of the four arms of the study.<sup>31</sup>

1996-2003: The German (GPOH) study NB97 compared outcomes of 295 high-risk NB patients randomized for **stem cell transplant** or **consolidation chemotherapy**. Results showed increased survival with transplant.<sup>32</sup>

2000-2006: The recent study (COG-A3973)<sup>33</sup> questioned the need for **purged stem cells** for CEM-LI (carboplatin, etoposide, melphalan, with local irradiation)<sup>34</sup> transplant, and accrued 486 patients. Purging stem cells was not found to improve survival.<sup>35</sup>

2000-2012: An additional study (COG-ANBL0032)<sup>36</sup> determined that the **antibody ch14.18** with interleukin 2 and GM-CSF improved survival when given after stem cell transplant (early analysis prompted the end of the randomization portion in April 2009) and will accrue a total of 423 patients.<sup>37</sup>

2002-2008: SIOP (International Society of Paediatric Oncology) formed the European SIOP Neuroblastoma Group (ESIOP NB) in 1994<sup>38</sup> and activated a phase III high-risk NB protocol in 2002 (SIOP-EUROPE-HR-NBL-1)<sup>39</sup> using "rapid" COJEC (8 cycles of chemotherapy given at 10-day intervals) followed by transplant randomization to CEM (carboplatin, etoposide, melphalan) or BuMel (busulfan, melphalan) and then randomization to with or without **ch14.18 antibody** treatment. This study will also evaluate the use of **growth factors** as well as compare **transplant regimens**, and all patients receive *cis*-retinoic acid. This trial will accrue 1000 patients (175 per year). There are eight arms to this study.

2005-2010: The current German NB2004 **randomizes topotecan** use in up-front therapy, includes MIBG therapy for positive lesions before transplant, and will accrue a total of 340. After transplant, the high-risk protocol includes six months of *cis*-retinoic acid, a three month break, and another three months of retinoic acid.  $^{40,41}$ 

2007: The COG phase III ANBL0532 $^{42}$  trial opened December 2007 for accrual of 495 and will compare **single versus tandem transplants**, and induction begins with two cycles of topotecan.  $^{43}$ 

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# Getting through Chemotherapy

Chemotherapy – or "chemo," as it is so often called — is what many of us associate with cancer treatment. The notion that your child must experience the thing you may have seen portrayed so graphically in movies or accounts from friends can be agonizing. Unfortunately, depending on the risk assignment of your child's NB at diagnosis, chemotherapy will likely be the first step in standard therapy for your child. Chemotherapy *does* cause significant side effects as it is killing the cancer, but experienced health care professionals will carefully monitor your child during all aspects of NB chemo.

Although your child will be in very good hands, you may wish to know more about what to expect and how you can help keep your child as comfortable as possible. The focus of this chapter is the potential short-term side effects of chemotherapy and coping strategies that have helped other NB parents during their children's chemotherapy treatments. (Please use the e-mail link at the end of this section to send comments about coping strategies that *you* have found helpful during your child's chemotherapy.) Although we hope it will be useful, please keep in mind that each child's situation is unique, and you should always address all of your questions and concerns about your child's specific situation to your medical team.

Chemotherapeutic agents are medications that destroy rapidly dividing cancer cells by targeting different phases in the cancer cell's life cycle. (**See "Overview of Treatment for High Risk NB."**) Since various agents attack the cancer cell differently, they are commonly given in combination for maximum beneficial effect. *Combination chemotherapy* decreases the possibility of the cancer's survival and lessens its ability to grow.

The manner in which the chemotherapy is prescribed for your child will be based on a clinical trial, a protocol or an institution's previous medical experience with NB. Your child will probably start on a regimen of *induction chemotherapy*, chemo that is given to shrink the tumor before surgical resection (removal). The child will then move on to *adjuvant chemotherapy*, a term used for chemo given to a child who is considered to have minimal evidence of disease after surgery.

At this time, most institutions administer induction chemo in-patient for high-risk NB and out-patient for low- and intermediate-risk NB. An exception to this rule includes Memorial Sloan-Kettering Cancer Center where most children do chemo in the Pediatric Day Hospital and are discharged with backpacks of IV fluids and/or medication infusing through portable pumps. It may sound daunting at first, but if your hospital utilizes this approach, rest assured that you will be trained in simple and time-tested procedures to make everything go smoothly during any at-home infusions.

The most common method of administering chemotherapy is intravenously. However, it can also be delivered by mouth, subcutaneously, intramuscularly, into a body cavity, or into the cerebrospinal fluid. The dose of chemotherapy will be determined by your child's body surface area or weight. Before every round of chemo your child's weight will be recorded in kilograms and height in centimeters in order to determine your child's body surface area (in square meters, or "m²").

After the chemotherapy consent is signed, the hospital pharmacist will prepare your child's specific chemotherapy dose. First, premedications (often referred to as "premeds") will be administered. They are commonly anti-emetics (anti-nausea medications). Then, typically, a specially trained nurse will administer the intravenous (IV) chemo agents by IV pumps into your child's central

catheter. You will probably watch anxiously the first round of the liquid medication dripping into your child's body. You may imagine it searching out and destroying the cancer. You might look to your child for some type of reaction, but he or she will probably continue watching TV, putting a puzzle together or chattering away. It will likely be an anti-climatic moment.

Along with the IV chemo, your child will receive carefully calculated intravenous fluids also. A lot of hydration can sometimes mitigate the toxic affects of some chemotherapeutic agents. These extra fluids may cause your child to urinate frequently during chemo and wake during the night. Even young children who have been toilet-trained for several years may have to wear "pull ups" or diapers due to the excessive amts of fluid. Any infant/child in diapers should be changed frequently, (even during the night), as this urine and chemo eliminated is irritating to the skin.

Usually blood work (CBC and chemistries) and a urine sample will be tested each day prior to chemo initiation and your child's urine output will be measured (from urinating in a hat or weighing wetdiapers.)

### Potential Side Effects of Chemotherapy

Once you understand that chemotherapy is designed to kill rapidly dividing cancer cells, you realize that it can also attack other rapidly dividing cells within your child's body. Your child's hair, skin, nails, gastrointestinal tract and bone marrow will be under assault. This hit on your child's non-cancer cells is what leads to the most common side effects of chemotherapy your child will likely experience.

Each specific type of chemotherapy, its purpose and its potential side effects will be explained by a member of your child's oncology team. (For example, doxorubicin and cisplatin generally cause nausea; cyclophosphamide can sometimes cause bladder bleeding; vincristine can cause loss of reflexes. Some side effects happen soon after the chemo is initiated and some are delayed-days, weeks and even years after the chemo is given. The most common short-term side effects are discussed below, along with various strategies that have helped some NB families cope with them. (As noted, please use the e-mail link at the end of this section to send comments about coping strategies that *you* have found helpful during your child's chemotherapy.)

#### Gastrointestinal (GI) Tract Issues

### Nausea, Vomiting and Diarrhea

During the first round of chemotherapy, nausea and vomiting often start within the first 12 hours and usually sooner with future rounds, depending on the agents used. These symptoms can occur because of the effect of chemotherapy on the GI tract and/or on the vomiting center of the brain. Each child's medication regimen is individualized and child-specific. You will need to work closely with your child's oncology team to determine which medications help ease your child's nausea and vomiting. It is good to keep your own notes on all the medications and write down how well they worked or didn't work (see "Keeping Records"). And keep in mind that it's best to have medications administered before the symptoms become pronounced. Also, if your child vomits chemo that was taken orally, it is imperative that you inform the oncology team immediately.

There are some dietary considerations that may be helpful to ward off nausea and vomiting. Most parents have found it helpful to encourage, but not force, the child to eat, and to avoid greasy, spicy, strong- smelling food. Cold food is commonly tolerated better than hot food. Try having your child drink, wait a about a half an hour, and then eat. High protein, high calorie foods--like shakes, high fat yogurts, and breakfast meals--are ideal. Some chemotherapy cause a metallic taste, and your child may ask for a favorite food and then reject it because it tastes wrong.

Food intake should not become a source of stress for your child. As parents we often obsess about every morsel of food our NB child consumes, but our children should not feel our stress. It's better to follow your child's lead. Some children develop strong cravings during chemotherapy and they commonly experience changes in taste. They intuitively know what their body may tolerate. Giving your child the power to make dietary decisions gives them a sense of control. And remember, anxiety can also cause nausea and vomiting.

Your child may experience diarrhea because chemo can damage the cells that line the intestinal wall. If this occurs it is usually advisable to avoid fatty foods. If your child can tolerate it, and it falls within his or her dietary restrictions (see "Surviving Neutropenia"), try foods naturally low in fiber and high in potassium like bananas and potatoes. Notify your health care team if your child's diarrhea is severe or if it occurs multiple times in one day.

## Constipation

Chemotherapy can also cause constipation, as it affects the intestinal nerves, slowing "peristalsis," the movement of food and wastes through the intestines. Pain medications and some tumor locations can also cause constipation. Encourage your child to drink fluids, especially apple juice, and eat high fiber foods like whole grain breads and cereals. Fruits and vegetables are beneficial if they can be tolerated and are allowed. Exercise can also encourage bowel regularity. You need to keep track of your child's bowel movements and inform the health care team if your child's bowel habits slow and constipation begins to develop. Medications such as stool softeners and laxatives may be prescribed (or available as over-the-counter drugs) to assist regularity. It often requires some trial and error to determine the lowest effective dose—too much can cause diarrhea.

#### Mucositis

Sores in the mouth and anywhere in the gastrointestinal (GI) tract, or "mucositis," can be a result of the chemotherapy destroying the mucus membranes. Mucositis occurs as a result of cell death caused by chemotherapy or radiation. This causes the mucosal lining of the mouth to slough off and then become red, inflamed, and ulcerated.

Oral mucositis can be severely painful, depending on the extent of the tissue damage, and can result in trouble speaking, eating, or even opening the mouth. These ulcers can also become infected. Make sure your child maintains good oral hygiene, and brushes with a soft toothbrush or sponge brush and rinses with water or water mixed with baking soda after each meal. A "swish and swallow" preparation and/or a "rinse and spit" mouthwash will usually be provided to assist in oral care. Different institutions have their own preferred mixtures. Just make sure no products contain alcohol, as this will almost surely cause a stinging pain. Try soft foods and avoid citrus, spicy, and hot foods. Popsicles, jello, sodas, ice cream, yogurt and shakes can be helpful.

For pain control, mild cases can be treated with home remedies such as ice pops, water ice, or ice chips. Some older children may fine sore throat lozenges help. Topical pain relievers, including lidocaine, benzocaine, dyclonine hydrochloride, chlorhexidine gluconate, and ulcerease, are often prescribed for severe mucositis, but it is hard to obtain an effective coating of all areas and the pain relief provided is usually brief. A medication called Magic Mouthwash, which is a mix of lidocaine, diphenhydramine, and Maalox, is sometimes prescribed for mucositis patients. Some say that Magic Mouthwash has not been proven effective and that the Maalox further dries the tissue, which can add to complications, so that it is best to use lidocaine alone in a swish and spit method. If a narcotic is used for pain control, remember to watch for constipation. Severe cases of pain with mucositis may require a hospital admission if IV pain administration is needed.

Because the mucous is present in the stomach and intestines, mucositis can also cause very gelatinous diarrhea. A diaper rash type paste, "Butt Paste," is often provided for rectal area skin.

#### Nutrition

Your child's weight and nutritional status will be monitored closely. During severe cases of mucositis and/or nausea, vomiting and diarrhea, a child may be unable to eat or drink any significant amount. Your child's weight, hydration, and nutritional status will be monitored closely. If there are signs of malnutrition and dehydration, your child's oncologist may order supplementary nutrition. This should not be seen as a failure for parents or the healthcare team, but as what is needed to help your child fight cancer.

Your child's oncologist will explain alternative feeding methods if they are needed. "Enteral" feedings are liquid feedings that are delivered by a tube--either a naso-gastric tube (a tube that is passed through the nose to the stomach referred to as NG-tube) or a gastric tube (a tube that is passed through the abdominal wall into the stomach referred to as G-tube.) Intravenous fluids can be administered to improve hydration. "Parenteral" feedings are carefully calculated nutritional intravenous feedings that are administered through your child's central line, bypassing the gastrointestinal tract. There are two types of parenteral nutrition: Total Parenteral Nutrition (TPN) or Partial Parenteral Nutrition (PPN). [Some good info is included on the use and pros and cons of parental and enteral feedings here—

http://www.cancer.gov/cancertopics/pdq/supportivecare/nutrition/Patient/page4 ie effect on organs such as liver etc]

#### Problems with Skin and Hair

Dry, flaky skin is common with chemotherapy. Mild soap, skin moisturizers, lip balm and sunscreen are a must for good skin care. Skin cracks and fissures need to be avoided, as they are potential places of entry for infection.

Special attention to diaper skin area is necessary for parents with infants and toddlers. The medications, in combination with the high amounts of IV fluids, make it nearly impossible to avoid diaper rash burns on the skin unless you are well-prepared to aggressively use preventative measures. Heavy barrier creams are needed as are more frequent diaper changes due to the extra fluids. Prevention goes a long way toward avoiding a rash and subsequent increased risk for infection.

Your child's hair follicles will be damaged by the chemo. This includes scalp hair, eyelashes, and eyebrows, as well as axillary (armpit) and pubic hair for teens. Hair loss or "alopecia" can occur gradually over weeks or months or it may happen suddenly. It is important that you explain to your child BEFORE hair loss begins, that the hair will come out, that it won't hurt, and that it will grow back. If your child would like a wig, it should be selected as early as possible, for matching purposes. Some parents and children opt to cut the hair or shave it, so the loss doesn't seem as dramatic. Regardless, when the strands start to fall, so may the tears--yours and your child's.

Although initially upsetting, hair all over the pillowcase, on the couch, and attached to the clothes eventually becomes an annoyance. Having a handy lint remover is helpful. Scarves, hats, and sunscreen should be used to protect the scalp.

Having a child going bald really brings home the reality that your child has cancer; there's no denying it anymore. At first you and your balding child may feel uncomfortable in public. But in time, your child will transition to acceptance and you to a feeling of parental pride in your child's strength during cancer treatment. It is not uncommon to see bald fathers in the cancer clinic, who

have decided to keep their heads shaved during their children's cancer treatment, to say to the child and to the world --bald truly is beautiful!

## **Bone Marrow Suppression**

Chemotherapy can suppress the bone marrow's ability to produce blood cells. This will affect your child in different ways.

Your child's white blood cell level may decline. Since white blood cells are needed to fight infection, this decline can put your child at high risk for potentially serious infections. A "colony stimulating factor" medication injected subcutaneously (i.e., by shots) may be prescribed in order to stimulate the bone marrow into white blood cell production. When the white blood cells that fight bacteria, the "neutrophils," get dangerously low, it is called "neutropenia". There is a lot of information about neutropenia and precautions that need to be followed during this condition. If your child is neutropenic and develops a temperature of 100.4 or any worrisome symptoms, the oncologist should be called immediately. Depending on your child's white blood cell level, hospital admission for observation and IV antibiotics is common to prevent sepsis (bacterial in the blood). (See "Surviving Neutropenia.")

In order to prevent a serious life-threatening infection called "pneumocystis carinii" pneumonia (PCP), various antibiotics are prescribed as a precautionary measure -- trimethroprim-sulfamethoxazole (Bactrim), dapsone, and/or pentamidine. (See "Surviving Neutropenia.")

Chemotherapy can also suppress your child's red blood cells and hemoglobin, causing "anemia." With anemia your child may seem pale, tired, irritable, have a shortened attention span and can get dizzy. When the hemoglobin level drops below a certain number (typically below 8), or there are worrisome symptoms such as mentioned above, your child will likely receive a transfusion of packed red blood cells at a dose of 10 milliliters per kilogram. (See "Blood Transfusions.")

Platelets, which are needed for clot formation and bleeding prevention, are also affected by chemotherapy. A drop in platelets to less than 100,000mm³ (also referred to as platelets of 100,000, 100K, or just 100) is called "thrombocytopenia." If your child's platelets are low and you notice any signs of bleeding--nosebleeds, "petechiae" (spatters of pinpoint, flat, red spots on your child's skin caused by broken capillary blood vessels), bruising on your child's extremities, blood in stools or urine (some bloody stools are actually black), bleeding from gums, or bleeding from intravenous access sites- you need to contact your child's health care team immediately.

When your child is thrombocytopenic, there are bleeding precautions that need to be followed. These include having your child avoid contact sports like soccer, bicycling and the trampoline and having them always use safety equipment like helmets, side-rails, car seats. Constipation needs to be avoided so stool softeners are often recommended. Emery boards should be used to keep fingernails and toenails trim and smooth; nail clippers and scissors should be avoided. In order to prevent oral trauma, extra soft toothbrushes or tooth sponges are preferred. For the adolescent patient who insists on shaving, electric razors are safer than a razor blade.

During chemotherapy and thrombocytopenia, children should not have rectal temperatures, suppositories or enemas due to the risk of injury, infection and bleeding. They should not receive non-steroidal anti-inflammatory (i.e. ibuprofen) or aspirin-containing medications (e.g., Pepto-Bismol) due to bleeding precautions and the potential for Reye's syndrome.

If your child's platelets are substantially low, invasive procedures (i.e., surgery, bone marrow biopsy, urinary catheterization) may be delayed or performed with great caution.

Platelet transfusions are usually administered when the platelet level is significantly low (<20,000/mm³, or platelets of 20,000, 20K, or just 20), your child is experiencing bleeding symptoms, or in preparation for surgery, a procedure or a platelet-depleting medication administration. (See "Blood Transfusions.")

### **Delayed Side Effects**

Chemotherapy can also affect your child's organs and body systems (i.e. heart, kidneys, liver, hearing, future reproductive function and growth). Your child will be continuously monitored for these effects on an individual basis, throughout his or her NB treatment and thereafter. See "Living with Long-term Survivorship Issues."

### Summary

Chemotherapy is an important aspect of the current treatment regimen for many children with NB. We parents should have basic information about each chemotherapeutic agent, their potential side effects, and the corresponding medication that our children can receive to combat these side effects. We need to know the dose of any such medication, how to give it, and any special instructions.

Keeping careful records of all drug names, dose administered, dates given, and any reactions is very important for reference during and after treatment.

Make sure that you completely understand when to notify your child's oncology health care team during chemotherapy, know the best manner to communicate with them at any hour of the day or night, and have all relevant phone numbers, pagers, e-mail addresses, and emergency services.

Before long, your child's first round of chemo will be completed. With the knowledge and experience gained, as a family you will feel more ready to begin the second round, and will quickly become "pros." Having a child who is receiving chemo is certainly a challenge, but together as a family you will conquer each hurdle so that the medications can rid your child of cancer.

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# Surviving Neutropenia

Chemotherapy's potential to kill NB cells means that it also will have effects on the normal cells in your child's body. General background information about these effects and some strategies from NB parents for coping with them can be found in **Getting Through Chemotherapy**. One side effect of chemotherapy that requires special attention is "neutropenia." Additional information about this important aspect of treatment is provided below, as well as some basic tips that have been helpful to some NB parents. (Please use the e-mail link at the end of this section to send comments about coping tips that *you* have found helpful during your child's neutropenia.) The information provided is not in the nature of medical advice - you should always consult with your NB team before considering any suggestions from a parent or any source other than your medical team. Most hospitals will have specific guidelines for caring for a neutropenic child. Your child is in a potentially life-threatening situation during neutropenia, so it is crucial to understand and follow the medical team's guidelines.

### What is Neutropenia?

Neutropenia is the medical term for having an abnormally low number of white blood cells called neutrophils. Neutrophils are the 'first responders' to a bacterial invasion, and surround and kill the bacteria. (See "Understanding the CBC.")

Neutropenia is dangerous because it makes the body more susceptible to bacterial infections. Children with NB often become neutropenic because neutrophils can be destroyed by chemotherapy and radiation. The children are typically at risk for neutropenia a week or two after completing a chemotherapy treatment. The timing will vary according to the specific chemotherapy and the particular child. But often neutropenia can be anticipated and parents should be on high alert at these times.

When neutropenia is expected, your child's temperature should be taken at least twice a day and whenever the child feels warm (tactile temperature). The temperature may be taken by mouth (orally), by ear (tympanic), or under the arm (works well on sleeping children), but be sure to record how the temperature was taken. Do not take a rectal temperature in a child undergoing treatment for cancer, as this can cause bleeding and infection.

## How is the Neutropenia Diagnosis Made?

Neutropenia is diagnosed by a blood test that will determine the patient's "absolute neutrophil count" or ANC. (See "Understanding the CBC.") The severity of neutropenia generally depends on the ANC:

- mild neutropenia exists when the ANC falls between 1000 and 1500;
- moderate neutropenia exists when the ANC falls between 500 and 1000; and
- severe neutropenia exists when the ANC falls below 500.

When the child's neutrophils are at the lowest point, the child is said to have reached the "nadir" of neutropenia.

## What are the Symptoms of Neutropenia?

At the onset of neutropenia, the child may have no symptoms. When a child is neutropenic and develops a fever of up to 100.4 degrees F, it is called "febrile" neutropenia. **This is potentially a life-threatening emergency.** Your child's immune system does not have the white blood cells to fight off infection, especially with the added risk of a central venous line, and you need to contact your child's oncology team immediately. Make sure you have your oncology team's 24-hour contact information with you at all times. Bacteria can grow rapidly in the blood (sepsis) and can be rapidly fatal.

Some symptoms that can coincide with neutropenia include any type of infection, cough, sore throat, shaking and chills, mouth ulcers, and diarrhea. (See "Getting Through Chemotherapy")

## What are the Signs of Infection?

The body's normal means of defense against infection is the immune system, comprised of the skin, the lining of the nose, mouth, gastrointestinal tract, and certain blood cells. When a patient has neutropenia, the body's immune system is compromised, putting the patient at a higher risk of infection. Most infections occur in the lungs, mouth and throat, sinuses, and skin.

Because infection can be extremely dangerous to a neutropenic child, it is important to be aware of the following signs of infection and to notify your child's oncologist if any of these symptoms appear:

- Tactile temperature
- Chills, shakes, sweating
- Fatigue
- Headache
- Body aches
- · Feeling confused, dizzy or weak
- Sore throat
- Cough or shortness of breath
- Stuffy nose
- Burning with urination
- Redness, swelling, or warmth at the site of an injury, surgical wound, or central line
- Swallowing problems
- Mouth sores
- Sinus tenderness
- Pain in the abdomen
- Diarrhea
- Rectal discomfort with bowel movement

Remember, however, that some common signs of infection, such as inflammation (pus, swelling, and redness), may be absent during neutropenia because the neutrophil cells that cause these symptoms are absent.

## When is Hospitalization Required?

The criteria for the hospitalization of a child with neutropenia may differ among medical institutions. However, the child with febrile neutropenia will be admitted. When your child is being considered for admission or admitted, expect blood samples to be taken for a complete blood count (CBC) and blood cultures (to determine if an infection is present). Broad-spectrum antibiotics will be administered and your child will have a minimum of once daily 'counts' (CBC) drawn. The results of the counts will be evaluated and treated as needed. The ANC will be monitored closely. (See "Understanding the CBC.")

## Visiting the Emergency Department

If your child runs a fever or has signs of infection during the evening or weekend when the oncology clinic is closed, a visit to the Emergency Room or Urgent Care will likely be necessary. It is important to call the hospital and ask for the "pediatric hematology/oncology fellow" on-call and if the doctor thinks you should bring in your child, the fellow will alert the ER to expect your arrival. When presenting to the ER, politely inform the triage nurse that your child has a fever and is neutropenic. Specifically ask that your child not wait in the general waiting room (to avoid exposure to other patients who are in the ER for communicable illnesses and because the treatment for febrile neutropenia is urgent).

In order to protect your immune-compromised child in the Emergency Department, have your child wear a mask and make sure any staff member who approaches your child washes their hands. Finally, it is prudent to bring a packed bag from home because such visits almost always result in hospitalization. It is best to bring along your child's toys and special items for comfort and entertainment, but also to decrease the likelihood of your child contracting an infection from any toys and products that have been used by other children in the ER.

### Discharge from the Hospital

There are no set criteria for a child to be released from the hospital following an admission for neutropenia. If no infection was found, the child may be released after a certain period of time without a fever and if evidence exists that the ANC is rising. (Remember, the ANC is typically checked at least daily during a febrile neutropenia admission.) However, if an infection or another complication was discovered, the child may have additional requirements to meet prior to being released.

One of the things most families experience in NB treatment is the feeling of being "trapped" in the inpatient ward of the cancer hospital after being hospitalized for neutropenia -- the child will start feeling better and better and pleading to go home, but his or her ANC will not yet be at the point required for discharge. One of the biggest frustrations during NB treatment is keeping your child engaged and happy during such hospitalizations! This is the time when the resources of the hospital's child-life program, those gifts of board games, crafts, and books, and if permitted, visits from friends and family members, provide a lifeline to the harried NB parent. Now is the time to reach out to those friends who are eager to help and don't know what to do. A well-timed visit and a gift of a set of Uno cards can work miracles!

## Treatment of Neutropenia

As mentioned above, once your child is admitted to the hospital during neutropenia, cultures will be performed on central venous access lines or ports and peripheral blood, and broad-spectrum antibiotics will be administered. Several antibiotics are given, because upon admission to the hospital it will not yet be clear if your child has a specific infection; by administering broad-spectrum antibiotics, the hope is to start treating any such infection that may exist. Blood cultures will be started immediately, and once any actual infection is identified the appropriate specific medication for the particular infection will be administered.

As a precautionary measure, many children with neuroblastoma take a specific antibiotic, sold under the brand names Bactrim or Septra among others, two to three days each week to prevent "pneumocystis carinii" pneumonia (PCP). (See "Getting Through Chemotherapy Treatments.") Alternatively, the child may receive a periodic IV injection of a specific antibiotic at the hospital. If you are administering such an antibiotic to your child at home and another antibiotic is prescribed

for your child to treat a suspected infection during a neutropenic phase, DO NOT discontinue the Bactrim or Septra unless your child's primary oncologist orders this. The other antibiotics may not protect the patient from PCP.

To stimulate a child's immune system during neutropenia, generally the child will be treated by the administration of a "growth factor" into the subcutaneous tissue. These growth factors are special proteins that naturally occur and stimulate the bone marrow to produce more white blood cells. "Granulocyte-Colony Stimulating Factor" (G-CSF) is a man-made product that stimulates the production of neutrophils and also enhances the activity of mature neutrophils.

G-CSF is usually administered by subcutaneous injection (an injection just under the skin). Cancer centers have varying schedules for these injections, which are commonly done by parents. If you are expected to administer G-CSF, your child's oncology nurse will give you all the necessary information and training. The recommended sites include the abdomen below the navel, upper outer arms, and upper outer thighs. Rotation of the sites is often recommended to prevent scarring and discomfort. The injection is not usually painful, but occasionally the preservative may sting.

Some families choose to have G-CSF injections accomplished through the use of a device called an Insuflon. The Insuflon is a soft plastic catheter that is inserted just under the child's skin. It allows several injections through the same injection port. The theory is that since it stays inserted under the patient's skin, it will alleviate the needle pain associated with injections. This technique works well to diminish the fear associated with daily injections in some children. Other children, however, find that having the Insuflon inserted is more stressful than the shots themselves. Also, much of the pain associated with the G-CSF injection is due to the medicine itself, and the Insuflon does not alleviate this.

If the daily injection of G-CSF is a stressful experience for your child, try experimenting with different techniques in an attempt to make the shot less painful. Some children feel that having EMLA cream or an ice cube placed on the injection site lessens the pain from the injections. Some children prefer having the G-CSF injected literally as fast as possible; others prefer it to be injected very slowly. Other coping tactics include distracting the child with television or books during the injection, and having the child participate as much as possible in the injection process. Some parents put together a toy box with a prize given to the child after each shot. The child's anticipation of the shot can be the worse than the actual experience (allowing the child to create and control the "rituals" to be done before administering the shot helps in some cases, but can also backfire). Occasionally, parents give the shot when the child is asleep. Some children actually prefer this method. (Just remember to hold the child securely at all times during the injection, whether given awake or asleep.)

If the child's central venous line or port is accessed for any reason at the time when G-CSF is being administered, the oncologists at some institutions may permit G-CSF to be given through the line. There is some data that suggests that giving the injection under the skin is more effective, but the child's discomfort with the shot may outweigh this concern. Of course, the risk of infection of the central line should always be weighed against the child's aversion to the injection.

Common side effects of G-CSF are bone, joint, or muscle pain (including muscle cramping) and injection site reactions. Tylenol and antihistamines such as Benadryl or Vistaril will generally alleviate some of these symptoms. Your child's oncology team will discuss any potential side effects and their appropriate treatments.

#### Neulasta

Neulasta is similar to G-CSF in a long-acting form and boosts white blood cells. NB patients usually use Neulasta less often than G-CSF because it is generally only administered to adults and, therefore, it is often difficult to obtain insurance coverage it. Those patients who have successfully

received Neulasta have been required to order an adult dosage from which they have to prorate their child's correct dosage amount. This may or may not necessitate the administration of the shot by the oncology clinic. The benefit of Neulasta is that it is given in a single shot 24 to 48 hours after the cessation of chemotherapy. This is obviously a significant quality of life issue for many children.

# Avoidance Tactics and Safety Precautions while Your Child is Neutropenic

There is nothing that a neuroblastoma patient can do to avoid neutropenia. The child and caregivers can, however, take measures to avoid infection. The most important thing a family can do is –WASH THEIR HANDS! A thorough 10-second hand wash can significantly help prevent spread of infection. (If you don't want to count to ten as you wash your hands, try singing a simple song like Happy Birthday!) Some families install hand sanitizers in conspicuous locations throughout the house to remind the child, family members, and visitors that clean hands are essential to avoiding infection.

Other basic measures to help your child avoid an infection are making sure your child gets enough rest, eats and drinks adequately, and avoids ill people. Remember -- these basic safeguards apply to all members of the family!

Depending on where your child is in treatment, your child's oncology team may or may not want your child to be immunized against influenza. If they do, the flu vaccine would be administered as a shot and not as a nasal mist. Every member of the child's household and anyone else in frequent contact with the child should be encouraged to get a flu shot. However, be aware that your child should not be near another person who received the nasal flu mist vaccine or any live virus vaccine.

Other measures that can be taken in order to try to avoid infection are:

- avoid large crowds and ill people, especially those who have chicken pox, measles, shingles, or the flu;
- avoid day care;
- avoid hot tubs and hot showers as this dries the skin;
- wear shoes at all times;
- avoid using razors or handling sharp objects;
- clean any cuts immediately;
- practice good oral hygiene with a soft tooth brush;
- avoid fresh flowers or plants;
- avoid cleaning up after pets;
- avoid swimming in ponds, lakes, or rivers;
- avoid sharing glasses, utensils, or towels with other people;
- avoid constipation;
- apply sunscreen and avoid sunburn;
- keep the house, especially the patient's room, very clean;
- minimize stuffed animals in the patient's room;
- teens with cancer who are menstruating should avoid tampons;
- have the child follow any dietary restrictions or guidelines recommended by your oncology team; common neutropenic dietary guidelines are to avoid raw foods including raw fruits and vegetables; cook and clean foods thoroughly; avoid unpasteurized food or liquids; and eat no leftovers or food that the parents do not prepare (unless the child is hospitalized).

Some parents have their neutropenic child wear a face mask when being in contact with the general public cannot be avoided, on public transportation, for example.

Indeed, the possibility of infection should be considered whenever the child comes into contact with

the general public - at home, at school, and any public places - whether or not the child is neutropenic! Naturally, you want your child to enjoy life to the fullest even though he or she is in cancer treatment, but avoiding unnecessary illnesses is always a concern to be considered for a child in NB treatment, and especially during neutropenia. Some decisions about safety precautions are very personal, and each family should discuss the necessary safety precautions for their child's particular situation with their oncology team.

Please contact editors@nbhope.org with any comments



# Special Issues with Stem Cell Transplants

Putting a child through a stem cell transplant (SCT) is one of the hardest decisions parents have to make during a child's treatment for high-risk neuroblastoma. Transplant can be a relatively smooth (albeit never "easy") experience for some children, but extremely difficult and even life-threatening for others. This section is not intended to offer guidance in making this very personal medical decision—but aims instead to provide tips for coping with the transplant experience for those undergoing it.

### Various transplant protocols

First, some background. Currently the majority of children with high-risk NB in the US are treated on the COG Phase III trial that randomizes children to one or two (tandem) transplants (COG-ANBL0532). Other hospitals treat children according to other protocols, which are not randomized and may include a single, double, or triple transplant; an allogeneic (donor) transplant; or *no* transplant (MSKCC in NYC). Parents may also decline to enroll their child on the Phase III ANBL0532 randomizing single vs tandem transplant and opt for single only. The current transplant "options" are thus complex and varied. For a brief discussion of current transplant trials and the history of phase III trials leading to the "standard" use of transplants, *see* Chapter 2, Overview of High-Risk Treatment.

Because a stem cell transplant for NB does not usually involve the use of marrow or stem cells from a donor (although there are exceptions to this), it is more accurately thought of as a "rescue" -- the child's own previously-harvested stem cells are infused (in the same fashion as a blood transfusion) after high-dose chemotherapy causing so much damage to the bone marrow that the child must be "rescued." The "transplant" term is prevalent because the cancer center's "transplant" team cares for the children undergoing this treatment and the often long and difficult period while the bone marrow rejuvenates. Occasionally you will see the term "stem cell rescue" or SCR used.

# Preparing for transplant

Once it has been determined your child will undergo transplant, you may be confused and nervous. After all, even though the stem cell transplant will involve "familiar" chemotherapy, the anticipated aftermath of prolonged low counts and severe side effects indicates a more challenging experience lies ahead for your child and your whole family. We hope this section will help allay your anxiety, by giving you an overview of the special precautions and lifestyle changes you may face during transplant. It is a lot easier to plan how to cope with the known challenge than the nerve-wracking unknown!

During your child's transplant, your child will be hospitalized probably for much longer than any other time during treatment. You will be spending a significant amount of time away from home, which can be uncomfortable and frustrating. If you have other children, or if you or your spouse must continue working during this time, your family may be split up for some time. Your child will spend several weeks in an inpatient isolation room, which requires much preparation and compliance with many hospital guidelines and restrictions. In addition, there will be several medications to keep track of before, during, and after his/her isolation period. You'll want to figure out ways to keep you and your child busy, as well as keep in touch with family and friends. And

after isolation, returning home will also require some specific preparation. The information below will help you with these as well as other aspects of your child's transplant.

### Home away from home

Probably one of the most difficult emotional aspects of the transplant process is all of the time you will spend away from home if you don't live near the hospital. Your transplant social worker or other hospital coordinator will help you arrange for housing if you live far away. During the weeks of outpatient transplant recovery most hospitals will require your child to be within a 30 minute drive (with traffic) from the hospital in case of fever or other medical issues. Although it's comforting to be close to your hospital, chances are you'll end up staying in a facility provided by your team, such as a Ronald McDonald House, local hotel, or temporary apartment. Some families are lucky enough to have friends or family near their hospital and able to accommodate them. Check with your child's transplant team before making any arrangements, as individual hospitals have various guidelines and preferences for where a child may stay during the transplant process. Such guidelines relate to disease-control issues and are imposed with your child's safety in mind.

Wherever you are, it isn't home of course. That said, there are many ways to make your surroundings feel more comfortable and familiar.

- Although lots of little knick-knacks can get dusty and are usually discouraged, bring a few favorite items from your child's room or your home.
- Consider laminating posters of your child's favorite characters or movies to put up in the transplant room. Laminate family photos (easier with a copy printed from your computer if you have digital photos). Laminated items are easy to clean and make a better choice than framed items (usually not allowed on the walls because of nail holes).
- If it is not provided, consider bringing a small lamp with a soft light. This can make any room more comfortable.
- Invest in a portable DVD player or CD player if the transplant room will not contain a TV. If you're staying for a couple of months, consider bringing a small TV if it is allowed (it may not be because of noise control).
- Bring your child's favorite towels, sheets, pillows, and blankets.
- Bring washable stuffed toys for your child's bed.
- Consider bringing an area rug or play mat for the floor to soften up the room. Make sure it is easily washable.
- If it isn't provided, bring a shower squeegee. You can get one of these at Target, Wal-Mart, or the like. It will help control mildew in the shower.
- Since food for caregivers is usually not allowed in individual rooms (to avoid germs), bring plenty of familiar snacks and foods to keep in the communal kitchen. Check with the medical team about any food since some are prohibited during transplant.

### Preparing for isolation

Although your stem cell team will help you prepare, getting your child and yourself ready for inpatient isolation can be stressful and intimidating. Guidelines and rules for isolation stay can vary greatly from hospital to hospital; however, some suggestions and general information are provided below to help you get ready.

- Insist that you be allowed to inspect your child's isolation room before he/she is closed in. Check that every surface has been properly cleaned, sanitized, and repaired. Look in the corners, closets, etc. (Some hospitals go so far as to clean these rooms with toothbrushes and re-paint the walls and re-wax the floors between each patient.) Don't be afraid to point out any dirty or damaged areas of the room. Check that your child's bed is comfortable, safe, and clean. You don't want to have to break isolation to get your child a new bed or have something repaired later.
- All your child's clothing will need to be freshly washed and completely dried in a dryer (no air drying) and placed in plastic sealable bags. This is for germ control. Hefty and Glad make oversized bags that make the transport a little easier. Once you get to your child's room, these clothes will probably need to be removed from bags before entering the room.
- You will also need to be freshly showered and dressed in freshly laundered clothes when you arrive at the hospital. Some hospitals will require you to shower again before entering your child's room. Some will allow you to shower at home but ask that you not make any stops (gas station, grocery, etc) before arriving. If you do, you may be asked to shower again. Leaving the hospital may mean another shower (even if it is to just get a Starbucks). Remember, it's all for your child's safety.
- Your child's toys will probably need to be new or sanitized. Toys that can be completely submersed in water by either washing them in a sink or a washing machine can usually come in the room. Some hospitals will purchase new toys for children undergoing transplant, so check with your transplant coordinator before you run out to buy all new stuff.
- Remember to sanitize and wipe down anything you plan to bring into the room. If it can go in the washer, put it in the washer. If it can go in the dishwasher, put it in the dishwasher. If not, seriously consider whether you need it or not. Check with your team about electronics, as anything electronic or with batteries will probably need to be cleaned by the environmental department of your hospital or otherwise may not be allowed. (Think laptops, DVD players, portable game devices, etc.) Notebooks, books, and other paper materials will probably need to be new or cleared by your transplant team.
- Your child's meals will need to be specially prepared, and the hospital will have a special menu for your child. Make sure your child's meal comes wrapped in plastic. Check to see whether or not you can have a meal delivered for yourself as well, since you probably won't want to leave your child to get a bite. Also check before you order any takeout. Some foods may be prohibited altogether in your child's room.
- As noted above, try to surround yourselves with familiar things -- photos, posters, pillows, blankets, towels, etc. It may mean a little extra laundry for you, but it will help your child feel more comfortable. Rugs will probably not be allowed.
- Make sure you purchase new toiletry items for your child- and COMPLETELY discard the old ones -- don't save them at home for use after transplant, because your child's immune system will not be normal for a long time. These items include toothpaste, hand soap, toothbrush, nail clippers, lotion, deodorant, etc. Anything that has touched your child's skin, hair, mouth, nails, etc. should be replaced, unless it can be washed or totally submersed in water (like a comb).
- Bring a lot of straws and disposable cutlery for yourself, and don't share with your child from your plate!!! This is not a time to be environmentally conscious or conservative. Don't keep leftovers or leave food out for more than an hour. Don't save a napkin from your takeout bag that wasn't used. Germs are a totally different thing for your family now.
- Consider bringing your own Swiffer and pads. Bring lots of anti-bacterial wipes and go over the computer keyboard, phone, door handles, counter tops, bed trays, buttons, blood pressure

cuff, bed frame, and thermometer handle several times a day. Although the room should still be cleaned daily by the custodial staff, you may want to go over it yourself. The room CANNOT be too clean!

- As convenient as it may have been during your child's initial rounds of chemo, DO NOT share bathroom facilities with your child. Use the parent restroom outside your child's room when possible. If your child does not use the toilet, make sure you wipe the toilet/sink after every use.
- Be extremely selective about visitors, especially children. Your hospital will have special visiting policies during transplant, but be extra vigilant yourself. NO ONE (including you) should be in your child's room if not feeling well. Young children (even siblings) should not be in the room at all (as they are less likely to report not feeling well). The smaller number of people you allow in, the better. Your child can get sick very easily during this time.
- Insist that cleaning staff, food service staff, nursing assistants and any visitors entering your child's room wear gowns and/or masks. Anyone entering your child's room should ALWAYS wash their hands with soap and dry with a paper towel. If ANYONE coughs, sneezes, or sniffles in your child's room, insist that they leave immediately. Small germs can cause big problems during transplant.

## Some medical issues during transplant

**Drugs.** Your child will probably be taking several different drugs before, during, and after his/her transplant. These drugs are primarily administered to prevent viral, bacterial, and fungal infections, which can of course be very dangerous to your child during this time. Some of them don't taste very good, so experiment if possible with your pharmacy's flavoring system. Choose something that generally tastes good to your child, or whatever is most likely to go in and not come right back out. Get into a routine for administering these drugs -- keep a schedule, checklist, calendar, or timer set, as each one is probably going to be administered at different times. Eventually you will be able to wean your child slowly off of each of these drugs as his or her counts begin to recover.

**Nausea and fatigue.** Not surprisingly, nausea and fatigue will be common for your child during transplant, as his or her body will be severely immune-suppressed. Expect lots of naps, easy fatigue even in low-activity situations, and overall crankiness while your child's counts are recovering.

**Food.** Make sure you are fully-informed by your child's medical team about food restrictions. The avoidance of fresh fruits or vegetables, deli meats, some breads, buffets, fast foods (unless freshly prepared), yogurt and some other dairy products, and tap water will be among the many restrictions for your child. Food also must be prepared in accordance with certain precautions, so make certain you understand all the requirements. Know what is safe and what is not. These restrictions are for your child's safety, and shouldn't be taken lightly. Some teams will refer to the rule "packaged, processed, frozen" as a guideline for foods for your child. As disgusting as it sounds, most of these foods are safe and should be the basis of your child's transplant diet. If you've been lucky enough to avoid an NG tube or TPN before now, you'll probably become familiar with one during transplant. Since most children don't eat or drink for several days or even weeks during this time, the provision of nutrition by IV infusion is likely. Both options have their pros and cons, so discuss both with your team so you can make the best decision for your child.

**Skin.** Shortly before your child's isolation, he/she will receive the final round of chemo. These high-dose chemos come with some added precautions to protect your child's skin and internal tissues that you probably have had to experience during induction chemo rounds. Again, discuss the requirements and side effects of these drugs with your team. Some of the protective precautions taken may include: use of a Foley catheter during the duration of the Cytoxan dose; 4-6 hour bathing

intervals (round the clock) during and a couple of days after a Thiotepa dose; frequent mouth care with lidocaine or similar mouthwash to counteract mouth and GI sores that accompany several drugs (ACT or lidocaine-free mouthwash helps for a young child that cannot spit yet, and offering frequent popsicles *before* onset of mouth sores help to reduce the incidence and pain); protective creams (also for the skin burns that can accompany Thiotepa- ask for the Remedy line if your hospital provides, otherwise ask other parents what they used). One cancer family concocted their own recipe -- equal parts Kaopectate, A&D ointment, and Aquaphor cream. Mix it all together in a big bowl, put it in a squeeze bottle (like a shampoo bottle), and rub on diaper area and any skin fold areas where irritation occurs. Keep away from the eyes, of course! Even if your child is out of diapers, his/her diaper area will be very irritated for some time. There are several creams that parents have found to work well during transplant. Dr. Smith's Diaper Cream, Flander's Diaper Ointment, or the homemade version mentioned are all standard choices. Be prepared to try lots of things until you find what works for your child.

**Pain.** Your child will most likely be on morphine or other pain control (either PC or continuous) at some point during the isolation period. This may seem extreme to us, but it really does help control the continuous irritation from mouth and GI sores, as well as the sometimes severe skin irritations. If your child is old enough, he or she may be able to control the dose, and the pump may be put on a continuous flow for some children. The doctors will slowly wean your child from the pump, and most children must clear the pump before leaving the hospital.

**Complications.** Talk to your child's team about the possibility of other medical complications that may occur and any symptoms to be aware of. Your child may experience changes in blood pressure, heart rate, temperature, water retention, consciousness, infections, or breathing ability. Although rare, VOD, respiratory distress requiring a ventilator, CMV, kidney failure, and other severe complications can happen. Know what to expect, but stay positive! Most children do not experience these severe complications.

### Keeping your family together during transplant

It's hard to keep your family together during this difficult time, especially if you are traveling to a distant cancer center, if there are other children in the home, or if one or both parents still need to work. Having a support system is very important. Many times neighbors, relatives, and friends will take turns with your other children. As much as you would like to help them with their every day activities, it may not be the best solution at the time. Because there are so many disease-control issues with your transplant child, you want to try to minimize the number of people who come into contact with him or her during this time. As much as possible, your child's only contact other than the medical team should be you and your spouse. Many hospitals will also not allow young visitors when your child is in isolation. Keep this in mind, and be sure to talk with your team before bringing siblings to visit in the hospital.

While your child is staying at a facility, hotel, or friend's house near the hospital (either before or after isolation) consider bringing siblings to these places to visit and/or stay the night. Most of the time accommodations can be made, although not usually every day, when siblings want to visit.

Also think about trying a web-cam service to keep your child in touch with siblings, other family members, or friends. Someone at the hospital may be able to help you hook up this service, either on your own laptop or on one loaned by the hospital. This way your child can chat live with his or her family and friends. It works out great for Grandma, too!

Older siblings might enjoy keeping a journal or tape-recording themselves for your child to read or hear. If your child is old enough, he/she may want to journal back or tape-record a message back. Hearing familiar voices is also good for little ones, as they are very responsive to familiar voices.

## Keeping yourself busy in the hospital

There are many things that you can do to keep your sanity while you're inpatient with your child. Although not always the case, some children sleep A LOT during transplant and may even be unconscious for periods of time. Although this may be scary for you and your child, it is generally normal and will pass. In the meantime, you'll have to find something to keep your mind busy. Since you probably won't want to come and go from the room very often (minimizing contact with germs), you should bring along lots of stuff to keep you occupied. Some suggestions are:

- Magazines, books, crossword puzzles
- Laptop computer with internet access (sometimes hospitals will loan one to you)
- Movies
- Sketch pad or journal
- Crochet, knitting, or scrapbooking
- Hand held game system (may sometimes be loaned by the hospital)
- Healthy munchie snacks (nuts, popcorn, etc.)
- A new address book to fill out
- Remember that your child's toys can also be therapeutic for you-coloring and crafting have actually been shown to reduce blood pressure and quiet the mind!

## Keeping your child busy in the hospital

You will need to bring some things from home to keep your child busy and happy while in the hospital. Many hospitals that offer transplant procedures do a great job of making your child's room comfortable and homey, and provide toys and other items to help entertain the child. Ask to speak with a child life specialist or social worker BEFORE isolation to see what can be done to help your child's stay more enjoyable. Remember that he or she will be very tired and may not feel well enough to play or do any activities. This doesn't mean you shouldn't try! Each day, encourage your child to get out of bed if possible, read, interact with you, watch favorite videos, bathe and change clothes, eat or drink, and walk. There will be some days that your child will not be able to do any of these things, but daily encouragement and motivation will help your child recover. Here are some suggestions:

- Bring new board games or puzzles.
- Buy or rent new movies or movies your child has been wanting to see.
- Encourage play that gets your child moving and out of bed -- bubbles, window markers, floor activities, tents, ball pits, video games like Wii, anything that might encourage your child to move! Most hospitals are supportive about bringing whatever you think might help your child. Just make sure it is either new or properly sanitized first.
- Many hospitals will stock your child's room with age appropriate activities, new toys or games, and other favorites based on information you provide about your child. New things are always a nice distraction!
- Talk about the view with your child and encourage him or her to get up and look out the window. Even if you can only see a wall, sunlight and a busy alley can even be exciting.

- Keep a calendar of your child's activities and status each day. Display a large classroom calendar (you can get one at a teacher supply store, make one yourself from a poster board, or even ask the hospital for one) and keep track of your child's days inpatient. Encourage him/her to decorate it too.
- Remember to be happy and upbeat as much as possible around your child. Even on the toughest days, being positive can help your child feel better.

## Preparing your home for your child's return

Preparing your home for transplant is a big job. Once again, check with your child's team as every hospital's guidelines are different, but here are some suggestions:

- At the very least, have all carpets in your home shampooed, steam-cleaned and sanitized. If you are financially able and your carpets are more than a few years old, you may want to consider replacing them. If you do this, don't forget to vacuum the floorboards before new carpet is laid. Usually the carpet-layers won't do that.
- Have your duct-work professionally cleaned if possible and change the filter in your furnace. Buy enough filters to change them every month for the next year, and if you're financially able, buy the really good ones.
- Have your home cleaned top to bottom. Whether this is done professionally or by you, family, and friends, be very picky about how your home is cleaned.
  - 1. Wash all draperies, throw rugs, throw blankets, pillows, sheets, and towels.
  - 2. Wash any stuffed animals.
  - 3. Vacuum or dust behind and under all furniture, including appliances.
  - 4. Clean out your refrigerator and freezer. If you have a door-front water dispenser, change the filter.
  - 5. Discard or give away any house plants. Ask your team if you're really attached. Some plants can just be moved to other rooms of the house.
  - 6. Put away or discard your portable humidifiers. You probably won't be able to use them in your home for at least 6 months.
  - 7. Wash out all cabinets (inside and outside) in the kitchen and bathrooms.
  - 8. Clean all blinds.
  - 9. Scour all bathrooms.
  - 10. Clean all light fixtures and fans.
  - 11. Vacuum or dust all ceiling corners and vent covers.
  - 12. Wash all windows and windowsills.
  - 13. Scrub floors and grout.
  - 14. Clean your child's toys with an alcohol/water solution. Add essential oil or lemon juice for a better smell!
  - 15. Dust, sweep, mop, clean, vacuum and scrub everything in sight! Again, your home CANNOT be too clean.
  - 16. Have your chimney swept.
- Don't forget to insist that everyone who enters your home be healthy. Anyone with a sore throat, cough, sneeze, or sniffle should not be near your child until it is okayed by your stem cell team. This includes grandma, siblings, and even you!
- Ask your transplant team about pets. Even the cleanest of pets carry germs, shed hair, and create bacteria in your home. Your team will be able to help you make the decision that is

right for your family regarding your pets. At the very least, your pets should be regularly bathed and up to date on all immunizations.

