THE OFFICIAL PARENT'S SOURCEBOOK *on*

CHILDHOOD NON-HODGKIN'S LYMPHOMA

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Dedication

To the healthcare professionals dedicating their time and efforts to the study of childhood non-Hodgkin's lymphoma.

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The collective knowledge generated from academic and applied research summarized in various references has been critical in the creation of this sourcebook which is best viewed as a comprehensive compilation and collection of information prepared by various official agencies which directly or indirectly are dedicated to childhood non-Hodgkin's lymphoma. All of the *Official Parent's Sourcebooks* draw from various agencies and institutions associated with the United States Department of Health and Human Services, and in particular, the Office of the Secretary of Health and Human Services (OS), the Administration for Children and Families (ACF), the Administration on Aging (AOA), the Agency for Healthcare Research and Quality (AHRQ), the Agency for Toxic Substances and Disease Registry (ATSDR), the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the Healthcare Financing Administration (HCFA), the Health Resources and Services Administration (HRSA), the Indian Health Service (IHS), the institutions of the National Institutes of Health (NIH), the Program Support Center (PSC), and the Substance Abuse and Mental Health Services Administration (SAMHSA). In addition to these sources, information gathered from the National Library of Medicine, the United States Patent Office, the European Union, and their related organizations has been invaluable in the creation of this sourcebook. Some of the work represented was financially supported by the Research and Development Committee at INSEAD. This support is gratefully acknowledged. Finally, special thanks are owed to Tiffany LaRochelle for her excellent editorial support.

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About ICON Health Publications

In addition to childhood non-Hodgkin's lymphoma, *Official Parent's Sourcebooks* are available for the following related topics:

- The Official Patient's Sourcebook on Childhood Acute Lymphoblastic Leukemia
- The Official Patient's Sourcebook on Childhood Acute Myeloid Leukemia - Other Myeloid Malignancies
- The Official Patient's Sourcebook on Childhood Hodgkin's Disease
- The Official Patient's Sourcebook on Childhood Liver Cancer
- The Official Patient's Sourcebook on Childhood Rhabdomyosarcoma
- The Official Patient's Sourcebook on Childhood Soft Tissue Sarcoma
- The Official Patient's Sourcebook on Neuroblastoma
- The Official Patient's Sourcebook on Retinoblastoma
- The Official Patient's Sourcebook on Unusual Childhood Cancers
- The Official Patient's Sourcebook on Wilm's Tumor and Other Childhood Kidney Tumors

To discover more about ICON Health Publications, simply check with your preferred online booksellers, including Barnes & Noble.com and Amazon.com which currently carry all of our titles. Or, feel free to contact us directly for bulk purchases or institutional discounts:

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INTRODUCTION

Overview

Dr. C. Everett Koop, former U.S. Surgeon General, once said, "The best prescription is knowledge."[1] The Agency for Healthcare Research and Quality (AHRQ) of the National Institutes of Health (NIH) echoes this view and recommends that all parents incorporate education into the treatment process. According to the AHRQ:

> Finding out more about your [child's] condition is a good place to start. By contacting groups that support your [child's] condition, visiting your local library, and searching on the Internet, you can find good information to help guide your decisions for your [child's] treatment. Some information may be hard to find—especially if you don't know where to look.[2]

As the AHRQ mentions, finding the right information is not an obvious task. Though many physicians and public officials had thought that the emergence of the Internet would do much to assist parents in obtaining reliable information, in March 2001 the National Institutes of Health issued the following warning:

> The number of Web sites offering health-related resources grows every day. Many sites provide valuable information, while others may have information that is unreliable or misleading.[3]

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[1] Quotation from http://www.drkoop.com.
[2] The Agency for Healthcare Research and Quality (AHRQ): http://www.ahcpr.gov/consumer/diaginfo.htm.
[3] Adapted from the NIH, National Cancer Institute (NCI): **http://cancertrials.nci.nih.gov/beyond/evaluating.html**.

Since the late 1990s, physicians have seen a general increase in parent Internet usage rates. Parents frequently enter their children's doctor's offices with printed Web pages of home remedies in the guise of latest medical research. This scenario is so common that doctors often spend more time dispelling misleading information than guiding children through sound therapies. *The Official Parent's Sourcebook on Childhood Non-Hodgkin's Lymphoma* has been created for parents who have decided to make education and research an integral part of the treatment process. The pages that follow will tell you where and how to look for information covering virtually all topics related to childhood non-Hodgkin's lymphoma, from the essentials to the most advanced areas of research.

The title of this book includes the word "official." This reflects the fact that the sourcebook draws from public, academic, government, and peer-reviewed research. Selected readings from various agencies are reproduced to give you some of the latest official information available to date on childhood non-Hodgkin's lymphoma.

Given parents' increasing sophistication in using the Internet, abundant references to reliable Internet-based resources are provided throughout this sourcebook. Where possible, guidance is provided on how to obtain free-of-charge, primary research results as well as more detailed information via the Internet. E-book and electronic versions of this sourcebook are fully interactive with each of the Internet sites mentioned (clicking on a hyperlink automatically opens your browser to the site indicated). Hard copy users of this sourcebook can type cited Web addresses directly into their browsers to obtain access to the corresponding sites. Since we are working with ICON Health Publications, hard copy *Sourcebooks* are frequently updated and printed on demand to ensure that the information provided is current.

In addition to extensive references accessible via the Internet, every chapter presents a "Vocabulary Builder." Many health guides offer glossaries of technical or uncommon terms in an appendix. In editing this sourcebook, we have decided to place a smaller glossary within each chapter that covers terms used in that chapter. Given the technical nature of some chapters, you may need to revisit many sections. Building one's vocabulary of medical terms in such a gradual manner has been shown to improve the learning process.

We must emphasize that no sourcebook on childhood non-Hodgkin's lymphoma should affirm that a specific diagnostic procedure or treatment discussed in a research study, patent, or doctoral dissertation is "correct" or your child's best option. This sourcebook is no exception. Each child is

unique. Deciding on appropriate options is always up to parents in consultation with their children's physicians and healthcare providers.

Organization

This sourcebook is organized into three parts. Part I explores basic techniques to researching childhood non-Hodgkin's lymphoma (e.g. finding guidelines on diagnosis, treatments, and prognosis), followed by a number of topics, including information on how to get in touch with organizations, associations, or other parent networks dedicated to childhood non-Hodgkin's lymphoma. It also gives you sources of information that can help you find a doctor in your local area specializing in treating childhood non-Hodgkin's lymphoma. Collectively, the material presented in Part I is a complete primer on basic research topics for childhood non-Hodgkin's lymphoma.

Part II moves on to advanced research dedicated to childhood non-Hodgkin's lymphoma. Part II is intended for those willing to invest many hours of hard work and study. It is here that we direct you to the latest scientific and applied research on childhood non-Hodgkin's lymphoma. When possible, contact names, links via the Internet, and summaries are provided. It is in Part II where the vocabulary process becomes important as authors publishing advanced research frequently use highly specialized language. In general, every attempt is made to recommend "free-to-use" options.

Part III provides appendices of useful background reading covering childhood non-Hodgkin's lymphoma or related disorders. The appendices are dedicated to more pragmatic issues facing parents. Accessing materials via medical libraries may be the only option for some parents, so a guide is provided for finding local medical libraries which are open to the public. Part III, therefore, focuses on advice that goes beyond the biological and scientific issues facing children with childhood non-Hodgkin's lymphoma and their families.

Scope

While this sourcebook covers childhood non-Hodgkin's lymphoma, doctors, research publications, and specialists may refer to your child's condition using a variety of terms. Therefore, you should understand that childhood

non-Hodgkin's lymphoma is often considered a synonym or a condition closely related to the following:

- Cancer Non-hodgkin's Lymphoma
- Histiocytic Lymphoma
- Lymphoblastic Lymphoma
- Lymphocytic Lymphoma
- Lymphoma Non-hodgkin's

In addition to synonyms and related conditions, physicians may refer to childhood non-Hodgkin's lymphoma using certain coding systems. The International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) is the most commonly used system of classification for the world's illnesses. Your physician may use this coding system as an administrative or tracking tool. The following classification is commonly used for childhood non-Hodgkin's lymphoma:[4]

- 201.9 lymphoma, non-hodgkin's
- 202.8 non-hodgkin's lymphoma, nos

For the purposes of this sourcebook, we have attempted to be as inclusive as possible, looking for official information for all of the synonyms relevant to childhood non-Hodgkin's lymphoma. You may find it useful to refer to synonyms when accessing databases or interacting with healthcare professionals and medical librarians.

Moving Forward

Since the 1980s, the world has seen a proliferation of healthcare guides covering most illnesses. Some are written by parents, patients, or their family members. These generally take a layperson's approach to understanding and coping with an illness or disorder. They can be uplifting, encouraging, and highly supportive. Other guides are authored by physicians or other healthcare providers who have a more clinical outlook. Each of these two styles of guide has its purpose and can be quite useful.

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[4] This list is based on the official version of the World Health Organization's 9th Revision, International Classification of Diseases (ICD-9). According to the National Technical Information Service, "ICD-9CM extensions, interpretations, modifications, addenda, or errata other than those approved by the U.S. Public Health Service and the Health Care Financing Administration are not to be considered official and should not be utilized. Continuous maintenance of the ICD-9-CM is the responsibility of the federal government."

As editors, we have chosen a third route. We have chosen to expose you to as many sources of official and peer-reviewed information as practical, for the purpose of educating you about basic and advanced knowledge as recognized by medical science today. You can think of this sourcebook as your personal Internet age reference librarian.

Why "Internet age"? When their child has been diagnosed with childhood non-Hodgkin's lymphoma, parents will often log on to the Internet, type words into a search engine, and receive several Web site listings which are mostly irrelevant or redundant. Parents are left to wonder where the relevant information is, and how to obtain it. Since only the smallest fraction of information dealing with childhood non-Hodgkin's lymphoma is even indexed in search engines, a non-systematic approach often leads to frustration and disappointment. With this sourcebook, we hope to direct you to the information you need that you would not likely find using popular Web directories. Beyond Web listings, in many cases we will reproduce brief summaries or abstracts of available reference materials. These abstracts often contain distilled information on topics of discussion.

While we focus on the more scientific aspects of childhood non-Hodgkin's lymphoma, there is, of course, the emotional side to consider. Later in the sourcebook, we provide a chapter dedicated to helping you find parent groups and associations that can provide additional support beyond research produced by medical science. We hope that the choices we have made give you and your child the most options in moving forward. In this way, we wish you the best in your efforts to incorporate this educational approach into your child's treatment plan.

The Editors

PART I: THE ESSENTIALS

ABOUT PART I

Part I has been edited to give you access to what we feel are "the essentials" on childhood non-Hodgkin's lymphoma. The essentials typically include a definition or description of the condition, a discussion of who it affects, the signs or symptoms, tests or diagnostic procedures, and treatments for the disease. Your child's doctor or healthcare provider may have already explained the essentials of childhood non-Hodgkin's lymphoma to you or even given you a pamphlet or brochure describing the condition. Now you are searching for more in-depth information. As editors, we have decided, nevertheless, to include a discussion on where to find essential information that can complement what the doctor has already told you. In this section we recommend a process, not a particular Web site or reference book. The process ensures that, as you search the Web, you gain background information in such a way as to maximize your understanding.

CHAPTER 1. THE ESSENTIALS ON CHILDHOOD NON-HODGKIN'S LYMPHOMA: GUIDELINES

Overview

Official agencies, as well as federally funded institutions supported by national grants, frequently publish a variety of guidelines on childhood non-Hodgkin's lymphoma. These are typically called "Fact Sheets" or "Guidelines." They can take the form of a brochure, information kit, pamphlet, or flyer. Often they are only a few pages in length. The great advantage of guidelines over other sources is that they are often written with the parent in mind. Since new guidelines on childhood non-Hodgkin's lymphoma can appear at any moment and be published by a number of sources, the best approach to finding guidelines is to systematically scan the Internet-based services that post them.

The National Institutes of Health (NIH)[5]

The National Institutes of Health (NIH) is the first place to search for relatively current guidelines and fact sheets on childhood non-Hodgkin's lymphoma. Originally founded in 1887, the NIH is one of the world's foremost medical research centers and the federal focal point for medical research in the United States. At any given time, the NIH supports some 35,000 research grants at universities, medical schools, and other research and training institutions, both nationally and internationally. The rosters of those who have conducted research or who have received NIH support over the years include the world's most illustrious scientists and physicians.

[5] Adapted from the NIH: **http://www.nih.gov/about/NIHoverview.html**.

Among them are 97 scientists who have won the Nobel Prize for achievement in medicine.

There is no guarantee that any one Institute will have a guideline on a specific medical condition, though the National Institutes of Health collectively publish over 600 guidelines for both common and rare disorders. The best way to access NIH guidelines is via the Internet. Although the NIH is organized into many different Institutes and Offices, the following is a list of key Web sites where you are most likely to find NIH clinical guidelines and publications dealing with childhood non-Hodgkin's lymphoma and associated conditions:

- Office of the Director (OD); guidelines consolidated across agencies available at **http://www.nih.gov/health/consumer/conkey.htm**
- National Library of Medicine (NLM); extensive encyclopedia (A.D.A.M., Inc.) with guidelines available at **http://www.nlm.nih.gov/medlineplus/healthtopics.html**
- National Cancer Institute (NCI); guidelines available at **http://cancernet.nci.nih.gov/pdq/pdq_treatment.shtml**

Among the above, the National Cancer Institute (NCI) is particularly noteworthy. The NCI coordinates the National Cancer Program, which conducts and supports research, training, health information dissemination, and other programs with respect to the cause, diagnosis, prevention, and treatment of cancer, rehabilitation from cancer, and the continuing care of cancer patients and the families of cancer patients.[6] Specifically, the Institute:

- Supports and coordinates research projects conducted by universities, hospitals, research foundations, and businesses throughout this country and abroad through research grants and cooperative agreements.
- Conducts research in its own laboratories and clinics.
- Supports education and training in fundamental sciences and clinical disciplines for participation in basic and clinical research programs and treatment programs relating to cancer through career awards, training grants, and fellowships.
- Supports research projects in cancer control.
- Supports a national network of cancer centers.
- Collaborates with voluntary organizations and other national and foreign institutions engaged in cancer research and training activities.

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[6] This paragraph has been adapted from the NCI: **http://www.nci.nih.gov/**. "Adapted" signifies that a passage has been reproduced exactly or slightly edited for this book.

- Encourages and coordinates cancer research by industrial concerns where such concerns evidence a particular capability for programmatic research.
- Collects and disseminates information on cancer.
- Supports construction of laboratories, clinics, and related facilities necessary for cancer research through the award of construction grants.