- If you haven't yet established this rule, insist that anyone who enters your home remove their shoes at the door or in the garage. They should also immediately wash their hands with anti-bacterial soap. This includes service professionals, nurses, family members, friends. This should become the new normal for your home. Shoes and hands carry way too many germs.
- Do not put hand towels in your bathrooms for about six months. Although it may seem wasteful to use paper towels, this is again an easy way to stop the spread of germs in your home for your child. Bath towels should be washed after every use for at least a few months. Same with bath mats and washcloths.
- For at least six months, wash everything your child wears, even if it doesn't "appear" dirty. Don't "re-hang" anything your child has worn. Wash or clean favorite toys as often as possible.
- Replace your child's toothbrush every week or two for about six months.
- Buy anti-viral tissues (Kleenex makes them)
- Wipe down all kitchen and bathroom surfaces daily with anti-bacterial wipes for about three months.
- Never leave a snack or cup (especially milk) sitting out for more than an hour. Again, what is normal bacteria for us can harm your child after transplant. Also, don't save an uneaten portion from your child's plate or cup. Be wasteful!
- Finally, as cruel as it may sound, be careful about how you and others touch, kiss and hug your child for a while. Kisses on the mouth should be limited, and make sure that anyone who touches your child is healthy and has washed their hands. If your child touches someone or something that you're not sure about, break out the anti-bacterial wipes. Again, it is difficult to think about limiting something as essential as human contact, but unnecessary contact with germs will definitely affect your child's recovery.

Take a deep breath! This is a lot to digest! Yes, transplant is a challenging process, but it is also an important step in your child's full recovery and remission. Although you may be feeling overwhelmed by the idea of your child's transplant in the future, know that you can do it! Become fully informed about the necessary safety precautions, make a plan, and stick to it! Also, don't try to go it alone – now is the time to rely on your Neuroblastoma community and your family and friends to support you during a trying time.

Please contact editors@nbhope.org with any comments



# Coping with 3F8 Antibodies

There are currently several clinical trials using intravenous 3F8 monoclonal antibodies being conducted at Memorial Sloan-Kettering Cancer Center (MSKCC) in New York City. Factual information about the purpose and scientific aspects of 3F8 treatment, and its role in various frontline, refractory, or relapse treatments, will be discussed elsewhere in this Handbook. The focus of this section is *coping with the side effects* of 3F8 treatment.

Regardless of which clinical trial a child is treated on, the side effects of 3F8 protocols are similar and are managed in the same ways. (Intrathecal 8H9 treatment is discussed separately in another section of this chapter.)

## How is 3F8 administered and how long does it take?

Ten to twelve children receive 3F8 treatments each week -- one group in the morning and another group in the afternoon. Antibody treatments are administered in a series of adjacent one- and two-patient rooms in the bed area of the MSKCC Pediatric Day Hospital (PDH). Patients who do not have a port or central line receive the treatments through a peripheral intravenous catheter (PIV) which is inserted for the week. As PIVs are not as stable as central lines, it is possible that the child will need will need it replaced.

Actual administration of the treatment takes about 90 minutes: 30 minutes for pre-meds, 30 minutes to administer the antibody, and 30 minutes for a flush. Patients often sleep for a few hours afterwards, so a child could be in the clinic anywhere from 3 to 6 hours.

On a typical treatment day, patients arrive at about 8:30 a.m. if they are on the "first shift" or 11:30 a.m. if they are on the "second shift" for antibody treatments that week. If you prefer to be on the earlier or later shift, let the staff know. Although they may not be able to accommodate your request that week, adjustments can usually be made for future rounds of treatment.

After checking in at the front desk, patients usually go to the area outside the IV room and wait to be called for a finger stick or other lab draws. After any required blood work is completed, patients may be "hooked up" to pre-treatment hydration, but they are usually free to stay in the clinic playroom or waiting area, attend class in the clinic school, or even go to the cafeteria while the fluids are running. Patients on 3F8 trials using GM-CSF may receive the shot at this time if they have not received it before coming to the PDH.

Patients are called to the bed area when it is time to administer pre-treatment medications. It is a good idea to have your child use the restroom before the pre-meds are administered, as some children feel a strong urge to urinate during the actual 3F8 treatment.

Once all of the pre-meds have been administered, a pre-treatment dose of pain medication is administered before the 3F8 infusion begins. The infusion begins when the research nurse pushes the syringe of 3F8 antibodies into the IV soluset, mixing it with saline solution. Often the patient is situated comfortably, watching TV or otherwise distracted, so the nurse may let the parent know the infusion is starting without announcing it to the child.

At sometime during the infusion the child will begin to experience pain and possibly other side effects (see discussion below). Because every child's experience is different, it is imperative that a parent stay with the child, since parents know their child best and can pick up on early signs of distress.

When the infusion and flush are finished, the treatment itself is complete. Patients usually are in a drug-induced sleep for a while after treatment as a result of the pain and allergy medications received. During the rest time after treatment, nurses continue to monitor the child for any adverse or late effects of the treatment. Patients are not released to leave the PDH until the medical staff is satisfied that they no longer need medical supervision.

#### What are the side effects of 3F8?

Although there definitely are side effects, these have all been short-lived, lasting (with rare exception) only during the week of the treatment. The common side effects are described below.

#### Pain

The most common and pronounced side effect of 3F8 is pain, which is controlled with narcotics (dilaudid or morphine) (see below). Pain occurs because the 3F8 antibody attaches to the GD2 antigen found on the surface of neuroblastoma cells. However, the GD2 antigen is also found on some normal nerve cells. When the antibody attaches to the GD2 antigen on a nerve cell, a message is sent to the brain, and the patient feels pain.

For most children the pain is severe, at least in the early rounds of treatment, and witnessing a child in pain can be extremely difficult for parents. As with everything in neuroblastoma treatment, the degree of pain experienced varies with each child. Many a mother watching her child experience 3F8 treatment has concluded that the pain seems similar to the pain of childbirth—although fortunately of much shorter duration--yet other parents have observed, "it's really not that bad."

Most patients seem to experience pain during the "flush" received during the last 30 minutes of the 90-minute treatment. However, for some the pain may start at the very beginning of the 3F8 infusion, and others may not experience pain until after the infusion is completed. The pain is generally localized to a certain area, such as the back, neck, abdomen, arms, hands, legs, knees, feet, or ankles, but some patients feel pain in more than one place. The pain tends to last 20-30 minutes for many patients, but other patients, especially older ones, continue to have residual symptoms of pain into the evening hours, often localized in hands, feet, knees, back, or other places. In general, the residual pain seems more severe for teenagers and young adults. If it is a continuing problem, additional medications can be prescribed.

Recovery time varies from patient to patient. Although some will sit up and feel totally recovered shortly after completing the treatment, many others, depending on the amount of pain medication, will sleep for an hour or so afterwards. Some parents find this an excellent time to crawl into their child's treatment bed to provide physical comfort and catch a nap themselves. Most patients will have some after-effects from the pain medications when they awake, and young children will generally be "fussy" and/or demanding until it wears off, so the after-treatment rest time provides a good opportunity for parents to recharge their own reserves. Some patients are back to normal by early evening, whereas others have residual pain and/or moodiness until late in the night. Many children do not remember the pain and return cheerfully to the clinic for the next day.

## **Allergic Reactions**

The second most common side effects are allergic reactions, usually hives, with or without itching. This side effect is controlled with Benadryl (diphenhydramine) or Vistaril (hydroxizine).

From time to time, children have been known to experience hives in the mouth or throat that cause swelling and result in breathing difficulties. All patients receiving 3F8 wear a pulse-oximeter to measure oxygen absorption. If a child's oxygen level drops, oxygen is on hand to be administered if needed.

As frightening as these rare events are, they can usually be resolved in the outpatient clinic, although sometimes a patient will be admitted to the hospital for overnight observation. In very rare

cases, a reaction is life-threatening and the doctors conclude that the risks of continuing treatment outweigh the benefits.

### High Blood Pressure

Children can also experience high blood pressure during and, very occasionally after, 3F8 treatment. High blood pressure is usually caused by increased heart rates that are a normal response to pain. Blood pressure is monitored periodically throughout the 3F8 treatment and afterward, and patients are not released from clinic until their vital signs are within normal ranges.

## Fever, Vomiting, Intestinal Distress

Patients may experience these side effects in varying degrees during treatment. Fever can be concerning if the patient has a central line or port, as it can be difficult to determine if the fever is treatment related, or a result of blood-borne infection. Blood cultures may be drawn and parents may need to watch the child closely after treatment and notify the clinic if fever returns. Aloxi (palonosetron) or Zofran (odansetron) are usually administered before treatment to prevent nausea. Some children experience diarrhea, which generally resolves after treatment, while a few others have had difficulty due to the constipating effect of the pain medications used.

There is no denying that 3F8 is a difficult treatment. Yet few patients object to returning the next day for treatment. In comparison to the pain, nausea, neuropathy, and debilitation of chemotherapy treatments, most children and parents seem to find 3F8 considerably more manageable.

## More on Managing Pain and Other Side Effects of 3F8

Naturally it is difficult going into a treatment for the first time knowing it will be painful, yet not knowing specifically what to expect.

MSKCC employs specially trained nurses that administer the antibody treatments, and the clinic nurses are very experienced in caring for patients receiving antibodies. Before beginning the infusion, each patient receives an antihistamine for allergic reactions (Benadryl or Vistaril), an antiemetic for nausea (Aloxi or Zofran), Tylenol for fever, and, just before the infusion, a narcotic (Dilaudid or morphine) for pain. Some children also receive Ativan to relieve any anxiety. Children that seem prone to breathing difficulties may receive a nebulizer treatment with Xopenex (levalbuterol) to relax and open up the airways before receiving 3F8.

At the first indication of pain, a "rescue" dose of the child's most effective painkiller—already drawn up and waiting at the bedside—is administered. Additional rescues of pain medication are available to be administered at 10 minute intervals if needed, up to a maximum of 5 during the infusion and flush. It's generally important to administer a rescue at the first indication of pain, otherwise the pain can be difficult to control.

Unfortunately it is difficult to manage the child's pain as effectively during the first few 3F8 treatments, because everyone is learning—the patient, medical staff, and parents—how the child reacts to treatment and what medicines and other measures are most effective in bringing relief. However, often a pattern emerges in later rounds of treatment that allows parents and staff to quickly address the child's needs.

In addition to medications, there are a number of non-medicinal palliative measures that may be used to relieve or lessen the side effects of 3F8 treatment. Each family will learn through trial and error which techniques work best for their child. For example, some find applying ice packs helps with the pain, while others prefer heat packs. Some children will use both ice and heat at different stages of the treatment.

Distraction can be effective for some children, who simply prefer to watch TV. Teens may opt to listen to a favorite CD or their iPod during treatment. Other children like the feel of the cool air from

the blow-by oxygen on their face, while still others may use massage or guided imagery to take their mind off the physical experience.

There are several complementary techniques available through MSKCC's Integrative Medicine Service for addressing the pain of antibody treatment. Success usually depends on a patient's (or parent's) willingness to try these approaches with an open mind. Families interested in complementary approaches can ask a nurse practitioner, one of the research nurses, or the Child Life staff for information on available options. The integrative medicine department will set up a time to teach visualization to the patient. All integrative medicine services are free of charge.

After a round or two of treatment the pain is almost always more manageable, because the child and the parents know what to expect, and because the parents and the medical staff have learned what techniques are best for managing the individual child's side effects. While some parents have observed that pain definitely diminished over the course of numerous rounds of 3F8, others have seen a less marked difference.

Once the last day of a week of 3F8 treatment is completed, it is extremely rare for a child to have any side effects. Blood counts are generally not affected, though children may lose a bit of weight if they do not eat much during the week of treatment. However, no long-term effects from 3F8s have been seen over the past twenty-plus years.

### Anxieties over the Presence/Lack of Pain and HAMA

As hard as it is to watch one's child in pain, most parents *want* their child to have pain through at least four cycles of 3F8 treatment, to get the most benefit from the antibodies before the body forms the immune response known as Human Anti-Mouse Antibody (HAMA) that blocks the effect of the treatments. You will hear parents and sometimes even nurses discussing the fact that if the child is experiencing pain, then he is *not* forming HAMA—or if the child is experiencing *no* pain, then the child *may be* forming HAMA. However, it seems that there simply is no single rule. While it is true that patients with an existing HAMA do not have pain during 3F8 treatment, nonetheless, patients *without* side effects sometimes do *not* develop HAMA, and patients often *do* form HAMA during a round of 3F8s in which they *did* have pain.

Try not to agonize over whether your child is having too little or too much pain, and try to resist the temptation to compare your child's experience with others. Every child is different, and there appears to be no correlation between long-term survival and the degree of pain experienced, or the lack thereof, during antibodies.

Generally one or more of the NB doctors makes rounds of the 3F8 treatment rooms and speaks individually with each family, at least once during the 3F8 treatment week. In addition to any scheduled meetings with the docs, this tends to be a good opportunity to ask questions about the 3F8 protocol and discuss your child's case with one of the NB doctors—the only ones other than you who understand all the facts of your child's particular case and his or her 3F8 history.

Please contact editors@nbhope.org with any comments



# Coping with 8H9 Intrathecal Antibodies

## What is Intrathecal 8H9 Antibody Treatment?

Intrathecal 8H9 antibody treatment is one part of a multi-modal protocol that also uses chemotherapy, surgery, and radiation to treat neuroblastoma relapses in the brain and central nervous system (CNS). The protocol, developed at Memorial Sloan-Kettering Cancer Center (MSKCC), employs a relatively new application of 8H9 that has only been in use at MSKCC since 2003.

The antibodies themselves are radiolabeled—i.e. liquid radiation is attached to them. Radiolabeled antibodies deliver radiation specifically to any neuroblastoma cells that remain after the surgery, chemotherapy and radiation therapies.

#### What does Intrathecal mean?

The term intrathecal refers to fluid filled space between the thin layers of tissue that cover brain and spinal cord known as the cerebrospinal fluid. The 8H9 antibody is injected directly into this fluid through an Ommaya Reservoir placed in the child's head for this purpose. Once the 8H9 is injected the central nervous system is bathed in cancer-killing antibodies and radiation.

## What is an Ommaya Reservoir?

The Ommaya Reservoir is a port placed under the scalp that has a catheter threaded down to a ventricle in the brain to provide access to the spinal fluid for treatment and testing. The Ommaya is placed by a neurosurgeon and placement requires a post-surgery overnight hospital stay. The Ommaya Reservoir is accessed with a thin needle with tubing attached. A syringe is then attached to the tubing to push medication in or draw spinal fluid samples out. Because the port protrudes a little above the skull it looks like a bump, but for the most part it is invisible when the child has hair. Ommaya Reservoirs require no maintenance; they do not need to be cleaned or flushed.

## How 8H9 antibody treatments administered?

Each treatment consists of two doses, a test dose and then the therapeutic dose, given exactly one week apart. If the therapeutic dose is delayed for any reason (e.g. low counts), it must be given within two weeks of the test dose or the test dose must be repeated.

Children are admitted to the hospital the day before the dose is given. The Ommaya Reservoir is accessed just before the 8H9 is administered and must remain accessed for about 90 minutes. The injection into the Ommaya is given and samples of the fluid are taken from it at specified intervals for one hour after the injection. The test and the therapeutic treatments are administered the same way except that the dose of the 8H9 antibody is doubled and the Radiation Officer is present during the therapeutic injection.

Scans are performed at 24 and 48 hours after the injection on the same machine used for MIBG scans. The child is usually discharged from the hospital after the 24 hours post-injection scan.

### What are the side effects?

The good news is that some children have had no side effects at all. Others have been observed to experience some or all of the following: fever, nausea, a tingling sensation lasting a few minutes, or

lowered counts requiring transfusions in the months following the treatment. Please note that this is not meant to be a complete list of possible side effects, just what has been observed by a few parents.

Because of the radiation level in the child's body after the therapeutic dose, it is recommended that the child stay several feet away from other children and women who are pregnant or considering future pregnancies for a few days after treatment.

## Coping with Treatment and Side Effects

You will learn a lot about how your child reacts to the intrathecal 8H9 antibody treatment after the first test dose. Many parents find that with this knowledge, the therapeutic treatment is much easier for their child because they know what side effects are most likely. For example, if a child experiences a very high fever during the test dose, parents can request Tylenol before the therapeutic dose and every four hours after even if there is no evidence of fever. Similar arrangements can be made for the provision of anti-nausea drugs if nausea is an expected side effect.

Families considering future pregnancies should plan, if possible, to have Dad stay overnight at the hospital after the therapeutic dose. Although mothers may be uncomfortable leaving their child for the night, it is probably better to have my Dad stay with the child than to be limited to providing comfort at arm's length.

Although accessing the Ommaya Reservoir is said to be painless, children generally don't like it. One child finds it tolerable if EMLA is placed on the port before access, but others find it extremely upsetting. The idea of having a needle put into their head is very frightening and may make children very angry. One child coped by using his dinosaur puppet to "bite" the doctors, who were all good sports about it.

Ommaya taps are a part of routine check-ups after 8H9 treatment, but they last only a few minutes. One Mom reported that after a tap her child felt tired and dizzy and would sleep for a while but felt better by evening. It may be possible to request that the routine taps be performed while the child is under anesthesia for bone marrow biopsies to spare additional trauma and emotional stress.

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# Coping with Accutane

Your child's Accutane treatment will likely require some "coping," possibly with the actual administration of the drug in addition to its side effects. Knowing what has worked for others will give you a good start on getting your child through the treatment.

The tips and insights below are based on the experiences of parents who have participated on the ACOR Neuroblastoma listserv over several years. Also, Dr. Patrick Reynolds, a neuroblastoma specialist, has occasionally shared information about Accutane on the listserv. Dr. Reynolds was one of the principal investigators into the effectiveness of Accutane in neuroblastoma treatment, and much of his advice to the listserv is summarized below. (He reviewed this document in June 2007.)

Although we hope the information below will be helpful, it is of course crucial that you discuss the details about Accutane administration and side effects with your oncologist, because new information may be available since this writing. Moreover, like everything else in NB treatment, each child's response to Accutane is very individual and needs to be carefully monitored by your oncologist.

Please note that Accutane is a trade name, as are Amnesteem, Claravis, and Roaccutane. The generic name of the drug is isotretinoin, and it is often called by its chemical name, 13-*cis*-retinoic acid. Also, please note that this section does not deal with the medical purposes of Accutane. See section on "Accutane" in "Understanding the Basics of Frontline Treatments: Overview of Treatment for High Risk NB."

## Helping your child take Accutane

Accutane is available only in capsule form and is given in two daily dosages for two weeks on and two weeks off, generally for about six months. Administering Accutane is really easy – IF your child can swallow capsules! Some parents have started training their child to swallow pills well in advance of Accutane treatment, and have had success using tiny candies such as M&Ms. If your child does not like to swallow pills, start by making sure you are getting a prescription for the minimum number of capsules required. For example, if your child is taking 60mg twice a day, you can get a prescription for one 40 and one 20 mg capsule, as opposed to three 20 mg capsules – and your child will have two fewer pills a day to swallow. Also, determine if you have the smallest size capsule available, and if not, using a smaller capsule may be helpful.

How to administer Accutane if your child cannot swallow pills and why it matters how you do it. Since so many neuroblastoma patients are very young and cannot swallow pills, parents are often uncertain how to get their child to take Accutane in the best way. The main concern is that Accutane is extremely sensitive to light and oxygen, and will degrade very shortly into other chemical forms after being exposed to oxygen and light. Also, the drug must be administered in a way to ensure that the child gets the prescribed dose. (See also warning below about danger of Accutane to pregnant women.)

Some parents have put the capsules into a food the child loves, such as pudding, or inside melted chocolate, and the child has simply eaten the capsules whole. This naturally achieves the same effect as swallowing the capsules, if the child will tolerate it. Dr. Reynolds points out that, to facilitate chewing and swallowing the capsules, carefully poking a hole in the capsule as it is being embedded into the food is known to help. Some children have enjoyed "popping" the capsules they find

embedded in the food, but the latter can't be done easily without the capsule first being pierced. Care should be taken to avoid loss of drug when doing this.

During early studies in children with Accutane, investigators recommended that the capsule can be pierced with a clean, large needle, and the contents of the capsule (a gel) can be squeezed out into a spoonful of food that the child likes. Other suggestions by parents are to pierce the capsule with a sharp toothpick or nail clippers. One parent found that a clean pair of pliers did the trick and squeezed out all of the liquid very quickly, with no mess and little contact with the product. One must be very careful to squeeze out the entire amount in the capsule so that the child will get the full dosage.

The original recommendation in clinical studies of Accutane for neuroblastoma was that the drug must be taken immediately after being squeezed out of the capsule, and also must be squeezed into the middle of the food and immediately covered over, so as not to be exposed to light and oxygen. Cottage cheese, ice cream, pudding or oatmeal with butter are foods recommended by investigators for the clinical trials, and they have been used successfully by many. Parents have also used yogurt, cool whip, peanut butter, applesauce, and others. In addition, protocols for the clinical trials have pointed out (and several NB experts have agreed) that oral absorption of Accutane is increased when taken with food or milk (or other liquid which contains fats).

Many parents have agonized about whether they were following the recommended procedures correctly. For example, some children have taken the Accutane when squeezed onto a spoon without other food, and washed it down with milk or another beverage. This raised the question of whether the brief exposure of the Accutane to light and oxygen meant the drug would not be effective.

On the one hand, Dr. Reynolds has warned on the listserv that there is serious risk of degrading the drug if you remove it from the capsule hours or days before use. However, Dr. Reynolds has also reiterated that the conversion of Accutane into another chemical is not an immediate event upon opening the capsule and exposing its contents to light or oxygen. He has written that there is clinical evidence that children did get sufficient amounts of the Accutane when their parents carefully squeezed out the contents and gave it to the child shortly thereafter, or if the child actually ate the capsule itself, in both cases in food or with milk. "I do not feel parents should feel it is essential for their child to swallow the capsules 'whole'," Dr. Reynolds has said. "Certainly if you can get whole capsules into the child that is the optimal way to administer the drug, but it should not be considered 'the only safe way'."

**Accutane should not be administered in a liquid form.** Although it is possible to have Accutane converted into an "extemporaneous" liquid formulation, Dr. Reynolds and other NB experts have strongly urged that this should not be attempted because the drug will likely degrade in the process and not be effective. Although it is possible an individual pharmacist may have developed a liquid formulation, there is too much of a risk that a liquid formulation will not deliver the drug effectively, or that such a liquid formulation could result in conversion of Accutane to a form that increases toxicity to the child.

Women of child-bearing age should carefully avoid contact with Accutane. It is important to be aware that Accutane has caused serious birth defects when taken by pregnant women. Any woman administering the drug who is of child-bearing age must take care not to accidentally swallow the drug (e.g., by getting some on your hands and inadvertently licking fingers, etc.). Dr. Reynolds has advised that any woman of child-bearing age who opens any of the capsules should wear gloves and carefully avoid contact with the Accutane inside of the capsules.

Standard daily doses of most vitamins are believed safe, but supplemental vitamin A should be avoided during Accutane treatment. Dr. Reynolds and other experts have advised against taking vitamin A during Accutane treatment, although the consensus is that a normal daily multi-vitamin should be safe. The data on this topic is based on the doses of Accutane for acne, which is very different from the dose for neuroblastoma, but nonetheless Dr. Reynolds doesn't feel comfortable

with a patient taking supplemental vitamin A during Accutane treatment. There has been no evidence that other vitamins such as vitamin E could interfere with the anti-neuroblastoma effect of the Accutane. Dr. Reynolds has said,

We did not find any evidence for vitamin E antagonizing the anti-neuroblastoma effects of Accutane. However, to truly determine this would require a clinical trial and I don't see that happening anytime soon. Our laboratory data make me very comfortable in recommending liberal topical use of vitamin E (such as vitamin E cream, especially on lips). As to other vitamins, I would think that giving standard 'recommended daily dose' supplemental vitamins (all except vitamin A) should be quite safe. There are no data to address this, but based on what we know about Accutane, there are no reasons to suspect any interactions with low doses of vitamins.

What is the timing of the doses? Accutane doses are generally given 12 hours apart (e.g., 8 am and 8 pm). Some parents have asked what to do if they are traveling or otherwise unable to administer the Accutane at the optimal time. Dr. Reynolds has said that a parent should not worry about adjusting the time between doses, especially if done only occasionally, but that it would be best to avoid more than 16 or fewer than 8 hours between the doses.

Can Accutane be given through a G-tube? Some parents have administered Accutane through their child's G-tube. The concern here is to make certain the Accutane gets through the tube without sticking to the sides, and to use a carrier which does not prevent the Accutane's absorption by the GI track. Some parents have suggested that fatty meals or vegetable oil is a good carrier, and that mineral oil is not a good carrier. The fear was that since mineral oil is not being absorbed by the intestine and the Accutane is dissolved well in it, the mineral oil may serve as a carrier that will take the Accutane out of the body and prevent the Accutane's absorption by the GI track.

One parent "primed" the tube with half a ml of oil, then pushed the Accutane and finally flushed with 5-10 ml of slightly warmed milk (suggested by the parent's hospital pharmacist, since it helps with absorption). Another parent mixed the Accutane with about 5 cc's of flax seed oil.

There does not appear to be any "official" advice on the best way to administer Accutane through a G-tube. The above is what some parents have done, and their children got the standard side effects, suggesting the child was getting a sufficient dosage. However, you should discuss this with your oncologist.

## Dealing with your child's side effects

The majority of children will have some sort of side effect from taking Accutane, although adverse reactions almost always disappear when the treatment is completed.

**Skin.** The most common side effect is severely dry skin and related issues. Almost all children taking Accutane develop extremely dry skin, especially on the face, lips and hands, but also on the ears, feet, arms, legs and sometimes the trunk. The child will likely experience itching, severe chapping, peeling skin, possibly dry eczema-like patches or rashes, and sometimes even cracking and bleeding of the affected area.

These symptoms are usually mitigated if the parent slathers some sort of ointment on the child – especially at night, since many children do not like having it applied during the day. You will have to experiment and determine which ointment or cream your child prefers and which is most effective. Some that parents have recommended are Vaseline, Aquaphor, Eucerin cream, Aveeno Oatmeal lotion, Cetaphil lotion, Cabot cream, Neutrogena Norwegian Formula Hand Cream, and vitamin E (squeeze it from the gelcaps onto the affected area). Some parents have found it helpful to apply the ointment liberally at bedtime and then put socks or gloves on the child's hands. Most parents apply the ointment even when the child is not on the Accutane to keep ahead of the dryness.

Most parents also apply chapstick, Blistex cream, or vitamin E to the child's lips frequently during the day. One parent discovered that the only thing to relieve the burning sensation on her son's severely chapped lips was "Bag Balm" – the antiseptic ointment used to protect cow udders.

Many parents have observed that it helped their child's comfort level when they increased the child's fluid intake substantially. Some parents have also found it helpful to use a cool mist vaporizer at night (which should be wiped down daily with an antibacterial and antifungal wipe or solution).

**Sun Exposure.** Most children are very susceptible to sunburn during Accutane, even during winter. Dr. Reynolds has warned that sun exposure should be very limited for any patient on Accutane. It is advisable to make the child wear a good sun hat, long sleeves and pants, and to apply sunscreen liberally (although a sunscreen may actually irritate the dry skin issues in some children). These measures are advisable even in winter and regardless of geographical area. Dr. Reynolds said that there isn't enough data to be certain of how many days after completing a course of Accutane you could be more relaxed about sun exposure. His recommendation was to avoid the sun until the 2nd week of the 2 weeks off drug and even then one should still use plenty of sunscreen.

Moodiness and other side effects. Individual children will likely experience additional side effects, which may be severe in some cases. Other side effects have included dry eyes, pink eye, dry nasal passages, headaches (some severe), neck, back, leg or knee pain or stiffness, leg cramps, muscle jerks, nausea, vomiting, constipation, diarrhea, lethargy, nosebleeds, and sensitivity to light. Crankiness, mood swings, flying off the handle, tantrums, and other "horrid" behavior are not uncommon. (One grandmother described her granddaughter's personality on Accutane as "satantic"!) Moodiness may be more severe for teenagers and adults. Warnings provided by the manufacturer of Accutane state that the prescribing doc should ask about family history of mental disorders and emotional stability of the patient, and that the patient's ongoing emotional status should be discussed at each check-up. It is important to note that although studies have reported rare but serious depression, suicidal behavior, and psychotic events in teens and adults, those studies refer to use of much lower dose used for acne.

**Treating side effects.** Each child's reaction to Accutane is unique to him or her, and you will have to respond accordingly. Most side effects are manageable with a little trial and error. For example, constipation can be alleviated by having the child drink more juice and by using stool softeners. Several parents have recommended that either oral or IV Zofran enabled their vomiting child keep down Accutane. One child was so sensitive to light that the parent had to keep shades pulled in the house and cover the child's eyes during car rides. Saline nose sprays and artificial teardrops have been used for dry nasal passages and eyes. One parent's dermatologist recommended Bactroban nasal during the days of Accutane, for preventing infections in the nose due to dryness. In addition to Tylenol or other pain medicines, a hot tub bath may ease leg or back pain.

However, some children on Accutane treatment have had even more serious health concerns. Some children have had such severe pain (such as headaches or leg pain) that morphine, oxycodone or other heavy painkillers were required. Some have experienced high blood pressure. One of the most serious side effects experienced by some children during Accutane is very elevated calcium levels, in some cases high enough to require hospitalization. It is therefore very important to have physical exams and blood tests while your child is on Accutane to see how his or her system is handling it. Any symptoms that concern you should be reported immediately to your child's oncologist.

High triglycerides can also be induced by retinoid use and fibrates can be used to lower triglycerides so Accutane treatment can be continued.

**Early or cumulative side effects.** The timing of Accutane side effects varies from child to child. Some children may experience a side effect that increases in severity with each dose; others experience the side effect only with the first couple of dosages or during the first few days of each dose. Most symptoms disappear during the time in between doses. The persistence of adverse reactions after Accutane treatment is completed is believed to be very rare.

The dose may need to be cut back if the adverse reaction becomes too severe. Dr. Reynolds has said that the recommended approach is to begin at the standard dose and then decrease it if necessary due to side effects. The oncologists of some children have added an additional round when the dose was lowered. Many children have been able to return successfully to the higher dose after the adverse reaction subsided.

### **Summary**

As explained above, Accutane can be difficult to administer to some children, but most parents have been able to get their children to take Accutane successfully. Accutane is an easily degradable drug, and it is important to administer it as recommended by neuroblastoma experts. Accutane can cause a wide spectrum of side effects, with dry skin problems the most common. Although we have summarized above many tips for administering Accutane and coping with side effects, each child is different; parents will have to determine what works best for their child and monitor individual reactions. Some side effects of Accutane can be very serious, and it is important that the child be carefully monitored by parents and his or her oncologist. Keep in mind that, as with any medical treatment, it is crucial to discuss all issues with your oncologist and get the most up-to-date advice.

Please contact editors@nbhope.org with any comments



# Coping with MIBG Therapy

MIBG therapy is a treatment for refractory or relapsed neuroblastoma using "radio-labeled" MIBG molecules. A radioactive isotope of iodine is connected to the MIBG molecule which is selectively taken up by NB cells. This therapy is very similar to the MIBG scans used to detect NB, but a much higher dose is used. The scans usually use iodine-123 (faster decay) whereas MIBG treatment uses the slower decaying iodine-131 isotope.

Some trials combine high-dose chemotherapy¹ with the MIBG therapy, and the side-effects and coping discussion that follows will not apply to the extra effects of the chemotherapy. In July 2008 a trial opened using a new MIBG "formulation" which is 20 times more concentrated with radio-labeled MIBG molecules and is known as MIP, Azedra, or Ultratrace.² Ultratrace has similar side-effects, but as of this writing few patients have been treated so we have little information about the differences, if any, between the two MIBG formulations.

MIBG therapy (without chemotherapy combination) is in some ways an easy treatment; unlike some other treatments, it is usually not painful and doesn't tend to make most children feel sick. Still, it is a major treatment that can bring significant upheaval with it. This section provides information on the special requirements of MIBG therapy and a few suggestions for coping from families who have experienced it.

## **Traveling for the Treatment**

One of the first hurdles for most families will be the need to travel to a distant city for an extended stay, since at present, MIBG therapy is available only in a few places around the country. Arrangements for housing can usually be made through the Ronald McDonald House or other similar program for families. For example, families traveling to San Francisco for treatment at the UCSF Children's Hospital utilize an organization called Family House. Usually the doctor's office at the hospital will put you in touch with the appropriate agency. If not, call the social workers at the hospital where your child will be treated. See "Finding Support Resources."

## **Receiving MIBG Treatment**

MIBG therapy is administered as an IV infusion that lasts about 90 minutes. Children receiving MIBG therapy are checked into a lead-lined hospital room. Their hospital bed is surrounded by two or three large lead shields, which protect parents and others from exposure to the radioactivity. Because children who receive the treatment are themselves radioactive, they must remain in the hospital room from two to five days and are confined to the bed except for necessary trips to the toilet or to another part of the hospital for a scan or medical procedure. The level of radiation being emitted from a child's body is constantly measured, and discharge is only permitted when the amount of radiation emitted drops to a certain level. The typical length of stay is 2 to 5 days, with smaller children generally having shorter stay times than larger children, since the dose administered is based on body weight.

The Children's Hospital of Philadelphia, one of the locations where MIBG therapy is available, has provided online, illustrated guides for parents at <a href="http://stokes.chop.edu/programs/maris/MIBG.pdf">http://stokes.chop.edu/programs/maris/MIBG.pdf</a> and for children at <a href="http://stokes.chop.edu/programs/maris/mibg4.pdf">http://stokes.chop.edu/programs/maris/mibg4.pdf</a> that describe the therapy experience.

## Limited Physical Contact with your Child

One concern parents always have about MIBG therapy is the limited physical contact with their child. For the first one to three days after the infusion, physical contact with the child must be very limited due to high levels of radioactivity. Only one parent or caretaker may stay with the child, and generally that person must remain on the far side of the room until the child's radiation level drops, although parents can assist with taking medications, going to the bathroom, eating, and other necessary activities. Children and pregnant women are NOT allowed in the room.

In some hospitals, it may be difficult to actually see the child, depending on how the lead barriers are placed. Often a large mirror is placed on one side of the bed so that parent and child can see each other. Some children find it difficult to have so little physical contact with their parents for several days, and very young children may need some light sedation. You may wish to start telling your child several days in advance that they will have to stay in bed, and that you will have to stay on the other side of the room.

Most of your time will be spent in a designated chair, which will probably be a sleep chair. It may be helpful to ask additional family members or friends to come in. Each individual can be in the room for a prescribed amount of time (a maximum of an hour at some hospitals) to help entertain and reassure the child.

## Coping with the Safety Precautions

Federal regulations require many safety precautions for patients receiving radiation therapy. You will be given detailed information on the various safety precautions required. Although the precautions for MIBG therapy vary from hospital to hospital, there are similarities. Every surface in the room, including the floor, will be covered with plastic, as well as any object the child touches, such as the telephone or video game controller. Parents are required to wear disposable gloves and a paper gown when caring for the child, and persons entering the room must wear paper shoe coverings that are disposed of upon leaving the room. Some hospitals may not allow parents to eat or drink, or use the bathroom, in the room.

Parents and visitors must wear a small badge or meter to measure the radiation exposure. The amount of radiation received by a parent staying with the child the entire time is at a safe level and will be explained to you. In order to limit the amount of time they spend in the room and the amount of radiation exposure they receive, nurses may rely on you to give any medications. This is necessary for their safety—parents may experience the radiation exposure that comes with MIBG therapy once or twice in a lifetime, but nurses are exposed to it frequently on the job, and need to limit exposure to avoid endangering their own health.

There will be several large cardboard boxes lined with red bags in the room, and all waste and linens must be disposed of in these boxes. Anything that you do not want to end up in the trash should be left at home. Toys and favorite blankies, stuffed animals, or other objects are usually allowed into the room, but if they become too "hot" (radioactive) they may not be allowed back out. Plan to bring disposable toys, coloring books, etc. for your child to play with during the treatment, because any item that your child handles, including toys and clothing worn, will generally be disposed of.

Several parents have reported that their child became attached to a particular toy and was upset when required to part with it at the end of the treatment. Some parents recommend buying a duplicate of a favorite toy to avoid this problem. Another parent coped with the problem by bringing a favorite doll wrapped in plastic so that it could be brought back home.

Some hospitals will allow items to remain in a locked storage to decontaminate and be recovered by you after about 3 months. However, you do not want to risk losing a favorite blanket or stuffed animal! Talk with the people at the specific hospital to find out their procedures in advance, so that you can begin forming a strategy for replacing, duplicating, or otherwise bribing your child to do without, his or her favorite comfort object.

You can bring your luggage and belongings into the room. However, these items will need to be stored away from the bed such as behind the chair that you will be sitting and sleeping on.

Each hospital has slightly different rules and practices, but most seem willing to do what is reasonable to help your child through the process.

## Coping with Boredom

Boredom tends to be the big issue with MIBG treatments because of the period of time the child is required to be alone as well as the fact that the child tends to feel quite well during the treatment. There will be video games such as Nintendo in the room and a VCR or DVD machine for the TV. If the video or game machine is beyond the lead barrier around the bed, videos and games from home may be used and brought home when you leave. Your child may be given a game controller or TV remote control wrapped in plastic, or otherwise will be required to wear plastic gloves while using them. Child life specialists can bring disposable craft materials, movies, and video games. Other inexpensive board games can be used in the room and later trashed if necessary. The age of the child will determine what activities are best for keeping them occupied and distracted, but packing a "bag of tricks" is certainly important. When all else fails, go to the cafeteria and bring back a big bowl of ice cream!

You may get pretty lonely yourself, so bring some good novels or other diversions. One parent stated that a prepaid calling card was a sanity saver, as some hospitals may restrict the use of cell phones, or the signal may be very poor.

### Physical Complaints during Treatment

Virtually every parent of a child that has received MIBG treatment found the most difficult issue for the child was having a Foley catheter in place for an extended period. The catheter is considered necessary because patients are given much hydration to protect the bladder and the catheter continually empties it, protecting the child from unnecessary exposure to radiation. Catheters are generally inserted under general anesthesia and remain in place for a couple of days. Some children find the catheter does not hurt at all. Others will feel some mild discomfort or be bothered by it, as it does restrict movement somewhat, while still other children complain that it does hurt. One parent recommends using lidocaine ointment topically as needed. When the child's radiation level is low enough the catheter will be removed. Older children may not be required to have a Foley catheter system but will need to be awakened every 2 hours to urinate.

Although the radiation dose is high, the only physical side effects generally reported during administration of the MIBG treatment are mild nausea and vomiting. Some parents have said their child just didn't feel well and refused to eat much during the treatment. MIBG affects the salivary glands and children may look swollen for a few days or have cheek pain requiring pain medication. One parent reported her child had diarrhea for about a week after finishing the treatment.

### Restrictions after the Treatment

After leaving the hospital, the federal regulations do not apply. However, your child will still be radioactive, and you will be given recommendations intended to minimize radiation exposure to others. You will need to avoid too much lap time, especially if you are expecting or may be pregnant in the relatively near future. It is usually recommended that the child not sleep in the same bed with anyone else for a period of time, and if you are remaining at a Ronald McDonald house (or similar) the hospital may send sheets with you to use until you are discharged to go home. Children must generally wait another week or so to return to school, and should eat off disposable plates and use disposable silverware for a couple of weeks after treatment.

## Follow-up after Treatment

After the treatment, children continue to take SSKI (potassium iodide) drops for quite a while. They will also have blood counts checked regularly and will probably require some transfusions as MIBG has a significant effect on bone marrow. Parents have reported that counts fell 3-6 weeks after the treatment. One parent said their child needed GCSF shots to boost white counts for a month; another mentioned that it took 3 months for her child's platelets to get to 75. Stem cells may be needed or required as part of the protocol, depending on the dosage of MIBG and whether or not there is more than one round of treatment. Getting the stem cells back is very easy, much like a platelet transfusion.

Follow up will continue until the counts are back up, and will also include follow up scans. The effects MIBG therapy has had on tumor burden can take several weeks to show up on scans, and the doctors may have your child do more than one scan to verify the impact of the treatment.

Overall, most parents say that, despite their prior anxieties, MIBG therapy is relatively easy and entails only minor inconveniences and manageable side effects. As one parent opined, MIBG treatment is "rather a dull affair," and another summed it up as follows: "It all seems scary and overwhelming, but it's actually quite a simple treatment. It's just a boring few days and then it's over."

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<sup>&</sup>lt;sup>1</sup> http://www.nant.org/nant2004-06.php



# **Advocating for Your Child**

## From the frying pan into the fire-becoming an Advocate for your child

If having a child with cancer isn't bad enough, parents of children with neuroblastoma must quickly become experts in navigating a dizzying array of medical tests and treatments—making decisions about which path to take without having much time to process or even learn about any options. So we become advocates for our children, politely getting them the treatment, dignity, and the control they deserve as they battle this disease.

## Getting people to help you advocate for your child

It can be a good idea to bring an extra adult helper/listener with you to meetings with doctors or other providers. It is helpful to have a second person to help you remember details, take notes, and ask questions when you will be hearing a large amount of medical information. If you don't have a family member or close friend available, ask the social worker at the hospital.

## Advocacy in the early rounds—knowing what to ask!

Few of us had any chance to really evaluate different protocols before our children are started on chemo. In many ways there aren't huge differences between the various protocols in terms of the upfront chemotherapy, but there are more differences as treatment progress. There are differences, changes are made over time, and some treatments may be leading the curve more than others. Remember you have a right to ask questions, and the right to a night to "sleep on" a decision. See "Patient's Rights and Responsibilities" and "Questions for Your Doctors" sections for more on this topic.

## Advocating for your child during treatment and procedures

Most clinics and hospitals where you will be treated specialize in pediatric care, and most are staffed with kind, caring professionals. Yet, there will still be many small ways in which you can advocate for your child to give them (if they are old enough to talk and have and opinion) and yourself a bit of control in what is often a frustrating and anxiety-ridden experience. All kids seem to develop little preferences—for example: one boy had to have orange flavoring for CT contrast, one girl didn't want anyone to touch her when she threw up, another preferred to have his G-CSF shots given "fast." Tune into your child's preferences, and step in and ask the nurses and doctors to respect and honor those small requests.

Some issues are a bit more involved and may require more knowledge, but the truth is there are some options patients and parents have but must be requested. This is especially challenging, because you may not know when to ask. For example, one child didn't respond well to the Dilaudid pain medication given during 3F8 treatments, and was eventually switched to morphine which had fewer side effects for her. But in this case, if the parent had been significantly frustrated and had not asked the nurses about alternatives, the child would have remained on Dilaudid because it was a standard part of the protocol. Other concerns might be making sure that protective measures are being taken to reduce damage caused by some of the chemotherapy agents. There are advances in protecting hearing, reducing heart damage, and reducing secondary cancer risks that may be worth considering while subjecting our children to the harsh chemotherapy that will potentially save their lives. This type of advocacy is difficult, and some of these issues are better addressed in other

sections of the handbook dealing with specific treatments, but underscore the importance of advocating for your child in medical areas as well as those areas where parents can truly have more control.

### Advocating for your child to be treated as a human being

Again, most medical professionals are extremely kind and child-focused, however everyone seems to have an encounter where that is not the case. You can and should advocate for you child to be treated in a way that is respectful. Even very small children should be talked to directly by medical personnel, and not only through the parent. If someone is talking to or interacting with your child in a way that makes you or your child uncomfortable, you have a responsibility to say something and step in to correct the problem. That being said, advocating for your child is not the same thing as starting a yelling match, throwing a fit, or otherwise threatening the person who you feel is acting in an inappropriate manner with your child. Asking them to stop for a moment, step in the hall, or even a gentle reminder will usually correct those kinds of issues. Frequently, it is just a matter of medical professionals doing their job in a bit too much of a hurry.

## Advocating for quality of life issues

Balancing quality of life with getting the needed treatment is an ongoing issue. Here, we are specifically referring to the ways you can continue life as "normally" as possible during treatment—school, activities, and routine medical appointments.

**School** can sometimes be a difficult challenge for kids and parents. Even for parents of preschoolers, where academic concerns are less the issue, it can be hard to know when to send the child back into the normal world. This is made even more difficult when the people at the school balk at having a child with cancer in the classroom. It is helpful to talk with a school principal or administrator, the teachers, and the school nurse to establish how to make everything work for your child, while reducing their worries. Some may be concerned about spreading contagious illness to your child—a valid concern no doubt! Suggest that children in the class be taught about hand washing, better ways to cover coughs and sneezes, and other general germ-spreading behaviors. In one girl's case, her class and school became so supportive of keeping the school germ-free for her that the school actually had one of the lowest rates of illness ever that year! It is up to the parents, however, to help pave the way for these win-win situations. For older children, especially those in larger school districts, there may be policies against wearing hats or bandanas in the school, so be sure to talk about this with the school.

If your child is school age, there can be concerns about not losing too much ground academically, as well as concerns about truancy laws if the child is not in attendance. It is important to be in contact with your child's school. Some schools will make things difficult, and it is important to insist that your child has a right to be in school. If the school is unwilling and your child needs some accommodations to make school work out, ask about a 504 plan (a legal document based on the Americans with Disabilities Act). The bottom line is that most of our children do best when their life can return as much as possible to normal activities. They benefit from social time with others their own age, and parents can benefit from a little time off as caregivers. Call in social workers, nurses, and doctors for support in talking to school staff about your child's situation—many will come and speak to a class to help make the transition back to the classroom smoother.

**Activities** like sports, dance class, art classes, and all the other things our children love are often easy to drop in all the chaos that cancer treatment can become. But, these activities can be really great outlets for children in treatment, a chance for them to feel more like themselves again. It is okay to ask that your child be able to participate, even if he or she can't participate as fully. Make sure to talk to the coach or instructor about any physical limitations or restrictions your child may have. If your doctor has told you not to participate, ask why, there may be ways to compromise.

**Routine medical appointments** for blood work, transfusions, and even chemotherapy can often be adjusted to allow for life to continue at least somewhat normally. As an advocate for your child, you can ask for a specific time for an appointment and have a reasonable expectation that you will be seen more or less on time. You can ask to have a transfusion after you child gets out of school. You may even be able to schedule some chemotherapy so that it allows for your child to have the weekend to recover and to be back at school. Or maybe, it is more important to have him feeling good for a birthday party on Saturday, so you push to have a transfusion a little earlier than usual. Ask, suggest, think about what is best for your child.

Please contact <u>editors@nbhope.org</u> with any comments



# **Understanding the CBC**

## What is Hematology?

Hematology is the science of blood and blood-forming tissues. Blood is made up of plasma and blood cells. Blood formation (hematopoesis) is a continuous process that occurs in the bone marrow. Within the bone marrow there is a pluripotent stem cell, *the Mother Cell*, the originator of all types of blood cells. The stem cell produces blood cells that exit the bone marrow and circulate in the blood system. Red cells circulate about four months, platelets last an average of ten days, and white cells range from only hours to a week or so. Stem cells that are found outside the bone marrow are called "peripheral stem cells" and are collected and frozen for stem cell transplants.

#### What is a CBC?

The CBC- the complete blood count, or *the counts*- is a lab test that will be ordered frequently on your child. This test determines the number, type, percentage, concentration and quality of the various types of blood cells that make up the blood. This test can be completed on blood that is collected by a finger stick, a lab draw from a central vein access and/or a *straight draw* from a peripheral vein, (usually from an arm, hand or foot).

The CBC is commonly performed on an automated analyzer. However when abnormalities are noted in the blood, parts of the test can be completed *manually*. That is when the blood sample is viewed under the microscope. Some institutions commonly perform an extensively complete CBC and others may perform just specific aspects of the CBC.

When evaluating a CBC it is important to remember that normal ranges can vary depending on many factors- the individual's age, their hydration status, and even can change between different laboratories. Compare your child's results with what is considered the normal range for that institution. When viewing your child's printed lab results, the normal range, or *reference* range, is usually printed alongside your child's results.

There are three different types of blood cells- erythrocytes, (red blood cells/ RBCs); leukocytes, (white blood cells/ WBCs) and thrombocytes (platelets).

### **Erythrocytes (RBCs)**

The primary function of erythrocytes is to carry oxygen from the lungs to the body and bring carbon dioxide from the body to the lungs. RBCs usually live for approximately 120 days. The liver, spleen and bone marrow cleanse them from the blood. In response to a low amount of circulating RBCs, the kidney releases a hormone that stimulates the bone marrow to make more RBCs. RBC is measured in millions of cells per microliter  $\mu L$  or cubic millimeter mm<sup>3</sup>.