The NCI, established under the National Cancer Act of 1937, is the Federal Government's principal agency for cancer research and training. The National Cancer Act of 1971 broadened the scope and responsibilities of the NCI and created the National Cancer Program. Over the years, legislative amendments have maintained the NCI authorities and responsibilities and added new information dissemination mandates as well as a requirement to assess the incorporation of state-of-the-art cancer treatments into clinical practice. Information dissemination is made possible through the NCI Online at **www.cancer.gov**. Cancer.gov offers to the public and physicians up-to-date information on the latest cancer research, current and upcoming clinical trials, statistics, research programs, and research funding.

The following guideline was recently published by the NCI on childhood non-Hodgkin's lymphoma.

What Is Childhood Non-Hodgkin's Lymphoma?[7]

Once childhood non-Hodgkin's lymphoma is found, more tests will be done to find out if the cancer has spread from where it started to other parts of the body. This is called staging. Your child's doctor needs to know the stage of the disease to plan treatment.

The following stages are used for childhood non-Hodgkin's lymphoma:

Stage I

Cancer is found in only one area outside of the abdomen or chest.

[7] The following guidelines appeared on the NCI website on Aug. 26, 2002. The text was last modified in August 2002. The text has been adapted for this sourcebook.

Stage II

Any of the following mean the disease is stage II:

- Cancer is found in only one area and in the lymph nodes around it.
- Cancer is found in two or more lymph nodes or other areas on the same side of the diaphragm (the thin muscle under the lungs that helps you breathe).
- Cancer is found to have started in the digestive tract. The lymph nodes in the area may or may not have cancer.

Stage III

Any of the following mean the disease is stage III:

- Cancer is found in tumors or lymph nodes on both sides of the diaphragm.
- Cancer is found to have started in the chest.
- Cancer is found in many places in the abdomen.
- Cancer is found in the area around the spine, around the outermost covering of the brain, or on the outermost covering of the brain (these tumors are called epidural tumors).

Stage IV

Cancer has spread to the bone marrow or to the brain and/or the spinal cord.

Recurrent

Recurrent disease means that the cancer has come back after it has been treated. It may come back in the area where it first started or in another part of the body.

Treatment Option Overview

There are treatments for all patients with childhood non-Hodgkin's lymphoma and patients can be cured. The main treatment used is

chemotherapy (using drugs to kill cancer cells and shrink tumors). Radiation therapy (using high-dose x-rays or other high-energy rays to kill cancer cells and shrink tumors) is sometimes used in special situations. Bone marrow transplantation is being tested in clinical trials for certain patients.

Chemotherapy uses drugs to kill cancer cells and shrink tumors. Chemotherapy may be taken by pill, or it may be put into the body by a needle in a vein or muscle. Chemotherapy is called a systemic treatment because the drugs enter the bloodstream, travel through the body, and can kill cancer cells throughout the body. Chemotherapy may also be put into the fluid that surrounds the brain through a needle in the brain or back (intrathecal chemotherapy) to treat certain types of non-Hodgkin's lymphoma that spread to the brain.

Bone marrow transplantation is a newer type of treatment. Sometimes lymphoma cells become resistant to treatment with radiation therapy or chemotherapy. Very high doses of chemotherapy may then be used to treat the cancer. Because the high doses of chemotherapy can destroy the bone marrow, marrow is taken from the bones before treatment. The marrow is then frozen and high-dose chemotherapy with or without radiation therapy is given to treat the cancer. The marrow that was taken out is then thawed and given back through a needle in a vein to replace the marrow that was destroyed. This type of transplant is called an autologous transplant. If the marrow given is taken from another person, the transplant is called an allogeneic transplant.

Treatment by Stage

Treatment for childhood non-Hodgkin's lymphoma depends on the stage of your child's disease, how the cancer cells look under a microscope (the histology), and your child's age and general health.

Your child may receive treatment that is considered standard based on its effectiveness in a number of patients in past studies, or you may choose to have your child go into a clinical trial. Not all patients are cured with standard therapy and some standard treatments may have more side effects than are desired. For these reasons, clinical trials are designed to test new treatments and to find better ways to treat cancer patients. Clinical trials are ongoing in most parts of the country for advanced stages of childhood non-Hodgkin's lymphoma. If you want more information, call the Cancer Information Service at 1-800-4-CANCER (1-800-422-6237); TTY at 1-800-332-8615.

Stage I and II Childhood Lymphoblastic Lymphoma

Your child's treatment will probably be systemic chemotherapy plus intrathecal chemotherapy.

Stage III and IV Childhood Lymphoblastic Lymphoma

Your child's treatment will probably be systemic chemotherapy plus intrathecal chemotherapy. Radiation therapy is sometimes given if there is a large mass in the chest.

Recurrent Childhood Lymphoblastic Lymphoma

Your child's treatment will depend on where the cancer comes back, the type of treatment that was given before, and your child's overall condition. Your child's treatment may be one of the following:

- Allogeneic bone marrow transplantation.
- Systemic chemotherapy with different drugs than were used before.
- A clinical trial of new methods of treatment.

Stage I and II Childhood Small Noncleaved Cell Lymphoma[8]

Your child's treatment will probably be systemic chemotherapy with or without intrathecal chemotherapy.

Stage III and IV Childhood Small Noncleaved Cell Lymphoma

Your child's treatment will probably be systemic chemotherapy plus intrathecal chemotherapy. Clinical trials are testing new combinations and doses of drugs.

[8] Includes Burkitt's and non-Burkitt's.

Recurrent Childhood Small Noncleaved Cell Lymphoma

Your child's treatment will depend on where the cancer comes back, the type of treatment that was given before, and your child's overall condition. Your child's treatment may be one of the following:

- Systemic chemotherapy.
- Allogeneic or autologous bone marrow transplantation.
- Systemic chemotherapy plus intrathecal chemotherapy.
- A clinical trial of new methods of treatment.

Stage I and II Childhood Large Cell Lymphoma

Your child's treatment will probably be systemic chemotherapy with or without intrathecal chemotherapy.

Stage III and IV Childhood Large Cell Lymphoma

Your child's treatment will probably be systemic chemotherapy with or without intrathecal chemotherapy. Clinical trials are testing new combinations of drugs.

Recurrent Childhood Large Cell Lymphoma

Your child's treatment will depend on where the cancer comes back, the type of treatment that was given before, and your child's overall condition. Your child's treatment may be one of the following:

- Allogeneic or autologous bone marrow transplantation.
- Systemic chemotherapy with or without intrathecal chemotherapy.
- A clinical trial of new methods of treatment.

To Learn More

Call

For more information, U.S. residents may call the National Cancer Institute's (NCI's) Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-

6237), Monday through Friday from 9:00 a.m. to 4:30 p.m. Deaf and hard-of-hearing callers with TTY equipment may call 1-800-332-8615. The call is free and a trained Cancer Information Specialist is available to answer your questions.

Web Sites and Organizations

The NCI's Cancer.gov Web site (**http://cancer.gov**) provides online access to information on cancer, clinical trials, and other Web sites and organizations that offer support and resources for cancer patients and their families. There are also many other places where people can get materials and information about cancer treatment and services. Local hospitals may have information on local and regional agencies that offer information about finances, getting to and from treatment, receiving care at home, and dealing with problems associated with cancer treatment.

Publications

The NCI has booklets and other materials for patients, health professionals, and the public. These publications discuss types of cancer, methods of cancer treatment, coping with cancer, and clinical trials. Some publications provide information on tests for cancer, cancer causes and prevention, cancer statistics, and NCI research activities. NCI materials on these and other topics may be ordered online or printed directly from the NCI Publications Locator (https://cissecure.nci.nih.gov/ncipubs). These materials can also be ordered by telephone from the Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237), TTY at 1-800-332-8615.

LiveHelp

The NCI's LiveHelp service, a program available on several of the Institute's Web sites, provides Internet users with the ability to chat online with an Information Specialist. The service is available from Monday - Friday 9:00 AM - 10:00 PM Eastern Time. Information Specialists can help Internet users find information on NCI Web sites and answer questions about cancer.

Write

For more information from the NCI, please write to this address:

National Cancer Institute
Office of Communications
31 Center Drive, MSC 2580
Bethesda, MD 20892-2580

About PDQ

PDQ Is a Comprehensive Cancer Database Available on Cancer.gov

PDQ is the National Cancer Institute's (NCI's) comprehensive cancer information database. Most of the information contained in PDQ is available online at Cancer.gov, the NCI's Web site. PDQ is provided as a service of the NCI. The NCI is part of the National Institutes of Health, the federal government's focal point for biomedical research.

PDQ Contains Cancer Information Summaries

The PDQ database contains summaries of the latest published information on cancer prevention, detection, genetics, treatment, supportive care, and complementary and alternative medicine. Most summaries are available in two versions. The health professional versions provide detailed information written in technical language. The patient versions are written in easy-to-understand, non-technical language. Both versions provide current and accurate cancer information.

The PDQ cancer information summaries are developed by cancer experts and reviewed regularly. Editorial Boards made up of experts in oncology and related specialties are responsible for writing and maintaining the cancer information summaries. The summaries are reviewed regularly and changes are made as new information becomes available. The date on each summary ("Date Last Modified") indicates the time of the most recent change.

PDQ Contains Information on Clinical Trials

In the United States, about two-thirds of children with cancer are treated in a clinical trial at some point in their illness. A clinical trial is a study to answer

a scientific question, such as whether one treatment is better than another. Trials are based on past studies and what has been learned in the laboratory. Each trial answers certain scientific questions in order to find new and better ways to help cancer patients. During treatment clinical trials, information is collected about new treatments, the risks involved, and how well they do or do not work. If a clinical trial shows that a new treatment is better than one currently being used, the new treatment may become "standard."

Listings of clinical trials are included in PDQ and are available online at Cancer.gov. Descriptions of the trials are available in health professional and patient versions. For additional help in locating a childhood cancer clinical trial, call the Cancer Information Service at 1-800-4-CANCER (1-800-422-6237), TTY at 1-800-332-8615.

The PDQ Database Contains Listings of Groups Specializing in Clinical Trials

The Children's Oncology Group (COG) is the major group that organizes clinical trials for childhood cancers in the United States. Information about contacting COG is available on Cancer.gov or from the Cancer Information Service at 1-800-4-CANCER (1-800-422-6237), TTY at 1-800-332-8615.

The PDQ Database Contains Listings of Cancer Health Professionals and Hospitals with Cancer Programs

Because cancer in children and adolescents is rare, the majority of children with cancer are treated by health professionals specializing in childhood cancers, at hospitals or cancer centers with special facilities to treat them. The PDQ database contains listings of health professionals who specialize in childhood cancer and listings of hospitals with cancer programs. For help locating childhood cancer health professionals or a hospital with cancer programs, call the Cancer Information Service at 1-800-4-CANCER (1-800-422-6237), TTY at 1-800-332-8615.

More Guideline Sources

The previous guideline on childhood non-Hodgkin's lymphoma is only one example of the kind of material that you can find online and free of charge. The remainder of this chapter will direct you to other sources which either publish or can help you find additional guidelines on topics related to

childhood non-Hodgkin's lymphoma. Many of the guidelines listed below address topics that may be of particular relevance to your child's specific situation, while certain guidelines will apply to only some children with childhood non-Hodgkin's lymphoma. Due to space limitations these sources are listed in a concise manner. Do not hesitate to consult the following sources by either using the Internet hyperlink provided, or, in cases where the contact information is provided, contacting the publisher or author directly.

Topic Pages: MEDLINEplus

For parents wishing to go beyond guidelines published by specific Institutes of the NIH, the National Library of Medicine has created a vast and parent-oriented healthcare information portal called MEDLINEplus. Within this Internet-based system are "health topic pages." You can think of a health topic page as a guide to patient guides. To access this system, log on to **http://www.nlm.nih.gov/medlineplus/healthtopics.html**. From there you can either search using the alphabetical index or browse by broad topic areas.

If you do not find topics of interest when browsing health topic pages, then you can choose to use the advanced search utility of MEDLINEplus at **http://www.nlm.nih.gov/medlineplus/advancedsearch.html**. This utility is similar to the NIH Search Utility, with the exception that it only includes material linked within the MEDLINEplus system (mostly parent-oriented information). It also has the disadvantage of generating unstructured results. We recommend, therefore, that you use this method only if you have a very targeted search.

The National Guideline Clearinghouse™

The National Guideline Clearinghouse™ offers hundreds of evidence-based clinical practice guidelines published in the United States and other countries. You can search their site located at **http://www.guideline.gov** by using the keyword "childhood non-Hodgkin's lymphoma" or synonyms.

Healthfinder™

Healthfinder™ is an additional source sponsored by the U.S. Department of Health and Human Services which offers links to hundreds of other sites that

contain healthcare information. This Web site is located at **http://www.healthfinder.gov**. Again, keyword searches can be used to find guidelines.

The NIH Search Utility

After browsing the references listed at the beginning of this chapter, you may want to explore the NIH Search Utility. This allows you to search for documents on over 100 selected Web sites that comprise the NIH-WEB-SPACE. Each of these servers is "crawled" and indexed on an ongoing basis. Your search will produce a list of various documents, all of which will relate in some way to childhood non-Hodgkin's lymphoma. The drawbacks of this approach are that the information is not organized by theme and that the references are often a mix of information for professionals and parents. Nevertheless, a large number of the listed Web sites provide useful background information. We can only recommend this route, therefore, for relatively rare or specific disorders, or when using highly targeted searches. To use the NIH search utility, visit the following Web page: **http://search.nih.gov/index.html**.

Additional Web Sources

A number of Web sites that often link to government sites are available to the public. These can also point you in the direction of essential information. The following is a representative sample:

- AOL: **http://search.aol.com/cat.adp?id=168&layer=&from=subcats**
- drkoop.com®: **http://www.drkoop.com/conditions/ency/index.html**
- Family Village: **http://www.familyvillage.wisc.edu/specific.htm**
- Google: **http://directory.google.com/Top/Health/Conditions_and_Diseases/**
- Med Help International: **http://www.medhelp.org/HealthTopics/A.html**
- Open Directory Project: **http://dmoz.org/Health/Conditions_and_Diseases/**
- Yahoo.com: **http://dir.yahoo.com/Health/Diseases_and_Conditions/**
- WebMD®Health: **http://my.webmd.com/health_topics**

Vocabulary Builder

The material in this chapter may have contained a number of unfamiliar words. The following Vocabulary Builder introduces you to terms used in this chapter that have not been covered in the previous chapter:

Abdomen: The part of the body that contains the pancreas, stomach, intestines, liver, gallbladder, and other organs. [NIH]

Adolescence: The period of life beginning with the appearance of secondary sex characteristics and terminating with the cessation of somatic growth. The years usually referred to as adolescence lie between 13 and 18 years of age. [NIH]