A significantly higher amount of RBCs than normal is called *polycythemia*. There are various causes of polycythemia in children, including congenital heart defects. A child undergoing treatment for neuroblastoma is more likely to experience *anemia*, a decrease in RBCs, as a side effect of chemotherapy and radiation. (Anemia can also be defined as a decrease in the hemoglobin.)

## **Reticulocyte Count**

When RBCs are released from the bone marrow, they are slightly immature. These immature cells are called reticulocytes. A reticulocyte count, or *retic count* measures the number of reticulocytes circulating in the blood. A low retic count can be seen in bone marrow failure. A high retic count can mean that the bone marrow is responding to the need for an increase in the production of RBCs. This can be seen in cases of anemia and blood loss. Retic counts are closely monitored in leukemia.

### Hemoglobin (Hgb)

Hemoglobin is a combination of protein and iron within the red blood cell. The hemoglobin is the part of the RBC that carries oxygen and is measured in grams per deciliter (g/dL). Anemia is a low hemoglobin level. It is the decrease in the oxygen- carrying capacity of the blood that can make your child tired when your child is anemic. Elevated hemoglobin can indicate dehydration or polycythemia. Hemoglobin is the first H in an H and H.

## Hematocrit (Hct)

Hematocrit is the second *H* in an *H* and *H*. The hematocrit or *crit* measures the percent by volume of blood that is comprised of RBCs. The hematocrit may be determined by spinning a blood sample in a centrifuge. That is why you may hear the phrase, *spinning* a *crit*. A low hematocrit can indicate blood loss, anemia, or bone marrow suppression, and dehydration can cause a "false" elevation in the hematocrit. (See "Blood Transfusions")

### **Erythrocyte Indices**

When the hemoglobin is low, it is important to look at the erythrocyte indices. Each of the indices evaluates a different aspect of the RBC. These indices are considered in relation to your child's diagnosis and current treatment.

## Mean corpuscular volume (MCV)

The MVC measure the average size of the RBC. Small RBCs can be seen in anemia, led poisoning, genetic diseases and cancers. Large RBCs are seen in other types of anemia and chronic liver disease.

## Mean corpuscular hemoglobin (MCH)

The MCH measures the weight of hemoglobin present in an RBC. This level can be low or high with different types of anemia.

## Mean corpuscular hemoglobin concentration (MCHC)

The MCHC measures the proportion of hemoglobin in the RBC. It can be decreased with anemia and is rarely high.

### Nucleated red blood cells (NRBC)

NRBCs are abnormal in peripheral blood except in newborns. The presence of NRBC in a CBC can indicate bone marrow recovery from anemia after chemotherapy.

# Leukocytes (WBCs)

Leukocytes help to protect the body from infection by a process called phagocytosis. This is when the WBC surrounds and destroys a foreign cell. WBCs also produce, transport and distribute antibodies. WBCs usually live for 13 to 20 days and are destroyed by the lymphatic system.

There are 5 different types of WBCs. Neutrophils, eosinophils and basophils are called granulocyte white blood cells. Granulocyte WBCs have granules when they are stained and viewed under a microscope. Lymphocytes and monocytes do not have granules and are called agranulocytes.

WBCs are usually evaluated in two different ways. The *Absolute number* is the total number of that type of WBC in a microliter (µL) which is equal to a cubic millimeter (mm³) of blood. The *differential*, the diff, reports the percentage of each of the 5 white blood cells, with the percentages adding up to 100%. Both aspects of the white blood cells are considered when making a WBC assessment.

The Total WBCs can be elevated (leukocytosis) with infection, trauma, leukemia and post-operative period. This level can be low (leukopenia) due to immune disorders, chemotherapy, radiation, and cancer. WBC levels can be affected by the body's own stimulating factors or those that are commonly injected subcutaneously when the child's WBC counts drop after chemotherapy.

## Neutrophils

Neutrophils kill bacteria. You may hear neutrophils called *segs*. This is because mature neutrophils have a segmented appearing nucleus. An elevated neutrophil (neutrophilia) count usually represents bacterial infection and/or inflammation. An Absolute low neutrophil count (neutropenia) can represent bone marrow suppression from chemotherapy and/or radiation, a severe infection, or a process known as sepsis. (*See* Chapter 3 "Surviving Neutropenia")

Immature neutrophils do not have a segmented nucleus; they have a band-shaped nucleus. So when young neutrophils are released from the bone marrow, they are called bands. The phrase a shift to the left is used when the band level has increased. It is a holdover phrase from the days when lab reports were handwritten and bands were written first on the left hand side of the report.

An important factor used in monitoring your child's ability to fight infection is called the ANC (Absolute Neutrophil Count). The ANC is not measured directly. It is determined by multiplying the WBC count by the percent of neutrophils in the differential WBC count. The percent of neutrophils consists of the segmented neutrophils plus the bands. The normal range for the ANC is 1.5 to 8.0 (1,500 to 8,000/mm³). When the ANC is under 500 (or 0.5) your child is at risk for serious infection and this is why fevers are treated with IV antibiotics in the hospital.

Sample calculation of the ANC

WBC count: 6,000 cells/mm<sup>3</sup> of blood (or 6.0)

Segs: 31% of the WBCs Bands: 4% of the WBCs

Neutrophils: segs + bands = 35% of the WBCs

ANC:  $35\% \times 6{,}000 = 2100 / \text{ mm}^3 \text{ or by convention} = 2.1$ 

Normal range: 1.5 to 8.0 (1,500 to 8,000/ mm<sup>3</sup>)

Interpretation: Normal

## **Eosinophils**

Eosinophils are commonly associated with hypersensitivity reactions or parasitic infections. A high eosinophil count would be expected in an allergic reaction. A low eosinophil count can occur when the child is receiving corticosteroids.

## **Basophils**

Basophils have a role in the body's immune response, by releasing histamine and heparin. Their small numbers increase during the healing process or when there is an alteration in bone marrow

function. A drop in the basophil level may occur with corticosteroid use, with an allergic reaction, or during an acute infection.

### Lymphocytes

Lymphocytes are active in immunity. They are produced in the bone marrow but mature in lymphoid tissue. The total lymphocyte count represents the total number of T and B-lymphocytes. Simply put, T cells (helper cells, killer cells, cytotoxic cells, regulator cells and memory cells) are the master immune cells and they tell the B cells to make antibodies. Lymphocytes increase with viral infections, tuberculosis, and leukemia and decrease with corticosteroids and other immunosuppressive medications.

### **Monocytes**

Monocytes are the largest cells in the blood. They are phagocytic, ingesting debris from cells when there is infection or inflammation. They have been likened to the Pacman video game. Some monocytes enter tissue where they enlarge and mature into macrophages. Monocytes typically increase after several days of infection or inflammation.

## **Thrombocytes (Platelets)**

Platelets are actually cell fragments, not true cells. They are made in the bone marrow and circulate in the blood for approximately 10 days, and are measured by thousands per microliter  $\mu L$ . Platelets are essential to blood clotting (coagulation). When blood comes into contact with anything other than the smooth lining of the blood vessels, platelets stick together to form a plug and release chemicals that further assist clot formation.

Thrombocytopenia, a platelet count below 50,000, can occur with bone marrow suppression from chemotherapy and/or radiation, leukemia, malignancies of the bone and autoimmune disorders. Medications that increase the production of white blood cells in the bone marrow, (i.e. G-CSF), may decrease the bone marrow's production of platelets.

Thrombocytosis, an increase in the platelet count, can occur with dehydration, spleen dysfunction, or as a response to injury or inflammation.

### **CBC** evaluation

When your child's treatment team evaluates a CBC, they do so in conjunction with understanding your child's present symptoms, physical exam, current treatment, treatment history, and any other factors that are pertinent to your individual child. It can be helpful to keep track of your child's counts yourself along with normal ranges and units for comparing results (see Chapter 10 "Keeping Records").

#### Sources:

RnCeus.com. Understanding the CBC by Maureen Habel, RN, MA, CRRN <a href="http://rnceus.com/course\_frame.asp?exam\_id=14&directory=cbc">http://rnceus.com/course\_frame.asp?exam\_id=14&directory=cbc</a>

RN.com. Assessment Series: Hematological Anatomy, Physiology and Assessment by Lori Constance MSN, RN, C-FNP

Ed Uthman, MD, American Board of Pathology <a href="http://web2.iadfw.net/uthman/blood\_cells.html">http://web2.iadfw.net/uthman/blood\_cells.html</a>

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# **Hearing Loss**

Hearing loss is unfortunately one of the most common adverse side effects of standard treatment for high-risk neuroblastoma. According to recent research, up to 62% of children treated for high-risk NB will end up with hearing loss. The hearing loss is caused by certain medications, most importantly the chemotherapy cisplatin. Your child may also have received other medications that damage the hearing, such as carboplatin, certain antibiotics, and Lasix (which is often administered if your child has extra fluid called ascites). The likelihood and severity of hearing loss seems to increase with higher doses of these medications and with younger age of the child. Older children seem less likely to be affected.

Many families are disheartened upon learning the news that their child, having completed a long and arduous treatment course, must now cope with the challenges of hearing loss. However, since the majority of children with post-NB treatment hearing loss are at an age when speech is developing, it is important not to delay intervention. Even a mild hearing loss can profoundly affect a child's ability to process language. Children who are cancer survivors are already at risk for learning problems due to radiation, chemotherapy, emotional trauma, and other reasons. Delays in effective interventions for hearing loss can only compound these problems.

This section is intended to be a resource guide to hearing loss, targeted especially at the young NB survivor. Topics that will be discussed include specialized terminology, audiograms, hearing loss professionals, and educational considerations, starting with a discussion of the first step you should take -- getting the most precise evaluation possible of your child's hearing status by a hearing loss professional.

### Getting Your Child Evaluated

When you read through the standard material on hearing evaluations for young children, you will see checklists of signs that a child may have a hearing loss. In some ways, your task is easier, since any child who has completed the standard protocol for high-risk NB may have hearing loss. **Any child who has received one of the platinum-based chemotherapy agents (cisplatin, carboplatin) should be evaluated for hearing loss.** If your child is very young, it is very important to find an audiologist who has experience working with young children, because it is notoriously difficult to get accurate audiograms with this age group. It is very common to hear parents of children with hearing loss tell stories of going through multiple audiologists before a hearing loss can be accurately measured. For example, it took over a year and three audiologists, before one two-year-old NB survivor was able to be evaluated precisely enough to equip him with hearing aids! The A.G. Bell website has good advice for finding a pediatric audiologist:

http://www.agbell.org/DesktopDefault.aspx?p=Find\_an\_Audiologist

Key points made include asking audiologists about their experience with young children, and asking other parents of hearing-impaired children for recommendations.

There are several methods of testing hearing, but for children over 6 months or so of age, behavioral assessments are most typical. In this type of test, the child's response to pure tones is assessed while sitting in a sound booth. For a very young child, this response may be as simple as a head turn. Preschoolers will be encouraged to make this into a game, tossing balls into a bin, for example, in response to the tones. Some young children may be frightened by the sound booth, which is often small and dimly lit. This is why it is so important to find an audiologist who has a lot of experience

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with small children and who has a good rapport with your child. Sometimes, the test is best run with two evaluators – one to run the equipment and the other to observe the child.

Here is a list of resources on hearing tests and how to interpret them.

### http://kidshealth.org/parent/general/eyes/hear.html

Hearing evaluation in children. This provides an overview of the types of tests used, types of hearing loss, and assistive technology such as hearing aids and FM systems.

## http://www.agbell.org/DesktopDefault.aspx?p=Testing\_for\_Hearing\_Loss

Another overview of the types of hearing tests that are used.

#### http://www.audiology.org/aboutaudiology/consumered/guides/audiogram.htm

How to read an audiogram. You'll want to be able to explain your child's audiogram when you are dealing with school personnel, who often have never worked with a hearing-impaired child before.

### http://www.earinfo.com/how-to-read

Here is another explanation of how to read an audiogram.

## http://www.handsandvoices.org/resources/coGuide/05\_Lossvseffct.htm

http://www.helpkidshear.org/resources/starter/degrees.htm

Good explanations of the degrees of hearing loss. This is also useful when dealing with school personnel.

### http://www.utdallas.edu/~thib/rehabinfo/tohl.htm

This site has simulations of what different types of hearing loss actually sound like.

## **Types of Hearing Loss**

This section presents a quick overview of the types of hearing loss, and then describes the type of hearing loss suffered by most NB survivors. You will want to understand the differences between types of hearing loss so that you can more effectively communicate with your child's audiologist, speech therapist, and educational personnel. It is often useful to memorize a quick phrase that summarizes your child's hearing loss: "bilateral moderate-to-severe sensorineural loss," for example.

Hearing loss can be categorized by general cause. A **conductive hearing loss** occurs when sound is not conducted through the outer and middle ears. This can be caused by otitis media or problems in the Eustachian tube. A **sensorineural hearing loss** is caused by damage to the inner ear, the cochlea, or to the nerves in the inner ear. This can be caused by disease, certain medications, genetic syndromes, and exposure to noise. This is a permanent hearing loss that cannot be corrected by medication or surgery. Finally, **central auditory processing disorders** originate in the auditory centers of the brain, and may be caused by injury or disease.

A hearing loss is also characterized in terms of its "shape". This refers to the shape of the line on the audiogram. A **sloping** hearing loss means that hearing is better in the lower frequencies and gets worse in the high frequencies. A **flat** hearing loss means that hearing is the same across all frequencies. A **rising** hearing loss means that hearing is worse in the low frequencies and better in the high frequencies. Finally, a **cookie-bite** hearing loss means that hearing is worst in the middle frequencies.

The type of hearing loss that is most common among children who have received ototoxic chemotherapy medicines is a bilateral, sloping, sensorineural hearing loss. The hearing loss may range from mild to profound, although moderate or moderate-to-severe seems to be most common. What this means is that the hearing loss is about the same in both ears, is worse in the higher (and

often middle) frequencies, is caused by damage in the inner ear, and is serious enough to require amplification. The fact that the hearing loss is often in the middle and high frequencies is important since those are the frequencies at which many speech sounds occur. It is very common for young children with this type of hearing loss to need speech therapy as a result. NB survivors often finish treatment at an age when language is being acquired, so it is important to keep this in mind.

Here are resources on types of hearing loss:

http://www.helpkidshear.org/resources/starter/types.htm

#### Mild Loss

http://www.sciencedaily.com/releases/2004/11/041123204642.htm

http://www.audiologycentre.com/child faq management.htm

### **Terminology**

http://www.helpkidshear.org/resources/starter/glossary.htm#S

A glossary of the types of terminology you are likely to hear.

## http://www.listen-up.org/htm/acronyms.htm

A glossary of acronyms that you are likely to encounter. Be forewarned – the area of hearing impairment abounds with acronyms.

#### Now What Do We Do?

The current thinking among audiologists is to aggressively aid hearing-impaired children as early as possible. This helps minimize speech and language delays. Most children with moderate or worse hearing impairments will need hearing aids, and many children with mild hearing impairments will need hearing aids as well. You will find that you will be spending a lot of time on hearing aid issues, so it is worth understanding the technology.

Besides aggressive amplification, the other important strategy is to obtain educational services for your child as quickly as possible. Such services may be through an early intervention program or through your school district, depending on your child's age.

## **Hearing Aids**

Hearing aids work by amplifying sounds coming into the ear. Hearing aids can be programmed to boost sounds selectively at different frequencies, depending on the individual needs of the wearer. Hearing aids may be either **analog** or **digital**. Digital hearing aids provide a cleaner signal and seem to be most typically recommended for children.

Hearing aids for children are most typically **behind-the-ear** hearing aids (BTE). These consist of the hearing aid itself, which fits behind the ear, and an **ear mold** which fits into the ear. This both anchors the hearing aid to the ear and sends sound into the ear. This type of hearing aid works well for children because it is easy to insert and because only the ear mold needs to be replaced as the child grows. Ear molds are available in many child-friendly colors – we have spotted children with swirling tie-dye style ear molds, and pink sparkly ear molds! Besides the BTE style hearing aids, **in-the-ear (ITE)** and **in-the-canal (ITC)** hearing aids are available and may be appropriate for teenagers whose ears have stopped growing.

Resources on hearing aids follow.

### http://www.childrenshearing.org/custom/hearing\_aids.html

A discussion of hearing aid types, as well as of other assistive technology.

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# http://www.agbell.org/DesktopDefault.aspx?p=Hearing\_Aids

A great overview of hearing aids.

### http://www.boystownhospital.org/Hearing/hearingaids/index.asp

Another overview, with more technical detail on digital hearing aids.

## http://www.asha.org/public/hearing/treatment/child\_aids.htm

Another overview of children's hearing aids, along with information on funding.

## http://www.utdallas.edu/~thib/rehabinfo/ao.htm

This page has pictures of the various kinds of hearing aids, and an extensive section on hearing aid maintenance and troubleshooting.

Hearing aids are unfortunately quite expensive. It is common for digital hearing aids to cost well over \$2000. And sadly, many insurance plans will not cover hearing aids. Many families who have been through NB treatment are already reeling financially, so this is a very unwelcome blow. In some states, Early Intervention and other state programs will pay for hearing aids, so check these options in your state. Medicaid will also cover hearing aids. Some states are introducing mandates that insurance pay for hearing aids. In some cases these mandates are so new that even the insurance company representatives may not be aware of the requirement, so always check the laws in your state if you have been turned down for insurance coverage.

Here is an entire page of links on funding for hearing aids. http://www.listen-up.org/haidfund.htm

## Other Assistive Technology

**FM systems** are commonly used in classroom settings, although they can also be useful in any noisy situation. These systems enhance the "speech to noise ratio" when the speaker is in a noisy setting (such as a classroom) and the listener is not physically close. The speech to noise ratio is the relationship between the loudness of the speaker and the loudness of the background noise level. Hearing-impaired children have difficulty picking out a speaker's voice when there is a lot of background noise. It isn't enough for a teacher to simply raise his or her voice since the hearing-impaired child will still have trouble picking out the differences between speech sounds, which is necessary to understand the speech. This is where an FM system can be a big help.

A **personal FM system** consists of a small microphone that the teacher wears and a receiver worn by the child. A common type of system involves 2 tiny receivers (called "boots") that plug into the child's hearing aids. The receivers pick up the signal transmitted from the microphone and transmit it directly into the hearing aids, thus boosting the teacher's voice significantly.

**Soundfield systems** consist of a microphone worn by the teacher, and small speakers that transmit the signal. Such systems are useful for children with mild hearing loss, but personal FM systems are more effective for children with higher degrees of hearing loss. Interestingly, some school districts have been experimenting with soundfield systems for all students, finding that amplification boosts attention and helps all children learn.

**Cochlear implants** are used in situations where a child has severe-to-profound hearing loss, with little or no residual hearing. This type of device bypasses the inner hear and directly stimulates the auditory nerve to send information. Most children who have lost hearing due to chemotherapy do not have this degree of hearing loss, so it is not common to see cochlear implants in this group.

**Closed captioning** is used in the classroom for films or video. It is common to write this accommodation into a child's IEP or 504 educational plan (more on those topics below in Educational Considerations). It is also possible to place the FM system mike in front of the speakers or to plug it directly into the audio output of the VCR.

When assistive technology is used in a school setting, it is important for the teacher(s) and other staff who interact with the child to be trained in the proper usage of the devices. These devices are fragile and unfortunately, break fairly often. The teacher and at least one other person in the school should know how to insert and remove the hearing aids and FM system receivers, and how to change batteries. As the child grows older, he or she can also take more responsibility for these tasks. If there is an IEP or 504 plan, these responsibilities should be spelled out. It is also useful if the school has the services of an educational audiologist, or can communicate with the child's private audiologist directly for assistance when there are problems. For example, one NB survivor's audiologist runs an in-service training session for his teachers each year, which is specified in the child's IEP.

#### **Educational Considerations**

Classrooms, as we all may remember, tend to be noisy, bustling places. A significant amount of the material learned in a classroom is learned through the ears, by listening. And part of that is learned not directly from the teacher, but through listening to other conversations. Children with hearing loss, even if they have hearing aids, tend to have trouble distinguishing speech sounds in a noisy situation. Hearing aids amplify background noises as well as speech. Thus, children with hearing loss have a lot of difficulty simply accessing the material to be learned. In addition, children with hearing loss often are behind other children in terms of vocabulary, which has a great impact when learning to read. Many children with hearing loss end up performing below grade level in reading, and the gap often progresses over time. (http://www.readingrockets.org/article/5135).

In addition, children with hearing loss often have social delays since they have trouble communicating with other children, and picking up information and social cues from other children's conversations. Children with hearing loss are often described by teachers as being "out of it" or having problems paying attention. Anecdotally, some parents have noticed that many children are misdiagnosed as having attention difficulties before finally being diagnosed with hearing loss.

Assistive technology such as personal FM systems are very important in overcoming the barriers experienced by children with hearing loss. If your child uses hearing aids, it is important that he/she wear them every day, and that they be maintained in working order. If your child uses an FM system, it is important that every teacher use the microphone when speaking to the class. For older children, it may also be useful to pass the microphone around when classroom discussions are taking place.

There are a number of classroom accommodations that can be made to further assist your child. These often need to be explicitly explained to the teacher, or better yet, specified in your child's IEP if he/she has one. Many teachers are not familiar with hearing loss issues and do not know the types of accommodations that can help. Here is a list of helpful accommodations:

- Preferential seating. A child should be seated near the front of the classroom where he/she can easily see the teacher. If the teacher regularly changes position, the child may need to be able to change seating as well. Many children with hearing loss use some degree of lip reading to augment understanding, so being able to see the teacher can be very important. The child should also be seated away from noisy equipment such as air conditioners or fans.
- The teacher should face the children when speaking, rather than facing a board.
- The teacher should write down important information, such as new vocabulary words, assignments, and announcements.
- The teacher should ask the child if important instructions have been understood.

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• The teacher should help the child understand when transitions are occurring, by using phrases that make the transition explicit. For younger children, it is especially important to make transitions to new types of activities explicit. One child's kindergarten teacher used a set of cards with pictures of children playing (for free time), children sitting quietly (for circle time), and children writing (for writing activities).

• The teacher should also assist with new vocabulary, since this is an area of particular difficulty for hearing-impaired children. The meaning of new words should be explicitly explained before using the new words to teach material. If the child has a Teacher of the Deaf as a support service, this specialist will usually preteach and reteach new vocabulary.

Here is a link which describes strategies for teaching hearing impaired children: http://www.as.wvu.edu/~scidis/hearing.html

In addition, there are steps that can be taken to reduce classroom noise. Noise often comes from sources such as air conditioning systems, pencil sharpeners, hallway noise, chairs and desks sliding on the floor, and of course, other children talking. Reverberation in the classroom can make such noise worse. Steps that can be taken include:

- Installing acoustic panels on the walls.
- Installing carpeting.
- Putting tennis balls on the chair legs this is a common solution since most districts will balk at installing carpeting as an accommodation.
- Requesting that tests be taken in quiet settings. This can be written into the child's IEP.
- Seating the child away from noise sources such as windows or corridors.
- Requesting that landscaping services (especially mowing) be done during non-instructional time.

Remind your school district that accommodations that reduce background noise will help all the students in the class, not just your child.

Finally, many children with hearing loss can benefit from the services of specialized support staff. Many parents are not even aware that some of these support services exist. One of the most important types of specialists that may be available to your child is the **Teacher of the Deaf**, or sometimes called an itinerant teacher of the hearing-impaired. This type of teacher, not to be confused with sign language interpreters, usually has completed a degree in Deaf Education. Typically, a school district will employ this type of teacher to travel to all the schools in the district and work with hearing impaired children. Smaller districts may use teachers contracted through regional consortia or a regional School for the Deaf. For example, in New York, such teachers are usually contracted for through a regional educational consortium called BOCES. A teacher of the deaf can provide many services, but the most important roles are to help other teachers develop strategies for working with your child, serve as a liaison between the various staff members and the parents, and provide one on one tutoring of your child in the area of vocabulary and strategies for understanding language. A Teacher of the Deaf is different from a speech therapist, whose role is to help a child produce comprehensible language. Often, a child with a serious hearing impairment will work with both types of specialists. School districts will usually have speech therapists on staff, and may try to argue that a hearing-impaired child only needs the speech therapist, so it is important to understand the distinction between the two types of specialists. Older children with hearing loss may also benefit from the services of transcribers to take notes, or from peer notetakers. Children who use sign language (which is less typical among cancer survivors) may also use a sign language interpreter.

## IEPs and 504 plans

This topic often causes the most stress for parents with special needs children, because these are the laws and regulations that govern your child's access to specialized services and accommodations.

The **Individuals With Disabilities Education Act (IDEA)** is the main law that governs access to specialized educational services. Schools are required to provide children with disabilities with a **free appropriate public education** (FAPE). A child who is determined to require such services will have an **Individualized Educational Plan (IEP)** which lists the educational goals to be met and the types and frequencies of services. Unfortunately, there are many areas of controversy, and possibilities for disagreements, within this law, especially as it relates to which children qualify for an IEP, and which types of services are appropriate. A child with hearing loss, and especially a child who is a cancer survivor, has a high likelihood of qualifying, so you should initiate the process of having your child evaluated as early as possible.

This article lists steps to take in order to request that your child be evaluated. <a href="http://www.fetaweb.com/01/faqs.evals.htm">http://www.fetaweb.com/01/faqs.evals.htm</a>

One tip – your child will almost certainly have a speech evaluation as part of this process. Request a speech evaluator that is trained in working with hearing-impaired children, since speech delays often manifest themselves differently in this group. Under the regulations, if you are not satisfied with an evaluation provided by the school, you can request an independent evaluation. Here is an article which discusses that process.

http://www.wrightslaw.com/info/test.iee.steedman.htm

Hearing-impaired children who do not qualify for an IEP will usually qualify for a 504 plan. **Section 504** is a law that prohibits discrimination against individuals with disabilities. Part of it (subpart D) mandates that children with disabilities have equal access to an education. Children who fall under this regulation (as all children with hearing loss do) will have a 504 plan drawn up by the school, which will typically mandate usage of hearing aids, an FM system, captioning of films/videos, notetakers, and sign language interpreters if needed. Very confusingly, some school districts will also provide services such as speech therapy in this plan, even though the child does not have an IEP. Keep in mind that a parent has far fewer procedural safeguards under Section 504 than under IDEA, so if your child needs support services to succeed in school, it is usually better to pursue an IEP.

The area of special education law is vast and difficult. It is impossible to delve into all of its complexities here. The WrightsLaw website and book series is an excellent resource which covers all of this material in depth. Links are provided below. School districts will also often have a parent advocate who participates in IEP meetings with families. This person may be helpful so you should try to locate your district's parent advocate. It is also possible to hire an independent educational advocate to assist you in obtaining needed services for your child from your school district. And finally, there are lawyers who specialize in special education law who can represent you at hearings. Hopefully you will never need such services!

#### **Additional Resources**

### **Organizations**

## www.handsandvoices.com

Hands & Voices is a nationwide non-profit organization dedicated to supporting families and their children who are deaf or hard of hearing, as well as the professionals who serve them.

### http://www.agbell.org/

The Alexander Graham Bell Association for the Deaf and Hard of Hearing helps families, health care providers and education professionals understand childhood hearing loss and the importance of early diagnosis and intervention. Through advocacy, education, research and financial aid, AG Bell helps to ensure that every child and adult with hearing loss has the opportunity to listen, talk and thrive in mainstream society. They have chapters located in the United States and a network of international affiliates.

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### http://www.clarkeschool.org/

The Clarke School for the Deaf has a number of branches in Massachusetts, Pennsylvania, and New York. In addition to educational programs, they also provide independent educational evaluations. Many other schools for the deaf will also provide this service; however, Clarke is particularly well known.

### **Online Resources**

## www.listenup.org

A wonderful collection of articles, and most importantly, the Listen-Up mailing list, for families of children with hearing loss. The mailing list is fairly high traffic, but you can learn almost everything you need to know there about topics from cheap sources of batteries and diagnosing problems in hearing aids, to negotiating with school districts for services.

### www.wrightslaw.com

The main "go-to" site for learning how to navigate the special education world, particularly focusing on IDEA regulations and parents' rights under that law. The people who run this site also run training sessions for parents all over the country.

#### **Books and Publications**

<u>Laverdière C, Cheung NK, Kushner BH, Kramer K, Modak S, LaQuaglia MP, Wolden S, Ness KK, Gurney JG, Sklar CA.</u> "Long-term complications in survivors of advanced stage neuroblastoma," Pediatric Blood Cancer, September 2005, pp. 324-332.

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From Emotions to Advocacy, The Special Education Survival Guide, 2<sup>nd</sup> Edition, Pam Wright and Peter Wright, Harbor House Law Press, 2006.

Wrightslaw: Special Education Law,  $2^{nd}$  Edition, Pam Wright and Peter Wright, Harbor House Law Press

Your Child's Hearing Loss: What Parents Need to Know, Debbie Waldman, Jackson Roush, Berkeley Publishing Group, 2005.

Please contact <a href="mailto:editors@nbhope.org">editors@nbhope.org</a> with any comments

<sup>&</sup>lt;sup>1</sup> Lavadiere et al, Pediatric Blood Cancer, Sept. 2005, 324-32

<sup>&</sup>lt;sup>2</sup> Li, Womer, and Silber: "Predicting ototoxicity in children: Influence of age and the cumulative dose," Eur. J. Cancer 40:2445-2451, 2004.



## **Treating Refractory NB**

After just a few months of your child's treatments, you may finally feel like you are getting the hang of cancer treatment. Then you find out that your child is "refractory"—i.e., one of the 20-50% of high-risk NB cases that does not respond to treatment adequately during frontline treatment. Once again, the wheels have come off the cart and you are bogged down in new information and emotions.

In this chapter, parents who have dealt with refractory disease share some of the information and insights they have learned along the way. Our hope is that the experience of others who have been in your situation will be helpful as you navigate this new stage of your child's treatment. As always, parents' observations are just that, and an experienced oncology team must always be your guide in medical matters.

### What does this mean for my child?

If you look up a definition of refractory, you will find it is "a condition that does not respond to treatment." However, in the world of NB, it is not that simple. Refractory NB may also be referred to as resistant, stable, or primary refractory disease. Your child may have had a very good partial response to treatment or only a very limited response -- there is a range of response that may be considered refractory. Keep in mind that "refractory" disease is different from "progressive" disease, in which the NB is not only **not** responding to treatment nor remaining stable, but is increasing or spreading despite treatment.

Whatever range of response has been seen, once your child has not responded to therapy as intended and is identified as refractory, he or she will no longer continue on the frontline protocol. It is time to consider alternatives. What this means is that you must become an even greater advocate for your child's medical care, be willing if necessary to consult with new doctors, and possibly even travel to new and distant places for treatment. It is important to keep in mind that each child responds differently and that a variety of new or improved treatments continually become available. There *are* long-term survivors whose once refractory disease was successfully treated with therapies that diverged from the "front-line" treatment the child had "failed." Your goal is to find that successful alternative path for your child.

### What is the first step?

So, how do you find out the best path for your child without enrolling in medical school yourself? An oncologist with expertise and long experience in NB, and most importantly, someone with whom you feel comfortable and can place your trust, is the key resource in making your next treatment decision for your child. If you are not already being treated at a medical center that has doctors who specialize in NB, *now* is the time to make contact with such institutions. The trick is to do so quickly—time can be critical in fighting NB.

You should regard your child's primary oncologist as an invaluable resource when determining subsequent treatment options, even if you decide to consult with additional NB experts. It is necessary to take into full consideration whether the child has responded favorably in a manner that might suggest the pursuit of a specific treatment and also whether the child has any medical

conditions that might preclude a certain course of treatment. Having intimate knowledge of the child's specific response to date and his or her present condition, your child's primary oncologist is in a unique position to help.

However, sometimes even your child's primary oncologist may not be fully informed about newer options available for children with refractory disease, and it may be necessary for you to do some research yourself. Alternatively, you may feel being more informed will enable you to have a more meaningful discussion with the medical professionals. Whatever your rationale, your research may involve exploring online the protocols offered at other cancer centers; speaking to NB experts at other cancer centers; speaking to principal investigators of new clinical trials; and/or obtaining second opinions from one or more NB specialists based on their comprehensive examination of your child and his or her history. Many parents also speak with others whose refractory children have been treated on certain clinical trials; be mindful that every child is different and the experience of others may have limited relevance to your child's situation.

If you decide to get a second opinion, a list of NB specialists in the U.S. and their contact information may be found in "Confronting the Diagnosis: U.S. NB Specialists." (This is not a comprehensive list.) Do keep in mind that these are doctors known around the country and even the world, and some have a very large number of patients; they often receive dozens of calls and emails a day. Hence, you might not get a return call or email, or at least not as quickly as you wish – which is immediately! It is often helpful to speak with the doctor's secretary first and find out if the specific doctor prefers to be contacted first by email or phone and the best time to call.

Keep in mind that a doctor cannot give you an informed second opinion over the phone, and will need to examine your child and his history to advise you medically. You must take the responsibility of having copies of all your child's medical records sent to a consulting physician. This can take time and may also involve some frustrating administrative steps, so you should determine as soon as possible how to get copies of your child's medical records.

Indeed, once you have realized your child is refractory, beginning the next phase of treatment as soon as possible and avoiding progressive disease is crucial. Yet, you do not want to rush into a treatment that may preclude a different, equally promising trial. In the experience of many parents of children with refractory disease, there are two very important and related considerations to bear in mind when deciding on the next course of action.

On the one hand, you wish to identify the treatment that will knock out the disease this time around, keeping in mind that such decisions rarely constitute the elimination of all other options. In many instances the failure to respond to a specific treatment -- or even emotional, financial, or social considerations -- will dictate a "return to the drawing board" in your effort to find the best care. Hence, this is also an opportunity to identify and set aside some options for later consideration. But, on the other hand, your preferred choice of treatment may have the effect of precluding some others. In particular, choosing an extremely harsh option, with potentially damaging, long-term side-effects, may render the child ineligible for other subsequent treatments, either by doing irreparable harm to organs or blood counts, or by changing the biology of the disease. For example, the high-dose chemotherapy that often accompanies transplant may affect organ function; high-dose MIBG might result in long-term suppression of blood counts; and a particular chemotherapy regimen may cause the cancer cells to develop an immunity to that agent. It is crucial to identify the "opportunity costs" of the various possible treatments (see further discussion below). It is also important to plan ahead in order to make the best use of a stem cell harvest.

### **Investigating Available Protocols/Clinical Trials**

NB protocols or trials are basically treatment options. Your induction chemotherapy or treatment regimen was a protocol used after initial diagnosis and staging of the disease. But whereas there is limited variation in "frontline" treatments around the country, treatment options for a child with

refractory disease are numerous and varied - and hence can be very confusing.

There are several centers that specialize in NB and some treatments may be available only at specific institutions. There are 14 hospitals across the countries that are affiliated with New Approaches in Neuroblastoma Treatment (NANT) (www.nant.org). NANT is a consortium of research institutions that share research protocols and support. Some trials may not be available at all of the NANT hospitals, but most will be. Another excellent resource is Memorial Sloan-Kettering Cancer Center (MSKCC, www.mskcc.org) in New York City. MSKCC has a team of several oncologists devoted to neuroblastoma and conducts research separate from NANT.

There is a wealth of information on the internet—but it is hard to pare down to a reasonable size. A good place to start is the websites from NANT, MSKCC, the National Cancer Institute <a href="http://www.cancer.gov/CLINICALTRIALS">http://www.cancer.gov/CLINICALTRIALS</a> and the National Institutes of Health <a href="http://clinicaltrials.gov">http://clinicaltrials.gov</a>. On most sites you will find a listing for clinical trials. These trials will be listed under "Neuroblastoma" or "Solid Tumors." Of course, on the NANT website, all of the trials are for NB.

You will find information organized in different ways, but should be able to determine which trials are currently open, why they think the drug/treatment/combination of drugs will work, what is being tested, and what results the drug has shown in the laboratory. Often the "consent forms" for the protocols can be read or downloaded from the internet. Each protocol will have specific eligibility criteria. Becoming familiar with eligibility criteria of trials is a good idea, so you know what items are often listed. Much of the information on the consent forms will be the same—basic information and disclaimers—but after you've looked at a few, you will be able to discern where the important information is. This information can help you determine whether or not the trial is targeting your child's particular situation and whether your child would be eligible for it.

For example, some trials have been primarily successful in reducing bone marrow disease, while others may be considered better for bulky tumors. In each case, you must ask whether there is sound reason to suppose that a particular treatment might be beneficial to your child's specific case and whether the potential for beneficial results outweighs the potential for further harm, either from progressive disease or side-effects. As noted, your child's induction treatment for NB may have resulted in certain physical impairments such as hearing loss, kidney or heart damage. These effects are important to consider as you determine the next course of treatment. Any viable option almost surely *will* have some favorable factors as well as the potential for both short and long-term harm.

It is wise to contact the oncologist conducting the research or those most experienced with the treatment strategy, in order to get answers to your specific questions, including the potential benefits and detriments for your child's specific case. In some cases, the data from previous clinical experience and scientific studies will provide clear support for the decision; in many cases the evidence is indirect and ambiguous. Anecdotal evidence of a favorable early response to a new, relatively benign treatment regimen (offering little harm to the child) may be all there is to go on in some cases. Do not be reluctant to ask probing questions of the doctors conducting the trials and get all the answers you need to make an informed decision.

Bottom line: you will need to discuss all possibilities with your child's primary oncologist and any consulting NB specialist, but reading the trial documents and conducting additional research, including talking to other parents whose children have been treated on such trials, can help you form questions and be better prepared to advocate for the best individualized treatment for your child. You, as the parent, are empowered to direct the care of your child.

## **Clinical Trials**

Whichever treatment you choose, it is likely to be a clinical trial of a newer drug than your child's initial induction chemotherapy. Parents sometimes refer to these newer treatments as "experimental

treatments." In the world of NB, each child's cancer is unique and thus, all treatments, even induction chemotherapy, can be considered experimental. Unfortunately, there is no existing NB treatment at this time that all children respond to successfully.

Clinical trials fall into three categories – Phase I, Phase II and Phase III trials. The distinctions between these categories are spelled out in this Handbook in "What is a Clinical Trial?" In a nutshell, a Phase I trial is defined by the NCI as the first step in testing a new treatment in humans. Before being approved as a Phase I clinical trial, the treatment has had promising results in a lab setting (ie testing on NB cells grown in dishes and NB tumors in mice). The clinical trial is established to determine the maximum tolerated dosage and the best means by which a treatment is given (i.e. orally, intravenously, etc). Pediatric Phase I clinical trials usually involve drugs that already have an established maximum tolerated dose in adults, and dosage levels are based on approximately 80% of the maximum tolerated dose used in adults for other cancers (typically other solid tumors). A Phase I trial agent for NB may be a completely new drug, a drug that never been used for NB, or a new combination of available drugs.

Phase II trials are typically a refinement of a Phase I trial that showed some success in treating NB. The purpose of a Phase II trial is to determine the anti-cancer effectiveness of the maximum tolerated dose established for a drug in its Phase I trial.

Phase III trials compare the current "standard" treatment to a new treatment, randomizing patients to either the new or the standard treatment. Most (but not all) children with high-risk NB are treated at diagnosis on a Phase III trial.

As the parent of a refractory patient, you are likely to be choosing between Phase I and Phase II trials. For a discussion of what is involved in enrolling in a clinical trial, see "What is a Clinical Trial." Enrolling in a trial is usually straightforward and the doctor will walk you through the paperwork. All clinical requirements, whether scans, blood work, etc will be managed by your oncology team. As a parent, it is wise to follow-up with your treating oncology team to ensure that any pre-trial tests are completed and sent to the trial coordinators in a timely manner. Any delays in obtaining pre-trial tests may delay treatment for your child. Repeating scans and tests that may have been done relatively recently can be an issue with insurance companies who don't like to pay for duplication. However, most of the insurance issues can be worked out with a phone call and sometimes a letter from the doctor.

You will be required to authorize treatment under the chosen protocol and sign waivers that outline the risks associated with the treatment regimen. Unfortunately, all cancer treatment options pose some risk to your child – as does the cancer itself. The trick is –

- 1) understanding the risks,
- 2) determining whether those risks pose a greater risk to the health of your child versus the risk posed by NB, and
- 3) evaluating whether the new protocol may preclude your child from enrolling on subsequent protocols.

Depending on the age of your child, he or she may be asked to give "assent" as well. See "What is a Clinical Trial."

Please know that your child can leave a trial early if it doesn't appear to be the best course of treatment.

#### **Maximizing the Options**

As noted above, it is important to take the long view when deciding between trials. Some trials may prevent you from being treated with another drug/trial down the road, or some may have long periods of recovery with low counts and transfusions. Recently, it seems that many trials require

stem cells in reserve. With that in mind, it might be worth discussing whether or not harvesting stem cells (new or to add to your current supply) is possible, and if so can be done immediately. It can take longer if done later in the treatment cycle, and may not yield as many cells, but stem cells have been collected at non-traditional times.

Read the trial documents and consent forms carefully, and talk with your doctors about a possible series of treatments that will make the best use of the available treatments while not precluding the possibility of other effective treatments down the road. It may seem unimportant now, when the situation is so critical—but it is also worth considering and asking the doctors about side effects from the treatment that may affect hearing, cognitive, and/or physical development.

Unfortunately there are no simple answers. Once you are dealing with refractory NB, you will likely be consulting with new and different doctors, traveling far from home to treatment centers that have NB specialists, and at times making decisions based on a leap of faith. However, the more informed you are, the more comfortable you will feel that you have made the best possible choice for your child.

#### Other Considerations

While amassing medical and logistical information on the various treatment options that are available, attention should be given to other, more personal concerns. In addition to direct financial cost of treatment, there are a host of social, psychological, emotional and even spiritual considerations that may bear on the treatment choices. One of the most important considerations may be whether a treatment would be available through a local facility, or only through a regional medical center. If the treatment requires travel and extended out of town stays, then careful consideration must be given to time away from school, a caregiver's time away from work, time away from other family members, and even time away from the ordinary, everyday sort of activities that might provide for a sense of stability for the child. Whether absence from home is either temporary or long-term (some families choose to stay near remote treatment centers for months and even years), careful consideration must be given to the impact on marriage, family, income, and the child's social development. If possible, it may be helpful to discuss these concerns with families who have experienced the course you are considering. Some parents have found it valuable to have fairly clearly established and regularly reviewed "rules of disengagement" – i.e, an exit strategy that will determine when it might be best to return home and/or suspend certain treatment regimens.

Participation by your child in the process of determining the next step in treatment will depend on the child's age and the specific case. As noted above, depending on the age of your child, he or she may be asked at some institutions to give "assent" to enrollment in a clinical trial. Many parents feel it is important throughout the decision-making process to talk with their child in an age-appropriate manner about what he or she might anticipate in the treatment scenarios being considered. For example, it may be appropriate to discuss with the child that certain options will involve frequent travel, long periods away from school, pain, additional hairloss, time in isolation, or other "costs." Some children may have concerns that need to be aired; even where their fears cannot be entirely avoided, they can be acknowledged and legitimized. Often, due consideration can be given to even a very young child's concerns and wishes, thereby allowing the child a sense of significance and ownership in the process. Again, these are very personal matters and dependent on the individual situation.

The most important factor to remember throughout this entire process is that, when a decision is made on the information available at the time, it is the best possible decision. You should trust fully in your decision insofar as you regard it as providing the best possible opportunity for the child to flourish as you work together with your child's oncologists toward a cure. There is, of course, no guarantee. Decisions are always based on imperfect information; there will always be another new drug you could not have known about at the time, another factor that may or may not impact the list of potential costs and benefits. Whether or not things go as you might have planned (and, of course,

they almost never do), it is pure folly to suppose that you could have known that it would have been better to have pursued a different course. You can no more determine the outcome of a course of treatment that you chose against, than you can fully anticipate the course actually chosen. Would it have been better or worse? No one, not even that nagging voice in your own head, can say with any certainty. Because in reality hindsight is not 20/20, you must go on, trusting the resources presently available to you, never forgetting that you have done your very level best for your child.

<sup>&</sup>lt;sup>1</sup> Kushner BH, Cheung NK <u>Induction for high-risk neuroblastoma</u>. Pediatr Blood Cancer. 2007 Sep;49(3):221-3. PMID: 17417798



# Dealing with Relapse

The focus of this chapter is on relapse after treatment for *high-risk* neuroblastoma. As always in the case of NB, the guidance of an experienced doctor you trust is absolutely crucial, especially in the complex decisions involved in relapse treatment. However, your knowledge can be a valuable ally. The more you know, the easier it is to understand the issues presented by relapse, have a meaningful dialogue with your child's doctor, and make informed decisions about the many treatment options.

This chapter draws extensively from "Treatment of Relapsed and Refractory Neuroblastoma," authored by Drs. K. Matthay and B. Kushner, in the 2005 pediatric oncology text *Neuroblastoma* (Cheung & Cohn, eds). There is some overlap with the previous chapter in this Handbook on treating refractory disease, because both are "resistant disease" -- standard frontline therapy has failed and new treatments options are needed. However, whereas refractory disease is considered "progressive" only if NB spreads to new sites or the size of a lesion is increased, relapsed disease (also referred to as "recurrent" disease) is always progressive disease at discovery, because it has *increased* from "no evidence of disease." The length of the time of remission, the location and nature of the disease, the prior treatment, and many other factors must be considered to determine how to treat this new, recurrent disease.

#### SOME BACKGROUND INFORMATION

A Note on Low-Risk and Intermediate-Risk Cases. The treatment strategies discussed here do not apply to relapse after low- or intermediate-risk NB. Risk of relapse is small after successful treatment for low- or intermediate-risk NB. Localized relapse in low- and intermediate-risk cases can often be successfully treated by surgery. In the case of metastatic relapse after low- or intermediate-risk treatment, the child's relapse treatment is usually very similar to high-risk frontline therapy. However, some of the general observations that follow may be relevant as well for low- and intermediate-risk relapse cases.

**Risk of Relapse for High-Risk NB.** Phase III and pilot studies from the past 15 years have revealed long-term survival after high-risk treatment ranging from 25% to over 50%. For example, follow-up of children with high-risk disease treated in 1991-1996 on clinical trial "CCG-3891" revealed nearly 60% long-term survival for the 50 children who reached remission and completed both transplant and six months of Accutane (13-*cis*-retinoic acid). In other words, about 40% relapsed after successful treatment. Since then, the dose of induction chemo has been intensified, transplant regimens have changed, and additional treatments for minimal residual disease such as antibodies have often been used, so it may be that the risk of relapse after successful treatment is now lower. It is also encouraging to know that the risk of relapse decreases every year after successful frontline therapy since most relapses occur within two years after stem cell transplant or completing chemotherapy.<sup>3</sup>

**What causes relapse?** No one has determined what causes NB relapse after clinical remission. Theories for its cause include:

- re-introduction of NB cells in contaminated stem cells at rescue:
- NB cells "hiding" in sanctuary sites such as brain or testes; and
- NB cells becoming resistant during frontline therapy.

The recent results of a clinical trial ("COG-A3973") comparing randomized patients receiving purged stem cells after transplant versus unpurged showed no difference in survival between the two groups, so contaminated stem cells are probably not the cause of most relapses.<sup>4</sup> Many researchers believe developing more effective treatments for minimal residual disease (MRD) will reduce the incidence of relapse in high-risk cases.<sup>5</sup>

By far the most common sites for relapse are bone and bone marrow, and sites not involved at first diagnosis (such as brain and lungs) are seen in up to 8% of relapsed children.<sup>6</sup>

**Monitoring after Frontline Treatment.** For about two years after finishing NB treatment, a child does follow-up tests and scans every three months, then every six months and eventually none; the schedule varies according to the institution and the particular case. It is certainly hard not to worry however far from treatment a child may be, because the symptoms of relapse can be similar to those of a host of childhood illnesses and conditions. Parents must continue to be vigilant -- but without being alarmist.

If your child has a complaint that persists over a few hours or days, depending on the symptom and its severity, naturally you should follow up with your pediatrician or your oncologist. Some parents recommend keeping a log of the child's complaints (discreetly, without upsetting the child), because it is important to be able to describe the precise symptoms and their duration to the doctors. It may take time, but ideally you will develop a good working routine for dealing with your professional team (which should include a pediatrician informed about your child's history) when you are troubled by your child's symptoms. You are the person most familiar with your child, and your invaluable instincts should be given careful consideration by your medical team.

**Establishing Conclusive Evidence of Relapse.** Just as with first diagnosis, relapse is not always obvious. Some NB relapses have no symptoms and are discovered by routine follow-up tests and scans; others present with similar symptoms as seen at first diagnosis (pain, fever, fatigue, anemia, etc.) or with new symptoms not present before (as with headaches in brain relapses).

Worrisome symptoms may require an oncology clinic visit for a physical exam, often followed by a CBC and urine HVA/VMA tests, and possibly even scans. NB relapse must be absolutely *proven* before treatment can commence, because some secondary cancers can resemble NB, and correct treatment must be given. Tests that evidenced the child's first diagnosis may no longer be reliable. One large German study found a relatively low incidence (54%) of abnormal HVA/VMA results at relapse<sup>7</sup>; occasionally relapsed NBs are MIBG-negative although previously MIBG-avid. Hence, other scans may be necessary, such as PET. *See* "Getting through Tests and Scans." Biopsy of bone marrow or suspicious spots on scans is often done in cases where a bone scan or PET is positive but catecholamines are normal. The possibility of residual matured (harmless) tumor can further complicate the determination of whether relapse treatment is needed, so rescanning may be required after a few weeks to determine if the disease is growing and active.

If relapse is confirmed, many of the same staging, pathology and genetic tests done at first diagnosis are performed, as well as baseline tests for heart, hearing, and other organ function. Since most treatment begins with some type of chemotherapy, a central venous access will be required. A port is often chosen rather than a Hickman or Broviac, depending on impending treatment choices. *See* "Broviacs, Hickmans, Ports, etc."

**Beginning Relapse Treatment.** After the whirlwind of scans, tests, and line placement, most often "retrieval" chemotherapy is begun. Depending on the relapse scenario, children very often respond to chemo again, especially if relapse occurs after more than one year of remission.<sup>8</sup>

However, relapse after high-risk treatment is a different scenario from first diagnosis. Whereas at first diagnosis a well-defined road map of the frontline protocol is provided, there is generally no set treatment path for a relapsed child. The NB team will often present several optional treatments to parents and discuss the various benefits and disadvantages of each. Some doctors even list "no treatment" as one of the options. Doctors may discuss the possible timing of various subsequent treatments that will depend on the child's response to the initial relapse chemo and on various personal considerations. In other words, relapse treatment is usually very individualized – and parents are generally expected to participate in the process of determining the particular treatment plan for their child.

Although perhaps less obvious, the considerations and analyses underlying relapse treatment are also different from those at first diagnosis. As Drs. K. Matthay and B. Kushner note in "Treatment of Relapsed and Refractory Neuroblastoma":

"The appropriate approach to the patient with recurrent or resistant neuroblastoma depends on the goals of the therapy. Although in previous studies the median survival for patients who relapsed after myeloablative therapy and bone marrow transplantation was only 3 months, with current multimodality approaches and judicious use of established as well as investigational agents, the survival can be prolonged for years, on and cure may be a possibility in some settings. Whether the goal is symptom palliation, prolongation of life, or complete remission depends on the timing and nature of the relapse, the prior therapy, and the tumor biology." 10

To participate fully in such difficult treatment decisions, parents of a relapsed child must have a basic understanding of the underlying rationales for the various treatment paths, and the benefits and detriments of these treatments for their child's specific case, both from a medical and a personal perspective. The following section will provide some general information on the various considerations to be weighed in determining relapse treatment – keeping in mind, of course, that the guidance of an experienced and trusted oncologist in these complex and difficult decisions is absolutely crucial.

# RELAPSE TREATMENT RATIONALE

Your doctor will take into consideration many factors when recommending treatment for relapse:

Age of child:

- $\Rightarrow$  less than one year
- *⇒* 1-21 years
- *⇒* over 21

How long the child was in remission after treatment:

- $\Rightarrow$  less than one year
- $\Rightarrow$  1-2 years
- *⇒ long remission*

Where disease is located:

- $\Rightarrow$  at primary site
- *⇒* lung; liver
- ⇒ central nervous system (CNS)
- *⇒ distant sites (bone, marrow)*

How much disease (tumor burden):

- ⇒ minimal or trace disease
- ⇒ many bone metastases or loaded bone marrow
- ⇒ bulky disease (soft tissue); many lymph nodes

#### Rate of tumor growth:

- *⇒* rapid progression
- ⇒ slow or stable disease

#### Prior treatment history

- *⇒ induction regimen (agents used)*
- ⇒ number of stem cell transplants (SCTs)
- ⇒ local, targeted, or total body irradiation
- *⇒* antibodies

# Organ function:

⇒ impaired kidney, liver, bone marrow function, hearing, etc

## Available stem cells:

- ⇒ number of rescues stored
- *⇒ length of storage time*
- *⇒ potential of another collection*

# Changing characteristics of the child's NB:

- ⇒ no longer MIBG-avid
- ⇒ chemo-resistance (loss of p53 function)

# Goals of treatment:

- $\Rightarrow$  cure
- ⇒ prolonging life
- ⇒ quality of life
- *⇒ palliative care*

# Your child's specific situation may present options and/or limitations for certain treatments.

A key factor is whether or not the NB still responds to chemotherapy. Having already been down that road, many parents want something new for their child, but the fact remains that chemo-sensitive NB will commonly be treated most successfully first with chemotherapy. However, the specific facts will be carefully considered. If a child had a certain chemo combination during induction, the oncologist may choose a different combination at relapse. If a child has recently undergone stem cell transplant, it is less likely high-dose chemo would be recommended due to the threat to bone marrow recovery and organ function; in contrast, a "late" relapse often allows for options of more aggressive therapy similar to frontline treatment. If, however, the NB is not responding to chemotherapy, then the oncologist will consider other treatment possibilities. Some children with very minimal bone marrow disease detected early may be a candidate for antibody therapy and/or retinoids. There is a treatment specifically for isolated CNS or brain relapse at MSKCC in New York City, using an antibody called 8H9 and surgery in addition to chemo. Surgery may be recommended for certain local tumor recurrences, but some cases are not ideal for surgery, such as multiple masses in the liver.

**Treatments for relapse vary in approach and intensity.** Some or all of the elements of frontline treatment for high-risk neuroblastoma --chemotherapy, surgery, radiation, Accutane, or antibodies --can potentially be used in the relapse setting, depending on the individual situation. Each of these treatments attack NB in a different way and with varying intensity.

The variety of intensity in treatment means there are weighty decisions to be made regarding treatments allowing good quality of life versus harsh treatments with potential to bring about cure or long term survival. There may be a sequence that starts out with harsh treatment, and then depending on the disease response, the child may move onto less aggressive treatments, or conversely, a child may respond to something lower dose at first, and then require harsher treatment later to elicit a response. Your child's oncologist must help you navigate this difficult dynamic, but

sometimes the decisions to be made are very personal. *See* discussion below regarding "maximizing your options" and "quality of life" considerations.

It is advisable to ask your oncologist about collecting stem cells (new or to add to your current supply) during the planning stage of relapse treatment, since the availability of stem cells can allow for treatments not otherwise possible.<sup>11</sup>

Can we know what will actually work against my child's NB? Truth is, no one knows for certain. NB cells can change and lose functions that make them chemo-sensitive. It also appears that every child's NB disease is unique. Research is ongoing of "individualized medicine," with the long-term goal of someday being able to determine the most effective treatment for each child (understanding and use of these technologies is limited thus far). One such effort is underway at the University of Texas in Houston. Analysis of a child's tumor characteristics ("morphoproteomics" or "Molecular Tumor Profiling Using Morphoproteomic Analysis by Immunohistochemistry") is being done to identify certain predominant weaknesses of the NB cells in a child's tumor sample. 12,13

There are no hard and fast rules, and currently relapse treatment relies on *educated* trial-and-error to see what works in each child. To reiterate, oncologists will recommend certain treatment options depending on all the variables in your child's specific case. The treatments mentioned below are merely examples to illustrate how varied the choices can be; furthermore, treatment for relapsed children is an ever-changing landscape. *The guidance of an experienced oncologist through this complex landscape is crucial.* 

**High-dose chemo/radiation.** Some treatments include high doses of chemotherapy or targeted radiation therapy, or a combination of the two, which may require stem cells for rescue. A current example of a high dose chemotherapy combination is known as ICE (ifosfamide, carboplatin, and etoposide). High-dose choices can require potentially long inpatient stays. MIBG radiation therapy, a type of "targeted" radiation using the radioactive iodine isotope 131-I, has been used to treat relapse and refractory NB since the mid-1980s. The child must be MIBG-avid – i.e., NB shows up on the child's MIBG scan. *See* "**MIBG Treatment"** for more information on treatment issues surrounding MIBG. "Hot antibodies" (3F8 antibodies with radioactive isotope131-I attached, currently given in conjunction with avastin) is another approach to high-dose, targeted radiation. Allogeneic (donor) or cord blood transplants, albeit less common, are additional aggressive possible treatment options considered for relapse.

**Medium-dose chemo.** Outpatient chemotherapy that is relatively easy on the blood counts is often chosen for certain relapse scenarios. One combination used frequently is topotecan and cyclophosphamide, which is usually administered IV at a clinic daily for one week out of every three or four weeks. <sup>14</sup> Topotecan with etoposide has been studied as a relapse regimen in Germany. <sup>15</sup> Another commonly used combination is irinotecan and temozolomide. <sup>16</sup> Irinotecan can be administered as an IV infusion daily for one or two weeks or taken orally, and temozolomide is an oral chemo taken in pill form daily for five days out of a three or four week cycle.

**Low-dose chemo.** Low-dose oral agents in pill form, such as topotecan, Cytoxan, temozolomide, or etoposide, may be used in some cases. These regimens are much easier on blood counts than high dose chemo so often transfusions and neutropenic fevers can be avoided. Occasionally combinations of oral chemos are used.

Timing, dosage and form of the various chemotherapy regimens can vary per patient based on the specific medical and personal factors.

**Targeted drugs ("small molecules") and biologics.** These drugs employ different mechanisms from chemo to destroy NB and sometimes are used in conjunction with medium- or low-dose chemo. Targeted drugs currently being tested in clinical trials for relapsed (or refractory) neuroblastoma include inhibitors of certain NB cell functions and signals such as CEP-701<sup>17</sup>; inhibitors of blood

vessels that support NB tumors— "anti-angiogenic" agents, such as ABT-751<sup>18</sup>; and stimulators of "differentiation" or apoptosis of NB cells (to mature or cause their death) such as the retinoids fenretinide or Accutane. <sup>19</sup> Nifurtimox, an anti-protozoal drug, is being administered to patients along with chemotherapy in a trial to determine if it enhances the effectiveness of chemotherapy. <sup>20</sup> Some new drugs are attractive for their low toxicity profile and may cause relatively minor side effects, but toleration does vary. From the child's perspective, the main advantage of low-dose regimens (chemo or targeted drugs) is allowing for near-normal activity.

**Immunological treatments.** Monoclonal antibodies may be an option for some relapsed children, generally those with minimal disease. For example, MSKCC has been treating children with 3F8 antibodies since the mid-1980s as part of frontline treatment. There are currently several different trials using the 3F8 antibody for certain refractory and relapse cases. This antibody, made in mice, generally must be preceded by high-dose chemo to prevent premature formation of an ultimately desirable immune response known as human anti-mouse antibody, or "HAMA." St. Jude's is producing a new "humanized" antibody hu14.18 to use with cytokines (immune stimulators). The *ch*14.18 antibody (*chimeric* refers to its part mouse and part human derivation) is not currently available to relapsed patients, but some refractory cases with minimal detectable disease may be eligible immediately after stem cell transplant. Efforts are underway at several institutions to produce various vaccines against NB, intended primarily for those with minimal disease or in second remission.

Clinical trials sometimes open and close, and then open again, so contacting the investigators is the best way to know the status of a specific trial. *See* discussion of research into clinical trials, below.

**Second remission treatment issues.** With advances in treating relapsed NB, more children are able to reach NED (no evidence of disease) again. While this is very good news of course, it poses a unique treatment dilemma. Once a child relapses, the likelihood of another relapse is very high, and therefore continued treatment of some sort is usually advised. However, there is no consensus on what agents should be used or for what length of time, and few drugs are available for an oncologist to prescribe beyond low-dose oral chemo. The problem is that almost all clinical trials of new treatments for relapsed NB *require evidence of disease*. Possible options for relapsed children in second remission include Acctuane, low-dose oral chemo in pill form (such as topotecan, Cytoxan, etoposide, temozolomide, thalidomide, Celebrex—separately or in various combinations), 3F8 antibody (requires high-dose chemo), and vaccines. As more studies are planned to treat minimal residual disease (MRD) occasionally eligibility for "second or greater response" is included, such as the CEP-701 NANT Phase I trial.<sup>21</sup> Some treatments may be available for "NED after relapse" via "compassionate use" such as ABT-751. This is an important item for discussion with your child's doctor.

**Special issues with late relapse.** While late relapses are rare, they have been observed and studied. Relapse diagnosis at any point is devastating, but a "late" relapse (3 or more years after finishing frontline treatment) can be especially unexpected. Being thrust immediately into treatment decisions after a hiatus from keeping up with the developments in the treatment of NB can be overwhelming. Quickly obtaining records of cumulative doses of chemotherapy and radiation received during frontline treatment is very important. After late relapse a child can sometimes receive aggressive therapy again, similar to frontline treatment. Late relapses often demonstrate prolonged response to treatment. <sup>23</sup>

**Maximizing your child's treatment options is an important part of the relapse decision process.** (This is also the case with refractory NB, hence very similar considerations are discussed in that chapter). Without knowing if the child will respond to any given treatment beforehand, it is wise to plan for more options later. This means looking at the eligibility criteria of trials and keeping a close eye on the child's organ function. For example, the liver enzymes may be elevated and eliminate the child from a particular trial. Some trials do not allow prior allogeneic (donor) transplants or radiation to more than 25% of the bone marrow. Others require the availability of stored stem cells.

There are many such criteria, and looking at all the possible trials (including those that may open in the near future) helps parents consider and determine the maximum possibilities.

In other words, it is important to take the long view when deciding between trials. Some trials may prevent you from being treated with another drug/trial down the road; some may have long periods of recovery with low counts and transfusions; and some may have high risk of side effects that will rule out subsequent treatments. Read the trial documents and consent forms carefully, and talk with your doctors about a possible series of treatments that will make the best use of the available treatments while not precluding the possibility of other effective treatments later. It may seem unimportant now, when the situation is so critical—but it is also worth considering and asking the doctors about side effects from the treatment that may affect hearing, cognitive, and/or physical development.

**Weighing Quality of Life and Other Considerations.** Providing a child with maximum quality of life during relapse treatment without eliminating some promising "harsh" treatment may present difficult choices. Every parent wants a treatment that ultimately brings cure, but after already seeing the hardships of frontline therapy, parents and children understandably may gravitate to what is "easiest" of the promising choices given. One of the goals of relapse treatment is commonly "tolerability," and researchers recognize this – the reason so many studies report something along the lines of "this combination was well tolerated in heavily-pretreated children with resistant neuroblastoma."<sup>24</sup>

Moreover, attention may have to be given to some non-medical concerns. In addition to direct financial cost of treatment, there are a host of social, psychological, and emotional considerations that may bear on the treatment choices. For example, one important consideration may be whether a treatment would be available through a local facility, or only through a regional medical center. Many families have elected and successfully maintained a treatment "partnership" between their local oncologist and an NB specialist in another part of the country. If the treatment requires travel and extended out of town stays, then careful consideration must be given to balancing time away from school, a caregiver's time away from work, time away from other family members, and even time away from the ordinary, everyday sort of activities that might provide a sense of stability for the child. Whether absence from home is temporary or long-term (some families choose to stay near remote treatment centers for months and even years), consideration of the impact on marriage, family, income, and the child's social development may be required. If possible, it may be helpful to discuss these concerns with families who have experienced the course you are considering. Some parents have found it valuable to have fairly clearly established and regularly reviewed "rules of disengagement" - i.e, an exit strategy that will determine when it might be best to return home and/or suspend certain treatment regimens.

These are difficult issues indeed, and very personal in nature.

#### INVESTIGATING DOCTORS AND CLINICAL TRIALS

Presented with such complex issues and decisions, it is not surprising most parents of relapsed children eventually find themselves doing research themselves. You may simply wish to understand better your child's situation and treatment options, or you may wish to bring more informed questions to your child's doctor about different treatment possibilities. Alternatively, you may feel your child's doctor is not sufficiently pro-active in exploring treatment options or is not fully informed about certain specific options available for children with relapsed disease.

Whatever the rationale, your research may involve exploring online the relapse protocols offered at other cancer centers; speaking to principal investigators (the oncologists heading up the research) of new clinical trials; and/or obtaining second opinions from one or more NB specialists based on their

comprehensive examination of your child and his or her history. Many parents also speak with others whose relapsed children have been treated on certain clinical trials; be mindful that every child is different and the experience of others may have limited relevance to your child's situation.

**Getting a Second Opinion.** If you are being treated at a medical center that sees very few cases of NB, you may decide upon your child's relapse that this is an appropriate point in the journey to get a second (or third) opinion.

For a list of NB specialists in the U.S. and their contact information, see "Confronting the Diagnosis: US NB Specialists." (This is not a comprehensive list.) Keep in mind that some of these specialists treat a large number of patients, and they often receive dozens of calls and emails a day. It is advisable to speak with the doctor's secretary first and find out if the doctor prefers to be contacted first by email or phone and the best time to call.

Also, a doctor cannot give you an informed second opinion over the phone or in an email! To recommend a course of treatment the consulting doctor will require:

- a complete treatment summary;
- recent medical records (such as scans and biopsies);
- a physical examination of your child; and
- possibly additional tests and scans.

You must take the responsibility to get a treatment summary completed by your child's current doctor and have copies of pertinent medical records sent to a consulting physician. This can take time and may require patience with some frustrating administrative delays.

Even if you decide to move your child's primary treatment to another center, your child's initial oncologist is an invaluable resource when weighing relapse treatment options. Having intimate knowledge of the child's specific history and his or her present condition, your child's initial oncologist is in a unique position to help you consult with additional NB experts as you seek new treatments for your child.

**Investigating available relapse treatments.** However knowledgeable your oncologist may be, you may decide yourself to investigate the available relapse treatments, in order to enhance your own understanding and comfort level. As noted, treatment options for a child with relapsed disease are numerous and varied, and there is much to investigate. The process is virtually identical to researching treatments for refractory NB, especially if the child has relapsed while still on treatment.

For starters, there is a wealth of information on the internet—but it can be daunting to sort through. Relapse NB trials can be found on these websites (using search mechanisms for recurrent neuroblastoma):

- New Approaches in Neuroblastoma Treatment (NANT), www.nant.org
- National Cancer Institute, <a href="www.cancer.gov/clinical trials">www.cancer.gov/clinical trials</a>
- National Institutes of Health, clinicaltrials.gov

Institutional websites also list trials available only at their locations, so be sure to search websites of institutions of interest. Notable examples are Memorial Sloan-Kettering (<a href="www.mskcc.org">www.mskcc.org</a>) and St Jude (<a href="www.stjude.org">www.mskcc.org</a>); also, some NANT institutions have their own trials that are NOT listed on the NANT website.

By contacting institutions of interest and principal investigators, you will learn pertinent information not only about current clinical trials, but may also learn about trials that are expected to open soon or treatments available "off-trial."

It is common for children to see one or more of the following treatment categories during the battle against relapse:

- **Enrollment on phase I or II clinical trials.** These may be specific to NB or for unspecified solid tumors. Phase III studies are rare for relapsed pediatric tumors including NB.
- Treatment "per" a clinical trial protocol although not enrolled, if not eligible and drugs are already FDA approved.
- Treatment with "off the shelf" agents that are FDA approved.
- Treatment on a "compassionate use" basis with drugs not yet FDA approved.

You will find on-line information about clinical trials organized in different ways, but key items to note are:

- whether trial is active/enrolling;
- any age limit;
- rationale for treatment on such trial;
- any requirement for disease sites/measurable disease;
- any organ function criteria; and
- any prior treatment limitations.

Becoming familiar with eligibility criteria of trials is a good idea, so you know what items are generally listed. Often the "consent forms" for the protocols can be read or downloaded from the internet. (See "Managing Emotions: Informed Consent" for personal perspective on consent forms from an NB dad.)

**Phase I and Phase II distinctions.** There is an important difference between phase I and phase II clinical trials. Drugs being administered in phase II studies have *possible* response results in children in a prior phase I study, and toxicities and maximum tolerated dose are known. Drugs in phase I studies do not have such information available—the purpose of a phase 1 study is to *determine* toxicities and maximum tolerated dose of a drug based on promising laboratory data from cell lines in glass dishes (*in vitro*) or activity in mice. Some agents look promising *in vitro* or in mice, but responses in children may be disappointing.

For further discussion of the distinctions between phase I, II, and III clinical trials, and background information about enrolling in a clinical trial, see "Clinical Trials."

**Timing of entry.** Another issue in considering enrollment in phase I studies has to do with timing. Many phase I studies enroll a small number of children (usually 3-6, called a *cohort*) at a certain dose level, observe for toxicities, and then the next cohort is enrolled at a higher dosage. Speaking with your child's oncologist and the principal investigator about the timing of enrollment is important, to determine if your child would be one of the first to receive the drug, or would be enrolling at a higher dose level. Trials also sometimes open and close and then open again, depending on drug availability, toxicities and other factors. The principal investigator will be able to give you the up-to-date status of enrollment and may give an indication of how the earlier cohorts have fared.

**Interpreting "response" from study reports.** As parents investigate available trials and try to discern what is most promising, they should be aware of the range of possibilities when studies report a "response" rate. Let's say you are considering a phase II study of drug X. You uncover the phase I drug X results reporting a "30% response rate." What does this mean? Does it mean 30% of the children on the study were cured? Unfortunately no, it does not. The 30% response rate may indicate that 30% of the children in the trial had some shrinkage or reduction in their NB, but often the duration of the response is unclear. Did some of the children have a complete response -- i.e., reach NED again? How long did the children respond before the disease progressed again? Did some of the children have shrinkage or reduction in their disease, and then experience stable disease for a

while? How long? Asking such questions and getting all relevant information is advisable before committing to a trial. Unfortunately, some promising drugs that have a "high response rates" actually produce responses that are very short-lived, and you are entitled to know that. Answers to these questions are usually not available until a phase I study ends.

It helps to know the terminology used to report "response" in studies. Clinical trial protocols include a plan for closely monitoring the disease response so that if the treatment is not working, the child can quickly move onto something else. The International Neuroblastoma Response Criteria (INRC) was established in 1993 and uses the following terms: <sup>25</sup>

- "complete response" (CR) is no evidence of disease;
- "very good partial response" (VGPR) is primary mass reduced by 90–99%, no evidence of distant disease except for skeletal residua, and catecholamines normal;
- "partial response" (PR) is greater than 50% decrease in measurable disease and 1 or no positive BM site;
- "mixed response" is greater than 50% decrease of any lesion with less than 50% decrease in any other;
- "no response" is less than 50% decrease but less than 25% increase in any lesion; and
- "progressive disease" (PD) is new lesion or greater than 25% increase in an existing lesion.

**Risks and benefits of treatment.** In evaluating any treatment, you must ask whether the potential for beneficial results outweighs the potential for further harm, either from progressive disease or side-effects. Your child's prior treatment for NB may have resulted in certain physical impairments such as hearing loss, kidney or heart damage. These effects are important to consider as you determine the next course of treatment. Any viable option almost surely *will* have some favorable factors as well as the potential for both short and long-term harm. *See* discussion on "maximizing your options," above.

It is advisable to contact the principal investigator or those most experienced with the treatment strategy in order to get answers to your specific questions about any clinical trial or new treatment.

#### **SUMMARY**

The rigors of relapse treatment cannot be minimized. You may be consulting with new and different doctors, traveling far from home for your child's treatment on various clinical trials, weighing difficult quality of life issues for your family, and at times making treatment decisions based on a leap of faith. An oncologist with experience in treating relapsed NB, and equally importantly, someone you feel comfortable with and can communicate with effectively, is the key resource in making your treatment decisions. However, the more informed you are, the more comfortable you will feel that you have made the best possible choices for your child.

There *are* successes in relapse situations. Unfortunately, because the relapse population involves such variation in relapse sites, in amount of disease, types of treatments tried, multiple treatment centers, and many other variables, it is virtually impossible to report long-term survival statistics. Even so, the reports of long-term survivors in some studies, the increasing numbers and approaches of available treatments, and the anecdotal evidence -- all suggest that the prospect for long survivorship after relapse is improving. There is increasing hope for relapsed children, and having an NB team who expresses and shares your hope is also essential to this stage of the battle.<sup>26</sup>

<sup>&</sup>lt;sup>1</sup> Cheung & Cohn (eds), Neuroblastoma, Springer (2005), p. 145

<sup>&</sup>lt;sup>2</sup> 2005 ASCO Annual Meeting - Session: <u>High-Risk Neuroblastoma</u>: <u>Beyond Intensification to Novel Therapy Approaches to Improve Outcome</u> (Education Session) Myeloablative Consolidation Therapy for Neuroblastoma Past, Present and Future; slide 10

<sup>&</sup>lt;sup>3</sup> Cheung & Cohn (eds), Neuroblastoma, Springer (2005), p. 194

<sup>&</sup>lt;sup>4</sup> S. G. Kreissman, J. G. Villablanca, R. C. Seeger, S. A. Grupp, W. B. London, J. M. Maris, J. R. Park, S. L. Cohn, K. K. Matthay, C. P. Reynolds, <u>A randomized phase III trial of myeloablative</u> autologous peripheral blood stem cell (PBSC) transplant (ASCT) for high-risk neuroblastoma (HR-NB) employing immunomagnetic purged (P) versus unpurged (UP) PBSC: A Children's Oncology Group study. *J Clin Oncol* 26: 2008 (May 20 suppl; abstr 10011)

<sup>&</sup>lt;sup>5</sup> Cheung & Cohn (eds), Neuroblastoma, Springer (2005), p. 145

<sup>&</sup>lt;sup>6</sup> Cheung & Cohn (eds), Neuroblastoma, Springer (2005), p. 194

<sup>&</sup>lt;sup>7</sup> Simon T, Hero B, Hunneman DH, Berthold F. <u>Tumour markers are poor predictors for relapse or progression in neuroblastoma</u>. *Eur J Cancer*. 2003 Sep;39(13):1899-903.

<sup>8</sup> Cheung & Cohn (eds), Neuroblastoma, Springer (2005), p. 196

<sup>&</sup>lt;sup>9</sup> Kushner BH, Kramer K, Cheung NK (September 2002). <u>Chronic neuroblastoma</u>. *Cancer* 95 (6): 1366–75.

<sup>10</sup> Cheung & Cohn (eds), Neuroblastoma, Springer (2005), p. 195

<sup>&</sup>lt;sup>11</sup> Grupp S.A., Cohn S.L., Wall D., Reynolds C.P. <u>Collection, storage, and infusion of stem cells in children with high-risk neuroblastoma: saving for a rainy day</u>, Pediatr. Blood Cancer, 46: 719-722, 2006.

<sup>&</sup>lt;sup>12</sup> Brown RE, et al. Morphoproteomic confirmation of constitutively activated mTOR, ERK, and NF-kappaB pathways in high risk neuro-blastoma, with cell cycle and protein analyte correlates. *Ann Clin Lab Sci.* 2007 Spring;37(2):141-7.

<sup>&</sup>lt;sup>13</sup> Consultative Proteomics Service Can Help 'Outsmart' Hard-to-Treat Cancers. Distinctions - October 2007

<sup>&</sup>lt;sup>14</sup> Recurrent neuroblastoma: Randomized treatment with topotecan + cyclophosphamide (T+C) vs. topotecan alone(T). A POG/CCG Intergroup Study. - ASCO.

<sup>&</sup>lt;sup>15</sup> Simon T, Längler A, Berthold F, Klingebiel T, Hero B. <u>Topotecan and etoposide in the treatment of relapsed high-risk neuroblastoma: results of a phase 2 trial.</u> *J Pediatr Hematol Oncol.* 2007 Feb;29(2):101-6.

<sup>&</sup>lt;sup>16</sup> Kushner et al. <u>Irinotecan Plus Temozolomide for Relapsed or Refractory Neuroblastoma.</u>. *J Clin Oncol.* 2006 Nov 20; 24 (33): 5271

<sup>&</sup>lt;sup>17</sup> CEP-701 in Treating Young Patients With Recurrent or Refractory High-Risk Neuroblastoma.

<sup>&</sup>lt;sup>18</sup> <u>ABT-751 in Treating Young Patients With Neuroblastoma That Has Relapsed or Not Responded to Previous Treatment.</u>

<sup>19</sup> Oral Fenretinide LXS Powder in Recurrent or Resistant Neuroblastoma Patients, NANT trial

<sup>&</sup>lt;sup>20</sup> Study of Nifurtimox to Treat Refractory or Relapsed Neuroblastoma or Medulloblastoma, NCI Clinical Trials

<sup>&</sup>lt;sup>21</sup> CEP-701 in Treating Young Patients With Recurrent or Refractory High-Risk Neuroblastoma.

<sup>&</sup>lt;sup>22</sup> Cotterill SJ, Pearson AD, Pritchard J, Kohler JA, Foot AB (January 2001). <u>Late relapse and prognosis for neuroblastoma patients surviving 5 years or more: a report from the European Neuroblastoma Study Group "Survey"</u>. *Med. Pediatr. Oncol.* 36 (1): 235–8.

<sup>&</sup>lt;sup>23</sup> Kushner BH, Kramer K, Cheung NK (September 2002). <u>Chronic neuroblastoma</u>. *Cancer* 95 (6): 1366–75.

<sup>&</sup>lt;sup>24</sup> <u>Phase I study of oral irinotecan and temozolomide in children with relapsed high-risk neuroblastoma: A New Approach to Neuroblastoma Therapy (NANT) Consortium study. - ASCO.</u>

<sup>&</sup>lt;sup>25</sup> Brodeur GM, Pritchard J, Berthold F, *et al* (August 1993). <u>Revisions of the international criteria for neuroblastoma diagnosis, staging, and response to treatment</u>. *J. Clin. Oncol.* 11 (8): 1466–77.

<sup>&</sup>lt;sup>26</sup> Mack JW, et al. Hope and prognostic disclosure. J Clin Oncol. 2007 Dec 10;25(35):5636-42.



# One Family's Insights

If you are reading this, then you already have felt the horror that comes with hearing the word Neuroblastoma. You may have gone through weeks or months trying to figure out why your child has unexplained fevers, or a limp that comes and goes. Or maybe there was a sudden change and a quick diagnosis. Whatever the facts, not one of us will ever forget that minute our world changed forever. The goal of this essay is to let you know that many have been down the path you are now on. We are sharing our observations to help you understand the feelings you may be experiencing, and to let you know you won't be in this state forever.

Once a diagnosis of neuroblastoma is made, there are often quick decisions to make concerning treatment options. The immediate shock of what you are facing can manifest itself in actual physical symptoms. Many parents report that they were physically ill—shaking, vomiting, or fainting during the first week of diagnosis. Try to remember that there is a lot of hope, a lot of promising treatment ahead. Relaxation and breathing can calm the mind and provide a temporary focus when your head feels like it is swimming in information. Taking a few moments several times a day to do relaxation techniques can help your physical symptoms, and put you in a more focused place emotionally.

This may be the first time you have ever faced with the types of decisions and challenges that you now are confronting. Doctors are giving you important information and you must think and make decisions while still reeling with fear and disbelief. You may feel absolutely overwhelmed. When meeting with doctors, it is very important to have someone with you so that discussions can be processed by two sets of ears. Don't be surprised if your short term memory is a little challenged-having someone else participate in these conversations, especially at first, will give you more of a sense of control.

The new learning curve you are on is much more manageable when you have support. Learning the routines of treatment, communicating about this with loved ones, entertaining your child for long stretches of time in the hospital, these are all new things for you to cope with. Don't be afraid to ask for help! People will offer to help, but may not know what to do. Tell them how to best support you! If you are unsure yourself of how others can assist your family, see the section "Reaching Out and Accepting Help" for ideas. There are no right or wrong ways, find what works for your family.

No one can imagine having to tell a son or daughter that he or she has cancer. The courage you find inside to be upbeat and positive in front of your child often turns to outrage and anger when you are alone. Parents of very young children may find themselves inventing words to help little ones understand the word *cancer*. Babies and toddlers have no frame of reference to understand cancer, so they really don't know what they are facing. You have to build a new world for them quickly, making up words and analogies to help them understand. You may be surprised at how well they adapt to treatment.

If your child is old enough to know someone who has been sick, then the conversations become a little more delicate. Around your child it is helpful to use simple terms. They need to know they are getting medicine to help the cancer go away. If they have experienced someone dying, give them a story of a survivor to focus on. Don't feel you have to go into great detail. Children are very concrete thinkers. They most likely will want simple, comforting explanations. Take each day as it comes!

Telling adolescents and young adults is also different. They understand the word cancer. They have prior experiences; they know cancer can mean death. Telling a teen or young adult of his or her

cancer diagnosis puts parents in the difficult position of dealing with their child's emotional response to a situation they themselves have likely never experienced.

It is difficult to know how to be most helpful as you struggle to explain to your child something that you cannot really explain to yourself. Focusing on the concept that you are a team and that you all will work together, emphasizing he/she is not alone, can be helpful. Even stubborn teens may become very needy and are thankful to know that your support is unconditional. Their emotions are all over the place. Try to react to their ups and downs with a steady, loving presence.

For all ages, sometimes the best thing to do is to just be there. Although it is hard not to take your child's reactions personally, try to remember that the combination of pain medications and chemotherapies creates temporary personality changes that are not to be taken to heart! More than one of us has cried from hurt feelings, but try to hold on to the fact that it is all temporary. When your child's fear shows, just being there and validating your fight together as a family is very comforting. Telling your child about other kids that are out of treatment and living a "normal" life again can help him or her create a vision to hold on to.

It may help to understand that you are probably going through a time of grieving. You may be mourning the loss of a seemingly healthy child to one whose future is not certain. You may be grieving the loss of being together as a family. Treatment often requires the family to be separated. Siblings may be shuffled around; spouses spend days, weeks, and sometimes months separated. You may be grieving the loss of a job. Friendships fade, new ones form. Extended family may or may not be helpful. You may feel you are facing the loss of everything you knew as your world. There is no longer the comfort of routine. Your life is on high alert at all times as you respond to the unpredictability of the illness and its treatment.

At first most of us feel incompetent and very unsure of ourselves when it comes to the new tasks we are handed. Please know that it isn't easy to assimilate new things in life even when you AREN'T grieving. Given the possibility that you are in a state of grief on top of trying to become quickly competent, sometimes you may feel downright paralyzed, but you won't stay there! Soon you will feel more relaxed with the new tasks that are your routine—one day you'll marvel at how you calmly flushed a line while playfully interacting with your child! Getting into new routines gets better rather quickly; what takes more time is allowing yourself the space to work towards an emotionally strong and healthy sense of self again.

Dr. Elizabeth Kubler-Ross has explained the grief cycle many people go through during any large, traumatic change in their lives. The grief cycle can be used to explain what you may feel you are going through. For some this helps to give some structure to the multitude of feelings that they cycle during their child's treatment and recovery.

The very primal emotions of shock, anger, and denial are often the first phases of grief. Many parents are in the first phases of grief during the initial month or two of treatment. Acclimating yourself to the world of a hospital or outpatient clinic can be something you go through feeling like a deer caught in the headlights. Many days you may think there has been a mistake, this just can't be happening. Your fears often have to be hidden as you watch your child receive treatment. You may feel like you are an actress, or cheerleader, even though your insides are in a panic! You learn to flush lines, give shots, change dressings, and collect urine, all during this phase when you may be feeling shock, anger and denial.

The sadness of watching your strong, well-developed, healthy child transform into a frail, thin, sickly child understandably can cause you to feel powerful emotion. You may feel shock again when hair falls out in clumps on the pillow and you suddenly have a bald child. It is then hard to deny that you have a child with cancer. Teens seem to get much more nauseous during chemotherapy. The nausea often can't be controlled and rapid weight loss can affect self-image. You may find yourself mourning this transformation, and yet you have to be the one to stay strong and upbeat for them.

You may feel, at first, that you live in a phase of angry, numb disbelief. Be comforted in knowing this phase will pass and you will feel better!

Your communications with those closest to you can be volatile. There may be misunderstandings and differences of opinion between spouses, as it is difficult to think clearly and logically, especially during the initial phase of treatment, when you spend hours on end by your child's side. You feel exhausted from the monotony of the days and may feel guilty for wanting to escape. But there is no choice but to remain strong. By simply recognizing that these reactions are normal you are taking the first step towards managing feelings that may be very unlike any you've ever experienced. Try to quickly resolve miscommunications with loved ones. It is ok to simply chalk disputes up to the situation at hand, and then lovingly move on.

Sometime during the initial phase of treatment, most people begin to settle into a new "normal" routine. You may find support groups online, at the hospital, or in your community. You may have established a website that gives you strength and support through messages people leave. Siblings settle in to a new routine. Everyone starts learning new roles and you have new hope that the chemicals dripping into your child are doing their job.

Ironically, as things get more routine, many parents find themselves feeling even more depressed. It's as though the initial adrenaline that you lived on as you started treatment is gone. You may find yourself making new "ifs and thens" about what you'll do differently if your child survives. You have a lot of time to think and reflect on where you have come from and where your life is heading. As you realize that treatment isn't quick, that healing takes time, you can find yourself feeling very flat and down.

Take advantage of the resources that are offered to you. Seek out the help this new routine is affording you. For parents who go from full time working parent to full time caretaker parent, there are many, many hours of downtime to fill. Use that time to invest in your own mental strength. Many parents have found that journaling, exercising, baking, knitting, or seeking support groups become ways to cope with the often flat feeling that accompanies hours and days of caretaking.

Depression can spiral up and down as you navigate through your child's treatment. Some feelings of depression are a normal phase of the grief cycle. The degree to which you, your children, and your spouse experience depression is important to monitor. Often it is a sibling, or the spouse who isn't the primary caretaker, who experiences depression first. Don't be afraid to talk to your child's doctor and your social worker if you, your spouse or any one of your children is feeling inordinately depressed. They will guide you to the right place to get help. Remember it is important to take care of yourself so that you can have the reserves needed to provide nurturing support and care.

Your child may have times during treatment where he or she is listless or just wants to quit. Often the drugs a child must take can exacerbate these feelings. If your child can find ways to express his/her feelings through art, music, writing or talking it may help. Trying to bring friends and siblings into the routine as often as possible helps you and your child cope.

Don't be surprised if your child takes on a more "controlling" personality. Children can get very specific about sizes, shapes, flavors, colors of EVERYTHING related to treatment, and may have temper tantrums over things that would not have bothered them before. This is normal. They are seeking to control a situation that they don't have a lot of say in! Try to be patient, but firm. Remember that when your child recovers you don't want to have a child who believes he or she will always get his or her way! It is a fine line, but one most parents have had to deal with on some level. Be mindful of the balance.

Older children may need more sophisticated outlets to avoid feelings of sadness and depression. Having a blog or website, arranging visits from friends during treatment, keeping in touch through cell phones and email, and keeping up with the latest video games are often the most significant

ways to help an older child cope. Each situation is so unique, it is a good time to really communicate with your older child and find out what makes him or her feel best, so you can work to create environments that support their needs.

Don't assume you know what your older child needs—they will surprise you! The isolation of treatment and loss of identity is a major challenge for many older children. Some may not want to become part of the clinic community, instead choosing to get in and out and gravitating more towards their family and friends away from treatment. Watch for signs of depression if teens are isolated for long periods away from their normal world. As with the younger children, there is very little over which older children have control, yet they are at an age when independence is important. You will understandably be protective, but try to let your teen be in charge as much as possible and do as many normal things as he or she is able.

At some time during your child's illness there generally comes a point of *acceptance*. This, too, is a phase of the grief cycle, but acceptance is different than getting in to a routine. Eventually you have a resolve about what your life is now. You pick up the pieces and try to establish new family dynamics. You try to accept that you are going through this experience called *cancer* with your child. You may get to this point of acceptance during treatment, or after your child has completed treatment.

Accepting that your life is in some way back to a new normal is a very fine line. You may be afraid to plan long term. You may be fearful of every ache and pain. You may even be afraid to discipline your child as you would your other children. Acceptance is not resignation. Resignation means staying stuck in the place of grief, without looking for ways to move forward and grow. Acceptance means you have had time to take in change and set new goals and benchmarks for you and your child. You have fear, but with a new wisdom. You know the reality of what you have been through, and yet you move forward.

Don't have unrealistic expectations about jumping back into being the person you were before your child was diagnosed. For many this experience becomes a catalyst for life change that can bring a new sense of purpose and priority. Your child will have wisdom beyond his/her years. Your other children will have the ability to be more compassionate, more aware. The friendships you keep will be the ones that are real. You won't ever be able to take the diagnosis away, but you will have found strength when you thought you had none; courage when fear burned inside; acceptance of challenges that once seemed insurmountable; and hope and joy in every day. You and your child are going through the unimaginable together, and yet the sun rises and a new day comes with the promise of more tomorrows.



# Parents Coping with Relapse

After our child was declared disease-free—after about ten months of treatment and some of the ugliest side effects we could have ever imagined—we felt secure enough to delve into the NB community and see what was going on out there. We had been through the dark forest and felt like we were coming out the other side and seeing glimmers of light. We never doubted the treatment, and said we had no concern for survival statistics because we were hopeful and faith-filled people and knew she was going to survive no matter what

In reading so many stories online and in papers every night, we would lament the number of kids who relapsed and asked ourselves this very poignant question: "What's worse, original diagnosis or the news of relapse?" This question was something that gave us hours of conversation, and it seemed relatively easy to discuss at the time, because it was always someone else's child.

While we had absolutely genuine sorrow for the family, it still wasn't that feeling of having the wind knocked out of you like when *you* get such news. It was almost therapeutic to have these and other conversations because again, it wasn't in our back yard and as long as we were big enough to discuss it, it felt like we were staying informed and didn't have our "heads in the sand." However, fearful as if just saying it would make it happen, we never said, "What would *we* do if *our* child relapsed?" As foolish as that may sound, we can at least reflect on those times and know now that we had real concern of the chances of a relapse occurring, and by discussing other children we tiptoed around the edges of our own fear.

We never really answered that "which is worse" question, and as best as we can tell, there is no right answer. Both original diagnosis and news of a relapse are devastating events, and while everyone deals with the two differently, there are some inherent truths about both that make them tough to swallow.

At original diagnosis, your biggest fear is the unknown. After all, before diagnosis, what was your biggest exposure to the world of pediatric cancer? Maybe you watched a St. Jude's Hospital fundraiser for ten minutes and said "gee that's sad, those poor kids." Consequently, it was disturbing to look at and you changed the channel to see what else was on. Unless you were a woman looking for a real good cry and in that case, it did its job because it is in fact sad. So while often people say ignorance is bliss, not knowing the next step when your child is diagnosed with cancer is anything but blissful. It is probably the most frightening event of your life.

In the case of relapse, however, you have still more complicated feelings and fears. You may think, "if I ever get that news, I can handle it, after all, I've been through the Neuroblastoma protocol, I've seen everything." **Not so!** 

When we first got news that our daughter had "suspicious findings" on her CT scan, we experienced a whole new range of emotions and none of them were good. Thinking back to all we had read and people we had met, we knew how serious this was, and for the first time, we had to face the question, "What if she has relapsed?" No more tiptoeing around the edges, this was here and in our face and the security blanket of discussing hypothetical situations and other people's kids was ripped away. In facing the possible news of relapse now, there were many layers of fear and concern. Some things were anger and frustration about why she had to go through this again, hadn't she been through enough? After a year of brutal chemotherapy, transplant, radiation, and the antibody therapy, it seemed she had paid her dues.

Other things were more pragmatic like, if our daughter had relapsed, who would travel to our cancer center in another state with her for treatment; who would pick her sister up from school every day; and what about her education? The problems of one of us quitting our job and restructuring our bills were also concerns.

But none of these issues rang out as loudly as the feelings of guilt and helplessness that arose. We thought we did everything right: we gave all her meds on time, attended every hospital appointment on time, kept her isolated from germs for months on end when necessary, and even chased down an experimental antibody therapy all the way across the country that our insurance wouldn't cover—yet she relapsed anyway. Did we put her through all this hell for nothing? Helplessness certainly sums up those feelings, and there was nothing we could do about it, but go back to our cancer center and face the music.

As mentioned in the beginning of this essay, we are a hopeful family and do not make our decisions based on statistics and percentages. It was hope that carried us to our cancer center in another state, the final stop on our journey from *maybe relapsed* to *starting treatment* for relapse. Even on the day of our daughter's surgery, we sat for hours on end talking about the possibility of the tumor being a ganglioneuroma, a benign mass that the surgeon could remove and then we would go home. After about five hours, the surgeon came in to tell us that it was in fact Neuroblastoma, and down came the ton of bricks. No more maybe this or maybe that, this was in-your-face cancer relapse, and it was every bit the kick in the stomach that the original diagnosis had been.

Once relapse is confirmed, the issue becomes how you *choose* to deal with the new world you have just been shoved into. Your perception is very powerful and your outlook is equally important, so the actions you take from day one may really be the true measure of your child's success in fighting "Round Two" of this horrible disease. Are you going to listen to the naysayer's stories of doom and gloom, or succumb to statistics (that in almost all cases are at least five years outdated by the time they are published) or are you going to grab your child's hand and muster up all the courage you have, and tell the doc, "Let's go, we're ready to fight"? It seems the answer is a no-brainer, but it's not always that easy—fear seems to weaken people, and if you give in to the numbers, it can be the beginning of the end right there.

So, once the crying was over, it was time to get it together for our little girl, and that meant putting on the war paint, and *fighting*. Of course our part of the fighting was the easy part; it was this poor little child who was going to go through the torturous therapy involved in treatment of relapse Neuroblastoma. This may be where relapse becomes tougher news to digest than original diagnosis.

In the beginning we were ignorant and didn't know what to expect other than what our doctors told us. But having lived this life for some time now, we knew how toxic the chemotherapy was, we knew her counts were going to drop, we knew she would once again be susceptible to infections. Now we would have been thankful to be ignorant and not know what we were about to put our little baby through. The good news in it all (if you can call it that) is that we've been through this before. We have no illusions or misconceptions about what's to come, and we have the resources of a caring medical team that has become, in effect, a part of the family. This combined with all of the other support systems both in person and online, makes it possible to take on another day, and do it with a good attitude.

As we sat with our doctors, things became a little more settled, and while we were upset about the circumstance, how much can you really expect to resolve by being mad at cancer? So, the treatment plan was laid out, we resolved the logistics for our home life, and all that was left was to try and explain it all to our little five-year-old who was waking up with a belly full of stitches. She came back with things like "Why did the doctor cut my tummy? I'm not sick", and "Why do all those kids have no hair?" So as you can see, there are many more ingredients to relapse than just the medical facts and treatment protocols.

We have always felt that attitude, hope and faith (and not in that order) are integral parts of fighting cancer. Very early after original diagnosis, we wanted to know everything and were charting our own drugs and terrorizing the nurses for every morsel of information when the doctor told us this: "Let the doctor's do what they do, let the drugs do what they do. Your job is to be a parent and keep your child safe, secure, and happy."

Anyone who has met our daughter knows that not only will this advice stay with us forever, but that it has proven itself. Any four-year-old who could run into an IV room, and put her arm out for a series of sticks into her vein depleted little arm—laughing the whole time and insisting that the parents wait outside—is a child whose parents did their job.



# **Informed Consent**

by Steve Dolling

Steve Dolling brightened many a dreary day for subscribers of the ACOR nblast listserv with stories of house repairs (in his underwear), hospital parking woes, sailing with a bread-loving Portuguese Water Dog named Scupper, and daily life fighting NB. Spencer (May 12, 1995 - May 21, 2008) said it best when he explained, "Aside from having cancer, you can see I have a pretty good life." The Dollings are now aboard the Blackdragon sailing where ever they fancy. http://www.sailblogs.com/member/blackdragon/

By now you are used to the familiar style. Deep sense of drama that sucks you along for a page and a bit followed by a quirky twist that tickles the funny bone. This isn't one of those, and if that is what you are hoping for, you are likely to be disappointed. Of course there is no way you are going to believe me here at the beginning. You've been fooled before. Fair warning. I had to advise you of the risk before we begin. It's your choice whether or not you care to read on.

Informed consent. It's the foundation of all the non-emergency treatment and diagnostic procedures that they do at the hospital. Whether it was created as the outcome of some enlightened medical care philosophy or it was thrust into the healthcare realm by an overly-zealous legal system doesn't really matter. Inherently, you have the right to choose. Nobody can do anything to your child without your OK. The decisions belong to you.

So how does it all start for the typical cancer family? Some hideous sequence of events brings you to Children's hospital. The first things they need to do are tests. Lots and lots of tests. "Yes we would like to do an ultrasound, x-ray, CT scan, bone scan, more blood tests, and an MIBG to accurately diagnose and stage your child's disease." Yes you get to choose whether or not to subject your child.

Inevitably follows some definitive diagnosis and a treatment protocol. The reams of chemotherapeutic agents all have side effects. "This one causes baldness, that one causes high frequency hearing loss, this one can affect the kidneys, that one can affect the heart, nausea is a common side effect, etc. etc." You listen with a sense of bewilderment and some amusement. You have a choice but don't even bother to ask about the alternative. You already knew the first time you heard them say the word "cancer".

Depending on what you're up against, surgery might be part of the game. A general anesthesia alone sounds like a bad risk. Once the surgeons fully detail all the potential complications of what might happen when your kid's particular tumor is removed, you sometimes wonder about the benefit of being informed. It doesn't leave you with a sense of comfort, but at least you have the choice.

Then there is the bone marrow or stem cell transplant. Now that meeting is a happy one. Let's contemplate the potential major organ failures: kidney, liver, lungs, bone marrow, and very occasionally, the heart. "Oh and of course there is some risk to the brain but generally not unless the other organs go first. Oh yes and of course there is infection. Your options are bacterial, fungal and viral. They are all potentially lethal, but we do our best." Strangely enough, they don't even mention hair loss as an adverse side effect on this one. Remind me again of the options please, I have a choice to make.

Informed Consent 9:031

These are all the impossible choices. Not that it is impossible to choose one way or the other. It just feels impossible to believe you are in the situation to begin with. Impossible to believe that you might eventually reach a point where you might want to consider option B.

But it's not all high-drama. Every day there are a bunch of informed medical decisions to be made. Would he like this medicine in liquid form or can he take a pill? Gravol now or should we wait and try to space it between the ondansetron doses? Platelets are low today, but not real low, we could hold off until tomorrow to transfuse if you can come back to the clinic then? He's losing weight; we should consider an NG tube. And on and on and on.

These are all the meaningless choices. Not meaningless in the sense that they are unimportant. Do a good job on all the day-to-day stuff and it can have a big impact in your child's comfort and your peace of mind. Make all the wrong choices though, and it won't likely have any effect on the final outcome. In that sense, they're all meaningless.

So of all the impossible and meaningless choices that you get to make, is control just an illusion? Isn't it just one great train ride you are on and at some point you pass a switch in the track that determines your final destination?