Allogeneic: Taken from different individuals of the same species. [NIH]

Antibiotic: A drug used to treat infections caused by bacteria and other microorganisms. [NIH]

Autologous: Taken from an individual's own tissues, cells, or DNA. [NIH]

Cell: The individual unit that makes up all of the tissues of the body. All living things are made up of one or more cells. [NIH]

Chemotherapy: Treatment with anticancer drugs. [NIH]

Diaphragm: The thin muscle below the lungs and heart that separates the chest from the abdomen. [NIH]

Epidural: The space between the wall of the spinal canal and the covering of the spinal cord. An epidural injection is given into this space. [NIH]

Histology: The study of tissues and cells under a microscope. [NIH]

Immunization: The induction of immunity. [EU]

Intrathecal: Describes the fluid-filled space between the thin layers of tissue that cover the brain and spinal cord. Drugs can be injected into the fluid or a sample of the fluid can be removed for testing. [NIH]

Lymphoma: Cancer that arises in cells of the lymphatic system. [NIH]

Oncology: The study of cancer. [NIH]

Pediatrics: A medical specialty concerned with maintaining health and providing medical care to children from birth to adolescence. [NIH]

Polysaccharide: A type of carbohydrate. It contains sugar molecules that are linked together chemically. [NIH]

Prophylaxis: An attempt to prevent disease. [NIH]

Staging: Performing exams and tests to learn the extent of the cancer within the body, especially whether the disease has spread from the original site to other parts of the body. [NIH]

Systemic: Affecting the entire body. [NIH]

Transplantation: The replacement of an organ with one from another person. [NIH]

Vaccine: A substance or group of substances meant to cause the immune system to respond to a tumor or to microorganisms, such as bacteria or viruses. [NIH]

CHAPTER 2. SEEKING GUIDANCE

Overview

Some parents are comforted by the knowledge that a number of organizations dedicate their resources to helping people with childhood non-Hodgkin's lymphoma. These associations can become invaluable sources of information and advice. Many associations offer parent support, financial assistance, and other important services. Furthermore, healthcare research has shown that support groups often help people to better cope with their conditions.[9] In addition to support groups, your child's physician can be a valuable source of guidance and support.

In this chapter, we direct you to resources that can help you find parent organizations and medical specialists. We begin by describing how to find associations and parent groups that can help you better understand and cope with your child's condition. The chapter ends with a discussion on how to find a doctor that is right for your child.

There are a number of directories that list additional medical associations that you may find useful. While not all of these directories will provide different information, by consulting all of them, you will have nearly exhausted all sources for parent associations.

The National Cancer Institute (NCI)

The National Cancer Institute (NCI) has complied a list of national organizations that offer services to people with cancer and their families. To

[9] Churches, synagogues, and other houses of worship might also have groups that can offer you the social support you need.

view the list, see the NCI fact sheet online at the following Web address: **http://cis.nci.nih.gov/fact/8_1.htm**. The name of each organization is accompanied by its contact information and a brief explanation of its services. Information on a number of organizations specializing in children's issues is also available.

The National Health Information Center (NHIC)

The National Health Information Center (NHIC) offers a free referral service to help people find organizations that provide information about childhood non-Hodgkin's lymphoma. For more information, see the NHIC's Web site at **http://www.health.gov/NHIC/** or contact an information specialist by calling 1-800-336-4797.

DIRLINE

A comprehensive source of information on associations is the DIRLINE database maintained by the National Library of Medicine. The database comprises some 10,000 records of organizations, research centers, and government institutes and associations which primarily focus on health and biomedicine. DIRLINE is available via the Internet at the following Web site: **http://dirline.nlm.nih.gov**. Simply type in "childhood non-Hodgkin's lymphoma" (or a synonym) or the name of a topic, and the site will list information contained in the database on all relevant organizations.

The Combined Health Information Database

Another comprehensive source of information on healthcare associations is the Combined Health Information Database. Using the "Detailed Search" option, you will need to limit your search to "Organizations" and "childhood non-Hodgkin's lymphoma". Type the following hyperlink into your Web browser: **http://chid.nih.gov/detail/detail.html**. To find associations, use the drop boxes at the bottom of the search page where "You may refine your search by." For publication date, select "All Years." Then, select your preferred language and the format option "Organization Resource Sheet." By making these selections and typing in "childhood non-Hodgkin's lymphoma" (or synonyms) into the "For these words:" box, you will only receive results on organizations dealing with childhood non-Hodgkin's lymphoma. You should check back periodically with this database since it is updated every 3 months.

The National Organization for Rare Disorders, Inc.

The National Organization for Rare Disorders, Inc. has prepared a Web site that provides, at no charge, lists of associations organized by specific medical conditions. You can access this database at the following Web site: **http://www.rarediseases.org/cgi-bin/nord/searchpage**. Select the option called "Organizational Database (ODB)" and type "childhood non-Hodgkin's lymphoma" (or a synonym) in the search box.

Cancer Support Groups[10]

People diagnosed with cancer and their families face many challenges that may leave them feeling overwhelmed, afraid, and alone. It can be difficult to cope with these challenges or to talk to even the most supportive family members and friends. Often, support groups can help people affected by cancer feel less alone and can improve their ability to deal with the uncertainties and challenges that cancer brings. Support groups give people who are affected by similar diseases an opportunity to meet and discuss ways to cope with the illness.

How Can Support Groups Help?

People who have been diagnosed with cancer sometimes find they need assistance coping with the emotional as well as the practical aspects of their disease. In fact, attention to the emotional burden of cancer is sometimes part of a patient's treatment plan. Cancer support groups are designed to provide a confidential atmosphere where cancer patients or cancer survivors can discuss the challenges that accompany the illness with others who may have experienced the same challenges. For example, people gather to discuss the emotional needs created by cancer, to exchange information about their disease—including practical problems such as managing side effects or returning to work after treatment—and to share their feelings. Support groups have helped thousands of people cope with these and similar situations.

[10] This section has been adapted from the NCI: **http://cis.nci.nih.gov/fact/8_8.htm**.

Can Family Members and Friends Participate in Support Groups?

Family and friends are affected when cancer touches someone they love, and they may need help in dealing with stresses such as family disruptions, financial worries, and changing roles within relationships. To help meet these needs, some support groups are designed just for family members of people diagnosed with cancer; other groups encourage families and friends to participate along with the cancer patient or cancer survivor.

How Can People Find Support Groups?

Many organizations offer support groups for people diagnosed with cancer and their family members or friends. The NCI fact sheet *National Organizations That Offer Services to People With Cancer and Their Families* lists many cancer-concerned organizations that can provide information about support groups. This fact sheet is available at **http://cis.nci.nih.gov/fact/8_1.htm** on the Internet, or can be ordered from the Cancer Information Service at 1–800–4–CANCER (1–800–422–6237). Some of these organizations provide information on their Web sites about contacting support groups.

Doctors, nurses, or hospital social workers who work with cancer patients may also have information about support groups, such as their location, size, type, and how often they meet. Most hospitals have social services departments that provide information about cancer support programs. Additionally, many newspapers carry a special health supplement containing information about where to find support groups.

What Types of Support Groups Are Available?

Several kinds of support groups are available to meet the individual needs of people at all stages of cancer treatment, from diagnosis through follow-up care. Some groups are general cancer support groups, while more specialized groups may be for teens or young adults, for family members, or for people affected by a particular disease. Support groups may be led by a professional, such as a psychiatrist, psychologist, or social worker, or by cancer patients or survivors. In addition, support groups can vary in approach, size, and how often they meet. Many groups are free, but some require a fee (people can contact their health insurance company to find out whether their plan will cover the cost). It is important for people to find an atmosphere that is comfortable and meets their individual needs.