That might be true. But there is one other choice you get to make that does have a lot of meaning. It may or may not affect the destination, but it certainly does affect the ride. It's not even an obvious choice because nobody will ever present it to you. You don't have to sign the consent form. You don't even have to announce your decision.

You get to choose how miserable you want to be.

OK. Life sucks. Your kid has cancer. But every day you get to choose if you want to be pessimistic or optimistic. You get to choose whether you want to be a victim or your kid's biggest champion. You get to choose if you want to endure the day or have some fun and make the best of it whatever it brings you. You get to choose what example you want to set for your kid. And you get to choose whether you want to teach your kid that he has a choice of whether or not to be miserable.

It's a choice that you actually get to make a dozen times a day in different circumstances. And you don't always have to make the "happy" choice. Sometimes it feels really good to just have a bad moment and tear the head off the incompetent idiot who appears not to have the skills to issue your parking pass.

Once you realize that you actually do have control over just about everything in your life except perhaps the impossible choices and impossible outcomes, it makes the journey a whole lot easier.

You might still be lumbering down the railroad, but if you believe you're flying the space shuttle, you might actually have a better chance of reaching escape velocity. And it's a whole lot more fun to eat astronaut food.



# Grooming a Pill Popper

by Patrick Lacey

Three-year old Will has been exhibiting his quest for independence and this is helping a lot as it relates to the fact that he has to take a lot of drugs. He started asking to help 'push' the syringe on his meds and has progressed to the point where now I give him the syringe (today with 12.5ml of Zofran) and he sticks the syringe in his mouth and pushes in the plunger.

I'm sure there are plenty of parents out there who secretly push their kids to excel at some unusual task for their age for various reasons. Perhaps they are competing with their neighbors kids, or they want little Johnny to appear to be the smartest 2 year old on earth, or maybe they just love their kids and want to give them every opportunity to succeed. In any event I have been secretly working on a skill with Will and I'm very proud of his progress. The skill we have been working on?

The art of swallowing a pill.

While it's not exactly reading a book or conducting a stuffed animal orchestra it is important in our world.

Will has been taking countless medications for the past 3 years and all his medication has been oral liquid or via IV. While he currently does not have an issue with any of his current oral meds (most likely due to the fact that he probably has no taste buds) there are treatment options that are pill only. It has been my goal to get him to be an Olympic quality pill swallower so that his next treatment option will not be restricted to clinical trials that don't require pills.

To do this I have started by buying a bottle of Motrin Jr. pills that are fairly small. While on ABT he takes Tylenol in the morning and at night to prevent any neuropathy related pain. I decided to replace his liquid or meltaway Tylenol with two of these pills in the morning and two at night. The first time I gave him one he promptly began to chew the pill....not the most auspicious of beginnings.....however we kept at.

My first attempt was to engage the 'cannonball' approach to pill taking. I would have Will pop in a pill and then start shouting "Cannonball!" as Will would pick up his milk and begin chugging it to launch the pills into his belly like cannonball.

This was going pretty well.

Will then stepped it up to a whole new level one day by simply tossing a pill in his mouth and dry swallowing it. Perhaps he was growing tired of my cannonball antics.

My reaction was completely over the top...and bordered on insanity....I acted as completely shocked and astonished as if a UFO had landed in our backyard. I actually employed the "there is NO way you did that!!!" approach. I basically started calling him a liar and demanded to look under his tongue. I told him to stop using his fancy magic tricks and to give me the pill because there was NO way on God's green earth that any 3 year old in recorded human history could have possibly swallowed a pill.

Tell a 3 year old he can't do something, especially a determined one, and you simply know that it is going to get done.

So this morning before his breakfast I brought out a paper plate with his Zofran syringe, multivitamin, and Motrin. He picked up the two Motrin off his plate popped them in his mouth and dry swallowed them both. I of course carried on, gave him a high five, and basically told him how amazed I was that he was doing things like a really big kid and at this rate he'd be driving a car pretty soon. He thought that was funny. Now I need to identify a bigger pill to start practicing on in the event one of these trials comes along with those giant horse pills that even us adults have a hard time gagging down. Perhaps I'll start a non-profit where we can have a Pediatric Cancer Olympics where the kids can compete in such events as pill swallowing, self injection, how to pause an infusion pump, who can flush their Broviac line the fastest, and projectile vomiting into a bucket.

These are all thing that, while not playing the piano, are skills and talents that are beyond these kids years and truly reflect just how normal our kids are even though they are forced to grow up in a very abnormal world. It's kind of hard to brag on your son at the playground about how incredible it is that your 2 year old wakes up at night and pukes into a bucket...there is no quantifying what an incredible thing that is... (So take THAT all of you preschool aged pilots, musicians, scientist, astronauts, and college grads.....Cancer kids kick your butt!)

Grooming a pill popper by Will's Dad with permission



# Why Keep Records?

# Reasons and Tips for Keeping Records for Neuroblastoma Treatment

If you multiply many patients by many hundreds of pages of records, you can quickly see the medical professionals deal with a vast amount of information about their patients. Electronic records allow quick recall of information from your child's chart, but there are times when it is handy for you to have important information at your finger tips. You can ask good questions about trends, check for accuracy in drug dosages, and quickly access pertinent information about your child. You have only one patient, and one disease. You can do it!

# Ask for copies of everything

Ask for copies of everything, including scans on CD. Persistence is occasionally required to get everything after each series of tests. Organize the records in a way that makes sense to you, so you can find what you need while at the hospital or clinic. It is helpful to keep a chronological log of counts, tests, results, chemo, and all drugs including dosage. Cumulative drug dose is important for several of the chemos.

Most oncologists and nurse practitioners will respect your desire to be a part of the team and appreciate your efforts to make his/her job easier. Keeping your child's chart up to date is important, so add to it as you go.

#### Tailor the charts to your child

This chapter includes example charts for you to use or modify. (The web version of this handbook has downloadable charts in Microsoft Word and Excel). Be sure to eliminate items that do not apply, and add in items of importance that concern your child. For example, if your child has asthma, you may want to make a column on your chart for pulmonary function tests. You can consider keeping a separate food diary (noting what foods stay down!) If weight is a non-issue, take it off the chart. By contrast, for infants you may have to keep careful track of fluids (in and out) or total calories, in addition to weight. Skin issues, infections, magnesium levels, cardiac function, seizures, moods, and a host of other possibilities may be very important in tracking the care and making decisions for your child.

Keeping track of anti-emetics (anti-nausea) drugs is very important, because each child is unique in how well certain combinations work, and some of these drugs have powerful and unpleasant side effects. The nurses and doctors will not remember the combination that works for your child, nor will they catch every unacceptable reaction to the drugs. Always record infections, reactions to drugs, and complications of any kind.

Color code any items you want to highlight, such as reactions to blood products or drugs, or inpatient versus outpatient days. Make a legend of what the color codes indicate, and a list of abbreviations are helpful if you give copies of your chart to medical professionals.

# **Terminology**

Drugs and tests often have more than one name, and you should make a list of all the drugs and tests and all their names and abbreviations, including common side effects of the drugs. Note that various abbreviations are used in the medical literature. For example, anthracyclines are a class of chemotherapy drug in the antibiotic family. One drug in this class is doxorubicin, which is sometimes referred to by the brand name Adriamycin (brand names are capitalized). You will need to know total dose of anthracyclines your child received because of potential long term heart damage from this class of drug.

#### EXAMPLE definition from:

http://www.medterms.com/script/main/art.asp?articlekey=20134

**Anthracycline:** A member of a family of chemotherapy drugs that are also antibiotics. The anthracyclines act to prevent cell division by disrupting the structure of the DNA and terminate its function. They do so in two ways: (1) they intercalate into the base pairs in the DNA minor grooves; and (2) they cause free radical damage of the ribose in the DNA. The anthracyclines are frequently used in leukemia therapy. The anthracyclines include daunorubicin (Cerubidine), doxorubicin (Adriamycin, Rubex), epirubicin (Ellence, Pharmorubicin), and idarubicin (Idamycin).

Common Misspellings: anthracyclin

#### Thou shalt know the side effects

Every drug administered to your child has potential side effects. You must know what they are. As wonderful as the nurses and doctors are, they simply will not be able to pin it down every time your child has an unpleasant side effect to something. Here is the really difficult part, and why you should have an honorary MD by the time you are done: many of the side effects over lap from drug to drug, so if your child is on 10 different meds, and is having blistering headaches, and five of the drugs can cause headaches, which one is it, Sherlock? Parents are often the most apt to figure this out, because they know their child and can keep careful track of responses.

An excellent resource for thorough information about many chemotherapy drugs can be found at <a href="http://www.bccancer.bc.ca/HPI/DrugDatabase/DrugIndexPro/default.htm">http://www.bccancer.bc.ca/HPI/DrugDatabase/DrugIndexPro/default.htm</a>

#### Units and reference ranges

Lab tests for blood and urine are reported by each institution with test name, units, and reference range. Be sure to record your results with units so that the results can be understood by different institutions, and also record what was tested (i.e. blood/serum, or urine). Reference ranges are established for each lab, and some are based on age and gender. You will become accustomed to interpreting the results of white cell counts, hemoglobin, and platelets. Other tests will be done less frequently, but will be important to determine organ function and possible tumor activity. Always ask why a particular test is done, so you understand the significance of the test and the result.

Become familiar with how drug dosages are written, so you can quickly copy chemo and other drugs onto your chart or drug list. See the list of dosage abbreviations below. Always indicate how the drug is administered (IV, oral, injection, etc) along with the dose. Ask a nurse if you don't understand the units. Drug dose is determined based on weight (kg or kilograms) or surface area (m² or "meters squared"). Surface area is calculated from height and weight, and an average five year old has roughly one meter squared of surface area. It is a good idea to record both the dose (amount of drug per kg or m²) and the actual amount given. This way you can keep track of dose errors. You should

keep track of both weight in kg and surface area, as these will change and affect the amount of drug given on a particular day.

Example: Doxorubicin 25 mg/m²/day IV x 3 days

This means 25 milligrams per meter squared of body surface area of doxorubicin is to be administered intravenously per day for 3 days. This is a continuous infusion, because there is no additional information on how long the infusion is—such as over 30 minutes. Total dose for this course would be 75 mg/m<sup>2</sup>.

Prescription abbreviations are handy to know, so you can check to be sure that administration of drugs prescribed is correct. See chart for abbreviations used for prescribing drugs below, with the Latin origin.

## **Drug Prescription Abbreviations**

| <u>Term</u>     | <u>Abbreviation</u> | Meaning       |
|-----------------|---------------------|---------------|
| ante cibum      | ac                  | before meals  |
| bis in die      | bid                 | twice a day   |
| gutta           | gt                  | drop          |
| hora somni      | hs                  | at bedtime    |
| oculus dexter   | od                  | right eye     |
| oculus sinister | os                  | left eye      |
| per os          | po                  | by mouth      |
| post cibum      | pc                  | after meals   |
| pro re nata     | prn                 | as needed     |
| quaque 3 hora   | q3h                 | every 3 hours |
| quaque die      | qd                  | every day     |
| quater in die   | qid                 | 4 times a day |
| ter in die      | tid                 | 3 times a day |

#### **Test limitations**

Even more tricky than keeping track of terminology, units, and results of all these tests, is understanding the limitations of each test. For example, your child may have a bone marrow biopsy that is reported as simply "positive for neuroblastoma" or "negative for neuroblastoma." What can you know from that result? In the case of "negative," it means that in the sample that was examined, no neuroblastoma cells could be found. These biopsies are usually bilateral, meaning two sites were checked at the same time. Those two sites are clear of tumor, but unfortunately, it does not mean the child's entire bone marrow is clear, because NB cells could be clumped in other locations (referred to as "sampling error"). How do you interpret the "positive for neuroblastoma" result? There is little chance of "false positive" in this case, unless there is very small amount of tumor, and it may be well-differentiated (matured) into harmless ganglioneuroma cells. These are items to discuss with your doctor and possibly the pathologist who reads the slides. Some pathologists will report the amount of neuroblastoma in a bone marrow biopsy as a percentage, but keep in mind this is visually estimated. In other words, there is no significant difference between 40% and 50% because this is difficult to estimate to a high degree of precision, especially since neuroblastoma often appears in clumps. The oncologist will be more interested in obvious trends in a series of biopsies over the course of several weeks or months, such as 100%, then 40%, then 5%.

Another example of understanding results with respect to limitations, is urine catecholamine metabolites (HVA and VMA). HVA and VMA indicate tumor activity in 82% of children with stage 1-3

neuroblastoma, and in 96% of children with stage 4 (Cheung 67), but in certain circumstances levels can be highly inaccurate. The spot test for HVA and VMA is much less accurate than the 24 hour urine test, unless done simultaneously with urinary creatinine (Cheung 68). Many food items will affect the results (such as apple juice), so you will want to know what foods your child should avoid so the test will be as accurate as possible. Finally, VMA/HVA are often tested during follow up visits after treatment is completed, but only 54% of patients in one study had elevated values at the time of recurrence (Cheung 68).

# Long term effects

Keeping a treatment summary for long term follow up is very important. A concise but thorough history of treatment, with all follow up tests should be kept up to date. Many children who are long term survivors of neuroblastoma know very little about their treatment when they become adults and become responsible for their own medical care. Recent studies have been published indicating the lack of knowledge about the disease and treatment can jeopardize the child's future health care: http://annalsfm.highwire.org/cgi/reprint/2/1/61.

# Overwhelming?

Do not be discouraged! This may appear to be an overwhelming task at first, but becomes easier as time passes. You will learn as you go, and develop your own strategies for keeping track of things as you see fit. The medical world respects your important role as advocate for your child. Your understanding of the disease and treatment can only benefit your child. Eventually you will want to pass this on to your child, so that as a survivor, your child will know how to become his or her own advocate.

Source:

Cheung, Nai-Kong V., and Susan L. Cohn, eds. Neuroblastoma. Berlin: Springer; 2005

Please contact <a href="mailto:editors@nbhope.org">editors@nbhope.org</a> with any comments



| Name:    |  |
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| Dhono:   |  |

# Neuroblastoma Diagnosis Phone:

| Date of Birth       |  |
|---------------------|--|
| Date of Diagnosis   |  |
| Age at Diagnosis    |  |
| Gestational Age     |  |
| If tumor discovered |  |
| before birth        |  |
| Parents             |  |

| Primary Doctor   |  |
|------------------|--|
| Type of practice |  |
| Hospital         |  |
| Address          |  |
|                  |  |
|                  |  |
| Phone            |  |

| Pediatric Oncologist   |  |
|------------------------|--|
| Cancer Center/Hospital |  |
| Address                |  |
| Phone                  |  |

| Allergies                         |
|-----------------------------------|
| Prior illness or hospitalization: |
|                                   |
| Family medical history            |
|                                   |

History leading up to diagnosis (list all symptoms, such as fever, lethargy, pain, weight loss, bruises, etc):

| Date(s) | Symptom(s) | Doctor/specialty | Tests | Results |
|---------|------------|------------------|-------|---------|
|         |            |                  |       |         |
|         |            |                  |       |         |
|         |            |                  |       |         |
|         |            |                  |       |         |
|         |            |                  |       |         |
|         |            |                  |       |         |
|         |            |                  |       |         |
|         |            |                  |       |         |

| OTHER | OTHER BASELINE TESTS AND EVALUATIONS |        |        |  |
|-------|--------------------------------------|--------|--------|--|
| Date  | Test                                 | Doctor | Result |  |
|       | Hearing test                         |        |        |  |
|       | Echocardiogram                       |        |        |  |
|       | Weight (lb and kg)                   |        |        |  |
|       | Surface Area (m <sup>2</sup> )       |        |        |  |
|       |                                      |        |        |  |

# **Diagnosis information:**

- ▶ be sure to obtain copies of every test result, including scans on CD
  ▶ reference ranges and units differ for some labs, so ask for reference ranges.

| Date        | SCANS                 |       | Doctor             | Results (note reference range and record units ie mL/min) |  |           |
|-------------|-----------------------|-------|--------------------|---|--|-----------|
|             | X-rays                |       |                    |   |  |           |
|             | Bone scan (Tc 99      | ))    |                    |   |  |           |
|             | CT scan               | •     |                    |   |  |           |
|             | MRI                   |       |                    |   |  |           |
|             | Ultrasound            |       |                    |   |  |           |
|             | PET scan              |       |                    |   |  |           |
|             | MIBG: □ I-123 □ I-131 |       |                    |   |  |           |
| BIOPSIE     |                       | 1-131 |                    |   |  |           |
| DIOI SIL    | Tumor biopsy          |       |                    |   |  |           |
|             | rumor biopsy          |       |                    |   |  |           |
|             | Bone marrow biog      | nev/  |                    |   |  |           |
|             | (bilateral)           | ЭЗУ   |                    |   |  |           |
|             | Marrow aspirate       |       |                    |   |  |           |
|             | Immunocytochemistr    | V     |                    |   |  |           |
|             | (ICC at CHLA, Dr. Se  |       |                    |   |  |           |
| BLOOD 8     | serum, list units     | Doct  | or/Hospital:       |   |  |           |
| Date        | Test                  |       | Result             | Date  | Test                                     | Result    |
|             | Hemoglobin            |       |                    |   | Phosphorus (P)                           |           |
|             |                       |       |                    |   |  |           |
|             | Hematocrit            |       |                    |   | Potassium (K)                            |           |
|             | Platelets             |       |                    |   | Magnesium (Mg)                           |           |
|             |                       |       |                    |   |  |           |
|             | WBC/differential      |       |                    |   | Sodium (Na)                              |           |
|             |                       |       |                    |   |  |           |
|             | Serum ferritin        |       |                    |   | Calcium (Ca)                             |           |
|             | Serum lactate         |       |                    |   | Serum creatinine                         |           |
|             | dehydrogenase (LDH)   |       |                    |   | Alarina ansiraturantana                  |           |
|             | neuron-specific       |       |                    |   | Alanine aminotransferase                 |           |
|             | enolase (NSE)         |       |                    |   | (ALT or SGPT)                            |           |
|             | Uric acid             |       |                    |   | Aspartate aminotransferase (AST or SGOT) |           |
|             | Alkaline phosphat     | taca  |                    |   | Total bilirubin                          |           |
|             | Alkalille pilospilai  | lase  |                    | างเลเ มีแทนมีก  |  |           |
| LIDINE in   | dicate 24 hour vol    | I     | l<br>Ooctor/Hospit | <u> </u>  |  |           |
| or spot tes |                       | _   - | octor/i iospit     | aı.   |  |           |
| Date        | Test                  |       | Result             | Date  | Test                                     | Result    |
|             | homovanillic acid     |       | . toodiit          |   | Dopamine                                 | - toodiit |
|             | (HVA)                 |       |                    |   |  |           |
|             | vanillylmandelic acid |       |                    |   | Metanephrine                             |           |
|             | (VMA)                 |       |                    |   | •  |           |
|             | Ratio: HVA/VMA        |       |                    |   | Normetanephrine                          |           |
|             | Epinephrine           |       |                    |   | Total urine                              |           |
|             |                       |       |                    |   | catecholamines                           |           |
|             | Norepinephrine        |       |                    |   | Creatinine clearance                     |           |
|             |                       |       |                    |   |  |           |
|             |                       |       |                    |   |  |           |

# **Stage and Tumor Classification:** Prognostic Factors at Diagnosis/Tumor Biopsy/Surgery Indicate if the information was obtained from tumor biopsy at diagnosis or from tumor resection after chemotherapy

| Tumor/Prognostic Risk Factors   | Favorable/Unfavorable <sup>1</sup>                                    | Child's NB Characteristics |
|---|---|----------------------------|
| Stage   | See INSS chart  |                            |
| Age at Diagnosis  | <18 months with no MYCN amplification, favorable                      |                            |
| Location of primary tumor   |   |                            |
| Size of primary tumor   |   |                            |
| Location of metastases  | No bone, marrow, favorable  |                            |
| Percent tumor present in bone marrow                                    |   |                            |
| Date of tumor biopsy  |   |                            |
| Date(s) of primary tumor resection                                      |   |                            |
| Surgeon   |   |                            |
| Percent, location tumor remaining                                       |   |                            |
| Shimada classification or histology, calcification                      | Differentiated, favorable Calcification, favorable                    |                            |
| DNA ploidy (DNA index 1.0 = diploid; 1.5 = triploid; 2.0 = tertraploid) | triploid, favorable di- and tetra-, unfavorable                       |                            |
| MYCN amplified copies   | Amplification > 10 copies unfavorable                                 |                            |
| Genetics: <u>1p deletion</u> , 3p deletion, 11q LOH, 17q gain, others   | alterations unfavorable   |                            |
| Serum GD2   | Presence unfavorable  |                            |
| CD44 antigen  | Lack of expression, unfavorable                                       |                            |
| Neurotrophin receptors TrkA, TrkB, TrkC                                 | High levels of TrkA expression, favorable TrkB expression unfavorable |                            |
| HVA/VMA ratio   | <1 is favorable   |                            |
| NSE   | < 100 ng/mL is favorable  |                            |
| LDH   | Normal is favorable   |                            |
| Serum Ferritin  | Normal is favorable   |                            |
|   |   |                            |

<sup>&</sup>lt;sup>1</sup>Cheung, Nai-Kong, and Susan Cohn, eds. Neuroblastoma. Berlin: Springer, 2005. (p. 79)



| Name: |  |  |  |
|-------|--|--|--|
|       |  |  |  |

# **Monitoring Disease Response to Treatment**

| BRIEF SUMMARY OF TREATMENT |            |  |
|----------------------------|------------|--|
| Dates                      | Course     | Chemo and dose, radiation location and dose, other |
|                            | 1          |  |
|                            | 2          |  |
|                            | Stem cell  |  |
|                            | Harvest    |  |
|                            | 3          |  |
|                            | 4          |  |
|                            | 5          |  |
|                            | 6          |  |
|                            | 7          |  |
|                            | 8          |  |
|                            | 9          |  |
|                            | Stem Cell  |  |
|                            | Rescue     |  |
|                            | Radiation  |  |
|                            | Retinoid   |  |
|                            | Antibodies |  |

| MONITORING DISEASE RESPONSE TO TREATMENT  |                 |                  |  |  |  |  |  |  |
|---|-----------------|------------------|--|--|--|--|--|--|
| List test, scan   | , tumor marker, | results, and inc | dicate what treatment was finished before test was performed (example: |  |  |  |  |  |
| after chemo course #2 MIBG I-123 scan showed reduced primary tumor >50% and bone lesions cleared) |                 |                  |  |  |  |  |  |  |
| Date  | Performed       | Test             | Results  |  |  |  |  |  |
|   | after           |                  |  |  |  |  |  |  |
|   | course #        |                  |  |  |  |  |  |  |
|   | Performed       |                  |  |  |  |  |  |  |
|   | at              |                  |  |  |  |  |  |  |
|   | diagnosis       |                  |  |  |  |  |  |  |
|   |                 |                  |  |  |  |  |  |  |
|   |                 |                  |  |  |  |  |  |  |
|   |                 |                  |  |  |  |  |  |  |
|   |                 |                  |  |  |  |  |  |  |
|   |                 |                  |  |  |  |  |  |  |
|   |                 |                  |  |  |  |  |  |  |
|   |                 |                  |  |  |  |  |  |  |
|   |                 |                  |  |  |  |  |  |  |
|   |                 |                  |  |  |  |  |  |  |
|   |                 |                  |  |  |  |  |  |  |
|   |                 |                  |  |  |  |  |  |  |
|   |                 |                  |  |  |  |  |  |  |
|   |                 |                  |  |  |  |  |  |  |
|   |                 |                  |  |  |  |  |  |  |
|   |                 |                  |  |  |  |  |  |  |



#### INSTRUCTIONS

# Daily Chart History and CBC Graphs EXCEL WORKBOOK FILE

This Excel workbook has some very useful features. With a running history in your hands when speaking to your child's doctor, you can quickly recall important treatment information, printing out pages of updated chart before hospitalizations or appointments with your child's doctor. If you have never used Excel, it is a fairly easy-to-learn application, and you will have the advantage of using a helpful record keeping tool.

Open (and save) the Excel file and look at the sheets in this workbook. You will note the first page has general instructions. The next sheet is entitled CHART HISTORY and contains sample information to give you ideas of what you may want to record. You can use color coding for certain events, like inpatient versus outpatient treatment and visits, chemo versus radiation, scan and bone marrow results, and so on. Look at the graphs on the following sheets. These graphs are useful ways to predict at a glance where your child's counts are going. The instructions explain how to clear the sample information and keep the formatting that generate the graphs when you enter your child's information.

Some hospitals use hematocrit (HCT) for determining red cell status, others use hemoglobin (HGB). Some hospitals rely primarily on white cell count (WBC) and others on absolute neutrophil count (ANC). If you wish to use HCT and not HGB, delete the column HGB and the sheet for the HGB graph. Alternately, you can delete the HCT column and graph sheet if you want to only keep track of HGB. You can rename the column WBC and replace it with ANC and rename the sheet WBC with the title ANC if you wish. By right clicking on the y-axis on the graph, you can change the range needed for your graphs, and change date formatting on the x-axis. Remember, the columns contain formatting to generate the graphs, so be careful in deleting columns on the chart. If you have any difficulties you can post in the record forum and we will help you.

With a little experimenting you can tailor this to your child's needs and you will have a powerful means of keeping medical professionals up-to-date on your child's treatment.

You can print this out and fill in by hand at the hospital, then type in the contents at home to keep the chart and graphs current.

We welcome any feedback on this record keeping tool.

| Neuroblastoma Chart Child's Name: Date of Birth: Date of Diagnosis: Page: |      |     |     |                               |                                     |   |                                       |  |  |
|---|------|-----|-----|-------------------------------|-------------------------------------|---|---------------------------------------|--|--|
| Date  | HGLB | WBC | PLT | tumor markers, organ function | blood products, reactions, cultures | tests, doctor, reason for clinic/hospital visit | chemotherapy, premeds, growth factors |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |
|   |      |     |     |                               |                                     |   |                                       |  |  |

| Neu             | rob      | lasto |             | hart | Child's Name:                       |           |                          |                          | ate of Diag | <del>-</del>                  |
|-----------------|----------|-------|-------------|------|-------------------------------------|-----------|--------------------------|--------------------------|-------------|-------------------------------|
| outP            | \ A (T   |       | WBC         |      | tumor markers,                      | transfusi | ion units<br>n, culture+ | tests, doctor, reason fo |             | chemotherapy, premeds,        |
| inP<br>Date     | WT<br>kg | HGB   | &/or<br>ANC | PLT  | organ function                      | PLT       | RED                      | clinic/hospital visit    |             | growth factors, complications |
| 5/9             | 78       |       |             |      |                                     |           |                          | Dr. John Smith           |             |                               |
| <del>5/10</del> |          | 9.1   | 4.7         | 115  | 24 hr urine: output<br>5050 ml/24hr |           |                          | chest x-ray              |             |                               |
| 5/11            |          |       |             |      | HVA=19.4mg/24hr                     |           | 2                        | BX1                      | 1           | tylenol and benedryl          |
| 5/12            |          | 9.5   | 4.5         | 98   | VMA=69.2mg/24hr                     |           |                          | hickman surgery/echo     |             |                               |
| 5/13            |          | 9.7   | 4           | 102  | metanephrines 1232<br>ug/24hr       |           |                          |                          |             | dox/vin/cyclo                 |
| 5/14            |          | 9.5   | 4           | 100  | normetanephr 49,894                 |           |                          |                          |             | dox/vin/cyclo                 |
| 5/15            |          | 9.3   | 2.4         | 91   | ug/24hr<br>total meta 51,126        |           |                          |                          |             | dox/vin                       |
| 5/16            |          |       |             |      | ug/24hr                             |           |                          |                          | ,           | vin                           |
| 5/17            |          |       |             |      | ferritin >5000                      |           |                          |                          |             | neulasta                      |
| 5/18            |          |       |             |      | LDH=641 serum                       |           |                          |                          |             |                               |
| 5/19            | 75       | 8.9   | 0.2         | 50   | uric acid=9.8                       |           |                          |                          |             |                               |
| <del>5/20</del> |          | 8.6   | 0.1         | 32   |                                     |           | 2                        | PET/CT                   |             |                               |
| 5/21            |          |       |             |      |                                     |           |                          |                          |             |                               |
| 5/22            |          |       |             |      |                                     |           |                          |                          |             |                               |
| 5/23            |          | 9.9   | 0.1         | 5    |                                     | 1         |                          |                          |             | dexamethazone                 |
| 5/24            |          |       |             |      |                                     |           |                          |                          |             |                               |
| 5/25            |          |       |             |      |                                     |           |                          |                          |             |                               |
| 5/26            | 74       | 8.6   | 0.1         | 6    |                                     | 1         | 2                        | Neutropenia – no fever   |             | hydrocortizone solucortef     |
| 5/27            |          | 9     | 0.2         | 22   |                                     |           |                          |                          |             |                               |
| 5/28            |          | 8.9   | 0.6         | 13   |                                     | 1         |                          |                          |             | hydrocortizone solucortef     |
| 5/29            |          | 8.4   | 1.3         | 27   |                                     |           | 2                        |                          |             |                               |
| 5/30            |          |       |             |      |                                     |           |                          |                          |             |                               |
| 5/31            |          | 11.1  | 5.1         | 30   |                                     |           |                          |                          |             |                               |
| 6/1             |          |       |             |      |                                     |           |                          |                          |             |                               |
| 6/2             |          |       |             |      |                                     |           |                          |                          |             |                               |
| 6/3             |          | 11.5  | 5.9         | 43   |                                     |           |                          |                          |             |                               |
| 6/4             |          |       |             |      |                                     |           | _                        |                          |             |                               |
| 6/5             |          |       |             |      |                                     |           |                          |                          |             |                               |
|                 |          |       |             |      |                                     |           |                          |                          |             | -                             |
|                 |          |       |             |      |                                     |           |                          |                          |             |                               |
|                 |          |       |             |      |                                     |           |                          |                          |             |                               |
|                 |          |       |             |      |                                     |           |                          |                          |             |                               |



# Instructions for Treatment Summary and an Example

Most institutions provide treatment summaries, but you can also prepare your own and include all follow up tests with various specialties (such as hearing tests, dental work, heart tests, etc.) You can use the summary provided from your hospital to create a complete summary of your own. Update your summary with every visit and make sure your pediatrician has a copy in your child's file.

You can individualize the summary to include the most significant issues for your child, such as paralysis, seizures, hearing loss, endocrine abnormalities, neurocognitive therapy, etc.

A treatment summary should contain the following important information:

- Name of child, birth date, allergies
- Name of disease, date diagnosed, age at diagnosis
- Symptoms leading to diagnosis, stage, location of metastases (type of scan)
- Date and description of any relapses
- Name, address, and phone number of treatment locations
- Name, address, and phone numbers of pediatric oncologist and other health team members
- **Chemotherapy**—list of all the chemotherapy drugs, dates given, type of administration (ie IV or oral), cumulative doses
- Surgeries—list of all surgeries, dates, location, and surgeon's name
- **Radiation**—list all dates, areas (fields), total doses, and number of treatments (fractions), and name of radiation oncologist
- Stem cell transplant(s)—dates, location, and types of transplant, and transplant doctor
- **Transplant conditioning**—list chemotherapy, radiation, and stem cell product (cell count and purged/unpurged)
- **Other treatment**—retinoids, antibodies, supplements
- Blood products received, and date of first blood product, significant reactions
- Names and dates of any significant complication(s), and treatments received for complication(s)
- Follow up exams and results

Keep a copy of your cancer treatment summary in a safe place, and give a copy to each of your health providers. Make sure your child always has a copy when he/she travels.

#### References:

http://asheducationbook.hematologylibrary.org/cgi/reprint/2005/1/507.pdf "Cancer Survivorship—Pediatric Issues" by Smita Bhatia, Hematology 2005

http://www.survivorshipguidelines.org/pdf/GuidelinesAppendixI.pdf
CureSearch Survivorship Guidelines; includes templates for Treatment Summary

Example Summary with fictitious information on next page

Please contact editors@nbhope.org with any comments

# Johnny Doe's\* Treatment for High-Risk Neuroblastoma 1995-1996

**UPDATED 5/1/2006** \*all names and phone numbers are fictitious

- ♦ Age at diagnosis: 3 years 9 months, stage 4, rt adrenal
- Allergies: sulfonamide antibiotics
- ♦ Diagnosed 12/30/95, DOB 3/19/92
- Presented with 3 weeks of fever, increasing bone pain in knees and pelvis; bone scan: widespread lesions (pelvis, distal and proximal femurs, ribs, skull, humerii, calcified abdominal mass), ultrasound, MRI, CT: 3 x 5 x 1.5 cm³ primary tumor on right adrenal gland, bone marrow bioipsy 100% replaced with NB, transfused with packed red cells for low hemoglobin, low WBC and PLT; HVA = 78.2 VMA = 235 (MIBG negative)
- ♦ 6/1/96 tumor biopsy (after 6 rounds of chemo): MYCN non-amplified, 1p deletion, poor histology, calcification, 4 x 1.7 cm tumor removed, plus affected nearby lymph nodes
- ◆ Treatment center: Children's Hospital/ ABC Cancer Institute
   123 Pleasant St, Anytown, NY 12345 (123) 345-6789
- ♦ Treatment team: oncologist Dr. Mary Jones; surgeon Dr. Robert Smith, transplant Dr. Tom Johnson, radiation oncologist Dr. Ruth Williams
- Discharged from SCT on 11/13/96.
- ◆ Last hospitalization 11/28/96 to 12/4/96 for shingles, on acyclovir. Single central venous line placed 12/30/95, removed 11/4/96.

Double lumen CVL placed 8/17/96, removed 1/13/97.

| Date     | Chemotherapy             | IV Dosage              | Amount Given                                 |
|----------|--------------------------|------------------------|--|
| Cycle 1  | Induction Protocol #1234 |                        | $wt = 18.7 \text{ kg BSA} = .98 \text{ m}^2$ |
| 12/31/95 | cyclophosphamide         | 1000 mg/m <sup>2</sup> | 980 mg x 3 days                              |
|          | cisplatin                | 100 mg/m <sup>2</sup>  | 98 mg x 1 day                                |

1/10 - 1/16 admitted for fever and neutropenia, given piperacillin and gentamicin

| Cycle 2 |                  |                        | $wt = 15.6 \text{ kg BSA} = .99 \text{ m}^2$ |
|---------|------------------|------------------------|--|
| 1/21/96 | cyclophosphamide | 1000 mg/m <sup>2</sup> | 990 mg x 3 days                              |
|         | cisplatin        | 100 mg/m <sup>2</sup>  | 99 mg x 1 day                                |

2/9 - 2/12 admitted for neutropenia and fever, given piperacillin and gentamicin 2/11 CT scan revealed no reduction in size of primary tumor; researched pilot protocol 2/18 L bone marrow biopsy: persistent NB, some maturation, aspirate clear

Changed to Pilot Protocol #5678

Cycle 3 (MESNA 496 mg/m² x 6 given with each dose of ifosphamide or cytoxan) wt = 15.6 kg BSA = 1.0 m² 2/18/96 ifosfamide 2 g/m² 2 g x 3 days etoposide  $150 \text{ mg/m}^2$  150 mg x 3 days

2/22 - 3/2 GCSF injections 10 mcg/kg/day, preventing fever and neutropenia

| Cycle 4 |             |                       | $wt = 16.6 \text{ kg BSA} = 1.04 \text{ m}^2$ |  |
|---------|-------------|-----------------------|---|--|
| 3/10/96 | carboplatin | 500 mg/m <sup>2</sup> | 520 mg x 2 days                               |  |
|         | etoposide   | 150 mg/m <sup>2</sup> | 155 mg x 3 days                               |  |

3/20 - 3/26 GCSF injections

| Cycle 5 |           |                       | $wt = 16.2 \text{ kg BSA} = 1.05 \text{ m}^2$ |
|---------|-----------|-----------------------|---|
| 3/31/96 | cisplatin | 40 mg/m <sup>2</sup>  | 42 mg x 5 days                                |
|         | etoposide | 150 mg/m <sup>2</sup> | 155 mg x 3 days                               |

4/5 - 4/14 GCSF injections

4/5 - 4/11 hospitalized for severe nausea and dehydration

| Cycle 6 |                  | _                     | wt = 16.1 kg BSA = $1.0 \text{ m}^2$ |
|---------|------------------|-----------------------|--------------------------------------|
| 4/22/96 | vincristine      | 1.5 mg/m <sup>2</sup> | 1.5 mg x 3 days                      |
|         | doxorubicin      | 60 mg/m <sup>2</sup>  | 60 mg x 1 day                        |
|         | cyclophosphamide | 600 mg/m <sup>2</sup> | 600 mg x 2 days                      |

4/25 - 4/30 GCSF injections 5 mcg/kg

5/1 - 5/6 GCSF injections 10 mcg/kg

5/22 CT: decreased tumor size to 4 x 1.7 cm, increased calcification, decreased adenopathy

5/22 BX: negative for NB

6/1 bilateral BX: positive for NB

6/1 surgery to remove primary tumor on RT adrenal and numerous affected lymph nodes

**Cycle 7**  $wt = 16.3 \text{ kg BSA} = 1.0 \text{ m}^2$ 

| - ,    |            |                       |                 |
|--------|------------|-----------------------|-----------------|
| 6/8/96 | ifosfamide | 2 g/m <sup>2</sup>    | 2 g x 3 days    |
|        | etoposide  | 150 mg/m <sup>2</sup> | 150 mg x 3 days |
|        |            |                       |                 |

# 6/12 - 6/22 GCSF injections 10 mcg/kg

**Cycle 8**  $wt = 16.4 \text{ kg BSA} = 1.0 \text{ m}^2$ 

| 7/10/96 | carboplatin | 500 mg/m <sup>2</sup> | 500 mg x 2 days |
|---------|-------------|-----------------------|-----------------|
|         | etoposide * | 100 mg/m <sup>2</sup> | 100 mg x 3 days |

<sup>\*</sup>note dosage change from what is listed on protocol (150 mg/m²)y

7/14 - 7/30 GCSF injections 10 mcg/kg

7/21 CT: 8 mm calcified node L of aorta; bone scan negative

8/11 bilateral BX: negative for NB

8/17 stem cell harvest; purged at CHLA

**Cycle 9**  $\text{wt} = 16.8 \text{ kg BSA} = 1.05 \text{ m}^2$ 

| -,      |              |                       |                  |  |
|---------|--------------|-----------------------|------------------|--|
| 8/24/96 | carboplatin* | 500 mg/m <sup>2</sup> | 525 mg x 1 day   |  |
|         | etoposide *  | 75 mg/m²              | 78.8 mg x 3 days |  |

<sup>\*</sup>dose reduction due to radiation treatment

#### Radiation Therapy

8/27 - 9/21 16 fractions of radiation to right abdomen, 150 cGy each for total of 2400 cGy Field size: 11.5 x 13.5 cm

| Stem Cell Transplant | $wt = 17.2 \text{ kg BSA} = 1.05 \text{ m}^2$ |
|----------------------|---|
|----------------------|---|

| 9/29/96 | carboplatin       | 667 mg/m <sup>2</sup>  | 700 mg x 3 days  |  |
|---------|-------------------|------------------------|------------------|--|
|         | etoposide         | 800 mg/m <sup>2</sup>  | 840 mg x 3 days  |  |
| 10/2/96 | cyclophosphamide* | 1800 mg/m <sup>2</sup> | 1890 mg x 2 days |  |

<sup>\*</sup>MESNA 348 mg Q3hrs

10/5/96 Stem cell infusion: 0.84 x 108 cells after purging.

During SCT, fevers were treated with piperacillin, gentamicin, vancomycin, and amphotericin 0.5 mg/kg. On 10/30, levels were high (gentamycin 13.4, vancomycin 46.6). Vanco, gent and pip were replaced with ceftozidine 1.5 g 3x/day. Although his hearing loss was credited to high levels of antibiotics, we first noted hearing deficit on 10/22. 11/13/96 Discharged on day +39 (after 47 days in the hospital) with ANC of 440.

Johnny received 17 platelet transfusions and 20 red cell transfusions during one year of treatment.

| TOTAL CHEMOTHERAPY DOSE 1995-1996 |                        |             |                       |  |
|-----------------------------------|------------------------|-------------|-----------------------|--|
| Etoposide                         | 4.725 g/m <sup>2</sup> | Doxorubicin | 60 mg/m <sup>2</sup>  |  |
| Carboplatin                       | 4.5 g/m <sup>2</sup>   | Ifosfamide  | 12 g/m <sup>2</sup>   |  |
| Cisplatin                         | 400 g/m <sup>2</sup>   | Vincristine | 4.5 mg/m <sup>2</sup> |  |
| Cyclophosphamide                  | 10.8 g/m <sup>2</sup>  |             |                       |  |

#### Follow-up Exams:

4/19/97 echo and electro cardiogram, nl 8/30/97 scoliosis films and immunizations, nl 3/3/98 eye exam, glasses 8/27/98 dental exam, no cavities 7/21/99 audiology exam (mild to profound hearing loss above 1500 Hz) 3/99 eye exam, new rx

7/99 echo and electro cardiogram (normal)

7/99 dental exam, no cavities

7/99 audiology exam (no change in hearing loss)

7/99 last physical exam and blood work with

oncologist (all labs normal) 7/99 Hepatitis C screening, neg

### HEALTH CARE PROFESSIONALS (1997-1999)

Dentist: Michelle Hauge, 1711 N Murray Blvd, CS 80996 (222) 596-1022

Audiologist: Marge Hale, Audiology Clinic, Evans Army Hospital Pediatrician: Rita Burt, Peterson AFB Clinic (222) 556-1121

Pediatric Oncologist: Anthony Christensen, Memorial Hospital, Colorado Springs CO

# CURRENT HEALTH CARE PROFFESIONALS (1999-present)

Physician: Vern E. Jones, 205 W 7<sup>th</sup> St, Fargo ND 58470 (111) 732-1234 Dentist: David Jackson, 19033 US 71, Fargo ND 58470 (111) 732-1122

Oncologist: Nathan Thomas, RMCC, 820 4th St N, Fargo ND 58122 (111) 234-2233

#### Other events:

Chronic infected toe nails 1996-1999 on various antibiotics on and off for 6 years, at age 9 given ciprofloxacin based on culture revealing resistant bacteria present (x-ray for growth plate closure in feet). Typical ingrown toenail surgery performed 5 times, problem resurfaced every time. In 2002 podiatrist (Dr. Williamson, Dakota Clinic) did surgery to remove sequestered infected tissue, problem resolved.

Broke right wrist 2001, surgeries in 2002 and 2003: required bone graft, and removal of pin, Olson, J Don MD (111) 222-3333; 2301 25th St S, Fargo, ND 58103

<u>Health Summary</u>: present health is good, with profound high-frequency hearing loss ( $\geq$  2000 Hz), no hearing aids, occasional respiratory problems, allergies, asthma

## **Prior History:**

DOB 03/19/92 Born Oakland Naval Hospital, Oakland CA Surgery for tubes in ears – repeated ear infections June 1993, Oakland Naval Hospital

Excellent health, normal hearing until NB treatment.

Immunizations complete until after transplant in 1996, reactions prevented more immunizations after transplant.

Family cancer incidence: (paternal side) grandmother breast and stomach cancer, aunt melanoma age 16 at death, aunt thyroid cancer



# Turning to End of Life

No parents should ever have to face the end of their child's life. The mere thought defies the natural order and is unbearable to each of us. Unfortunately, some children do lose the battle. Still, they and their families always remain a part of our NB family. Because this handbook is intended for the entire NB community, we concluded it should acknowledge the struggle of parents coping with their child's last illness. Thus, this chapter is our attempt to support those facing the most challenging thing imaginable.

Like every stage of a family's NB journey, the issues that arise at end of life vary depending on the child's disease and many other factors. Below are questions that have presented themselves to some parents, along with thoughts and guidance on these topics from NB angel parents. The statements below should not be taken as definitive--there simply are no "right" or "wrong" answers when one is facing the loss of a child. What follows are merely the very personal reflections of individual angel parents.

Despite the painful memories this topic evokes, these angel parents have lovingly shared their thoughts and insights, in the hope that they might allay another parent's particular concern, answer a troubling question, or merely let a parent know that others have had these experiences. We are very grateful for their courage, generosity and willingness to help others.

This is a work in progress, and we welcome assistance and any suggestions for improving it.

\* \* \* \* \*

# How do I know when it is the time to stop treatment? To stop transfusions?

"A lot will depend on how far the disease has spread; whether the major organs are involved; how much treatment the child has had already; what are the child's blood counts; will the child qualify for any clinical trials; how old is the child (may sound like a strange reason); can you travel to other parts of the country; financial situation for the family; religious beliefs; whether the child is responding to any treatment; whether the child is having severe pain; and many other things. A thought I had was -- is it better to have my child die of disease or from treatment, i.e., what is the best quality of life for the end of life."

"This is a very tough and difficult question and there is no correct answer to it. I think a parent will always think that, if I stop treatment, then I haven't done all I'm supposed to do for my child. 'A good parent doesn't give up!' At least that is the thought you will probably grapple with in your head."

"An older child may want to have a say in whether or not they want to continue with treatment. If the treatment will make them throw up or feel worse than they already are, they may not want to have more."

"I think most parents will go as far as they can with some sort of treatment until weeks or even days before the child's life ends".

"When to stop transfusion is a difficult question. One of the biggest fears a parent may have is having their child bleed to death because of low platelets, so they will continue with transfusions for as long as

they can. One thing to keep in mind and to discuss with your doctor and hospice nurse is whether or not transfusions will be effective. Depending on the extent of disease in the body, additional fluids such as red blood or platelets may actually cause even more harm, as the body may not be able to process it properly and they may basically cause the child to 'drown."

"When to stop transfusions? For us this was the easy decision. If the doctors couldn't save him, then why put him through having to go to the hospital every other day for transfusions. We kept him at home where he was happy. He was only 3 years old, but he told us he was tired of the hospital and going to the doctor's all the time."

# What do I consider in choosing whether to have my child on hospice at home or in the hospital?

"This may depend on a few factors: one may be your comfort level in helping your child at home with the medicines, such as morphine or other narcotics for pain control, and your comfort level in working with the morphine pump when the hospice nurse is not there. The other factor may be how sick your child is and where the disease has spread. If your child is still somewhat mobile and wanting to do things or go places, then your child can be cared for at home under the guidance of the hospice nurse. If the disease has spread to areas where your child needs special care and you feel more comfortable with having someone with you every minute, then the hospital may be a better place for you and your child. However, if you are at home then you can be more of a family, and not have to worry about traveling to and from the hospital if you want to bring other family members to visit. You may all be more comfortable at home."

"For us the hospital was just not an option. The hospital couldn't save him, so why make him be in a place he didn't like to be. He was home where he was most comfortable and had all of his toys and could do whatever he wanted to do."

"It is important to know that hospice can be available not only in the hospital setting, but also in specialized hospice centers and in the home. Some hospitals allow a child to remain in the current hospital room and transfer to hospice care with the appropriate hospital physicians and supportive staff coming to the child's room. Some families welcome the ability to remain in a room that they already know with familiar staff still available to them. Some hospitals require a move to a different floor, with transfer of care to physicians and staff that provide hospice care. In some cases this transfer of care may be to a different organization that provides hospice care for that hospital. Some families find this preferable because all care transitions completely towards supporting the child without the distractions of other families who are still fighting cancer. Hospice can also be transferred to the home setting, which can be the choice for some families who want their son or daughter to have all the comforts of home. In this setting, hospice provides the necessary medical devices and hospice staff comes to the home in order to provide care for the child."

# What sort of care is available for my child on hospice? What do I need to know about hospice to get the best care?

"Hospice does not have the goal of prolonging life, nor does hospice have the goal of hastening death. In order to be considered for hospice, a child must have a life expectancy of less than 6 months. The focus for the child transitions from treatment for the purposes of a cure to providing treatments that facilitate quality of life through pain control and supportive care. . . . most hospice providers will state that their primary goal is to provide comfort, peace, and dignity with the primary goal of pain control."

"It is important to learn what you can of the hospice organizations available to you, how they define hospice, and the point at which they limit their interventions."

"Parents should find out if the specific hospice organization regularly deals with children. Too many parents find out after the fact that their hospice provider only cares for children on an "occasional" basis. Pain control for children and other special issues of children are difficult for hospice professionals to understand if they don't work with children on a somewhat regular basis."

"The ability of the hospice to provide staff that can communicate and give the explanations you need, in order to understand what your child is going through, is vital to achieving the best care you can for your child. Hospice representatives should be willing and able to meet with and speak with you. . . . Unless the oncologist is able to write orders for and in conjunction with that specific hospice organization, ask your questions specifically of an individual employed by the hospice organization you are considering and who will be one of the employees implementing your child's care. Be sure to write your questions and the answers down, because as you have already learned, it is frequently difficult to remember all of the details later. This is a time of great stress, and your ability to remember the easiest of things will be challenged."

"Once care is transferred to hospice, treatments like red blood cells transfusions and platelet transfusions may or may not be able to be carried out depending upon the scope of practice of the specific hospice organization. Depending on the length of time since the last round of chemo this may or may not be a concern. Other treatments such as TPN nutrition may be able to be continued, or may need to be discontinued. Possibly nutrition may need to be administered via a nasogastric tube, jejunostomy tube, or G-tube if already in place. The determination of these types of decisions can be limited by the hospice's scope of practice. For some, it can ultimately be a source of relief that certain options are no longer available, as each intervention can have its risks and these risks can become more difficult to handle as a child becomes increasingly debilitated."

"Hospice care is covered differently depending upon whether your child's care is covered by private insurance provided by employers or individual policies, state-provided insurance, Medicaid, or in some cases on a charitable basis. Good social workers, caseworkers, and hospice social workers will be able to make this transition smooth. Unfortunately, wrong information can make a very difficult time even more difficult, and sometimes questions must be asked more than once and of more than one person in order to get the help needed even when one legally qualifies for it."