Online Support Groups

In addition to support groups, commercial Internet service providers offer forums and chat rooms to discuss different illnesses and conditions. WebMD®, for example, offers such a service at their Web site: **http://boards.webmd.com/roundtable**. These online communities can help you connect with a network of people whose concerns are similar to yours. Online support groups are places where people can talk informally. If you read about a novel approach, consult with your child's doctor or other healthcare providers, as the treatments or discoveries you hear about may not be scientifically proven to be safe and effective.

The Cancer Information Service[11]

The Cancer Information Service (CIS) is a program of the National Cancer Institute (NCI), the Nation's lead agency for cancer research. As a resource for information and education about cancer, the CIS is a leader in helping people become active participants in their own health care by providing the latest information on cancer in understandable language. Through its network of regional offices, the CIS serves the United States, Puerto Rico, the U.S. Virgin Islands, and the Pacific Islands.

For 25 years, the Cancer Information Service has provided the latest and most accurate cancer information to patients and families, the public, and health professionals by:

- Interacting with people one-on-one through its Information Service,
- Working with organizations through its Partnership Program,
- Participating in research efforts to find the best ways to help people adopt healthier behaviors,
- Providing access to NCI information over the Internet.

How Does the CIS Assist the Public?

Through the CIS toll-free telephone service (1–800–4–CANCER), callers speak with knowledgeable, caring staff who are experienced at explaining medical information in easy-to-understand terms. CIS information specialists answer calls in English and Spanish. They also provide cancer information to deaf and hard of hearing callers through the toll-free TTY number (1–800–

[11] This section has been adapted from the NCI: **http://cis.nci.nih.gov/fact/2_5.htm**.

332–8615). CIS staff have access to comprehensive, accurate information from the NCI on a range of cancer topics, including the most recent advances in cancer treatment. They take as much time as each caller needs, provide thorough and personalized attention, and keep all calls confidential.

The CIS also provides live, online assistance to users of NCI Web sites through LiveHelp, an instant messaging service that is available from 9:00 a.m. to 7:30 p.m. Eastern time, Monday through Friday. Through LiveHelp, information specialists provide answers to questions about cancer and help in navigating Cancer.gov, the NCI's Web site.

Through the telephone numbers or LiveHelp service, CIS users receive:

- Answers to their questions about cancer, including ways to prevent cancer, symptoms and risks, diagnosis, current treatments, and research studies;
- Written materials from the NCI;
- Referrals to clinical trials and cancer-related services, such as treatment centers, mammography facilities, or other cancer organizations;
- Assistance in quitting smoking from information specialists trained in smoking cessation counseling.

What Kind of Assistance Does the CIS Partnership Program Offer?

Through its Partnership Program, the CIS collaborates with established national, state, and regional organizations to reach minority and medically underserved audiences with cancer information. Partnership Program staff provide assistance to organizations developing programs that focus on breast and cervical cancer, clinical trials, tobacco control, and cancer awareness for special populations. To reach those in need, the CIS:

- Helps bring cancer information to people who do not traditionally seek health information or who may have difficulties doing so because of educational, financial, cultural, or language barriers;
- Provides expertise to organizations to help strengthen their ability to inform people they serve about cancer; and
- Links organizations with similar goals and helps them plan and evaluate programs, develop coalitions, conduct training on cancer-related topics, and use NCI resources.

How Do CIS Research Efforts Assist the Public?

The CIS plays an important role in research by studying the most effective ways to communicate with people about healthy lifestyles; health risks; and options for preventing, diagnosing, and treating cancer. The ability to conduct health communications research is a unique aspect of the CIS. Results from these research studies can be applied to improving the way the CIS communicates about cancer and can help other programs communicate more effectively.

How Do People Reach the Cancer Information Service?

- To speak with a CIS information specialist call 1–800–4–CANCER (1–800–422–6237), 9:00 a.m. to 4:30 p.m. local time, Monday through Friday. Deaf or hard of hearing callers with TTY equipment may call 1–800–332–8615.
- To obtain online assistance visit the NCI's Cancer Information Web site at **http://cancer.gov/cancer_information** and click on the LiveHelp link between 9:00 a.m. and 7:30 p.m. Eastern time, Monday through Friday.
- For information 24 hours a day, 7 days a week call 1–800–4–CANCER and select option 4 to hear recorded information at any time.
- Visit NCI's Web site at **http://cancer.gov** on the Internet.
- Visit the CIS Web site at **http://cancer.gov/cis** on the Internet.

Finding Cancer Resources in Your Community[12]

When your child has cancer or is undergoing cancer treatment, there are places in your community to turn to for help. There are many local organizations throughout the country that offer a variety of practical and support services to children with cancer and their families. However, parents often don't know about these services or are unable to find them. National cancer organizations can assist you in finding these resources, and there are a number of things you can do for yourself.

Whether you are looking for a support group, counseling, advice, financial assistance, transportation for your child to and from treatment, or information about cancer, most neighborhood organizations, local health care providers, or area hospitals are a good place to start. Often, the hardest part of looking for help is knowing the right questions to ask.

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[12] Adapted from the NCI: **http://cis.nci.nih.gov/fact/8_9.htm**.

What Kind of Help Can I Get?

Until now, you probably never thought about the many issues and difficulties that arise with a diagnosis of cancer. There are support services to help you deal with almost any type of problem that might occur. The first step in finding the help you need is knowing what types of services are available. The following pages describe some of these services and how to find them.

- **Information on Cancer.** Most national cancer organizations provide a range of information services, including materials on different types of cancer, treatments, and treatment-related issues.
- **Counseling.** While some parents are reluctant to seek counseling, studies show that having someone to talk to reduces stress. Counseling can also provide emotional support to children with cancer and help them better understand their illness. Different types of counseling include individual, group, family, self-help (sometimes called peer counseling), bereavement, patient-to-patient, and sexuality.
- **Medical Treatment Decisions.** Often, parents need to make complicated medical decisions. Many organizations provide hospital and physician referrals for second opinions and information on clinical trials, which may expand treatment options.
- **Home Health Care.** Home health care assists patients who no longer need to stay in a hospital, but still require professional medical help. Skilled nursing care, physical therapy, social work services, and nutrition counseling are all available at home.
- **Hospice Care.** Hospice is care focused on the special needs of terminally ill cancer patients. Sometimes called palliative care, it centers around providing comfort, controlling physical symptoms, and giving emotional support to patients who can no longer benefit from curative treatment. Hospice programs provide services in various settings, including the patient's home, hospice centers, hospitals, or skilled nursing facilities. Your child's doctor or social worker can provide a referral for these services.
- **Rehabilitation.** Rehabilitation services help people adjust to the effects of cancer and its treatment. Physical rehabilitation focuses on recovery from the physical effects of surgery or the side effects associated with chemotherapy.
- **Advocacy.** Advocacy is a general term that refers to promoting or protecting the rights and interests of a certain group, such as cancer patients. Advocacy groups may offer services to assist with legal, ethical,

medical, employment, legislative, or insurance issues, among others. For instance, if you feel your insurance company has not handled your child's claim fairly, you may want to advocate for a review of its decision.

- **Financial.** Treating cancer can be a tremendous financial burden. There are programs sponsored by the government and nonprofit organizations to help parents of cancer patients with problems related to medical billing, insurance coverage, and reimbursement issues. There are also sources for financial assistance.
- **Housing/Lodging.** Some organizations provide lodging for the family of a patient undergoing treatment, especially if it is a child who is ill and the parents are required to accompany the child to treatment.
- **Children's Services.** A number of organizations provide services for children with cancer, including summer camps, make-a-wish programs, and help for parents seeking child care.

How to Find These Services

Often, the services that people with cancer are looking for are right in their own neighborhood or city. The following is a list of places where you can begin your search for help.

- Your child's hospital, clinic, or medical center should be able to give you information. The doctor or nurse may be able to tell you about your child's specific medical condition, pain management, rehabilitation services, home nursing, or hospice care.
- Most hospitals also have a social work, home care, or discharge planning department. This department may be able to help you find a support group or a nonprofit agency that helps people who have cancer and their families. While your child is undergoing treatment, be sure to ask the hospital about transportation, practical assistance, or even temporary child care. Talk to a hospital financial counselor in the business office about developing a monthly payment plan if you need help with hospital expenses.
- The public library is an excellent source of information, as are patient libraries at many cancer centers. A librarian can help you find books and articles through a literature search.
- A local church, synagogue, YMCA or YWCA, or fraternal order may provide financial assistance, or may have volunteers who can help with transportation and home care. Catholic Charities, the United Way, or the American Red Cross may also operate local offices. Some of these

organizations may provide home care, and the United Way's information and referral service can refer you to an agency that provides financial help. To find the United Way serving your community, visit their online directory at **http://www.unitedway.org** on the Internet or look in the White Pages of your local telephone book.

- Local or county government agencies may offer low-cost transportation (sometimes called para-transit) to individuals unable to use public transportation. The Federal government runs the Hill-Burton program (1–800–638–0742), which funds certain medical facilities and hospitals to provide children with cancer with free or low-cost care if their families are in financial need.

Getting the Most From a Service: What To Ask

No matter what type of help you are looking for, the only way to find resources to fit your needs is to ask the right questions. When you are calling an organization for information, it is important to think about what questions you are going to ask before you call. Many people find it helpful to write out their questions in advance, and to take notes during the call. Another good tip is to ask the name of the person with whom you are speaking in case you have follow-up questions. Below are some of the questions you may want to consider if you are calling or visiting a new agency and want to learn about how they can help:

- How do I apply [for this service]?
- Are there eligibility requirements? What are they?
- Is there an application process? How long will it take? What information will I need to complete the application process? Will I need anything else to get the service?
- Do you have any other suggestions or ideas about where I can find help?

The most important thing to remember is that you will rarely receive help unless you ask for it. In fact, asking can be the hardest part of getting help. Don't be afraid or ashamed to ask for assistance. Cancer is a very difficult disease, but there are people and services that can ease your burdens and help you focus on your child's treatment and recovery.

Finding Doctors Who Specialize in Cancer Care[13]

A common way to find a doctor who specializes in cancer care is to ask for a referral from your child's primary care physician. Sometimes, you may know a specialist yourself, or through the experience of a family member, coworker, or friend.

The following resources may also be able to provide you with names of doctors who specialize in treating specific diseases or conditions. However, these resources may not have information about the quality of care that the doctors provide.

- Your local hospital or its patient referral service may be able to provide you with a list of specialists who practice at that hospital.
- Your nearest National Cancer Institute (NCI)-designated cancer center can provide information about doctors who practice at that center. The NCI fact sheet *The National Cancer Institute Cancer Centers Program* describes and gives contact information, including Web sites, for NCI-designated cancer treatment centers around the country. Many of the cancer centers' Web sites have searchable directories of physicians who practice at each facility. The NCI's fact sheet is available at **http://cis.nci.nih.gov/fact/1_2.htm** on the Internet, or by calling the Cancer Information Service (CIS) at 1–800–4–CANCER (1–800–422–6237).
- The American Board of Medical Specialties (ABMS) publishes a list of board-certified physicians. The *Official ABMS Directory of Board Certified Medical Specialists* lists doctors' names along with their specialty and their educational background. This resource is available in most public libraries. The ABMS also has a Web site that can be used to verify whether a specific physician is board-certified. This free service is located at **http://www.abms.org/newsearch.asp** on the Internet. Verification of a physician's board certification can also be obtained by calling the ABMS at 1–866–275–2267 (1–866–ASK–ABMS).
- The American Medical Association (AMA) provides an online service called AMA Physician Select that offers basic professional information on virtually every licensed physician in the United States and its possessions. The database can be searched by doctor's name or by medical specialty. The AMA Physician Select service is located at **http://www.ama-assn.org/aps/amahg.htm** on the Internet.
- The American Society of Clinical Oncologists (ASCO) provides an online list of doctors who are members of ASCO. The member database has the

[13] Adapted from the NCI: **http://cis.nci.nih.gov/fact/7_47.htm**.

names and affiliations of over 15,000 oncologists worldwide. It can be searched by doctor's name, institution's name, location, and/or type of board certification. This service is located at **http://www.asco.org/people/db/html/m_db.htm** on the Internet.

- The American College of Surgeons (ACOS) Fellowship Database is an online list of surgeons who are Fellows of the ACOS. The list can be searched by doctor's name, geographic location, or medical specialty. This service is located at **http://web.facs.org/acsdir/default.htm** on the Internet. The ACOS can be contacted at 633 North Saint Clair Street, Chicago, IL 60611–3211; or by telephone at 312–202–5000.
- Local medical societies may maintain lists of doctors in each specialty.
- Public and medical libraries may have print directories of doctors' names, listed geographically by specialty.
- Your local Yellow Pages may have doctors listed by specialty under "Physicians."

The Agency for Healthcare Research and Quality (AHRQ) offers *Your Guide to Choosing Quality Health Care*, which has information for consumers on choosing a health plan, a doctor, a hospital, or a long-term care provider. The Guide includes suggestions and checklists that you can use to determine which doctor or hospital is best for you. This resource is available at **http://www.ahrq.gov/consumer/qntool.htm** on the Internet. You can also order the Guide by calling the AHRQ Publications Clearinghouse at 1–800–358–9295.

If you are a member of a health insurance plan, your choice may be limited to doctors who participate in your plan. Your insurance company can provide you with a list of participating primary care doctors and specialists. It is important to ask your insurance company if the doctor you choose is accepting new patients through your health plan. You also have the option of seeing a doctor outside your health plan and paying the costs yourself. If you have a choice of health insurance plans, you may first wish to consider which doctor or doctors you would like to use, then choose a plan that includes your chosen physician(s).

The National Comprehensive Cancer Network (NCCN) Physician Directory lists specialists who practice in the NCCN's 19 member institutions across the U.S. To access the directory, go to **http://www.nccn.org/** and click on "Physician Directory". To use this service, you will be required to scroll to the bottom of the page and select "I agree." Enter your search criteria and select "Find" at the bottom of the page. To obtain more information on a

physician or institution, contact the institution's Physician Referral Department or the NCCN Patient Information and Referral Service at 1-888-909-NCCN or **patientinformation@nccn.org**.

If the previous sources did not meet your needs, you may want to log on to the Web site of the National Organization for Rare Disorders (NORD) at **http://www.rarediseases.org/**. NORD maintains a database of doctors with expertise in various rare diseases. The Metabolic Information Network (MIN), 800-945-2188, also maintains a database of physicians with expertise in various metabolic diseases.