". . . it is nearly impossible to think of all situations and make all possible preparations. As you have learned throughout the time in treatment, you do the best you can with all that you are given and can find."

# How can I most effectively manage my child's pain?

"Hospice is nationally recognized as the expert on pain control, particularly for cancer patients. . . . the types of medications used for the purposes of pain control, the amounts used, and the frequency with which they can be used are based on how much medication has been used in the past, how much is currently in use, and how much (possibly several medications in conjunction with each other) may need to be used in order to effectively achieve pain control. Depending on the child's age and ability to communicate, the child and the parents are asked about symptoms, effects from the medications, and the level of medication at which the pain is controlled and, if possible, still allows the child to interact with her or his parents, family, and friends."

"If you have a good pediatric hospice service they will be around whenever you need them. Ask them any question you can think of. Make sure they are used to giving children narcotics, as some services are reluctant to do so and that is not what you want. Always talk with the hospice nurse and coordinate pain control between him/her and your oncologist. You want to maintain a good quality of life for your child with as little pain as possible. If your child is having "break through" pain you may have to up the regular dose of pain meds so as not to have too many boluses in between the regularly scheduled infusion. Use more than one drug if you have to in order to get the pain under control. Bone pain is very severe and can come on very suddenly and last for a long time until you can get the dosing

right. Be aware that a drug-induced coma may be the only solution to keep your child from suffering with severe pain. Every child is different, and some do not have any pain and can succumb to the disease quickly and peacefully."

"I did everything myself but adjust the morphine pump. The hospice nurse came once a day to check on him, but we did the rest."

### How do I make the most of my child's time?

"This will depend on your child's condition. Some children are still able to go places and do things with reasonable comfort. Do the things they want to do. Take a lot of movies of your child, take pictures, make hand prints, tape record their voice, touch them all the time, smell them, take a lock of their hair. Do as many things as a family as you can even if it is just sitting and watching TV. "

"I wish that someone had told me from the very beginning to take a million pictures, videos, recordings, etc. I don't know how you tell someone that from the beginning, but there has to be a way. Rather than waiting until near the end of life to record your child's voice etc, because we are not all given that opportunity in the end. . . ."

"Let them do whatever they feel like doing and want to do. Take tons of pictures and videos, take a lock of hair if they have any. Get their hand and foot print. Just spend every moment with your dying child."

"It is such a difficult situation and decision when hearing the word hospice. For so long you believe in the hope for a cure for your child. You have to maintain hope but transition the focus of hope for precious quality time spent with your child and hope for a peaceful passing. Make each moment of each day count and create positive family memories that you will treasure in the days and years to come. One thing I am so thankful that we did was to get many family photographs taken. Even though you have probably taken more pictures that you can count of your child, make sure that you have photographs that capture your family unity and love."

#### How do I talk to my child with neuroblastoma?

"This can be difficult. Some parents are afraid to tell their child they are dying. And it depends on the age of the child. With many older children, you have to tell them it is okay to stop fighting and they can now rest. I think some of the children want to know that you will be okay once they are gone. They worry about you since you are so sad and you cry a lot. Some parents can't say anything to their child about dying. If the child is very young, they would not understand what dying is. I don't think there is a right or wrong way to do this. Some say speak honestly about it. I couldn't tell my son he was dying. I just couldn't."

"No matter the age and developmental level, always listen to your child, whether verbal or nonverbal, and be open to discussing your child's illness and how they are feeling. I felt with my four year old daughter that she knew more about her prognosis and what was happening than I did at times. Surround them with your love and emotional support. Be sensitive to their needs, questions they may have and stories they may tell you. Many children may talk about angels or heaven and I believe it is so important to be open to exploring their visions or ideas and to respond sensitively. My daughter spoke often about her fairy friends that were helping her, loved her, and would show her heaven and bring her back again. I truly believe my daughter's words and I treasure the discussions we had about the fairies. They brought a sense of comfort to both her and me and I believe with all my heart that my daughter was telling me about the fairies to reassure me that everything was going to be okay. Maintaining open communication with your child can provide them with a sense of trust and confidence through which they can express their feelings and thoughts."

# What do I tell the siblings of my NB child?

"I think it is important to be honest with the brothers & sisters and tell them the truth so they can prepare themselves too. This will depend on the age(s) of the siblings."

# How to I get the support I need from family, friends & others?

"If anyone offers to help, let them. If you don't want a lot of visitors have a person designated to kick everyone out if need be. Take it easy on yourself and your other children. Let friends take your other kids out for a while to give you and them a break."

"Support from family and friends runs all across the board. Some are very helpful and are there all the times that you need them. And others will only stay around for a little while before they get tired of it and move on with their lives. They expect you to do the same. Seek counseling if you have to. It is difficult to get siblings to go for counseling depending on their age(s)."

# What do I need to know about the dying process (since no one is telling me about this)?

"This will depend on where the disease has spread to I think. In our case it took a while before the major organs were affected. The urine will slowly turn an orange/brown color from the liver starting to fail. The darker it is the worse the liver is getting. The child will have difficulty urinating due to the morphine or other narcotics. The child's breathing will get more labored. They will sleep more. The pain may intensify causing the need for more morphine or other painkillers. The child may get delusional from the spread of the disease and/or the narcotics. The actual act of dying itself is very peaceful. The heart stops and that is all."

"Thankfully for our son it was very peaceful. He just closed his eyes and was gone five minutes later."

"Unfortunately some children do not have a "peaceful" ending. Some lose their sight, experience seizures, vomit blood, or have respiratory distress syndrome that can last a short time or a version that stretches out over a day or more, which is very, very hard to hear and watch. There are other very difficult scenarios. One possibility is to speak at length about what is to come with a physician or hospice nurse who knows the child's specific situation. Of course, they don't know everything, but an educated guess about what may happen can be better than having nothing else to go on. One mom told me her hospice nurse warned her to have dark colored towels so her pre-teen daughter would not be scared when she began to vomit blood. The mother was so very glad she was told that, because it helped so much in their situation."

# What do I need to know about planning and making final arrangements?

"Many parents will make final arrangements prior to their child's death. This is so, so hard! It is an unnatural act. But they may plan a celebration rather than a sad ceremony."

"My husband and I had made the decision shortly after we were told our son's diagnosis that we would have him cremated if in fact he died. I am glad that we made that decision then. It gave us the knowledge that the decision was made  $\dots$ "

"We didn't make any arrangements until after our son had died. I wish we had planned earlier, then I would have remembered everything I had wanted to do (like have a balloon release)."

"I was fortunate in that my son's memorial was recorded. I have listened to it once since then. I am glad, because I remember so little."

"Although we made our son DNR in the hospital, once we got him home we did not have the necessary paperwork in place to keep the local paramedics from trying to intervene if they were called in. Due to this, I waited several hours after he died before we called the oncologist to tell them that he had died and what time. The oncologist was good to us to simply sign the death certificate for the time that I reported. Due to certain laws, etc, the paramedics had to be called anyway to state that there did not appear to be any child abuse, etc. That is certainly something I would never have thought of then, but of course now it makes sense ... I remember this huge fireman walking into our bedroom. The doorway and ceiling is only 6 foot at that one point, and he was muscular and filled the doorway. I told him, "Don't you touch him. It is too late now." I think that fireman actually knew that in that moment it would be over my dead body before he laid a hand on my son. He wisely agreed..."

"I remember that some ladies at my church organized a meal for the extended family that came in from out of town. Stuff like this helps so much as entertaining all of the extended family and friends is simply beyond one's capability."

"I had let my primary care physician know that I expected I would need some medicinal help after my son died. I most certainly did. Although I was already on an antidepressant before we learned he had relapsed, the day he died I became a non-functioning human. I took Xanax after his body was taken from me, and it helped me keep from losing my mind. I literally felt as though I would lose my mind. It is more difficult than can be put into words. I know some people can cope, but I could only get through each day waiting for time to pass until I could begin to cope. It is a very, very long and difficult process ..."

# How do I let go? What is my role in releasing my child to a journey I have not experienced?

"I didn't let go until he stopped breathing and his heart stopped. I knew the day he died that he was going to die that day. I got up that morning and I felt God tell me that was the day. He slept most of his last day. He woke up right before he died and told me again that he loved me forever and made me promise again that I would be ok. I told him I would and how much I loved him too. I told him to go to God when he was ready and five minutes later he was gone. I felt his soul leave his body and felt him watching us cry from above."

"At the funeral home if your child is small enough for you to hold and you want to hold your child, then DO IT! The funeral director we had laid our son in my lap and I slept in the funeral home holding him all night the night before his funeral. It gave me some closure."

"Although I kept my son with me for several hours after he died, I have read about other parents keeping their son or daughter with them for a day, and then even going to the funeral home and spending more time with their son or daughter's body to say goodbye in their time as they needed. I find that few people realize they have choices that they can make, but in that state it is very, very hard to make those choices. My husband carried my son from my lap in a chair in our bedroom to a stretcher the funeral home brought into our house. I wish I had had my husband carry his body all of the way to the waiting van. It is not something I tear myself up over, but had we been thinking, we would have done that. The gentleman that took his body out on the stretcher asked us if we wanted to wait before he covered up his face and head. I told him to wait, and we all watched from our porch as they took his body to the van, and then covered his face and body."

"Watching your child endure so much and decline in the end and the helplessness knowing there is nothing more you can do to save your child is the most painful experience a parent can ever go through. The one thing that you can do is let your child know the wonderful impact that they have had on so many peoples lives. Let them know how very proud of them you are and that they are so brave. Let

them know how much you love them and will forever and ever. What a good brother or sister, daughter or son, granddaughter or grandson, cousin, niece or nephew they are. Let them know what a good mother or father they have been to their pets or favorite doll or stuffed animal. No matter how difficult, promise them that you will be okay and that is okay for them to go."

# What thoughts do you have about the time ahead without our children?

"In the coming days and years remember your promise you made to your child, "I will be okay" and live by that promise for your child...they will want you to."

"In my own way, by my posts on NB Angels and now on Angel On My Shoulder, I keep a journal of sorts that I print out and put in my scrapbooks. Shortly after my son died I asked people to write to me about memories they had of him, and one lady had saved every email update I had ever sent out. I am really glad to have all of those updates now. Time is a thief, and I write down as many specific memories of my son that I can."

"The isolation you feel, after your child dies, is beyond words. So many people give you unsolicited advice ("you should go back to work", "you should move on") that you isolate yourself just to get away from these people. These people tend to be those that you love even, and so the isolation becomes even worse. People mean well, but you learn to stay away from them. Life takes on new perspectives in that you are no longer capable of putting the time and energy into people who talk to hear themselves talk without having any real clue. There occasionally is a wise person who will ask you how you feel, and then after you give them the words that shut them up, will quietly ask you, "Ok, how do you really feel?", and then actually listen. These are precious people who tend be older and wiser souls despite their young physical age, and they are few and far between. Mostly, they tend to be other parents who had a child die. So the lists like NB Angels and Angel On My Shoulder are a support system where we can say the things we can't say anywhere else."

"A quote I really like is 'the measurement of one's life is their enduring impact.' All of our children will be remembered forever until we meet again."

Please contact editors@nbhope.org with any comments



# **Directory of Online Resources**

This Directory is an evolving list of resources for parents of children with cancer. We need your input to add to it and make it as helpful as possible to NB parents! If there is a resource you have found to be helpful that is not listed here or if you have further information about (or corrections to) any of the following, please send the information to <a href="mailto:editors@nbhope.org">editors@nbhope.org</a> Be sure to check with your hospital social worker for *local* resources, especially with regard to lodging.

# **Advocacy**

#### Childhood Cancer Ombudsman Program

http://www.childhoodbraintumor.org/ombuds.html

Provides complaint investigation and resolution for families of children with cancer and adult survivors of childhood cancer. A service of the <a href="Childhood Brain Tumor Foundation">Childhood Brain Tumor Foundation</a>.

http://www.childhoodbraintumor.org/services.html

Fax: (804) 580-2502

# Children's Cause for Cancer Advocacy

http://www.childrenscause.org

Advocacy and education for safer and effective treatments for childhood cancer.

#### National Coalition for Cancer Survivorship

http://www.mcmcllc.com

Oldest survivor-led cancer advocacy organization in the country.

# Patient Advocacy Coalition

http://medicalreporter.health.org/tmr0497/PAC.HTM

Helps resolve insurance coverage issues.

#### Patient Advocate Foundation

http://www.patientadvocate.org

Safeguards patients through effective mediation to assure access to care, maintenance of employment, and preservation of their financial stability. (800) 532-5274; fax: (757) 873-8999

# **Bone Marrow Transplant Information and Fundraising**

#### **BMT** Infonet

http://www.bmtinfonet.org

Information and emotional support to patients and survivors of transplant.

#### The Bone Marrow Foundation

http://www.bonemarrow.org

Resources, information, programs, and services about bone marrow and stem cell transplantation.

# Cord Blood Donor Foundation (CBDF)

http://www.cordblooddonor.org

Provides educational and public awareness and promotes further research into use of umbilical cord blood stem cells from live birth for the treatment of disease.

### Cryobanks International

http://www.cryo-intl.com

For-profit organization for collection, processing and banking of umbilical cord blood stem cells.

### National Foundation for Transplants (NFT)

http://www.transplants.org

Helps patients fundraise for transplant expenses.

# National Marrow Donor Program

http://www.marrow.org

Donor registry and information about donor blood and marrow transplants.

# National Transplant Assistance Fund and Catastrophic Injury Program

http://www.transplantfund.org

Helps patients fundraise for transplant expenses.

800-642-8399

# ViaCord - Cord Blood Banking and Research

http://www.viacord.com

For-profit umbilical cord blood banking and information.

### Caregivers - Advocacy and Support

#### CancerCare

#### http://www.cancercare.org

Support for cancer patients and their families. Financial assistance, information and referrals, community and professional education, counseling, and practical help.

# CaringBridge

# http://www.caringbridge.org/

Free website service for keeping friends and family informed during treatment.

### CarePages

# http://www.carepages.com/

Free website service for keeping friends and family informed during treatment.

#### Family Caregiver Alliance

http://www.caregiver.org/caregiver/jsp/home.jsp

A public voice for caregivers; programs include information, education, services, research, and advocacy guidance for how caregivers can affect public policy.

#### Lotsa Helping Hands

http://www.nfca.lotsahelpinghands.com

A volunteer coordination service for friends, family, colleagues, and neighbors to assist loved ones in need. It's an easy-to-use, private group calendar, specifically designed for organizing helpers. <a href="mailto:info@lotsahelpinghands.com">info@lotsahelpinghands.com</a>

## National Alliance for Caregiving

http://www.caregiving.org

Supports family caregivers and professionals who help them; increases public awareness of issues facing family caregivers.

# National Family Caregivers Assoc

http://www.nfcacares.org/

Support and advocacy for caregivers of loved ones with a chronic illness or disability.

Never-Ending Squirrel Tale

Practical tips, encouragement, humor, sharing, for the parents of kids with cancer—just like sitting around the clinic, only more stories!

# Share the Care

http://www.sharethecare.org/

A grassroots organization dedicated to preventing "caregiver burnout by promoting and educating people about the benefits of group caregiving using the SHARE THE CARE $^{\text{TM}}$  model."

(646) 467-8097

Email: info@sharethecare.org

# Strength for Caring

http://www.strengthforcaring.com/

An online resource and community for family caregivers that helps family caregivers take care of their loved ones and themselves.

866-466-3458

# The Wellness Community

http://www.thewellnesscommunity.org/

Connect with others who know what you're going through as a cancer patient or a caregiver.

### Children as Patients - Support

#### Chai Lifeline

http://www.chailifeline.org/index.php

Chai Lifeline is a not for profit organization dedicated to helping children suffering from serious illness as well as their family members. We offer a comprehensive range of services to address the multiple needs of patients, parents, and siblings.

### Chemo Buddy Club

http://www.chemobuddyclub.com/

Unique gifts and gift baskets for the cancer/chemo patient, information, and encouragement.

# Children's Miracle Network

http://www.childrensmiraclenetwork.org/

Improves the lives of children by raising funds for children's hospitals across North America. 801.278.8900

# The Hole in the Wall Gang Camps

http://www.holeinthewallgang.org/about/mission.asp

Provides children with cancer and other serious illnesses and conditions a high quality camping experience.

# Believe In Tomorrow Children's Foundation

http://www.believeintomorrow.org/

Provides hospital and retreat housing services to critically ill children and their families.

## Songs of Love Foundation

Provides personalized songs to chronically or terminally ill children and young adults.

#### Chemo Angels

Brightens the lives of cancer patients while they are going through this challenging time.

### Make A Child Smile Organization (MACS)

Provides emotional support to children with chronic or life-threatening illnesses and their families.

#### HopeKids

http://www.hopekids.org/index.aspx

# Hugs & Hope Club for Sick Kids

A ministry of encouragement for children battling critical illness.

#### Post Pals

Cards for ill children.

# Children's Cancer Camps

## ACOR list of camps

http://www.acor.org/ped-onc/cfissues/camps.html

# Children's Oncology Camping Association

http://www.coca-intl.org/

currently has 65 member camps in the US

http://www.cancerindex.org/ccw/guide2s.htm

#### **Clinical Trial Information**

# Clinicaltrials.gov

http://clinicaltrials.gov/

Search database of thousands of clinical trials, provided by the US National Institutes of Health (NIH), through its National Library of Medicine (NLM).

# National Cancer Institute

http://www.cancer.gov/clinicaltrials

Search NCI's list of 5,000+ clinical trials, find recent clinical trial results, learn what clinical trials are, how they work, why they're useful, patient care costs, and more.

# **Drugs and Supplements**

#### BC Cancer Agency - BCCA Cancer Drug Manual

www.bccancer.bc.ca/HPI/DrugDatabase/DrugIndexPro/default.htm

A fairly comprehensive database on oncology drugs—health professional summaries give information on indications, pharmacokinetics, dosing, and side effects.

#### Mayo Clinic Drugs and Supplements

http://www.mayoclinic.com/health/drug-information/DrugHerbIndex

# Memorial Sloan-Kettering: Herbs, Botanicals, and other Products

http://www.mskcc.org/mskcc/html/11570.cfm

#### National Center for Complementary and Alternative Medicine

http://nccam.nih.gov/

# Financial Resources - Private & Nonprofit

American Cancer Society (ACS)

# http://www.cancer.org

Through local offices has some assistance available for expenses such as transportation, home care equipment, wigs, and babysitting; scholarships for cancer survivors.

#### CancerCare

# http://www.cancercare.org

Support for cancer patients and their families. Financial assistance, information and referrals, community and professional education, counseling, and practical help.

#### Cancer Fund of America

http://www.cfoa.org/

Free products, such as nutritional supplements, candy, small toys, and miscellaneous items, application

http://www.cfoa.org/downloads/APPLICATION.pdf

# Children's Cancer Fund of America

http://www.ccfoa.org/

For cancer related expenses not covered by insurance. Average grant \$50.00.

# Disabled Children's Relief Fund (DCRF)

http://www.dcrf.com/

Provides disabled children with assistance to obtain wheelchairs, orthopedic braces, walkers, lifts, hearing aids, eyeglasses, medical equipment, physical therapy, and surgery.

#### First Hand Foundation

# http://www.cerner.com/firsthand/

Helps families of children with health problems address the financial aspects of their child's healthcare.

# Jessica's Hope Chest

#### http://www.4jhc.org/index.html

Assists families with critically ill children and helps with costs of necessities not covered by private medical insurance and/or government medical assistance programs.

#### National Children's Cancer Society (NCCS)

http://www.nationalchildrenscancersociety.com

Some financial assistance for travel, meals, lodging, medical expenses not covered by insurance for families with need: application

http://www.nationalchildrenscancersociety.com/NetCommunity/admin/NetCommunity/Document. Doc?&id=22

# The Partnership for Prescription Assistance

https://www.pparx.org/Intro.php

Help for qualifying patients who lack prescription coverage to get needed medicines free or at reduced

1-888-4PPA-NOW (1-888-477-2669)

Partnership for Prescription Assistance for Kids

http://kids.pparx.org/

#### Financial Resources - Government

Medicaid (called "Medical Assistance" in some states)

http://www.cms.hhs.gov/MedicaidGenInfo/

For disabled children (and adults) who qualify; apply through your county. Eligibility varies by state. Jointly funded by federal and state. Pays medical expenses, travel, lodging, meals, and drugs -- works as a secondary insurance (paying co-pays, deductibles, other) after your primary insurance is billed.

### State Children's Health Insurance Program (SCHIP)

http://www.insurekidsnow.gov/

A Federal-State partnership that offers low-cost or free health insurance coverage to uninsured infants, children, and teens.

See information for each state

http://www.insurekidsnow.gov/states.asp

1-877-543-7669 (1-877-KIDS-NOW)

# Supplemental Security Income (SSI)

http://www.ssa.gov/d&s1.htm

Information about SSI for under 18

http://www.ssa.gov/applyfordisability/child.htm

& for over 18 http://www.ssa.gov/applyfordisability/adult.htm

Note: High-risk and recurrent neuroblastoma are listed as disability indications (but other factors are considered for determination). Benefits are retroactive to DATE OF APPLICATION not date of diagnosis, so it is important to apply immediately after diagnosis for maximum benefit. See the SSA's disability evaluation for childhood cancers in the Blue Book

http://www.ssa.gov/disability/professionals/bluebook/113.00-NeoplasticDiseases-Malignant-Childhood.htm#113.21Neuroblastoma

SSI monthly payments are for those with disability, very low income, and minimal resources. For child over 18, the family's income and resources are not included even if the child lives at home. In most states, once disability is approved (with or without SSI payments) the child is automatically eligible for Medicaid (also called Medical Assistance), which serves as a primary or secondary insurance.

## **Health Insurance**

healthinsuranceinfo.net

http://healthinsuranceinfo.net/

What Cancer Survivors Need to Know About Health Insurance

http://www.canceradvocacy.org/resources/pubs/pdf/Health%20Insurance\_Book.pdf

Insure Kids Now!

www.insurekidsnow.gov

A Federal-State partnership that offers low-cost or free health insurance coverage to uninsured children of low-wage, working parents.

#### Managing Care, Managing Claims (MCMC)

http://www.mcmcllc.com

Offers customized managed care, medical bill review, and integrated service programs.

Ph: (800) 227-1464 Fax: (617) 375-7777

Patient Advocacy Coalition

http://medicalreporter.health.org/tmr0497/PAC.HTM

Helps resolve insurance coverage issues.

# **Hearing Device Assistance & Resources**

The Starkey Hearing Foundation

http://www.sotheworldmayhear.org/contactus/

Committed to assisting deaf and hard-of-hearing persons with limited financial resources who permanently reside within the United States.

John Tracy Clinic

http://www.johntracyclinic.org/

Free services worldwide for parents of infants and preschool children with hearing loss.

Miracle Ear Children's Foundation

http://www.atk.ku.edu/hearingaidfunding.htm

Provides new or reconditioned "Miracle-Ear" hearing aids and services free of charge to families who have hearing impaired children ages 16 years or younger, with an income level that does not allow them to receive public support.

http://www.hdhearing.com/Learning/Part3.htm

http://www.hdhearing.com/Learning/Part2PDF.PDF

# Hospice

### Information/Medical Research about Neuroblastoma & Treatment

CancerGuide

http://cancerguide.org/scurve\_basic.html

Primer explaining survival curves and statistics used in medical literature.

Especially good essay on "The Median is not the Message" by Stephen Jay Gould http://cancerguide.org/median\_not\_msg.html

http://www.ncbi.nlm.nih.gov/sites/entrez?db=PubMed

MedlinePlus

http://medlineplus.gov/

A service of the US National Library of Medicine and the National Institutes of Health; includes descriptions of diseases, medical dictionary, encyclopedia, index of drugs and supplements.

emedicine

http://www.emedicine.com/

Cell Stem Cell

http://www.cellstemcell.com/

Nature Medicine

http://www.nature.com/nm/index.html

OncoLink

http://www.oncolink.com/

Harvard Links

http://mcb.harvard.edu/BioLinks/Immunology.html

AMA

http://www.ama-assn.org/

Online Medical Dictionaries

http://cancerweb.ncl.ac.uk/omd/

http://www.nlm.nih.gov/medlineplus/mplusdictionary.html

http://www.medterms.com/script/main/hp.asp

Science in the News Weekly http://www.americanscientist.org

Walter Reed Army Institute of Research

http://wrair-www.army.mil/Resources/library/Library.asp

U.S. Food and Drug Administration

http://www.fda.gov/

Harvard Health & Medical Information

http://www.health.harvard.edu/

National Library of Medicine

http://www.nlm.nih.gov/

Cancer Survival Toolbox

http://www.cancersurvivaltoolbox.org/

In Chinese, English, and Spanish

National Cancer Institute http://www.cancer.gov/

Rare Cancer Alliance (RCA)

http://www.rare-cancer.org/

Disseminates information and provides support to all pediatric and adult rare cancer patients.

Patient-Centered Guides

http://www.patientcenters.com/

Patient-Centered Guides are a mix of medical, practical and emotional information, grounded in Western medicine, told by people who have been there.

# Lodging

ITM Hospitality Fund

http://www.itmhospitalityfund.com/pages/512431/index.htm

Joe's House

http://www.joeshouse.org/

Ronald McDonald House Charities

www.rmhc.org

Provides a "home away from home" for families of seriously ill children receiving treatment at nearby hospitals.

# **Support for Parents and Patients**

Neuroblastoma Foundations Pediatric Cancer Foundations

Alex's Lemonade Stand

http://www.alexslemonade.org/

St. Baldricks Foundation

http://www.stbaldricks.org/#

American Red Cross

http://www.redcross.org/index.html

Cure Search

http://www.curesearch.org/

Hope Street Kids

http://www.hopestreetkids.org/

Gilda's Club

http://www.gildasclub.org/

Advocates the importance of emotional and social support for anyone touched by cancer.

The Sparrow Foundation

http://www.sparrowfoundation.org/

Assists with fundraising for medical needs.

517.364.5680 call to verify

Kristin's Friends

Financial assistance - computers, laptops medical equipment and help with insurance-related issues for families with life-threatening illnesses.

410-239-8154

Kelly Ann Dolan Fund

www.kadmf.org

Financial assistance with rent. Provides video on family financial management.

215-643-0763

Justin Scott Foster Foundation

http://www.jsffoundation.com/index.html

Creates public awareness about childhood cancer, gives special awards to children in treatment and financial assistance to families are in financial crisis, funds pediatric cancer research.

Special Love, Inc.—Virginia

http://www.speciallove.org

Emergency funds for families participating in the camp program who are in need; college scholarships for children diagnosed with cancer.

The Candlelighters Childhood Cancer Foundation

http://www.candlelighters.org

Provides information, peer support, and advocacy through publications, an information clearinghouse, and a network of local support groups, and maintains a list of organizations to which eligible families may apply for financial assistance. 800-366-2223

# Association Cancer Online Resources

http://www.acor.org/

Provides support, information, and community to everyone affected by cancer and related disorders

#### Cancer Kids

http://www.cancerkids.org/

A web-based organization that helps children with cancer tell their stories to the world.

# Survivorship & Late Effects

# The Cancer Survivors Project

http://www.cancersurvivorsproject.org/index.html

An organized, international community of long-term cancer survivors and their friends working together to improve the lives of children and adults after cancer.

## Survivor Alert

Part of ongoing efforts nationally to educate adolescent and young adult cancer survivors about research showing that an early history of cancer creates a need for lifelong follow-up care, and to motivate them to take charge of their health.

# National Coalition for Cancer Survivorship

Survivor-led cancer advocacy organization.

### Long Term Follow-up Guidelines

Prepared by COG (Children's Oncology Group) and provides recommendations for screening and management of late effects after childhood cancer treatment.

# **Long-Term Treatment Complications**

Prepared by Memorial Sloan-Kettering, with detailing potential late effects from specific chemotherapy agents, and other treatments. See a brief overview at after childhood cancer.

#### <u>Candlelighters</u>

Good information, including two articles published in 2006 *New England Journal of Medicine* on results of the Childhood Cancer Survivor Study and information on late effects on the drop-down menu under the "Treatment" button on the home page. Parents also can order a copy of Nancy Keene's book "Educating the Child with Cancer" from their store.

#### ACOR's Ped-Onc Survivors listserv

a great source of information and support

ACOR also maintains a list of survivorship clinics

# **Transportation**

#### Air Care Alliance

Supports the Nationwide Community of Charitable Aviators

Maintains a list of all free air flight services for medical and other needs; updated regularly.

#### American Airlines Miles for Kids in Need

Provides transportation (with donated miles) for children up to the age of 23 in need of medical treatment; patient must be recommended by a social worker.

(800) 421-0600

#### **AMTRAK**

Offers a rail fare discount to passengers with disabilities. To receive the discount you must book your reservation by telephone or at a ticket counter. Discounts are not available through online booking.

# **Continental Airlines**

Compassion (Bereavement) Fares

Corporate Angels

## Northwest Airlines KidCaresSM

Donated WorldPerks® miles are used to provide free air travel for a child, accompanied by one parent or guardian, to obtain needed medical treatment.

Phone: (612) 726-4206 Fax: (612) 726-3942

## National Patient Travel Center

Facilitates patient access to appropriate charitable medical air transportation resources in the United States.

1-800-296-1217

# **Operation Liftoff**

Provides transportation for children with a life-threatening illness for treatment or dream trip

# Wish Granting Organizations

List of wish granting organizations

http://www.familyvillage.wisc.edu/general/wish-grant-orgs.html

Make-a-Wish Foundation

http://www.wish.org/

Children's Dream Fund

http://www.childrensdreamfund.org/ez/

Helps make critically ill children's dreams come true.

Please contact editors@nbhope.org with any comments

# Travel Guide: Bethesda MD (NIH)

One of the places you may end up taking your child for NB treatment is the National Institutes of Health, or NIH. This is the U.S. government's National Cancer Institute, and it is located in Bethesda, Maryland, right outside of Washington, DC.

If you fly into Washington, DC, the NIH offers shuttle buses free of charge from the major airports. There is a schedule on the NIH website. You can also drive to the NIH. Since 9/11, there is very tight security. Your vehicle and your belongings will be inspected upon entry onto the campus. You will also be given a security badge that is just temporary. Ask the staff at the clinical center about arranging for a permanent security badge. It will last a year, and it will make coming and going from the campus very easy. You will also need a security badge to enter the campus from the Metro. There is a Metro station right on the campus, and it makes it a breeze to go enjoy Washington, DC and all it has to offer.

Once a patient at the NIH, your expenses are paid for, as well as the treatment. Travel is covered, as well as meals, scans, tests, and the drugs administered. Literally the only expense you will have is the cost of travel to get to the NIH for the first visit.

You will most likely stay at The Children's Inn at NIH. It is a wonderful facility, renovated just a few years ago. The accommodations are very comfortable and the staff there is used to dealing with all kinds of patients and their families. You will stay in a hotel room that includes a television with cable, a full bathroom, and two double beds. Linens are provided free of charge, but you are expected to keep your room clean and to clean it when you leave. There is maid service but not daily. There are washers and dryers provided, as well as laundry detergent. Whether you stay one day or two months, The Children's Inn staff will try to make your stay as comfortable as possible.

One restriction enforced is that you cannot eat in your room. That is fine, because there are several very large kitchens with eating areas. You are assigned a refrigerator that you share with two or three other families, as well as a pantry. The Inn provides a lot of basics, like condiments, dishes, pots and pans. There are also daily grocery store runs to stock up on what you need. There are even grills outside to use when the weather is nice. You can also order out from a large variety of restaurants in Bethesda and the surrounding area that will deliver. The main desk keeps a folder of menus.

The Children's Inn provides specific refrigerators for medicine that needs to be kept cold or things like a 24-hour urine collection. There is a bank of computers specifically for children, and a business office for adults. The Children's Inn also has an exercise room. There are flat screen televisions throughout the Inn with the schedule of activities, the airport shuttle schedule, the local date and time, and a running ticker of the latest news. A constant shuttle service is provided from the Inn to the clinical center for treatment, which is good since the walk to the clinical center is straight uphill!

Another benefit of the Inn is free long distance calls, so having no cell phone is no problem. The room phones can be used only for local calls, but free long distance calling is available on the many telephones in the hallways at the Inn. The NIH staff likes for you to sign in and out of the Inn, just so they know where you are, and how to get in touch with you should they need to discuss any changes in treatment or other items.

The NIH has a cafeteria that, while small, is still quite good, and has a small coffee shop that stocks snacks and other items you may need. It also has a library and a chapel.

The NIH has an active child life organization, and The Children's Inn provides several activities for children and parents to enjoy. For example, there are trips to the local zoo and sporting events, and dinners at local hotels. There is bingo (with great prizes), and arts and crafts activities. There are large screen televisions, air hockey and video games, and an outdoor play area. Each child is assigned a mailbox - not for regular mail, but for regular gifts! Each day your child will receive a special little gift - or maybe several.

The NIH voucher office is where you will be reimbursed for travel and meals. This will need to be coordinated with your clinic. When the first appointment is made for your child, you will be discussing these matters with the patient coordinator. Also, the coordinator will make the first reservation at the Children's Inn. After that point, you will make all the follow up reservations at the Children's Inn yourself, either at your discharge from the first visit, or on-line or by phone.

Many families from all over come to the NIH and stay at The Children's Inn. Right beside the main desk is a map of the world; take the pin related to your room, and put it on your hometown. It is amazing to see how far some children come for treatment. There always seems to be someone to talk to or play with at the Inn and at the clinical center. Other parents reach out to each other, and children make lifetime bonds within moments, let alone days.

These two websites have all the information you will need about the NIH: www.childrensinn.org and www.nih.gov

Please contact editors@nbhope.org with any comments



# Travel Guide: Memorial Sloan-Kettering Cancer Center (MSKCC)

Address: 1275 York Avenue, New York, NY 10065

Website: www.mskcc.org

The prospect of taking your child for cancer treatment to any city other than your hometown is daunting -- make that city New York and it is even more so for most families. But, New York City can also become like a second home. The hospital is located in a safe, friendly, residential Upper East Side neighborhood, and the city has much to offer on days when your child is feeling well and free from the hospital. We hope to make the adjustment easier by providing information on many of the things that may impact your stay.

#### Directions:

From the airports—Cabs are the most convenient way to get to the hospital area from the area's airports, especially if you are carrying much luggage. However, cabs can be expensive, running from \$25-\$30 from LaGuardia to \$40-\$50 from JKF or Newark. A car service can be comparable in cost in some cases. One useful website for transportation options is <a href="www.nysubway.com/airport">www.nysubway.com/airport</a>. It gives you approximate costs, times, and 'best bets' on all the alternative methods of transportation.

By car --If you are driving your own car, you have several options for local parking garages, but there is only one garage that MSKCC validates parking for patients at the Pediatric Day Hospital; however, first you have to fill out a form registering your car, which is available from the Pediatric Day Hospital staff. More information on parking and driving directions is available on the MSKCC website at the following link: <a href="http://www.mskcc.org/mskcc/html/5308.cfm#286690">http://www.mskcc.org/mskcc/html/5308.cfm#286690</a>

# Where to stay:

**Ronald McDonald House:** 405 E. 73rd Street, New York, NY 10065 (On 73<sup>rd</sup>, between 1<sup>st</sup> Avenue and York Avenue, 6 blocks from the hospital) 212-639-0100.

If this is your first treatment away from home, 'the Ronald' (as the locals call it) can be a great place to feel connected to other people going through exactly what you are going through. Kids tend to make new friends very easily and the Ronald soon becomes your home away from home. You can find a good photo tour of the property at their website <a href="www.rmdh.org">www.rmdh.org</a>, which will give you a sense of what the facility looks like. There is also a link for making a reservation via email, if you choose. The charge for the rooms is very low or free depending on income—work through the MSKCC social worker to determine the current cost. There is sometimes money to subsidize the cost for families. The rooms at this Ronald McDonald House are much like hotel rooms. Each floor has laundry facilities and guest rooms. The first two floors and the basement are the primary shared living areas, including a large living room, kitchens and dining area, and a great playroom.

#### More details on the NYC Ronald McDonald House:

1) You may go through the MSKCC NB social worker to reserve your room, and you can usually confirm your room a day or two in advance.

- 2) Each family is assigned to one of several shared kitchen spaces, which are located just off the large communal dining room. Each family is given a kitchen number, an assigned storage space, and a refrigerator that is shared by the small number of other families assigned to the same kitchen.
- 3) The kitchens are fairly well stocked with cooking equipment, but there isn't much in the way of a shared pantry for basics. You may decide it is just easier to order carryout from the hundreds of restaurants in the area that deliver. The front desk has a folder of menus. (A favorite is Delizia Pizzeria, just around the corner on 1st Ave.)
- 4) Although there is no regular evening meal served by volunteers as in some other Ronald McDonald Houses, on many days and evenings there are special events, often with food and drinks provided.
- 5) Linens and towels are provided. You are expected to leave all linens clean and folded when you check out. (If you have an early check-out/departure flight, you should consider bringing your own linens from home).
- 6) Laundry facilities are free of charge, but are frequently busy.
- 7) The front desk is staffed 24 hrs a day and staff is available to help in any late-night emergencies.
- 8) Rooms are equipped with DVD players, VCRs, flat-screened TVs, and cable, and a library of DVDs is available for check-out at the front desk. The living room and playroom also have libraries of books for all ages.
- 9) There are many grocery stores, drug stores and delis close by on 1st Avenue.

# Transportation to/from RMH:

In good weather, it is a pleasant 10-minute walk to the hospital, but there is weekday shuttle to and from the hospital (sign-up at the RMH front desk). They also have a limited amount of strollers and wheelchairs available to loan out. If you prefer to take a taxi, they are easy flag down from either 1st Ave or York Ave. It is not possible to call for a taxi for a pick up, but there are car services that can be called (e.g, Carmel at 212-666-6666).

#### If RMDH is full:

There a many hotels within a short distance of the hospital. The Ronald McDonald staff may make suggestions, you can consult with the social worker, or you may find additional hotel and long-term housing help on the hospital website <a href="www.mskcc.org">www.mskcc.org</a> (go to New Patients and then look under Accommodations). Hotel rates are high, running about \$200 or more per night. The hospital website also provides help through the Patient Representative Department at 212-639-7202.

#### Things to do in the area:

Central Park is within walking distance from the hospital and the Ronald. There you can find playgrounds, the historic Carousel (\$1.50 per ride) and the Children's Zoo with its penguins, polar bears, and petting zoo. Down the street from the RMH towards York Ave. is The Little Shop of Crafts where kids love to pick out and paint ceramic pieces (50% discount to guests of the Ronald.) Other city favorites are the huge Toys R Us in Times Square, FAO Swartz, American Girl Store, Dylan's Candy Bar, the Museum of Natural History, the Metropolitan Museum of Art and the Children's Museum of Manhattan, Broadway shows, and the Mets or the Yankees. There is of course tons to do and see in NYC, so you might want to do some on-line research before arrival to identify things of particular interest to your family.

## **NAVIGATING THE HOSPITAL**

Prior to your first visit to MSKCC, it can be helpful to look through the hospital's website, starting with the Pediatric Cancer Care homepage, where you can find a photo tour of the pediatric facilities, pictures of the neuroblastoma team members, and much more. The site lists all the things you need

to bring with you—insurance information, social security number of your child, etc. There is a lot of very helpful information there to help prepare you for coming to MSKCC.

# To find the Pediatric Day Hospital (PDH):

You may enter the hospital through four different entrances (through main entrance at York Ave., or from 67<sup>th</sup> or 68<sup>th</sup> Street or First Ave.), so learning the layout can be helpful. The PDH is located on the 9<sup>th</sup> floor and is accessed from the "B" elevators (on the 68<sup>th</sup> Street side of the building). There are staff/security near all of the street entrances who can direct you.

#### The first visit:

You will first check-in with the staff at the registration desk near the elevator on the 9<sup>th</sup> floor or the registration desk at the end of the lounge area. They will give the patient a bracelet, should be able to tell you whom you are seeing and where you need to be, and can often give you a printout of your appointment schedule for the day. On your first visit to MSKCC you will probably meet with the financial consultant, one of the NB doctors and/or nurse practitioners, and will have bloodwork and other tests run. These events may happen in any order, and there may be lots of waiting. You may be able to take care of most of the insurance issues beforehand over the phone, but may still need to sit down briefly with the insurance/financial consultant, who is conveniently located nearby.

# A few tips:

- 1) Come prepared to stay for several hours—there are lots of activities, games, and even Nintendo systems in the playroom, but not much for adults.
- 2) There are complimentary coffee, juice, and some food available in a small kitchen off of the waiting area. Depending on the time of day and day of the week there may be bagels, sandwiches, donuts, and other surprises. Mini-boxes of cereal are available virtually all the time.
- 3) If you want to use the internet, there are a couple of computers in the waiting area available for patient/family use. You may also bring your own laptop and plug into one of their high-speed internet connection outlets—but this requires the right cable which you must bring yourself. These outlets are also located in each treatment room.

# Dining options:

- 1) The hospital cafeteria has a wide range of things available and can be convenient. The surrounding neighborhood has a huge number of food options from Dunkin' Donuts to gourmet fare—all within one block of the hospital. Many will deliver to the hospital.
- 2) If you are receiving treatment and assigned a room in the PDH, you may order lunch for your child and one caregiver as part of the hospital's service. There is a limited menu that you order from in the morning, and it is delivered directly to your treatment room.

# Other services:

- 1) The child life staff arranges events and activities every day. Check out <a href="www.mskcc.org">www.mskcc.org</a> for more details under Pediatric Cancer Care. From regular visits by clowns to karate, yoga, cooking, and crafts, there is always something happening.
- 2) There are also group sessions for teens and tweens, as well as for caregivers, that meet at least once each week.
- 3) School services are provided through the New York Public Schools with several teachers who are in the PDH each weekday. (These are provided for those who are of a legal age to attend school in NY, i.e., kindergarten and above, with a different teacher for lower and higher grades.) You may bring materials from your home school or the teachers will provide lesson materials for your child. Sometimes they work one-on-one with your child, and other times they work with a small group.

4) Depending on what type of treatment your child will be having, there are other support services available through the hospital. Ask the social worker to help you navigate which will be most appropriate for your child.

# Inpatient Unit:

The inpatient unit is also located on the 9<sup>th</sup> floor. Although it is connected to the PDH, access between the two is not allowed. Direct access is from the M elevator bank right off the main waiting room (these elevators are reached most easily from either the main entrance on York Ave. or the 68<sup>th</sup> Street entrance). The inpatient side has its own smaller playroom with a few computers for patient and caregiver use. If patients are not feeling up to it, or are in isolation, child-life specialists or volunteers are usually available to bring toys, games, books and DVDs to rooms. Arrangements can be made to have someone play and watch over your child while you shower or just take a break. For caregivers there are a kitchen with free coffee and juice, showers and a laundry room available (laundry soap is for sale in the gift shop). The clowns stop by inpatient rooms a few times a week, and there are activities for patients each night throughout the week; e.g., Thursday there's bingo and Friday is candy-cart and movie night.

### Unique to MSKCC:

Because there is a team of several doctors and nurse practitioners who specialize in NB, you may see a different doctor each day of treatment, or maybe not even see the doctor at all. They may check on your child indirectly if you are established in a treatment plan and things are going along smoothly and as intended. However, this is not to say they are not involved or that you will not see them regularly and whenever you need to. The doctors are always available and are checking on you, but you will have the most direct daily contact with the nurse practitioners on the NB team.

If you have been treated at other large-city hospitals, MSKCC shouldn't be too different. However, if you are from a small town, the size of the hospital, the large number of patients, and the general hustle-bustle can be a bit of an adjustment. You may feel at first that you are a very small cog in a large institutional wheel. However, very shortly you will grasp that you are in a world-class facility, that your child is being cared for by the finest experts, and that the myriad of support services are second to none. You will get to know not only the routine at MSKCC but the best place to get coffee and pizza on First Avenue, and will be on a first-name basis with the many wonderful people involved in your child's care -- and soon you will feel like an honorary New Yorker.

Please contact editors@nbhope.org with any comments



# Travel Guide: Philadelphia, PA (CHOP)

#### CHILDREN'S HOSPITAL OF PHILADELPHIA

Address: 34th and Civic Center Blvd., Philadelphia, PA 19104

Website: www.chop.edu

**Directions:** For driving directions and public transportation to CHOP, as well as maps and a virtual tour, go to www.chop.edu. You may also call the Travel Directions Hotline at 215-590-7275.

**Parking:** Signs will direct you to the Wood Center Parking Garage. Once you park, take the building elevator to the building you are visiting – either the Wood Center for clinic or the main hospital. Get more specific directions from the information desk, a security guard, or a CHOP employee. *Make sure you get your parking validated so that parking will be \$3.00.* 

#### WHERE TO STAY:

Ronald Mc Donald House 3925 Chestnut Street Philadelphia, PA 19104 215-387-8406

This "home away from home" is available to those traveling more than 25 miles to CHOP. Cost is \$15/night per family based on room availability; reserve by calling the House directly or through the nursing or social work staff.

Sheraton University City Hotel 36<sup>th</sup> and Chestnut Streets 215-387-8000

For additional hotel information, go to www.chop.edu.

#### More on the Ronald McDonald House:

- 1) Call the house **on the day of your attended arrival between 10am and 1pm** to confirm your room. If the house is full, RMH will try to place you in a local hotel. The Ronald McDonald House in Camden, NJ is also an option.
- 2) All families, no more than 5/room, must check in by 8pm on the day of arrival. There is free parking in the RMH parking garage.
- 3) Sheets and towels are provided.
- 4) The kitchen pantry contains free food for families during their stay, based on availability of donated items. A home-cooked meal is provided for guests each evening by volunteers from the community. Free milk and juice is also provided.
- 5) Shuttle Service: Two vans provide transportation on a regular schedule to and from CHOP.
- 6) Laundry rooms are available. Bring quarters. If you are in-patient at CHOP, there is a free laundry room in the Ronald McDonald lounge on the oncology floor. Transplant patients will need to wash special blankies or stuffed animals daily so bring extras.
- 7) Ask the Philly RMH to send you a welcome packet containing directions, rules, and alternate housing.
- 8) An RMH social worker is available to assist families.

9) Best of all is the large playroom with craft area, computers, puppet theater, playhouse, and loft area with video games and books. There is also a teen area with billiards and large screen TV. A small exercise area and a nice outdoor playground provide physical activity.

#### NAVIGATING THE HOSPITAL

Before You Arrive: Go to <a href="www.chop.edu">www.chop.edu</a> and select "Programs and Services" and "Your Visit." These online resources introduce you to the CHOP:

# Welcome Folder (752K)

This downloadable folder prepares you for your stay at The Children's Hospital of Philadelphia. You'll get quick tips on how to talk to your child about hospitalization, what to bring, how to get here, where to stay, and how to keep in touch while your child is in the hospital.

# Patient and Family Guide video

This online video shows you what to expect during your stay at The Children's Hospital of Philadelphia. You'll learn how to identify caregivers, find your way around, access family resources, get visiting policies, arrange for school classes and more.

#### Hospital Virtual Tour

Our interactive Virtual Tour lets you visit the Hospital in the comfort of your own home. See points of interest such as our child-friendly Atrium, patient rooms, Operating Room, Connelly Resource Center for Families, cafeteria and ATMs, and call our contact numbers for more information.

Wonderful Website for Children: www.kidshealthgalaxy.com

# What you'll find on Kidshealthgalaxy.com

- Information for children ages 6 to 12 about coming to the hospital, and what to bring with you for an overnight stay
- A kid-friendly virtual tour of Children's Hospital
- Descriptions of some of the people you may meet when you visit
- Animated movies describing some common medical procedures, like having an x-ray or getting an IV
- Definitions of medical equipment kids are frequently exposed to in a hospital setting
- An online pre-operative tour, describing what it's like to have an operation at Children's Hospital
- Games and activities

Research has shown that children who are prepared for healthcare experiences have better outcomes. Whether your child is coming to Children's Hospital for the first time or has visited us before, this site will help your visit go more smoothly.

| what to Bring to CHOP for an Outpatient Clinic | V1S1t |
|--|-------|
|--|-------|

| Appointment information           |
|-----------------------------------|
| Doctor's name                     |
| Department building name/location |

|   | Name and telephone number of your referring physician  |  |  |  |
|---|--|--|--|--|
|   | Name and telephone number of family physician (if different from above)  |  |  |  |
|   | Insurance cards  |  |  |  |
|   | Insurance referral immunization record   |  |  |  |
|   | Medical or personal records (X-Rays, lab tests). If you are unsure of what to bring, please call the outpatient office you are scheduled to visit.   |  |  |  |
|   | A list of questions you may have for the physician. If your child is old enough, help him or her to add to the list too.                             |  |  |  |
|   | Social security number of the patient and both parents (for insurance purposes)  |  |  |  |
|   | Child's birth certificate (if name has been legally changed)   |  |  |  |
|   | Another adult to assist you if you must bring other children   |  |  |  |
|   | Books, games, snacks, formula, diapers, change of baby clothes or other necessities. (Please do not bring food if your child must fast for testing.) |  |  |  |
| Wha   | at to Bring to the Hospital for a Day Surgery Procedure  |  |  |  |
| If your child is staying overnight, pack a suitcase with a change of clothing for yourself and your child. Children's pajamas and slippers are available at the hospital. Also, pack an empty bottle or sippy cup to use after the surgery. Older children may bring headphones or a hand-held game to help them relax. |  |  |  |  |
| Wha   | at to Bring to the Hospital for an Inpatient Stay  |  |  |  |
|   | Bathrobe   |  |  |  |
|   | Infants/toddlers: favorite toy or item from home (please limit to one or two small items)  |  |  |  |
|   | School age/teenagers: books, magazines, cosmetics, school work   |  |  |  |
|   | Insurance and Medical Assistance Information (including subscriber and access cards)   |  |  |  |
|   | Name/phone # of your family physician & others involved in your child's care   |  |  |  |

#### AMENITIES AND SUPPORT AT CHOP

#### Family Services:

# Connelly Resource Center

The Connelly Resource Center for Families and other family resource rooms are quiet places to take a break or nap; browse through information on healthcare, finances, parenting and education; speak with the family librarian; surf the Internet; attend a coffee hour or select children's books and videos. A Family Learning Center in the Connelly Center offers many classes to help families learn new skills needed to care for their children in the hospital or at home.

# **Child Life Services**

The staff of the Child Life, Education and Creative Arts Therapy Department help children, teens and family members cope with the healthcare experience through developmentally appropriate activities

for children, education about and preparation for medical procedures and through emotional support.

Social Worker - Stephanie Fooks, fooks@email.chop.edu, 215-590-3445

Religious - Chaplain Jack Rodgers and Sister Alice Strogen, 215-590-1147

<u>Sibling Support</u> – **Sibshops** is a program run quarterly and is open to all siblings in the hospital. Child Life and Social Work is available to work with siblings one-on-one.

Hospital Pharmacy - 1st floor of the Main Hospital, 215-590-1147

# **Inpatient Services:**

<u>Unit Playroom</u> – open all the time. If your child is in transplant, you must schedule time daily. <u>Ronald McDonald House Lounge</u> – open all the time. This cozy lounge has a kitchen with refrigerators, coffee, and a sink. There's also a seating area with magazines, books and a TV. You'll find a free washer and dryer. Special events include weekly suppers, massage, haircuts, and support or informational meetings.

<u>Internet Availability</u> – most rooms have wireless internet

Wheel Chairs - found throughout the hospital

Inpatient Kitchen - The Ronald McDonald Room

<u>Sleeping</u> – 2 parents are allowed to sleep on the South side, however CHOP will only provide bedding for one. Families can bring an air mattress or sleeping bag.

# Dining:

<u>Cafeteria</u> – located on the main lobby/atrium level. Large cafeteria has a deli, sushi, fresh fruit, snacks and sweets. Vending machines and a coffee bar are available in the main dining area.

McDonald's - located on the main lobby level/atrium

#### Fun at CHOP:

<u>Gift Shop</u>- located next to glass elevator in main lobby/atrium. You'll find candy, toys, toiletries, cards, jewelry, plush animals and more.

<u>Atrium Play Area</u> – located in main lobby/atrium. Experience the moving art. Touch and play with health related displays. Gaze at the fish tank. Bring anti-bacterial wipes, especially if your child is immuno-suppressed.

# Activities, Stores and Restaurants near CHOP and RMH: NEED ADDRESS and (phone #'s just for restaurants)

- 1) Grocery Store The Fresh Grocer, 40th and Walnut St.
- 2) Post Office 30th and Market St.
- 3) Ben and Jerry's 40th between Walnut and Sansom
- 4) Drug Stores CVS, 34th and Walnut (next to the food court)
- 5) Penn Book Store 3601 Walnut St.
- 6) Food Court 34th and Walnut St.
- 7) Chinese Restaurant Beijiing Chinese Rest. on Spruce St. below 38th
- 8) Marathon Grill 40th and Walnut

9) Potbelly Restaurant – across from CHOP, attached to Penn Towers

# **Helpful Tips:**

- 1) When staying at a hospital or RMH, it's helpful to have a "pre-packed" 2 or 3 drawer plastic cart on wheels. You can store your child's favorite games and toys, art supplies, DVDs, snack items, restaurant menus and maps, storage containers and baggies, a corkscrew, etc. It's wise to have your own sponge in a sealable dish to wash your child's dishes so you don't have to worry about germs on a communal sponge. One of the drawers is a good place to stash little wrapped gifts for daily rewards. You'll find other "must-haves" to add to your drawers!
- 2) Some sanity stress-busters at CHOP include:
  - Strolling through the University of Pennsylvania campus. There's also an easy walk through the university to get to CHOP from the Philly RMH. Just ask at the RMH desk.
  - Enjoy coffee and browse books at the Penn Bookstore.
- 3) Visit CHOP's award winning website for even more at www.chop.edu

Please contact editors@nbhope.org with any comments



# Travel Guide: Chicago, IL Children's Memorial Hospital (CMH)

# Children's Memorial Hospital

Address: 2300 Children's Plaza Chicago, IL 60614

Phone: (773) 880-4000

Website: www.childrensmemorial.org

**Directions:** For driving directions and public transportation to Children's, as well as maps and a virtual tour, go to <a href="www.childrensmemorial.org">www.childrensmemorial.org</a> and click on "For Patients and Families" on the header bar. There is an excellent overview of shuttles and cabs from the airport as well.

**Parking:** Parking is on Lincoln Avenue across from the hospital. Parking is frequently limited, however there is complimentary valet parking in the garage once it is full. Once you park, cross the street to the main hospital building. *Make sure you get your parking validated so that parking will be \$4.00*. You can also pull up in the breezeway of the building and a valet will park your car for you and bring it to you upon leaving for \$1 more (per day- if you are inpatient, just get your keys from valet and move your car to a parking space in the evening).

# WHERE TO STAY:

# Ronald Mc Donald House

622 W. Deming Chicago, IL 60614 (773) 348-5322

This "home away from home" is available to those traveling more than 25 miles to Children's. Reserve by calling the House directly or through the nursing or social work staff.

# Kohl's House

2422 N. Orchard Chicago, IL 60614 (773) 975-8881 (ask for Michelle)

This facility is available to families who have selected a transplant procedure for their child. You can stay here during any transplant related activity, such as stem cell harvest, transplant preparation, or during the transplant process. More information about KH is available on the Children's website. Coordinate your stay by speaking with your stem cell social worker or nurse.

# **Discounted Hotels**

The following hotels offer discounted rates for families. Mention that your child is a patient at Children's Memorial Hospital when calling.

Children's Memorial shuttle service is available to select hotels. Please call the hospital's security services at 773.880.4223 to arrange transportation.

Travel Guide: Chicago, IL 13:081

- Belden-Stratford 2300 Lincoln Park West Chicago, IL 60614 1.800.800.8301
- <u>Days Inn Lincoln Park North</u> 644 W. Diversey Chicago, IL 60657 773.525.7010
- Inn at Lincoln Park 601 W. Diversey Chicago, IL 60657 773.348.2810

# Downtown hotels

Marriot Residence Inn 201 E. Walton 312.943.9800

# Neighborhood inns

- The Willows 555 W. Surf Chicago, IL 60657 773.528.8400
- Majestic Hotel 528 W. Brompton Chicago, IL 60657 773.404.3499
- City Suites Hotel 933 W. Belmont Chicago, IL 60657 773.404.3400

#### NAVIGATING THE HOSPITAL

Before You Arrive: Go to www.childrensmemorial.org and select "For Patients and Families" for a wonderful resource on the basics of the hospital and procedures.

# What to Bring to Children's for an Outpatient Clinic Visit (Clinic or Day Hospital)-

| □ Appointment information   |
|---|
| □ Doctor's name   |
| □ Department building name/location   |
| □ Name and telephone number of your referring physician                           |
| $\square$ Name and telephone number of family physician (if different from above) |
| ☐ Insurance cards   |
| ☐ Insurance referral immunization record  |

Travel Guide: Chicago, IL 13:081

| ☐ Medical or personal records (X-Rays, lab tests). If you are unsure of what to bring, please call the outpatient office you are scheduled to visit.  |
|---|
| $\Box$ A list of questions you may have for the physician. If your child is old enough, help him or her to add to the list too.   |
| ☐ Social security number of the patient and both parents (for insurance purposes)   |
| ☐ Child's birth certificate (if name has been legally changed)  |
| ☐ Another adult to assist you if you must bring other children  |
| Books, games, snacks, formula, diapers, change of baby clothes or other necessities. (Please do not bring food if your child must fast for testing.)  |
| Sanitizing wipes if your child is immuno-supressed  |
| -There is a great playroom in the waiting area for day hospital and clinic with volunteers. Your child and/or any siblings can play here while waiting. Anything from this playroom can be checked out during your stay at Day Hospital as well.  -There are coffee, tea, and snacks available in the lobby for you and/or your child. You can also order a meal for your child at Day Hospital. Just ask your nurse for a menu.  |
| What to Bring to the Hospital for a Day Surgery Procedure   |
| If your child is staying overnight, pack a suitcase with a change of clothing for yourself and your   |
| child. Make sure your child has items that make them comfortable, such as a favorite toy, blanket, or stuffed friend, game, or snack for after surgery (nothing too spicy or greasy, as they will be nauseous from anasthesia). Also, pack an empty bottle, sippy cup, or cup to use after the surgery. The hospital can also provide one for you. Older children may bring headphones or a hand-held game to help them relax. TVs are available in all pre and post-op rooms. DVDs available upon request. |
| or stuffed friend, game, or snack for after surgery (nothing too spicy or greasy, as they will be nauseous from anasthesia). Also, pack an empty bottle, sippy cup, or cup to use after the surgery. The hospital can also provide one for you. Older children may bring headphones or a hand-held game to help them relax. TVs are available in all pre and post-op rooms. DVDs available upon   |
| or stuffed friend, game, or snack for after surgery (nothing too spicy or greasy, as they will be nauseous from anasthesia). Also, pack an empty bottle, sippy cup, or cup to use after the surgery. The hospital can also provide one for you. Older children may bring headphones or a hand-held game to help them relax. TVs are available in all pre and post-op rooms. DVDs available upon request.  |

nurse)

DVDs, CDs, and video games are available to check out at the hospital- just ask your

| Insurance and Medical Assistance Information (including subscriber and access cards)  |
|---|
| Name/phone # of your family physician & others involved in your child's care  |
| Personal Care items for yourself and your child (there are limited basic items available if you forget)   |
| Book, magazine, or laptop computer for yourself (all of which are available to check out at the hospital as well). WiFi is available throughout the hospital. |

### AMENITIES AND SUPPORT AT CMH

# **Family Services:**

# Brown Family Life Center

The Brown Center is a fabulous place for parents and siblings to relax. It is sometimes available to oncology patients, but check with your nurse first. Usually germ control prohibits 4 West patients from leaving the ward. The Brown Center has a business center for parents, coffee, magazines and books, movies and video games, toys and activities, a teen center, and special programs throughout the week. It's a great place to step out and unwind a little. There are also free massages- just ask in the Brown Center and sign up on the weekly schedule.

<u>ParentWISE</u>- MAKE SURE YOU MEET SOMEONE FROM THIS PROGRAM WHILE YOU ARE HERE! This program, which stands for Parent Wisdom In Shared Experience, is a group of people who have had children going through treatment. They can share your experiences and give you advice about the hospital and procedures, as well as hope for your child's future. This is an amazing program!

<u>Family Ambassador</u>- This individual is a "wealth of knowledge" about the hospital and can fill you in on anything and everything you need to know. Ask your nurse or social worker who this is. It is typically written in on the board in your child's room.

<u>Child Life Specialist</u>- Heidi Thomalla- The staff of the Child Life Department help children, teens and family members cope with the healthcare experience through developmentally appropriate activities for children, education about and preparation for medical procedures and through emotional support. Heidi can also get your child on the schedule for an ART or MUSIC therapist. There are several at the hospital. A great video is available on the website: <a href="https://secure.childrensmemorial.org/parents/an-introduction-to-child-life-video.aspx">https://secure.childrensmemorial.org/parents/an-introduction-to-child-life-video.aspx</a>

<u>Social Worker</u> – The Social Workers will help you through any issues that arise, positive or negative, throughout your stay. They will help you manage financial, emotional, organizational issues you might have. Your social worker will vary depending on whether or not your child is transplanting. Please contact the Family Services Department at 773-880-4485

<u>Religious Services</u> – There are several chaplains available, but most prevalent on 4 West is Jim. Contact him or any other chaplain at 773-880-4005

<u>Case Manager</u>- Because of the overwhelming nature of the bills your family may be facing, you can request a case manager to act as a liason between you, the hospital, and your insurance company. Sometimes one is automatically sent to meet you, regardless of your financial or insurance situation. This person is very helpful and can help you as much or as little as you need.

Other services available at the hospital to families and detailed on the website are: Patient Relations, Interpreters, Educational Services, and Family and Child Advisory Boards

# **Inpatient Services:**

<u>Pharmacy</u>- On the first floor by the C elevators

<u>Unit Playroom</u> – This playroom is specifically for 4 West patients and their siblings. Please ask your nurse about times, as it is volunteer run and times vary.

<u>DVDs</u> and <u>Video Games</u>- You or your child can check out DVDs and Video Games at the 4 West desk. You can also rent a Video Game system or laptop based on availability.

<u>Internet Availability</u> – most rooms have wireless internet

<u>Parent Lounge</u>- Just outside the door to 4 West. Talk with your nurse about a key. You can use the microwave and refrigerator, rent a locker for your extra stuff (as storage in the room can be limited) as well as two private restrooms and a private lounge. You can request the private lounge for sleeping as long as you let your nurse know in advance.

<u>Parent Shower</u>- This is a private shower room with toilet and sink right outside the doors to 4 West. Talk with your nurse about securing a key. There are parent showers on every inpatient floor, so if yours is full, go upstairs to 5 or another inpatient floor. 5 is especially nice.

<u>Errand Solutions</u>- This is a great service, located in the basement across the hall from the cafeteria. There you can rent movies, drop off and pick up drycleaning, and receive help with other errands you may need while you are in town or in the building. Ask in the office for a full range of services.

<u>Sleeping</u> – 2 parents are allowed to sleep on 4 West, however only one is allowed in the room. You can check out a cot or reserve the private room by speaking with your nurse. The private room is nice, but truthfully if there aren't a lot of people, the playroom is a much quieter place since people are coming in and out of the lounge all night to use the bathroom.

<u>ATM and Stamps</u>- Both are located next to the back entrance to the cafeteria in the basement.

# Dining:

<u>Cafeteria</u> – Located in the basement. Offers a full salad bar with many unique choices, soup, pizza, full menu grill, daily lunch and dinner specials (usually have a Southern cooking theme), soda, baked goods, fresh sandwiches and salads, fresh fruit and yogurt parfaits, nuts and sweets, ice cream, and vending machines

<u>McDonald's</u> – Located in the basement. If you let them know your child is an oncology or stem-cell patient, and you request, they will cook your food fresh. Every employee, however, has been trained with very strict dietary rules and is very good about making sure your child is safe.

<u>Café</u>- Located on the main level in the lobby (just past the gift shop). Here they serve Starbucks coffee as well as tea, eclectic snacks, and a variety of little gifts. If your child has an audiology screening, he or she will undoubtedly fall in love with the "moving aquarium" which can be purchased here.

Ordering in the Room- You can always order a meal for your child in the room. If your child's current situation does not allow you to leave (i.e. transplant), you can also order a meal for yourself. Just let the person taking your order know that you are ordering two separate meals. You can always order a low-bacteria diet meal for your child while on transplant (they won't let you order anything else for them, but the menu is moderately varied). You can always order from the regular menu. If there is something you want that is not on the menu, just ask. They can send up special orders as well as portions of whatever is in the cafeteria, including specials of the day.

<u>Cruising Cart</u>- Several times a day, a cruising cart of sandwiches and snacks comes around. Ask your nurse about times for the day/week. This is a great way to grab a snack without leaving your child.

### Inside CMH:

<u>Gift Shop</u>- Located on the main level in the lobby. Here you can buy the traditional t-shirts, stuffies, balloons, crayons, etc. as well as unique jewelry or keepsakes. Gifts can also be purchased here or online to send up to a child's room.

<u>Café</u>- Along with a great cup of tea or coffee, you will find some fun gifts here.

<u>Lobby Play Area-</u> You can't miss all the buttons and displays in the main lobby when you walk in. Most kids will not be able to control themselves. There is also currently a mock patient room for the new hospital, coming in 2012. Kids love to play in there, too. It's a great "get acquainted" space before you head upstairs. Bring sanitizing wipes!

<u>Garden Courtyard</u>- Visible from the main lobby, this courtyard is a nice place to eat, sit, or play. It has some fun little animal statues hidden in the bushes for kids to find. Lots of great trees and fresh air. Many parents enjoy "breaking" here during transplant, when you aren't supposed to leave the hospital without showering upon re-entry. Access in the basement around the back corridor.

# **Outside CMH**

Chicago is an amazing city, and there's plenty to do if you're in the position to venture far enough. Check out <a href="www.cityofchicago.org">www.cityofchicago.org</a> for a great tourism guide. Click on the blue tab at the top "Exploring Chicago". If you're just in the Lincoln Park area around the hospital, though, check out the following places to eat, shop, or relax.

- 1) Grocery Store Dominicks- West on Fullerton Ave.
- 2) Post Office You may be able to do some basic stuff in the hospital at Errand Solutions, but a full post office is on Sheffield. Go west on Fullerton to Sheffield, then north (right). It's a decent walk (half mile)
- 3) Public Library- Walk west on Fullerton several blocks. Open every day but Sunday. (312) 744-1926
- 4) CVS- on Lincoln, north of hospital
- 5) Clarkes- great sandwiches- north on Lincoln- about 3/4 mile walk- worth the walk and the wait
- 6) Chipotle- South on Lincoln till you hit Orchard
- 7) Nan's Asian Food and Sushi- Across from the hospital on Lincoln- north of the garage
- 8) America's Dog Hot Dogs- Across from the hospital on Lincoln- south of the garage

- 9) Spicy Pickle Soups, Salads, Sandwiches- Across from the hospital on Lincoln- south of the garage- not for those with sensitive stomachs...
- 10) Subway- North on Lincoln past the McDonalds- next to CVS
- 11) Swirlz- the very best cupcakes you have ever tasted- next to Chipotle
- 12) Great shopping on Halsted, south of Fullerton, or on Webster which intersects with Halsted and Lincoln down by Oz park The shopping is west of the park, though- great little stores and boutiques. Also a pleasant walk if you need to get away. Clark Street (go east on Fullerton) is also a fun collection of restaurants and shops. Make sure you check during transplant to see whether or not your child can go inside public places.
- 13) Walk east on Fullerton to the lake, or as you pass, to Lincoln Park Zoo (large and free!) or the Notebaert Nature Museum. There's also a great harbor and lagoon to watch the boats, rowers, and ducks.
- 14) Catch an "El" Train (Elevated Train) to the city or airports on Fullerton, west of the hospital, just before the Dominicks. It's reasonably priced and safe. A train schedule, fares, and map can be downloaded or viewed at <a href="http://www.transitchicago.com/maps/">http://www.transitchicago.com/maps/</a>

#### Stress Busters-

- DePaul University is across the street on Halsted and a pretty walk.
- Oz Park is south of the hospital on Webster. A great playground is here along with sprawling areas to play Frisbee, read, or sit and relax. During lunchtime, though, it may be crowded with high schoolers from the nearby school as they have off-campus lunch.
- Park West Park is a beautiful little park nestled on Wrightwood. Walk north on Orchard to Wrightwood, turn west (left) and walk about a block and a half. It's tucked in on your lefthand (south) side so don't miss it! A nice alternative to sometimes crowded Oz Park, especially if you're staying at Kohl's House during your transplant and your child is very susceptible to germs.
- Starbucks just south on Lincoln has a nice indoor atmosphere.
- Origins on Halsted smells great and has bath products you can try in the store. If you ask, you may also receive a neck massage with some of their fantastic products.
- Brown Family Life Center is an excellent place to unwind or take siblings.
- Catch a cup of coffee or a meal and take it to the Garden Courtyard to be alone.
- Walk east on Belding, all the way to Lincoln Park Zoo if you want. It's a nice walk, and there are plenty of pretty homes to gaze at. The same is true for Fullerton, but it's not quite as peaceful.
- The Lincoln Park Zoo is a wonderful, large zoo. There are paddleboats and plenty of places to tuck yourself in and have a quiet moment. It's also FREE!

Please contact editors@nbhope.org with any comments



# Travel Guide: Burlington, Vermont (UV)

One of the options for treatment of either refractory or relapsed neuroblastoma is at Fletcher Allen Health Care/Vermont Cancer Center in Burlington, Vermont. Dr. Giselle Sholler and her team have developed a clinical trial utilizing nifurtimox along with two chemotherapy agents (topotecan and cyclophosphamide) as well as Zometa to treat our children. Other preclinical studies are ongoing.

### THE HOSPITAL

Fletcher Allen Health Care is located in Burlington, Vermont on the campus of the University of Vermont. Several neuroblastoma families are seeking treatment there, primarily those who have already tried other options for refractory or relapsed NB. It is a small center for such a busy oncology practice, but Dr. Sholler and her team do everything practicable to make it easier for the families.

For example, there is no pediatric oncology unit - neither a specialized clinic or inpatient unit. Pediatric oncology outpatient treatment is at the Children's Specialty Clinic - where other specialties are housed as well. The infusion bay is for the entire Specialty Clinic. There are three very small bays where chemo and transfusions are handled. Bone marrow aspirates and biopsies are done in the Specialty Clinic as well - not in outpatient surgery. If you do go there, ignore the people in Admissions - it does not matter how many times you tell them, they still insist you go to outpatient surgery for a bone marrow procedure.

The hospital itself is a maze of different buildings built at different times. The Children's Specialty Clinic is in the main hospital, as is Admissions and Registration. Scans and the inpatient unit are done in an older part of the hospital. It can be confusing, but everyone is very helpful, and once you get to the main hospital entrance, someone will point you in the right direction. We always found a wheelchair if we needed it, and there is plenty of underground parking at the hospital. The clinic will stamp your ticket so that you do not have to pay for parking. Additionally, if you have a handicapped placard from your home state, parking is free.

Vermont does not issue handicapped placards to non-residents; however, the state does honor any other state's handicapped placard. If your child needs handicapped parking, then do this before you come to Vermont and bring the placard with you. Even if your child is ambulatory when you leave your home state, this might be a good idea, since the nifurtimox trial can cause pain and problems with walking.

The food in the hospital is relatively good. Vermont is known for lots of food products, including Ben & Jerry's ice cream, Cabot cheese, and of course, maple syrup. Vermont locals are also proud of being "green" and eating lots of organic foods.

There are a lot of child life therapists at Fletcher Allen, and they are very good at entertaining the children.

### WHERE TO STAY

There are many hotels in the area, and the hospital is only about ten minutes away from the airport.

The Ronald McDonald House in Burlington is on South Winooski Avenue. The hospital is just about a mile up the road - but it is a long mile and straight uphill. The RMH does have a shuttle van, and the social worker (Penny DeGoosh at the time this was written) can help with cab fare vouchers if necessary.

The RMH is an old Victorian house that has been renovated, and was given to the RMH organization by the church that sits next door. Some rooms do not have televisions, and even though there is WiFi access for computers, it can be spotty. The rooms are comfortable, and can fit four nicely. A few of the rooms are actually suites, with a bedroom, living room, and bathroom. The kitchen is fully stocked and every day someone brings dinner. The RMH also provides staples like eggs, milk, butter, and juice, and has some donated items like cereal, soup, and spaghetti sauce and noodles. There are two large refrigerators, but they are usually packed to the hilt with leftovers and guests' personal items. There is very little dry storage for guests. There is a playroom and a large yard with a playground. The director, Pam, and house manager, Amy, are very accommodating and can arrange for anything you need. During a recent visit, they were acquiring small refrigerators in each guest room for medications that must be refrigerated.

The best part of the RMH is its location. It is one block away from Church Street - a five-block section of downtown Burlington that is closed to vehicle traffic, and has tons of restaurants and shops. It is a very pleasant place to spend time for everyone in the family. It is also only a few blocks away from the waterfront. Burlington sits on the shores of Lake Champlain. There is a beach close by, and the waterfront has a walking/running/biking path.

The RMH has also arranged for guests to have temporary passes to the YMCA and the local library. Some people stay at the RMH for an extended time, and some families have even enrolled their children in the local schools. There is an elementary and middle school four blocks away from the RMH.

### **ACTIVITIES**

Vermont is very small, and filled with things to do to keep your family active. It is also relatively easy to find your way around. Some examples:

Ben & Jerry's ice cream factory - tours, samples and museum Cabot cheese factory - tours, samples and museum Vermont Teddy Bear factory - tours Pizza Putt - kind of like a big Chuck E Cheese Fairbanks Museum - lots of stuffed (real) animals, Vermont history Skiing - Vermont has so many ski resorts, too many to mention! ECHO - an aquarium and Lake Champlain museum

### TRAVEL

Burlington has an international airport, although it is very small. There is only one waiting room for outgoing flights. There are a lot of rental car places in the airport. It takes ten minutes to get to the hospital and the RMH from the airport. Turbulence can be expected when you fly in because of the mountains that surround Burlington.

### **WEATHER**

Expect eight months of winter - and tons of snow. Still, everyone there knows how to deal with it. The roads are usually plowed promptly and everything continues on as normal during a big snowstorm. The summer months usually have ideal weather with comfortable highs and lows. If you are going in the winter, take snow boots and layer everything. Sometimes the highs don't get above

the teens. Each business and the hospital overcompensate, and heat inside buildings is usually very warm.

#### Websites for more information

Details about the clinical trial:

http://www.cancer.gov/search/ViewClinicalTrials.aspx?cdrid=558526&version=HealthProfessional&protocolsearchid=4711221

Story and slide show about Dr. Sholler with some patients: www.burlingtonfreepress.com/legacy/slideshows/040808neuroblastoma/index.html

Ronald McDonald House Vermont:

www.rmh-vermont.org

Ben & Jerry's Factory Tour:

www.benjerry.com/scoop shops/factory tour/

Cabot Cheese Factory Tour:

www.cabotcheese.com/f1.php?left=menu-visit.html&right=visit.html

Vermont Teddy Bear Factory Tour:

www.shop.vermontteddybear.com/tour-essentials.html

Fairbanks Museum:

www.fairbanksmuseum.org

ECHO Museum:

www.echovermont.org

Pizza Putt:

www.pizzaputt.com

Please contact editors@nbhope.org with any comments



# Finding Other Families: Listservs and On-line Communities

After our children were diagnosed with neuroblastoma, most of the parent authors of this Handbook felt alone in a way never known before. Family and friends circled around us in support, many of them with stories of family members and friends who had been cured of cancer. But it didn't always help. What we wanted was to connect with other neuroblastoma parents, and know that their kids were okay. We wanted to hear success stories from people who had experienced exactly what we were facing.

One parent recalls the day she finally met another stage 4 neuroblastoma family at her hospital -- the child was close in age to hers and had responded successfully to treatment. She recalls needing to meet them like needing to eat that day. It gave her the first real sense of hope she had felt since her child's diagnosis.

If you are reading this, chances are you're a parent, family member, or close friend of a child with neuroblastoma. Whether you're right at the beginning of the journey or several months into it, you may have few or no acquaintances in the neuroblastoma community. If you wish to reach out and connect with other neuroblastoma families (and not every parent does), know that it can easily be done. After reading this short section of the Handbook, you will have the ability to connect with hundreds of neuroblastoma families -- online, by phone, or even in person. Support, hope, and neuroblastoma success stories from those who have walked the walk are definitely out there.

The largest support group of NB parents can be found online –on the N-BLASTOMA listserv sponsored by the Association of Online Cancer Resources, or "ACOR." For many of us, finding this group was like finally glimpsing a lighthouse from a stormy sea. You can subscribe to the group on the ACOR website. Click on "MAILING LISTS" at <a href="www.acor.org">www.acor.org</a> and look under "N" or go to <a href="http://listserv.acor.org/archives/n-blastoma.html">http://listserv.acor.org/archives/n-blastoma.html</a>. You will see N-BLASTOMA listed. Click on "join or leave the group" and you can join the group immediately.

N-BLASTOMA is an active online group of parents from hospitals across the country and around the world. Its members offer general support as well as information and personal insights about any and all aspects of neuroblastoma treatment (including frontline and relapse). Currently there are over 650 subscribers, all of them families and friends of children with neuroblastoma. Posting a question or a "hello" on the N-BLASTOMA listserv will get you responses within hours, or sometimes even minutes, depending on the urgency of your message. You will find lasting, valuable connections with parents who have experienced in the past or are facing now exactly what you're going through.

Once you join, posts can be sent directly to your e-mail. Some parents have found it helpful to create a filter using N-BLAST as the filtering keyword, and a separate folder for this mail to be sent to, like "NB" or "N-BLAST". This way, any e-mail from the forum will be sent to a separate folder and will not take over your Inbox. The emails can also be received in a daily or weekly digest.

Keep in mind that there is no requirement to "post." The N-BLASTOMA listserv is in effect an online bulletin board and, if desired, you can monitor and benefit from it without ever revealing your presence.

Another online support group (newer and currently less active) can be found on the Children's Neuroblastoma Cancer Foundation website. Go to <a href="www.nbhope.org">www.nbhope.org</a>, and at the top of the home page, under "Community," select "Forums." Here you can join the forum, and posts can be viewed on the website or sent to your e-mail.

Many neuroblastoma parents have found it invaluable to become friendly with the other pediatric cancer families at their hospital. Even if you connect with a family whose child does not have neuroblastoma, chances are they know someone who does. They can connect you with other families, and so on. It often evolves into a network of local parents that you can talk with, meet for coffee, or even schedule time together with your children. No one understands your child's weakened immune system like another family who's been there, and issues such as special accommodations or last minute cancellations won't bother a parent who has had to cope with a sick child of their own. Many parents form close relationships that continue long after their children's treatments have ended.

You could also mention to the nursing staff and social worker of your hospital that you would like to meet other neuroblastoma families. Although privacy laws prohibit them from giving you names, phone numbers, room numbers, or any other information, once you tell the hospital staff that you'd like to be contacted, they will pass your contact information along to someone else with your permission.

If you have a local cancer resource center, it may offer the opportunity to connect personally with local cancer families. Many such centers, primarily those in urban areas, offer programs, networks, and support groups for families. Even if support groups are not available, your local center may be able to connect you with other families in the area just by taking down your contact information and spreading the word.

You can also network with parents of children with neuroblastoma at annual conferences and other events held by various pediatric cancer foundations. The Children's Neuroblastoma Cancer Foundation has an annual conference for neuroblastoma families, offering presentations by neuroblastoma specialists and social events for the families. Many of the parents on the N-BLASTOMA listserv attend this annual conference in order to connect in person with each other. Events for families are also sponsored by Curesearch, Alex's Lemonade Stand, the Rally Foundation, etc. (although these are foundations focusing on funding research for all pediatric cancers). By registering on the websites of such foundations you can receive updates of their events.

If you haven't done so already, consider starting a <u>CaringBridge</u> or <u>Care Pages</u> website for your child (see "Keeping Friends and Family Informed"). Not only will such a website help you communicate updates to people without being bombarded by e-mail and phone calls, but you will be surprised at how quickly word of your website spreads. Through friends of friends of friends, you will receive messages from other cancer families, and eventually from neuroblastoma families, in the online "guestbook" these free website services provide. For example, one parent learned her sister-in-law's best friend worked with a neuroblastoma mom living about an hour away. She posted in the parent's guestbook and that parent then visited her son's website. This simple connection created a lasting friendship, yet they would never have found each other on their own. When visitors leave contact information in your online guestbook, you can then visit their websites and in this way gradually become part of a network.

Ultimately, whether and how you wish to connect with others in the neuroblastoma community is a very personal decision. You may learn that connecting in person with other neuroblastoma parents is an invaluable source of support and hope for you – or you may decide to be a "silent" member of an online support group and absorb the available information privately at your own pace. Each parent copes in a different way. Our purpose in setting forth these various suggestions is to merely to make sure that you know that these various sources of support and information are available. Neuroblastoma treatment can be long and arduous, and we wish you to know there is a uniquely caring community of neuroblastoma parents available for any who feel it would be helpful.

Please contact editors@nbhope.org with any comments



# **Keeping Family and Friends Informed**

Along with the whirlwind of emotions and medical demands after your child's diagnosis, you will probably find yourself deluged with questions, tears, and offers of help from family and friends. Chances are you're being bombarded with phone calls and e-mails from just about everyone in your life, as well as a stream of visitors bringing gifts, flowers, food, and even advice. It's natural for people to want to help and stay in the loop – but, however well-meaning, the overtures can sometimes be overwhelming. Responding to so much attention from others while coping with the emergency at hand can become still another challenging task.

One parent recalls the stress and exhaustion of those first days after diagnosis – and at this worst of all possible times she was constantly fielding phone calls! What she desperately needed was to focus on taking care of her son, but it seemed everyone she knew wanted to know what was going on. Not only did she have barely a minute to spare, but telling and retelling the story of her child's diagnosis was nothing short of traumatic.

There are several strategies you can use to communicate with others while still reserving your time and energy for your sick child and family.

One of the best ways to keep people informed, especially if you have a large network of friends and family, is to start a blog or website dedicated to updating folks on your child's progress. This website will enable loved ones in your life to "check in" on you and express their support without calling you constantly. It will free you up to focus on your family, as a few minutes of typing will instantly update everyone you know! Some parents appoint a very close relative or friend to handle the updating of the website or blog for them.

The most popular websites for this type of communication are <u>CaringBridge</u> and <u>Care Pages</u>, both free and managed by non-profit organizations for this specific purpose. If you think one of these sites might be for you, browse both, because their formats are very different. However, both are extremely user-friendly, even for inexperienced internet users, and easy to set up. You can post journal entries as many times as you want-- hourly, daily, weekly, monthly ... whatever suits your needs. These journal entries are instantly sent to the e-mail inbox of anyone who subscribes to your child's site.

You can also upload pictures, set up links to other websites of interest, and, most importantly, receive messages in the online "guestbook." You will find that the messages in this guestbook become lifelines at times -- knowing there are so many out there that care about your family can be very comforting. If you wish, you will also be able to connect in this way with other neuroblastoma families. This can become an important source of support and information, as it will enable you to build a network of resources that will last throughout your child's treatment and beyond. See "Finding Other Neuroblastoma Families."

There are also sites available for forming your own blog, such as <u>Blogspot</u>. You might like to try one of these if you want more control over your own format, but it will probably take a little more time to put together. One downside of a blog is that anyone in the world can view it with a little googling, making it more public than a CaringBridge or Care Page, since a viewer must be aware of and register with the latter services. Just know there are many choices when it comes to blogs, and setting one up will save you time, energy, and emotion. You may even find that journaling your experiences publicly will itself be therapeutic, allowing an outlet for your emotions on good days as well as difficult ones.

A similar option is simply creating an e-mail group. This operates in effect like a blog, but is considerably more private. You select the recipients of your e-mail by creating a group, and hence the people receiving your child's updates are those you approve (and whom you can advise on whether your updates should be further circulated or not). Although you can create some filters on a blog or website, your own e-mails are always more restricted. Another plus is that each e-mail can be tailored for a specific set of recipients. You can select your group based on the particular message, giving you even more control of the information you send.

If you don't have internet access handy, or if talking to people helps you cope, consider a phone tree. By "assigning" calls to several persons closest to you, you can create a communication circle that still gives you extra time. For example: you call only your parents, in-laws, and best friend. Your parents call your aunts and uncles, your in-laws call your husband's sibling and grandparents, your best friend calls your closest work colleague and college roommate, with each of them calling other designated persons, and so on. This way everyone is informed without keeping you away from the person who needs you most -- your child.

Don't forget the power of your child's own words and messages in keeping people informed. When he or she is up to it, consider helping your child create cards, send e-mails, update your website, or make phone calls to people they want to talk to. Many children feel bombarded by the constant attention during their treatment. Reciprocating the gesture may help them sort their emotions.

Whatever decision you make regarding how you communicate, be sure to keep a record of who should be contacted if there is an important update. Don't forget your child's "extended family"- e.g., pediatrician, teacher, soccer coach, etc. Also include your or your spouse's co-workers if possible. Ensuring certain important updates are communicated can be invaluable when you are required to be away from work due to your child's treatment needs.

Finally, don't be afraid to make your own needs known. If you are too harried or preoccupied for calls and visitors or to keep others in the loop, or if you need a specific type of help, don't shrink from letting people know. Many people are desperate to help but have no idea what is needed -- and sometimes there are people who do not grasp what is not needed. You have too much on your plate to worry about the perceptions and needs of so many others. Doing what is best for you and your family is the goal of those who really care about you, and such people will understand if you have no time for them or share that a particular thing is not helpful.

It can be hard to find the time or the words to communicate your needs to others. Sometimes a close friend or family member can help run interference. One aunt, after helping her family during her niece's three-year battle with neuroblastoma, put together a list of suggested ways to help the family of a sick child, as well as a list of things not to do. This list can be distributed to friends or perhaps can just give you some ideas. See "Reaching Out and Accepting Help."

There is no right way or wrong way to communicate with others about your child's treatment and your family's needs. Each of us is unique in our preferences and the amount of privacy or support needed. Of course, whether stressful or comforting to you, it is very likely that throughout your child's treatment you will continue to receive calls and messages from people who want to know how things are going. On the one hand, these inquiries come because people care so much about you and your family -- so, although it doesn't always make your life easier, do keep in mind that family and friends have your best interests at heart and only want to help and be involved. On the other hand, keeping everyone in the loop may at times become difficult for you to handle. We hope the suggestions included here will help you find ways to strike the right balance and relay messages and information to all those who care about you, yet still maximize your time with your sick child and family.

Please contact editors@nbhope.org with any comments



# **Reading List**

#### **Medical Texts and Reference Books**

Childhood Cancer: A Parent's Guide to Solid Tumor Cancers, 2nd ed., by Honna Janes-Hodder and Nancy Keene. Covers neuroblastoma, Wilms, liver cancers, soft tissue sarcomas, bone sarcomas, and retinoblastoma. 560 pages, 2002.

Contact info@candlelighters.org for free copy.

#### FreeBooks4Doctors

Free, online, full-text medical texts. The *Cancer Medicine 5th edition* text, 2000, has comprehensive sections on childhood cancer and childhood cancer survivorship issues.

*Neuroblastoma*, by <u>Nai-Kong V. Cheung</u> and <u>Susan L. Cohn</u> (Editors). Neuroblastoma reference work providing a concise up-to-date reference for practitioners, students, and researchers. Springer, 298 pages, 2005.

Psychosocial Aspects of Pediatric Oncology, by Shulamith Kreitler and Myriam Weyl Ben Arush (Editors)

Comprehensive text on the all-important psychosocial aspects of cancer in children. 470 pages, 2004.

# Caring for the Child with Cancer

Armfuls of Time, by Barbara Sourkes.

The psychological experience of the child with a life threatening illness.

Cancer and Self-Help: Bridging the Troubled Waters of Childhood Illness, by Chesler, Mark A., PhD, and Barbara Chesney, The University of Wisconsin Press, 1995.

Explains how self-help groups are formed, how they function and recruit, and why they are effective.

Cancer Pain Relief and Palliative Care in Children

World Health Organization, 1999, 76 pages (available in English and French; Spanish in preparation).

A Child In Pain: How to Help, What to Do, by Leora Kuttner, PhD., Hartley & Marks, 1996.

Children With Cancer: Communication and Emotions, by Anna M. Van Veldhuizen and Bob F. Last, 1991.

Reports the findings of a study (funded by the Dutch Cancer Society and the Foundation for Pediatric Cancer Research) on the communication between parents and their child with cancer.

Choices: The Most Complete Sourcebook for Cancer Information, by Marion Morra & Eve Potts, 2003. Great information on cancer basics: staging, medications, procedures, etc.

100 Questions & Answers About Your Child's Cancer, by William Carroll, MD.

This book is an invaluable resource for anyone coping with the physical and emotional turmoil of cancer. 160 pages, 2004.

Healing Images for Children: Teaching Relaxation and Guided Imagery to Children Facing Cancer and Other Serious Illnesses, by Nancy C. Klein.

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Muscle relaxation, calm breathing, visual imagery, stories, music, humor, and positive affirmations are techniques that enhance a child's healing process. Companion items include: Healing Images for Children Activity Book: For Days When Quiet Activities Are Best Healing Images for Children: Relax and Imagine (Audio CD).

Helping the Fearful Child: A Parent's Guide to Everyday and Problem Anxieties, by Johnathan Kellerman, W.W. Norton, 1981.

Helping Your Children Cope with Your Cancer: A Guide for Parents and Families, by Van Dernoot, Hatherleigh Co., 2002.

Real life stories and experiences of over 20 parents who have been diagnosed with cancer. Provides valuable advice on how to discuss the impact of cancer on the whole family.

Home Care for the Seriously Ill Child: A Manual for Parents, by Modlow, D. Gay, and Ida M. Martinson, 2003. \$18 from Children's Hospice International (703) 684-0330.

Living with Childhood Cancer: A Practical Guide to Help Familiess Cope, by Leigh Woznick and Carol D. Goodheart, American Psychological Association, 2001.

My Child Has Cancer: A Parent's Guide to Diagnosis, Treatment, and Survival (The Praeger Series on Healing and Managing Injury and Disease), by Della L. Howell, 2008.

*The Relaxation Response* by Herbert Benson, MD. and Miriam Z. Klipper, Avon Books, 1990. Relaxation method of pain relief.

Shelter From the Storm: Caring for a Child With a Life-threatening Condition, by Joanne Hilden, MD, Daniel R. Tobin, MD, and Karen Lindsey.

Your Child has Cancer: A Guide to Coping, by Joan Taksa Rolsky, MSW.

Your Child in the Hospital: A Practical Guide for Parents, Nancy Keene. 3rd ed. Sebastopol, CA: O'Reilly & Associates, 2002.

# Informative Books for Kids with Cancer and their Siblings

Order a **FREE** copy of the following from info@candlelighters.org.

*Childhood Cancer: A Parent's Guide to Solid Tumor Cancers*, 2nd ed., by Honna Janes-Hodder and Nancy Keene. Covers neuroblastoma, Wilms, liver cancers, soft tissue sarcomas, bone sarcomas, and retinoblastoma. 560 pages, 2002.

Childhood Cancer Survivors: A Practical Guide to Your Future, 2<sup>nd</sup> edition, by Kathy Ruccione, Nancy Keene, & Wendy Hobbie. Covers the issues of long-term survivorship: medical late effects, relationships, overcoming employment or insurance discrimination, maximizing health and follow-up schedules. 482 pages, 2000.

Chemo, Craziness & Comfort, My Book about Childhood Cancer, by Nancy Keene and Trevor Romain. A 200 page resource that provides practical advice for children diagnosed with cancer between 6 and 12 years of age. Warm and funny illustrations and easy-to-read text help the child (and parents) make sense of cancer and its treatment.

The Amazing Hannah, Look at Everything I Can Do! By Amy and Dave Klett Available in English or Spanish, this 28 page picture book is written for the preschool (1 to 5 years) child who has been diagnosed with cancer. Through real-life photos, children will be able to identify with Hannah's hospital stay, special friends, tests, treatment and germ care.

Oliver's Story: For 'Sibs' of Kids with Cancer, is a 40 page illustrated book targeted for the 3 to 8 year old sibling of children diagnosed with cancer. Illustrated by Mike Dodd and written through the eyes of his six-year-old son Oliver, this resource focuses on the many questions that siblings have when their brother or sister is diagnosed with cancer, and offers constructive ways on how they can provide support. Also in Spanish.

# **Educational Issues**

*Educating the Child With Cancer: A Guide for Parents and Teachers*, edited by Nancy Keene, 2003. Available free through Candlelighters

Negotiating the Special Education Maze: A Guide for Parents and Teachers 3rd ed., by Winifred Anderson, Stephen Chitwood, and Deidre Hayden, Woodbine House, 1997.

*Keeping a Head in School: A Student's Book About Learning Abilities and Learning Disorders*, by Mel Levine, MD., Educator's Publishing Service, Inc., 1991.

Suggestions for Teachers and School Counselors. Write to:

The Compassionate Friends. P.O. Box 3696, Oak Brook, IL 60522.

Grief Comes to Class: A Teacher's Guide

Gliko-Braden, Majel. Centering Corporation, 1531 N. Saddle Creek Rd., Omaha, NE 68104. (402) 553-1200.

Comprehensive guide to grief in the classroom.

# **Finances During Medical Treatment**

Finding the Money: A Guide to Paying Your Medical Bills, by Diane Pammenter Tolley, Tynsdale House Publishers, 2001. Available from BMT Infonet

A book to help families of people who need transplants.

One Small Sparrow: The Remarkable Real-Life Drama of One Community's Compassionate Response to a Little Boy's Life, by Jeffe Leeland, Multnomah Books, 1995.

Available at www.randomhouse.com/waterbook.

Contains numerous ideas for methods to raise funds. Christian perspective.

A Special Way to Care, by Sheila Peterson, 1988. Available from Friends of Karen, Box 217, Croton Falls, NY 10519.

Free guide for those who wish to provide financial/emotional support for families of ill children.

### Books for Children Ages 4 to 8

Alex and the Amazing Lemonade Stand, by Alex, Jay and Liz Scott, 2004.

The true story of NB fighter Alexandra Scott and her plan to help all kids with cancer!

Chemo Girl: Saving the World One Treatment at a Time, by Christina Richmond, 1997. About a super heroine named Chemo Girl.

H is for Hair Fairy: An Alphabet of Encouragement for Kids (and Kids at Heart!) with Cancer, by Kim Martin and Wend Boomhower, 2005.

I Can Too! Boys! by Christine Thomas, 2006.

An imagination journey of what all kids with cancer can do – this one with Cancer Kid Boy. *Imagine a Rainbow: A Child's Guide to Soothing Pain*, by Brenda S. Miles, Ph. D. and Nicole Wong, 2006.

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Beautiful illustrations and verse help the child use imagery to refocus the mind away from pain. A Note to Parents discusses pain management and guides parents in teaching imagery and deep breathing.

Kathy's Hats: A Story of Hope, by Trudy Krisher, Concept Books, 1992.

Let's Talk About When Kids Have Cancer (The Let's Talk Library), by Melanie Apel Gordon, Hazelden Information Education, 1999.

Little Tree: A Story for Children with Serious Medical Illness, by Joyce C. Mills, 2003. An inspiring story that also provides coping techniques such as visualization and relaxation exercises.

My ABC Book of Cancer, by Shannon Chamberlain, 1991.

Ten year old Shannon tells about her fight with cancer in a hope-filled ABC format. Also contains a discussion on childhood cancer, a glossary, and reading list.

My Book for Kids With Cansur: A Child's Autobiography of Hope, by Jason Gaes Written by cancer child and illustrated by his brothers. Jason's parents also wrote a book that is very informative: A Child's Autobiography of Hope by Jason Gaes, Melius & Peterson Publishing, South Dakota, 1987.

My Brother Matthew, by Mary Thompson, Woodbine House, 1992.

Sammie's New Mask: A Coloring Book for Friends of Children with Cancer
The National Children's Cancer Society (www.nationalchildrenscancersociety.com) will send multiple
copies of this booklet to schools, etc. if requested on behalf of a child with cancer.

What Is Cancer Anyway? Explaining Cancer to Children of All Ages, by Karen Carney, Dragonfly Publ, 1998.

You and Your Cancer: A Child's Guide, by Lynda Cranston, BC Decker, 2001.

# Books for Children Ages 9 to 12

Cancer (What's It Like?), by Angela Royston, Heinemann Library, 2005.

Drums, Girls and Dangerous Pie, by Jordan Sonnenblick.

A 13-year old boy's pesky 5-year old brother is diagnosed with leukemia.

Our Family Has Cancer, Too! by Christine Clifford, Jack Lindstrom (Illustrator), Pfeifer-Hamilton Publ, 2002.

You and Your Cancer: A Child's Guide, by Lynda Cranston, B.C. Decker, 2001.

# **Books for Young Adults**

Cancer (Diseases and People), by Steven I. Benowitz, Enslow Publishers, 1999.

The C-Word: Teenagers and Their Families Living with Cancer, by Elena Dorfman, 2nd ed., New Sage Press, 1993.

### **Inspirational Books for Adults**

The Anatomy of Hope: How People Prevail in the Face of Illness, by Jerome Groopman, MD., 2005.

Every Second Counts, by Lance Armstrong, 2004.

It's Not About the Bike: My Journey Back to Life, by Lance Armstrong.

The story of a world-class athlete nearly struck down by cancer who recovers and wins the Tour de France.

I want to grow hair, I want to grow up, I want to go to Boise, by Erma Bombeck, 1989.

*LiveSTRONG.* Lance Armstrong Foundation Inspirational stories from cancer survivors.

Love, Medicine, & Miracles, by Bernie Siegel, MD.

Peace, Love, & Healing, by Bernie Siegel, MD.

There's No Place Like Hope: A Guide to Beating Cancer in Mind Sized Bites - A Book of Hope, Help and Inspiration for Cancer Patients and their Families, by Vickie Girard.

When Bad Things Happen to Good People, by Harold S. Kushner A Jewish rabbi facing his own child's fatal illness asks, "Why me?

# **Books for Siblings**

Straight from the Siblings: Another Look at the Rainbow, by Gloria Murray (Photographer), Gerald G. Jamplosky (Editor), Celestial Arts, California, 1982

Written by sixteen children who have brothers and sisters with a life-threatening illness.

What About Me? When Brothers and Sisters Get Sick, by Allan Peterkin, Frances Middendorf

When Molly Was in the Hospital: A Book for Brother and Sisters of Hospitalized Children, by Debbie Duncan

# Biographical/Families' Stories

Amanda's Gift, by Scott MacLellan (1998).

Fighting Chance: Journeys through Childhood Cancer. A photo-journal by Harry Connolly, Tom Clancy, and Curt Civin, 1998.

This book follows three children through treatment for childhood cancer.

I Never Signed Up for This!: An Upfront Guide to Dealing with Cancer at a Young Age, by Katie Strumpf, 2006.

Written by a 25 year old who had cancer as a young girl.

I Will Sing Life: Voices from the Hole in the Wall Gang Camp, by Larry Berger and Dahlia Lithwick, 1992.

*Kids with Courage*: *Thoughts and Stories about Growing Up with Cancer*, by Kelly and Maury Cotter. Board of Regents of the University of Wisconsin System, 1998.

Ya Can't Let Cancer Ruin Your Day: The James Emails, by Syd Birrell, 2005. Order at www.greentrainbooks.com

This true story about a young boy battling cancer will inspire you to seek life, love, laughter and adventure. Foreword by Tom Hanks.

# End of Life and Grief - Children's Books

The Fall of Freddy the Leaf: A Story of Life for All Ages, by Leo Buscaglia, Holt, Rinehart and Winston, 1982.

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I Had a Friend Named Peter: Talking to Children about the Death of a Friend, by Janice Cohn and Gail Ownes. 1987.

Last Week My Brother Anthony Died, by Martha Hickman and Randie Julien, Abingdon, Tennessee: 1984.

Lifetimes: The Beautiful Way to Explain Death to Children, by Bryan Mellonie, New York: Bantam Books, 1983.

Painting the Sunsets with the Angels, by Vann Wesson and Moira Michaels, 1996. A sister is given hope after the death of her brother.

Thumpy's Story: A Story of Love and Grief Shared, by Nancy Dodge.

What is Death? by Etan Boritzer and Nancy Forest, 2000.

Simple illustrations, like a child's colorful drawings, fill the pages of this book. The book asks questions as a child might--the answers are sensible, including different cultures.

The Empty Place: A Child's Guide Through Grief, by Roberta Temes, PhD., New Horizon Press, 1992. Explains and describes feelings after the death of a sibling, such as the empty place in the house, at the table, in a brother's heart.

Gentle Willow: A Story for Children about Dying, by Joyce C. Mills, 1992.

This is a book for children who may not survive their illness. This comforting story about a tender-spirited tree and her forest friends will also help children with the death of friends or family members. A healing metaphor, it addresses our feelings of sadness, love, disbelief, and anger, and provides children with a transformational way of viewing dying.

On the Wings of a Butterfly: A Story about Life and Death, by Marilyn Maple, 1992.

The Everlasting Snowman, by Hunter Darden & Tamara Adams, 1997.

The Next Place by Warren Hanson, 1997.

An inspirational journey of light and hope to a place where earthly hurts are left behind.

What on Earth Do You Do When Someone Dies? By Trevor Romain,: Free Spirit Publishing, 1999. Help children understand and cope with grief.

When Good-bye is For Ever, by Lois Rock, 1969.

All through our lives we learn to say many good-byes. Some are easy; some are hard. This book will help you find hope when you have to say the hardest good-bye of all.

# End of Life and Grief - Books for Teens

I Remember You: A Grief Journal, by Laynee Wild, HarperCollins, 1994.

A journal for recording written and photographic memories during the first year of mourning.

Straight Talk about Death for Teenagers: How to Cope with Losing Someone You Love, by Earl Grollman, Beacon Press, 1993.

*Teenagers Face to Face with Bereavement, by* Karen Gravelle and Charles Haskins, J. Messner, 2000. The perspectives and experiences of seventeen teenagers coping with grief.

When a Friend Dies: A Book for Teens about Grieving & Healing, by

Marilyn E. Gootman and Pamela Espeland, 2005.

# End of Life and Grief - Books for Adults

The Next Place by Warren Hanson.

An inspirational journey of light and hope to a place where earthly hurts are left behind.

Bereavement: A Magazine of Hope and Healing.

For a free copy or to subscribe, call: Bereavement Publishing, Inc., (888) 604-4673 (HOPE).

Beyond Tears: Living After Losing a Child, by Ellen Mitchelll, Carol Barkin, Audrey Cohen, and Lorenza Colletti, 2005.

Children Mourning, Mourning Children, by Kenneth Doka, Hemisphere Publications, 1995.

Closer to the Light: Learning from Near Death Experiences of Children, by Melvin Morse, MD. and Raymond Moody, New York: Villard Books, 1991.

Final Gifts: Understanding the Special Awareness, Needs, and Communications of the Dying, by Maggie Callanan and Patricia Kelley, Bantam Books, 1997.

From My Son's Garden: A Personal Story of Growth and Healing after the Loss of a Child, by Brenda Hahn Greene, 2002.

How Do We Tell the Children? A Step-by-Step Guide for Helping Children Cope When Someone Dies, 3rd ed., by Dan Schaefer and Christine Lyons and David Peretz, Newmarket Press, 2002.

I Remember You: A Grief Journal, by Laynee Gilbert, 1994.

A journal for recording written and photographic memories during the first year of mourning.

Letters I Never Wrote, Conversations I Never Had, by Charles Ben Bissell, Tilden Press, 1983.

Living When a Loved One Has Died, by Earl A. Grollman, 1997.

On Children and Death, by Elisabeth Kubler-Ross, MD. New York: Macmillan, 1997.

Parental Loss of a Child, by Therese Rando, PhD, Research Press, 1986.

Remember the Secret, by Elisabeth Kubler-Ross & Heath Preston, 1998.

*Talking About Death: A Dialogue Between Parent and Child*, 3rd ed., by Earl Grollman, Beacon Press, 1991.

The Grieving Garden: Living with the Death of a Child, by Suzanne Redfern and Susan K. Gilbert, 2008.

The Worst Loss: How Families Heat from the Death of a Child, by Barbara D. Rosof, 1995.

*There Is a Rainbow Behind Every Dark Cloud*, by Gerald G. Jampolsky. Eleven children share their experiences with terminal illness, 1979.

When the Bough Breaks: Forever After the Death of a Son or Daughter, by Judith Bernstein, Andrews & McMeel, 1998.

Please contact <u>editors@nbhope.org</u> with any comments



# **Common Abbreviations**

# Quick Reference Chart of Abbreviations and Acronyms

| 123-I MIBG    | isotope of iodine with quick half-life (13 hours) connected to MIBG, used for scanning                       |
|---------------|--|
| 131-I MIBG    | isotope of iodine with longer half-life (8 days) connected to MIBG, used for scanning and therapy to kill NB |
| 131I-3F8      | "hot antibodies" used for radioimmunotherapy   |
| 1p, 1p36, 3p, | genetic aberrations in NB: unbalanced loss and/or gain of these chromosomal                                  |
| 4p, 11q, 14q, | arms are subjects of research for prognostic significance  |
| 16p, 17q, 19q |  |
| 3891          | randomized study published in 1999: compared results with and without  |
|               | transplant and accutane  |
| 3973          | randomized study (closed 2006) to compare with and without purged stem cells                                 |
| 3F8           | antibody for neuroblastoma at Sloan-Kettering  |
| 4HPR          | fenretinide  |
| 8H9           | antibody used at Sloan-Kettering especially for NB relapsed in CNS   |
| ABMT          | autologous bone marrow transplant  |
| ABT-751       | anti-angiogenesis drug in phase 1  |
| ACS           | American Cancer Society  |
| ANBL0032      | randomization study for ch14.18 antibody   |
| ANC           | absolute neutrophil count  |
| ANR           | Advances in Neuroblastoma Research (international meeting held every 2 years)                                |
| ASCT          | autologous stem cell transplant  |
| BMT           | bone marrow transplant (or blood and marrow transplant)  |
| BSO           | buthionine sulfoximine   |
| BUN           | blood urea nitrogen  |
| BX or BMX     | bone marrow biopsy   |
| CAM           | complementary and alternative medicine   |
| CBC           | complete blood count   |
| CCG           | Children's Cancer Group  |
| CD34+         | antigen expressed on healthy blood-forming <u>stem cell</u> , used to count stem cell collection             |
| CD44          | cell surface glycoprotein, advanced neuroblastomas often have low CD44                                       |
|               | expression   |
| CEM           | carboplatin, etoposide, melphalan  |
| CEM-LI        | carboplatin, etoposide, melphalan, and local irradiation   |
| CEP-701       | receptor tyrosine kinase inhibitor, lestaurtinib   |
| CEV           | carboplatin, etoposide, vincristine  |
| ch14.18       | chimeric anti-GD2 antibody (part human, part mouse)  |
| CHLA          | Children's Hospital Los Angeles  |
| СНОР          | Children's Hospital of Philadelphia  |
| cisRA         | 13-cis retinoic acid, brand name Accutane, Amnesteem, Claravis   |
| CMV           | cytomegalovirus  |
| CNCF          | Children's Neuroblastoma Cancer Foundation   |
| CNS           | central nervous system   |
| COG           | Children's Oncology Group  |

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| COJEC       | "Rapid COJEC" European protocol: cisplatin, vincristine, carboplatin, etoposide |
|-------------|---|
| COOLC       | cyclophosphamide given in rapid delivery schedule (10 day cycles)               |
| CPT-11      | irinotecan  |
| CR          | complete response   |
| CT          | computerized tomography   |
| CVL         | central venous line, Broviac or Hickman   |
| DFCI        | Dana-Farber Cancer Institute  |
| DMSO        | preservative used in frozen stem cells  |
| DNA index   | ploidy, copies of DNA   |
| DX          | diagnosis, diagnosed  |
| EFS         | event free survival   |
| EKG or ECG  | electrocardiogram   |
| ESIOP       | European pediatric oncology study group   |
| ESR         | erythrocyte sedimentation rate (also called "sed rate")                         |
| FDA         | Federal Drug Administration   |
| FISH        | Fluorescent <i>in situ</i> hybridization  |
| GCSF or     | granulocyte colony stimulating factor   |
| G-CSF       | Similarious to corony diminarating factor                                       |
| GD2         | antigen expressed on the surface of neuroblastoma                               |
| GM-CSF      | granulocyte macrophage colony stimulating factor                                |
| GNB         | ganglioneuroblastoma  |
| GPOH        | German pediatric oncology study group   |
| G-TUBE      | gastrostomy tube for feeding  |
| HAMA        | human anti-mouse antibodies   |
| HLA         | human leukocyte antigens  |
| HSCT        | hematopoietic stem cell transplant  |
| hu14.18-IL2 | humanized anti-GD2 antibody fused to interleukin-2                              |
| ICE         | ifosfamide, carboplatin, etoposide  |
| IL2         | interleukin-2   |
| IND         | investigational new drug  |
| INRC        | International Neuroblastoma Response Criteria:                                  |
| INRG        | International Neuroblastoma Risk Group  |
| INSS        | International Neuroblastoma Staging System                                      |
| IORT        | intraoperative radiation therapy  |
| IRB         | institutional review board  |
| IV          | intravenous   |
| LD or LDH   | lactate dehydrogenase   |
| LI          | local irradiation   |
| LOH         | loss of heterozygosity  |
| LP          | lumbar puncture   |
| MIBG or     | meta-iodobenzylguanidine  |
| mIBG        |   |
| MKI         | mitosis-karyorrhexis index  |
| MR          | mixed response: > 50% decrease of any lesion with less than 50% decrease in     |
|             | any other   |
| MRD         | minimal residual disease  |
| MRI         | magnetic resonance imaging  |
| MSKCC or    | Memorial Sloan-Kettering Cancer Center  |
| MSK         | 6   |
| MYCN        | myc myelocytomatosis viral related oncogene, when amplified (more copies)       |
|             | unfavorable prognostic factor; same as N-myc                                    |
| N9          | Memorial Sloan-Kettering neuroblastoma protocol                                 |
| NANT        | New Approaches to Neuroblastoma Therapy   |

| NB or NBL   | neuroblastoma  |
|-------------|--|
| NCI         | National Cancer Institute  |
| NED         | no evidence of disease   |
| NIH         | National Institutes of Health  |
| NG-tube     | nasogastric tube for feeding   |
| N-MYC or N- | myc myelocytomatosis viral related oncogene, when amplified (more copies)        |
| myc         | unfavorable prognostic factor; same as MYCN                                      |
| NP          | nurse practitioner   |
| NSAIDs      | nonsteroidal anti-inflammatory drugs   |
| NSE         | neuron-specific enolase  |
| OMS         | opsoclonus-myoclonus syndrome  |
| OS          | overall survival   |
| p53         | tumor suppressor gene  |
| PA          | physician's assistant  |
| PBSCT       | peripheral blood stem cell transplant  |
| PD          | progressive disease: new lesion or >25% increase in an existing lesion           |
| PET         | positron emission tomography   |
| PET-CT      | positron emission tomography and computerized tomography performed at the        |
| PET/CT      | same time; images fused  |
| PFS         | progression-free survival  |
| PI          | principal investigator   |
| pNTs        | peripheral neuroblastic tumors   |
| POG         | Pediatric Oncology Group   |
| PR          | partial response: >50% decrease in measurable NB and 1 or no positive BM site    |
| RA          | retinoic acid  |
| RT-PCR      | reverse transcription-polymerase chain reaction                                  |
| S-100       | stain used to identify neuroblastoma in biopsies                                 |
| SAHA        | suberoylanilide hydroxamic acid  |
| SCR         | stem cell rescue   |
| SCT         | stem cell transplant   |
| SD          | stable disease   |
| SIOP        | Society International Oncology Pediatrics  |
| SSKI        | Lugol's potassium iodine solution  |
| TBI         | total body irradiation   |
| TMI         | total marrow irradiation   |
| TPN         | total parenteral nutrition   |
| trkA, trkB, | tyrosine kinase family of neurotrophin receptors: high levels of trkA expression |
| trkC        | favorable, high levels trkB unfavorable, high level trkC favorable               |
| TVD         | topotecan, vincristine, and doxorubicin  |
| VGPR        | very good partial response: tumor reduced by 90-99%, no distant disease except   |
|             | skeletal residua, catecholamines normal  |
| VOIT        | temozolomide, oral irinotecan and vincristine                                    |
| VP-16       | etoposide  |
| VZV         | Varicella-zoster virus   |
|             | Varietha zoster viras  |

Please contact <a href="mailto:editors@nbhope.org">editors@nbhope.org</a> with any comments



# **Glossary of Medical Terms**

# A

**Absolute Neutrophil Count (ANC):** The real number of white blood cells (WBCs) that are <u>neutrophils</u>. Neutrophils are key components in the system of defense against infection. Having few neutrophils present is called <u>neutropenia</u>.

**Acyclovir:** An anti-viral drug used to treat or prevent cytomegalovirus and herpes simplex infections.

**Adenovirus:** A set of viruses that induce respiratory tract and eye infections. Gene therapy uses adenoviruses that are modified to carry a particular tumor-fighting gene.

**Adrenal glands:** Glands located on top of each kidney that secretes several important hormones into the blood. The inner portion of the adrenal gland, the adrenal medulla, stores and releases catecholamines that are measured by testing urine samples.

**Alkylating Agents:** A class of anticancer drugs that interferes with the cell's DNA and restrains or halts cancer cell growth.

**Allogeneic:** (Bone Marrow or Peripheral Blood Stem Cell Transplant) a transplant using bone marrow or stem cells from a matched sibling donor infused into recipient after high dose chemotherapy.

**Angiogenesis:** Blood vessel formation. Angiogenesis involves the growth of blood vessels from surrounding tissue into a solid tumor. **Antiangiogenesis** drugs are drugs that prevent the growth of new blood vessels into a solid tumor.

**Anthracyclines**: A class of antibiotics used in many induction chemotherapy regimens for high-risk neuroblastoma. It is important to keep track of the cumulative dose of anthracyclines a child receives because these drugs can damage the heart muscle.

**Antibiotics:** Drugs used to fight bacterial infections.

**Antibody:** A substance made by the immune system, used to defend the body against bacteria, viruses, toxins or tumors. Neuroblastoma treatment may include the use of man-made monoclonal antibodies (MoAb) in an effort to train the immune system to fight neuroblastoma.

**Antiemetics:** Drugs used to control nausea and vomiting.

**Apheresis:** Procedure in which blood is withdrawn from the patient and circulated through a machine that removes specific components, such as stem cells or platelets, and returns the remaining blood components to the patient. High risk neuroblastoma patients have peripheral blood stem cells collected through apheresis for use in stem cell transplant or after certain other types of therapy.

**Apoptosis:** Programmed cell death.

**Ascites:** Excess fluid in the abdominal cavity, which causes swelling. Ascites is a possible complication of surgery to remove abdominal tumors and a symptom of VOD.

**Ataxia:** A problem of muscle coordination causing loss of balance. Ataxia is sometimes seen in neuroblastoma with opsoclonus/myoclonus syndrome (OMS).

**Audiogram:** A graph showing a person's hearing capacity, based on a set of tests examining perception of distinct sound frequencies.

**Autologous bone marrow or peripheral stem cell transplantation (ABMT or auto PBSCT)**: Transplant in which the patient receives his or her own marrow or stem cells.

В

Benign: Not-malignant.

**Beta-glucan:** Sugar molecule derived from yeast or barley, used with 3F8 antibody therapy to enhance immune response against neuroblastoma.

**Bile:** A yellow-green liquid made in the liver whose purpose is to eliminate waste from the liver and break down fats as food is digested.

**Bilirubin:** The orange-yellow pigment in bile. Jaundice occurs if bilirubin builds up in the blood and skin. Bilirubin can be measured to check for liver disease.

**Biological response modifiers:** Substances (natural or man-made) that increase or revive healthy immune defenses. Granulocyte Colony Stimulating Factor (GCSF) is often given after chemotherapy to quicken white cell count recovery, and Granulocyte Macrophage Colony Stimulating Factor (GM-CSF) is a biological response modifier often used with antibody therapies.

**Biopsy:** Surgical removal of tissue for examination by a pathologist to determine diagnosis.

**Blood type:** Identification of a person's blood according to the kinds of proteins present on the surface of the red blood cells.

**Bolus:** One dose of drug usually injected into a blood vessel over a short time period.

**Bone Marrow:** The spongy material that fills the inner cavities of the bones and makes all types of blood cells.

**Bone Marrow Aspiration:** The removal and examination of a small portion of bone marrow cells by suctioning into a syringe.

**Bone Marrow Biopsy:** The removal and examination of a small portion of bone using a hollow biopsy needle.

**Bone Marrow Harvest:** A process that collects healthy bone marrow to be stored and used at a later date for a bone marrow transplant.

 $\mathbf{C}$ 

**Carboplatin:** Platinum compound (<u>DNA</u> <u>alkylating agent)</u> chemotherapy commonly used in frontline therapy for neuroblastoma; less toxic to hearing than cisplatin.

**Cardiomyopathy:** A disease of the heart muscle. It can be caused by the toxic effects of some anticancer drugs.

**Catecholamine:** Any of many substances (such as epinephrine, norepinephrine, and dopamine) that function as hormones or neurotransmitters or both. Most neuroblastomas will cause an increase in urinary catecholamines.

**Central line (central venous line, CVL):** A catheter (tube) that is passed through a vein to end up in the chest portion of the vena cava (the large vein returning blood to the heart) or in the right atrium of the heart.

**Central Nervous System (CNS):** the largest part of the nervous system, including the brain and the spinal cord.

Chimeric Antibodies (ch 14.18): part-mouse and part-human anti-GD2 antibody.

**Cisplatin:** Platinum compound (<u>DNA alkylating agent)</u> chemotherapy commonly used in frontline therapy for neuroblastoma; can cause hearing damage.

**Complete response (CR):** A term for labeling response to treatment, in this case, no detectable disease present.

**Computed tomography scanning (CT scanning):** A technique for producing cross-sectional images of the body which may show cancer more accurately than other imaging methods in some circumstances. CT passes x-rays through the body at different angles and these images are analyzed by a computer.

**Conditioning Regimen:** The chemotherapy and/or radiation given transplant patients to destroy remaining cancerous cells and/or create space for healthy new marrow to be transplanted.

**Consolidation:** A course of treatment with chemotherapy given to the patient while in remission to further reduce the number of cancer cells.

**Creatinine:** A waste product of protein metabolism that is filtered from the blood by the kidneys and expelled in urine. Creatinine can be measured to assess kidney function.

**Cyclophosphamide (brand name Cytoxan):** Alkylating chemotherapy in the nitrogen mustard family, commonly used in frontline and relapsed neuroblastoma; can cause bleeding in the bladder, so bladder protectant Mesna is given also.

**Cytogenetics:** A branch of biology that studies the structure of chromosomes.

**Cytomegalovirus (CMV):** a herpes virus that occurs in healthy individuals without causing symptoms. In immune compromised individuals, CMV may cause serious illness including retinitis (inflammation of the retina), pneumonia, colitis (inflammation of the large bowel), and encephalitis. Blood products are screened to prevent passing CMV to cancer patients.

 $\mathbf{D}$ 

**Debulking Surgery**: Surgically removing as much of the tumor as possible.

**Differentiation:** The process of maturation of a cell line of cancer cells. When fully differentiated, the cells more closely resemble the normal cells in the tissue of origin. In high-risk neuroblastoma, 13 cis-retinoic acid (Accutane) is used as a differentiation therapy to encourage any remaining undetectable neuroblasts to mature into normal cells.

**Diploid DNA:** A tumor characteristic in which the basic chromosome number in the neuroblastoma cells is doubled (also referred to as DNA Index = 1.0). This is an unfavorable prognostic factor.

**DNA Index:** A measurement of the amount of DNA material in neuroblastoma cells. An increase in the number of chromosomes is called hyperdiploid DNA. Diploid is the same as DNA index = 1.0; triploid is DNA Index = 1.5; tetraploid is DNA index = 2.0. Diploid and tetraploid are unfavorable prognostic characteristics, and triploid is favorable.

**DNA**: Deoxyribonucleic acid; responsible for passing genetic information in nearly all organisms. DNA passes hereditary characteristics and information on cell growth, function, and division. Tumor cells have damaged DNA.

**Dopamine:** A catecholamine hormone and neurotransmitter that transmits messages in the brain and plays a role in movement. Dopamine is a precurser of adrenaline and noradrenaline.

**Doxorubicin (brand name Adriamycin):** an <u>anthracycline</u> <u>antibiotic</u> chemotherapy drug that interacts with DNA, commonly used in frontline and relapsed neuroblastoma. Can cause heart damage.

 $\mathbf{E}$ 

**Echocardiogram:** A test to image the heart and surrounding tissues that uses high-frequency (ultrasound) sound waves.

**Electrocardiogram (EKG or ECG):** A record of the electrical impulses that trigger the heartbeat, recorded on a moving strip of paper.

**Electrolyte:** Minerals, such as sodium potassium, that are found in the blood plasma and must be maintained at certain levels to prevent organ malfunction.

**Enteral:** General term for intestines.

**Epinephrine:** Another name for adrenaline. Epinephrine is a hormone produced by the adrenal glands in response to stress, exercise, or fear.

**Erythrocyte Sedimentation Rate (ESR):** A measure of the time it takes for red blood cells to collect at the bottom of a sample of blood. It is a non-specific sign of inflammation, and can be caused by many diseases such as arthritis or wide-spread cancer. It is also called "sed rate."

**Esthesioneuroblastoma:** A malignant tumor distinct from neuroblastoma (not a peripheral neuroblastic tumor or pNT) arising from the olfactory epithelium of the superior nasal cavity and cribriform plate. It is rare and its cause is unknown. The type of treatment depends on tumor size and location.

**Etoposide (VP-16):** An inhibitor of the <u>enzyme</u> <u>topoisomerase II</u>, chemotherapy commonly used in frontline and relapsed neuroblastoma. Can cause leukemia.

F

Febrile: Feverish; with fever.

**Ferritin:** An iron storage protein that is found especially in the liver and spleen.

<u>Fluorescent</u> <u>in situ</u> <u>hybridization</u> (FISH): A <u>cytogenetic</u> technique which can be used to detect disseminated neuroblastoma cells in blood or bone marrow aspirate and can distinguish between malignant and benign cells. This method localizes the presence or absence of specific <u>DNA</u> <u>sequences</u> on <u>chromosomes</u>. It uses <u>fluorescent probes</u> which bind only to those parts of the chromosome with which they show a high degree of sequence similarity.

G

**Ganglion:** A <u>tissue mass</u>, which is composed mainly of <u>somata</u> and <u>dendritic structures</u> (parts of nerve cells), which often interconnect with each other to form a complex system of ganglia known as a <u>plexus</u> (network). These structures provide relay points and intermediary connections between different neurological structures in the body, such as the <u>peripheral</u> and <u>central</u> nervous systems.

**Ganglioneuroblastoma (GNB):** A cancerous growth composed of nerve fibers and mature ganglion cells. It is regarded by many as a differentiated neuroblastoma. Nodular ganglioneuroblastoma has "nodes" of neuroblastoma.

**Ganglioneuroma:** A neuroma (benign) derived from ganglion cells. Ganglioneuromas are often found in the hands or wrists.

**Ganglioside GD2:** GD2 is a serum marker found in large amounts on the surface of some neuroblastoma cells. Some institutions are researching the use of antibodies that attack GD2 while limiting damage to healthy cells.

**Gastric Tube (G Tube):** A tube inserted through a small incision in the abdomen into the <u>stomach</u> and is used for long-term enteral nutrition.

**Granulocyte:** A type of white blood cell that protects the body against bacterial infections. Patients receiving high dose chemotherapy may receive granulocyte colony stimulating factor (GCSF, Neupogen, or Neulasta) to help the immune system recover more quickly.

н

**Hematocrit:** The percentage of total blood volume that consists of red blood cells.

**Hematoma:** A collection of blood from a broken blood vessel.

**Hematopoietic:** To make blood, another word for blood-forming stem cells.

**Hematuria:** Blood in the urine. Gross hematuria means the blood is obvious; microscopic hematuria means the blood is hidden.

**Hemoglobin:** The pigment in red blood cells that carries oxygen to tissues; hemoglobin bound to oxygen gives blood its red color. A complete blood count (CBC) reports hemoglobin as a measure of red blood cells.

**Hemorrhagic cystitis:** Bladder ulcers; ifosfamide and cyclophosphamide can cause bleeding in the bladder, so chemo-protectant Mesna is given to protect the bladder.

**Hepatomegaly:** Enlargement of the liver.

**Hickman Catheter:** A type of central venous line which consists of a flexible plastic tube inserted into the large vein above the heart, used for administering IV drugs and drawing blood samples.

**Hirschsprung's Disease:** A congenital condition in which nerve cells do not develop in parts of the intestine, causing the colon to function poorly.

**Histology (histopathology):** the study of <u>tissue</u> sectioned as a thin slice, using a <u>microtome</u>. It can be described as microscopic <u>anatomy</u>. <u>Histopathology</u> is the microscopic study of diseased tissue, is an important tool of <u>anatomical pathology</u> since accurate diagnosis of <u>cancer</u> and other diseases usually requires histopathological examination of samples. This gives prognostic information about neuroblastomas, and is an important part of risk assessment.

**Homovanillic acid (HVA):** A dopamine metabolite. HVA is excreted in human urine. High HVA concentrations can be an indicator of active neuroblastoma.

**Horner's Syndrome:** A complex of abnormal findings marked by sinking in of the eyeball, contraction of the pupil, drooping of the upper eyelid, and vasodilation and anhidrosis of the face. Horner syndrome is caused by injury to the cervical sympathetic nerve fibers on the affected side.

**Hot Antibodies (131I-3F8):** radioactive iodine connected to 3F8 antibodies that deliver radiation directly to the neuroblastoma, also called radioimmunotherapy.

**Human Anti-Mouse Antibodies (HAMA):** antibody produced by immune system in response to mouse antibodies 3F8.

**Human Leukocyte Antigen (HLA):** Genetic information on the surface of white blood cells and platelets. HLA is composed of proteins that play an important role in activating the body's immune system to respond to foreign organisms. HLA typing is done to identify potential donors as a match to provide bone marrow or stem cells to a patient who cannot use their own stem cells for stem cell transplant (allogenic).

**Humanized monoclonal antibody (hu 14.18-IL2):** this antibody combination is called a fusion protein. The humanized antibody retains only 2% mouse antibody and is fused to interleukin-2. The patient does not form an antibody to this because it is humanized. The antibody delivers the interlekin-2 directly to the neuroblastoma cell, which creates an immune response against the tumor.

Ι

**Ifosfamide:** Alkylating chemotherapy in the nitrogen mustard family, less commonly used in frontline and sometimes in relapsed neuroblastoma; can cause bleeding in the bladder, so bladder protectant Mesna is given also.

**Immune System:** The network of cells and organs that protect the body against infection or disease. Activation of this system against foreign substances is referred to as the immune response. The ability to produce cells that work to combat infection or disease is referred to the immune function.

**Immunocompromised:** Having a depressed immune system. A person can become immunocompromised because of certain diseases or treatments.

**Immunocytology (Immunohystochemistry):** Cell surface antigen detection technique using one or more mouse antibodies. This is used to detect very small amounts of neuroblastoma cells in peripheral blood or bone marrow aspirate.

**Immunodeficiency:** The reduced capacity of the body to combat infection and disease.

**Immunoglobulins:** Proteins that perform as antibodies.

**Immunoscintigraphy:** An imaging technique in which antibodies labeled with radioactive substances are administered, and then a picture is taken of areas in the body in places where the antibody localizes.

**Immunotherapy:** Treatment to activate or return the capacity of the person's immune system to combat infection and disease.

**Incidence:** The total of new cases of a disease diagnosed annually.

**Indolent:** A slow growing cancer.

**Induction Therapy:** Treatment that is used as a first step to shrink a tumor and assess it's response to drugs. Additional therapy is given after induction therapy to destroy remaining cancer.

**Infusion:** The administration of drugs and other fluids into the blood stream.

**Insufion:** Trade name of an infusion cannula allowing multiple subcutaneous injections through the same injection port, reducing needle pain that usually comes from frequent daily injection therapy.

**Integrative Medicine:** Focus to complement mainstream medical care and address the emotional, social, and spiritual needs of patients and families; includes herbal medicine, music, aroma, visual therapy.

**Interferons:** Substances that can increase the body's normal response to disease (biological response modifiers). Interferons are normally produced by the body, but they can be made in the lab for use in treating cancer. Interferons hinder the division of cancer cells.

**Interleukins:** Substances that can increase the body's normal response to disease (biological response modifiers) that aid the immune system to combat infection and cancer. Interleukins are normally produced by the body, but they can be made in the lab for use in treating cancer.

**International Neuroblastoma Response Criteria (INRC):** Definitions of response to NB treatment used in trial results include complete response (CR), very good partial response (VGPR), partial response (PR), mixed response (MR), no response or stable disease (NR or SD), progressive disease (PD).

**Intracranial Tumors:** Tumors arising in the brain.

**Intraoperative Radiation Therapy (IORT):** Radiation aimed directly at a tumor during a surgical procedure.

**Intraperitoneal:** Within the area containing the abdominal organs (the peritoneal cavity).

**Intrathecal:** The thin space between the lining of the brain and spinal cord. Children with central nervous system (CNS) disease may receive intrathecal therapy using liquid radiation or antibodies administered into this space.

Intravenous (IV): Injection of fluids into a blood vessel.

**Iodine-131-Metaiodobenzylguanidine (I-131-MIBG):** a radioactive isotope of iodine connected to a compound that is selectively taken up in neuroblastomas and pheochromocytomas.

**Irinotecan (CPT-11, Camptosar):** A <u>topoisomerase 1 inhibitor</u> chemotherapy drug that is frequently used in relapsed neuroblastoma. It is a semisynthetic analogue of the natural alkaloid <u>camptothecin</u>.

**Isotretinoin:** A member of the retinoid family of drugs. Also known as 13-*cis*-retinoic acid, or by the trade name Accutane, Amnesteem, Roaccutane, and Claravis.

J

**Jaundice:** A condition characterized by yellowing of the skin, the whites of the eyes, and a darkening of the urine. Jaundice indicates that the liver is not working properly.

K

**Karyorrhexis**: The destructive fragmentation of the <u>nucleus</u> of a dying <u>cell</u>. It can occur either as a result of <u>programmed cell death</u> or <u>necrosis</u>.

**Kidneys:** A pair of organs found in the abdomen. The kidneys remove waste from the blood, which leaves the body as urine.

**Killer Cells:** A type of white blood cell that attacks tumor cells and other cells that have been invaded by foreign substances.

L

**Lactate dehydrogenase (LDH):** An enzyme present in most tissue, often used as a marker of tissue breakdown. This can be used as a marker for disease progression in neuroblastoma in some cases.

**Laparoscopy:** The insertion of a laparoscope (a thin tube with an attached light) through the abdominal wall to view the inside of the abdomen. Laparoscopy is also used to remove tissue samples.

**Laparotomy:** An incision made in the wall of the abdomen.

**Lasix:** a loop diuretic that prevents system from absorbing too much salt, allowing the salt to instead be passed in your urine. Lasix uis used to treat fluid retention (edema).

Leukocytes: Cells that help the body combat infections and diseases. Also called white blood cells.

**Lugol's (SSKI):** Potassium and iodine solution used to protect thyroid from MIBG scans and MIBG therapy

**Lumbar Puncture:** The penetration of a needle into the lower part of the spinal column to gather cerebrospinal fluid or to give chemotherapy drugs intrathecally. Also called a spinal tap. This procedure is not recommended during tests for diagnosis of suspected neuroblastoma due to possibility of spread of disease to central nervous system.

**Lymphatic System:** The tissues and organs that produce, store, and carry white blood cells that combat infection and other diseases. This network includes the bone marrow, spleen, thymus, and lymph nodes and a system of thin tubes that carry lymph and white blood cells. These tubes branch, like blood vessels, into all the tissues of the body.

# M

**Magnetic Resonance Imaging (MRI):** A procedure in which a magnet linked to a computer is used to create detailed images of areas inside the body.

**Malignant (Malignancy):** A cancerous growth with a tendency to invade and destroy nearby tissue and spread to other parts of the body.

**Mediastinum:** The area between the lungs, which includes the heart, trachea, esophagus, bronchi, and lymph nodes.

Mediport: (brand name) a venous catheter in the chest that has access under the skin.

**Megestrol (megace):** A hormone that is used to increase appetite in people with cancer.

**Melphalan:** A chemotherapy drug that belongs to the family of drugs called alkylating agents.

**Melphalan:** Alkylating chemotherapy in the nitrogen mustard family, commonly used in stem cell transplant regimens for neuroblastoma; can cause severe mucositis.

**Meninges:** The three membranes that cover and protect the brain and spinal cord.

**Mesna:** A drug that helps safeguard the kidneys and bladder from the damaging effects of the chemotherapy drugs ifosfamide and cyclophosphamide.

**Meta-iodobenzylguanidine (MIBG or mIBG):** synthetic analogue of the neurotransmitter norepinephrine; selectively taken up (metabolized) by neuroblastoma cells.

**Metastasis:** Cancer that has spread from one part of the body to another.

**Minimal Residual Disease (MRD):** Undetectable cancer cells left behind after treatment that cause relapse. Accutane (cis-retinoic acid) and antibodies are treatments for minimal residual disease.

**Mitosis:** The process in which a cell duplicates its chromosomes to generate two, identical cells.

**Mitosis-karyorrhexis index (MKI):** A count of dividing tumor cells for classifying tumor pathology and one factor used for neuroblastoma risk assessment. A high MKI (≥200/5,000 cells) at any age is unfavorable. A low MKI (<100/5,000 cells) for those <60 months of age) is favorable.

**Mixed response:** Greater than 50% decrease of any lesion with less than 50% decrease in any other as defined by the INRC.

**Monoclonal Antibodies (MoAb):** Substances made in a laboratory that can locate and attach to cancer cells in the body. Monoclonal antibodies are used to fight cancer by recognizing certain proteins on specific cancer cells. They can be used alone, or used to deliver drugs or radioactive material directly to a tumor. Types of monoclonal antibodies used in neuroblastoma treatment include 3F8, 8H9, hu14.18 and ch14.18.

**Monoclonal Antibody 3F8:** 3F8 was produced by white blood cells of mice, and it must be carefully prepared for human use. It attaches to GD2, which is a marker on the surface of neuroblastoma cells. 3F8 is part of the standard treatment for high-risk neuroblastoma and is only available at Memorial Sloan-Kettering.

**Monoclonal Antibody 8H9:** A murine (mouse) IgG1 antibody. The 8H9 antibody is highly reactive with a range of neoplastic tissue, including human brain tumors, childhood sarcomas, and neuroblastomas. The majority of primary brain tumors tested positive with 8H9 antibody. The 8H9 antigen is expressed on cell membranes of a broad spectrum of tumors of neuroectodermal, mesenchymal, and epithelial origin.

**Monocyte:** A type of white blood cell.

**Morphology:** The science of the structure and form of organisms.

**Mucositis:** A complication of cancer treatment that causes the lining of the digestive tract to become inflamed. Mucositis sores can develop in the mouth, throat, stomach or intestinal tract.

**Multimodal Treatment:** Approach to therapy that uses more than one type of treatment.

**MYC-N Amplification:** myc myelocytomatosis viral related oncogene, when amplified (more copies) unfavorable prognostic factor for neuroblastoma; same as MYCN

Mycostatin: A drug that treats fungal infections.

**Myelin:** The fatty material that covers and protects nerves.

**Myeloablative Therapy:** Chemotherapy and/or radiation that destroy the blood-producing cells in the bone marrow and requires blood stem cells to recover.

**Myelodysplasia:** Abnormal bone marrow cells that may lead to a type of leukemia.

**Myelofibrosis:** A condition in which bone marrow is replaced by fibrous tissue.

**Myelosuppressive Therapy:** Treatment that inhibits blood cell production.

N

**Naso-gastric (NG) Tube:** A plastic tube inserted through the <u>nose</u>, past the <u>throat</u>, and down into the <u>stomach</u>, used for feeding and administering drugs.

**Neoplasm or Neoplasia:** A new growth of benign or malignant tissue.

**Nephrectomy:** Surgical removal of the kidney.

**Neuroblastoma:** A malignancy that arises in immature nerve cells, occurring in mostly infants and children.

**Neuroectodermal Tumor:** A tumor of the central or peripheral nervous systems.

**Neuroendocrine:** Refers to the nervous system and the endocrine system and their hormones.

**Neuropathy:** A term used to describe changes in the peripheral nervous system. Some drugs used in treatment of neuroblastoma can cause numbness, tingling, or pain in extremities.

**Neurotoxicity:** The propensity of some treatments to damage the nervous system.

**Neutropenia:** An abnormal reduction in the number of infection-fighting white blood cells called neutrophils. Neutropenic patients have no ability to fight infections and generally require hospitalization if they develop a fever.

**Neutrophil:** A type of white blood cell necessary for fighting infection..

**N-MYC Amplification:** myc myelocytomatosis viral related oncogene, when amplified (more copies) unfavorable prognostic factor; same as MYCN

No Evidence of Disease (NED): No detectable disease.

**No Response:** Less than 50% decrease but less than 25% increase in any lesion as defined by the INRC.

Nonsteroidal anti-inflammatory drugs: A group of drugs that decrease swelling, pain, and redness.

**Nystatin:** A drug that treats fungal infections.

O

**Octreotide:** A drug similar to the naturally-occurring growth hormone inhibitor somatostatin, used for scans and therapy like MIBG.

**Ommaya reservoir:** a plastic, dome-shaped device surgically placed under the scalp with thin tubing that passes through an opening in the skull for delivering drugs to the brain and spinal cord.

**Oncogene:** A gene that normally directs cell growth. If an oncogene is altered, it can encourage or permit the uncontrolled growth of cancer.

Ondansetron (Zofran): A drug that prevents or diminishes nausea and vomiting.

**Opsoclonus-Myoclonus Syndrome:** a syndrome which includes ataxia and encephalopathy. "Opsoclonus" is an unusual disorder of eye movement in which both eyes dart involuntarily (dancing eyes). "Myoclonus" simply means brief muscle jerks and "ataxia" indicates incoordination..

**Ototoxic (ototoxicity):** Damaging to hearing. Some chemotherapy and antibiotics can cause hearing damage and are termed ototoxic drugs.

**Overall Survival (OS):** The percentage of subjects in a study who have survived for a defined period of time. Usually reported as time since diagnosis or treatment. Also called the survival rate.

P

**p53 Gene:** A tumor suppressor gene that normally inhibits the growth of tumors that has been found to be altered in many types of cancer.

**Palliative Therapy:** Treatment given to alleviate symptoms caused by cancer or its treatment with the goal to improving the quality of life.

**Palpation:** Examination by feeling an area of the body with the fingers to feel the organs or tissues underneath.

**Partial Response (PR):** The shrinking, but not entire disappearance, of a tumor in response to treatment, defined by the INRC as greater than 50% decrease in measurable disease and 1 or no positive bone marrow site.

Pathologic Fracture: A fracture in a bone to an area that has been weakened by cancer.

**Peripheral Blood Stem Cell Transplant (PBSCT):** Stem cells collected from the peripheral blood as opposed to directly from bone marrow, and used to "rescue" patient from high-dose chemotherapy and/or radiation.

**Peripheral IV line:** A short <u>catheter</u> inserted through the skin into a <u>peripheral vein</u>, any vein that is not in the chest or abdomen

**Peripheral neuroblastic tumors or pNTs:** The spectrum of tumors classified by pathologists that arise from sympathetic nervous tissue; includes neuroblastoma, ganglioneuroblastoma, and ganglioneuroma.

**Peripheral Stem Cells:** Immature cells found circulating in the bloodstream from which new blood cells develop.

**Peripherally Inserted Central Catheter (PICC Line):** A long, thin, flexible tube known as a catheter. It is inserted into one of the large veins of the arm near the bend of the elbow. It is then slid into the vein until the tip sits in a large vein just above the heart.

Petechiae: Pinpoint bleeding under the skin usually caused by a low platelet count.

**Pilot Study:** The initial study examining a new method or treatment.

**Placebo:** An inert substance that resembles an actual medication, and is administered in the same way as a drug in a clinical trial.

Plasma: The clear, yellowish, fluid portion of the blood. Cells are suspended in plasma.

**Platelets:** One of three types of circulating blood cells that helps prevent bleeding by causing blood clots to form. Also called thrombocytes.

**Platinum:** A metal that is a significant ingredient of some chemotherapy drugs, such as cisplatin and carboplatin.

**Ploidy:** The number of sets of chromosomes in a cell or an organism. For example, haploid means one set and diploid means two sets.

Port (or "port-a-cath"): Catheter placed in chest with access just under the skin.

**Positron Emission Tomography (PET) Scan:** Positron emission tomography scan. A computerized representation of areas of increased glucose uptake which is used to ascertain the presence of disease.

**Progressive Disease (PD):** New lesion or greater than 25% increase in an existing lesion as defined by the INRC.

**Prophylaxis:** An effort to prevent disease.

**Purging:** Removing neuroblastoma cells from bone marrow or peripheral stem cells in laboratory.

R

**Radiation Therapy:** The use of high-energy radiation from x-ray machines, cobalt, radium or other sources for control or cure of cancer. Systemic radiation involves giving a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body.

**Radioactive Iodine:** A radioactive form of the chemical element iodine often used for imaging tests or as a treatment for cancer.

**Radiolabeled:** Any compound that has been joined with a radioactive substance.

**Recurrence:** The reappearance of cancer, at the same site as the original tumor or in another location, after treatment had caused it to apparently disappear.

**Red Blood Cells:** Cells that carry oxygen to tissues and take carbon dioxide from them. Also called erythrocytes.

**Refractory:** Disease that persists after intensive frontline chemotherapy.

**Remission:** Disappearance of the signs and symptoms of cancer. A remission is not necessarily a cure.

**Resection:** Surgical removal of part of an organ.

**Residual Disease:** Cancer cells left behind after surgery or other treatment.

**Retinoid:** Vitamin A or a vitamin A-like compounds such as 13-cis retinoic acid, isoretinoin or accutane.

**Reverse transcription-polymerase chain reaction (RT-PCR):** Method to identify a target gene and transcript level in order to detect minimal residual disease.

**Risk Assignment:** Neuroblastomas are divided into three risk groups based on prognostic factors determined from cytogenetics, histology, stage and age. The risk assignment determines the treatment. About 40% are low-risk, 10% are intermediate-risk, and about 50% are high-risk.

S

**Sagramostin (GM-CSF):** A recombinant therapeutic agent which is chemically identical to or similar to endogenous human GM-CSF. Binding to specific cell surface receptors, sargramostim modulates the proliferation and differentiation of a variety of hematopoietic progenitor cells with some specificity towards stimulation of leukocyte production and may reverse treatment-induced neutropenias

Saline: A solution of salt and water used for IV hydration.

**Second-look Surgery:** Surgery performed after primary treatment to determine whether tumor cells remain.

**Sedimentation (SED) Rate:** A measure of the time it takes for red blood cells to collect at the bottom of a sample of blood. It is a non-specific sign of inflammation, and can be caused by many diseases such as arthritis or wide-spread cancer. It is also called ESR.

**Shimada classification:** The histopathology classification of neuroblastoma tumors. The classification groups tumors based on morphological features such as degree of maturation, structure, and mitosis. Favorable histology includes tumors that are Schwannian stroma-rich, and unfavorable tumors are Schwannian stroma-poor.

**Shingles:** Herpes zoster, or shingles, is the reactivation of <u>varicella zoster virus</u> (<u>chickenpox</u>), producing a crop of painful <u>blisters</u>. This is common after stem cell transplants or immune suppressive therapy and is treated with acyclovir.

**Shunt:** A surgically created redirection of fluid from one area of the body to another.

Stable Disease: Cancer that is not decreasing or increasing in bulk or severity.

**Staging:** A process of determining how far a cancer has spread. Staging involves a physical exam, blood tests, x-rays, scans, and sometimes surgery. Knowing the stage of disease helps to determine treatments and prognosis.

**Stem Cells:** A cell from which other types of cells develop. Blood cells develop from blood-forming stem cells.

**Stroma:** The connective, non-functional supportive framework of a biological <u>cell</u>, <u>tissue</u>, or <u>organ</u>. Stroma-rich neuroblastomas are favorable and stroma-poor neuroblastomas are unfavorable.

Subcutaneous: Beneath the skin.

T

Teniposide: A chemotherapy drug that belongs to the family of drugs called mitotic inhibitors.

**Thiotepa (ThioTEPA):** A chemotherapy drug that belongs to the family of drugs called alkylating agents, used in some stem cell transplant regimens for neuroblastoma.

**Thoracotomy:** An operation to open the chest.

Thrombocytes: See Platelets.

**Thrombocytopenia:** An abnormally low number of platelets due to disease, reaction to a drug, or toxic reaction to treatments.

**TNP-470:** A drug that belongs to the family of drugs called angiogenesis inhibitors and blocks the growth of further blood vessels into a solid tumor.

**Topoisomerase inhibitors:** A substance that blocks topoisomerase enzymes, which are involved in DNA structure and cell growth, and the action of some chemotherapy drugs.

**Topotecan:** A <u>topoisomerase 1</u> <u>inhibitor</u> chemotherapy drug that is frequently used in relapsed neuroblastoma. In study for future use in frontline therapy.

**Total Marrow Irradiation (TMI):** Radiation therapy delivered to all the bones and marrow, sparing the organs. Also called TomoTherapy.

**Total Parenteral Nutrition (TPN):** The practice of feeding a patient intravenously, circumventing the <u>gut</u>. This is commonly required in small children undergoing intense chemotherapy and stem cell transplants.

**Total-body Irradiation (TBI):** Radiation therapy delivered to the whole body.

**Transfusion:** The infusion of components of blood or whole blood into the bloodstream.

**Trimethoprim-sulfamethoxazole (Bactrim, Septra):** An antibiotic used to treat infection and to prevent *pneumocystis carinii pneumonia* (pcp pneumonia).

**Tumor Infiltrating Lymphocytes:** White blood cells that have moved from the bloodstream and migrated into a tumor.

**Tumor Marker:** Substances sometimes discovered in an increased amount in the blood, other body fluids, or tissues and which may imply the presence of some types of cancer.

**Tumor Necrosis Factor:** A natural protein substance produced by the body, which may make tumors shrink.

**Tumor Suppressor Gene:** Genes in the body that can suppress or block the development of cancer.

**Type and Crossmatch:** To protect patients from adverse reactions to unmatched blood from blood donors, a type and crossmatch is performed to check antigens and antibodies. This process takes 45 minutes (see more).

U

**Ultrasound:** A study which uses high-frequency sound waves to create an image of the inside of the body.

**Umbilical Cord Blood:** Blood collected from the placenta at birth that contains high concentrations of stem cells needed to produce new blood cells. Parents of neuroblastoma children often are able to collect and store cord blood from later-born siblings at low or no cost.

**Ureter:** The tube that carries urine from the kidney to the bladder.

**Urethra:** The tube which empties urine from the bladder.

**Urinalysis:** Examination of the content of the urine.

**Urokinase:** A drug that dissolves blood clots or prevents them from forming.

 $\mathbf{v}$ 

**Vaccine:** A compound or group of compounds designed to produce an immune response to a tumor or disease.

**Vancomycin:** An antibiotic drug used to fight resistant bacterial infections.

Varicella: varicella-zoster virus that causes chicken pox, also one of the herpes family of viruses

**Vascular:** A tumor that is heavily endowed with blood vessels and thus richly supplied with <u>blood</u>.

**Very good partial response (VGPR):** Define by INRC as primary mass reduced by 90–99%, no evidence of distant disease except for skeletal residua, catecholamines normal.

**Vincristine:** Vinca alkaloid chemotherapy (made from the <u>Madagascar periwinkle</u>) commonly used in frontline and relapsed neuroblastoma; can cause neuropathy and loss of reflexes.

**Virus:** A tiny infectious agent that is smaller than bacteria. Many common infections are caused by viruses. Viruses invade cells, alter the cells' chemistry and cause them to produce more viruses. In cancer therapy, some viruses may be made into vaccines that help the body build an immune response to kill tumor cells.

W

White Blood Cells: Infection and disease fighting cells.

More general cancer terms can be found in the <u>NCI Dictionary of Cancer Terms</u> and the <u>NCI Drug</u> <u>Dictionary</u>. Some items used with the permission of Honna Janes-Hodder

Please contact editors@nbhope.org with any comments