Selecting Your Child's Doctor[14]

There are many factors to consider when choosing a doctor. To make the most informed decision, you may wish to speak with several doctors before choosing one. When you meet with each doctor, you might want to consider the following:

- Does the doctor have the education and training to meet my child's needs?
- Does the doctor use the hospital that I have chosen?
- Does the doctor explain things clearly and encourage me to ask questions?
- What are the doctor's office hours?
- Who covers for the doctor when he or she is unavailable? Will that person have access to my medical records?
- How long does it take to get an appointment with the doctor?

If you are choosing a surgeon, you may wish to ask additional questions about the surgeon's background and experience with specific procedures. These questions may include:

- Is the surgeon board-certified?[15]
- Has the surgeon been evaluated by a national professional association of surgeons, such as the American College of Surgeons (ACOS)?
- At which treatment facility or facilities does the surgeon practice?

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[14] This section has been adapted from the AHRQ: **www.ahrq.gov/consumer/qntascii/qntdr.htm.**

[15] While board certification is a good measure of a doctor's knowledge, it is possible to receive quality care from doctors who are not board certified.

- How often does the surgeon perform the type of surgery that my child needs?
- How many of these procedures has the surgeon performed? What was the success rate?

It is important for you and your child to feel comfortable with the specialist that you choose, because you will be working closely with that person to make decisions about your child's cancer treatment. Trust your own observations and feelings when deciding on a doctor for your child's medical care.

Other health professionals and support services may also be important during cancer treatment. The National Cancer Institute fact sheet *Your Health Care Team: Your Doctor Is Only the Beginning* has information about these providers and services, and how to locate them. This fact sheet is located at **http://cis.nci.nih.gov/fact/8_10.htm** on the Internet, or can be obtained by calling the CIS at 1–800–4–CANCER (1–800–422–6237).

Working with Your Child's Doctor[16]

Research has shown that parents who have good relationships with their children's doctors tend to be more satisfied with their children's care. Here are some tips to help you and your child's doctor become partners:

- You know important things about your child's symptoms and health history. Tell the doctor what you think he or she needs to know.
- Always bring any medications your child is currently taking with you to the appointment, or you can bring a list of your child's medications including dosage and frequency information. Talk about any allergies or reactions your child has had to medications.
- Tell your doctor about any natural or alternative medicines your child is taking.
- Bring other medical information, such as x-ray films, test results, and medical records.
- Ask questions. If you don't, the doctor will assume that you understood everything that was said.
- Write down your questions before the doctor's visit. List the most important ones first to make sure that they are addressed.

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[16] This section has been adapted from the AHRQ: **www.ahrq.gov/consumer/qntascii/qntdr.htm**.

- Ask the doctor to draw pictures if you think that this will help you and your child understand.
- Take notes. Some doctors do not mind if you bring a tape recorder to help you remember things, but always ask first.
- Take information home. Ask for written instructions. Your child's doctor may also have brochures and audio and videotapes on childhood non-Hodgkin's lymphoma.

By following these steps, you will enhance the relationship you and your child have with the physician.

Getting a Second Opinion[17]

Once you have chosen a doctor and discussed a diagnosis and treatment plan, but before treatment has started, you may want to get a second opinion - that is, you may want to ask a different doctor to review the diagnosis and plan. Some insurance companies require a second opinion; some may pay for it if you ask. A second opinion may also be obtained during the course of treatment if it is not working as hoped. Most doctors support a parent's decision to get a second opinion and many even suggest you do so. To find specialists to get a second opinion, you might:

- Ask your child's doctor to suggest a specialist for a second opinion.
- Get the names of doctors who specialize in treating childhood cancer from the local medical society, a nearby hospital, or a medical school. You can find the telephone numbers for these organizations in your telephone directory or the Yellow Pages.
- Contact an NCI Comprehensive Cancer Center for a second opinion and possible treatment. Considered "Centers of Excellence," these cancer centers' programs have been reviewed and selected by NCI. They offer the most up-todate diagnosis and treatment of cancer and are devoted to both basic and clinical research. To obtain information about the location of the different cancer centers, call the CIS at 1-800-4-CANCER (1-800-422-6237) or TTY at 1-800-332-8615.
- Contact the Pediatric Oncology Branch, NCI, located in Bethesda, Maryland, to ask for a second opinion appointment. They can be reached at 1-877-624-4878.

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[17] This section was adapted from the NCI:
http://www.cancer.gov/CancerInformation/youngpeople.

Finding a Cancer Treatment Facility[18]

Choosing a treatment facility is another important consideration for getting the best medical care possible. Although you may not be able to choose which hospital treats your child in an emergency, you can choose a facility for scheduled and ongoing care. If you have already found a doctor for your child's cancer treatment, you may need to choose a facility based on where the doctor practices. The doctor may be able to recommend a facility that provides quality care. You may wish to ask the following questions when considering a treatment facility:

- Has the facility had experience and success in treating my child's condition?
- Has the facility been rated by state, consumer, or other groups for its quality of care?
- How does the facility check and work to improve its quality of care?
- Has the facility been approved by a nationally recognized accrediting body, such as the American College of Surgeons (ACOS) and/or the Joint Commission on Accredited Healthcare Organizations (JCAHO)?
- Does the facility explain patients' rights and responsibilities? Are copies of this information available to patients?
- Does the treatment facility offer support services, such as social workers and resources to help me find financial assistance if I need it?
- Is the facility conveniently located?

If you are a member of a health insurance plan, your choice of treatment facilities may be limited to those that participate in your plan. Your insurance company can provide you with a list of approved facilities. Although the costs of cancer treatment can be very high, you have the option of paying out-of-pocket if you want to use a treatment facility that is not covered by your insurance plan. If you are considering paying for treatment yourself, you may wish to discuss the potential costs with your child's doctor beforehand. You may also want to speak with the person who does the billing for the treatment facility. In some instances, nurses and social workers can provide you with more information about coverage, eligibility, and insurance issues.

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[18] Adapted from the NCI: **http://cis.nci.nih.gov/fact/7_47.htm**. At this Web site, information on how to find treatment facilities is also available for patients living outside the U.S.

The following resources may help you find a treatment facility for your child's care:

- The NCI fact sheet *The National Cancer Institute Cancer Centers Program* describes and gives contact information for NCI-designated cancer treatment centers around the country.
- The ACOS accredits cancer programs at hospitals and other treatment facilities. More than 1,400 programs in the United States have been designated by the ACOS as Approved Cancer Programs. The ACOS Web site offers a searchable database of these programs at **http://web.facs.org/cpm/default.htm** on the Internet. The ACOS can be contacted at 633 North Saint Clair Street, Chicago, IL 60611–3211; or by telephone at 312–202–5000.
- The JCAHO is an independent, not-for-profit organization that evaluates and accredits health care organizations and programs in the United States. It also offers information for the general public about choosing a treatment facility. The JCAHO Web site is located at **http://www.jcaho.org** on the Internet. The JCAHO is located at One Renaissance Boulevard, Oakbrook Terrace, IL 60181–4294. The telephone number is 630–792–5800.
- The JCAHO offers an online Quality Check service that parents can use to determine whether a specific facility has been accredited by the JCAHO and view the organization's performance reports. This service is located at **http://www.jcaho.org/qualitycheck/directry/directry.asp** on the Internet.
- The AHRQ publication *Your Guide To Choosing Quality Health Care* has suggestions and checklists for choosing the treatment facility that is right for you.

Questions and Answers about Children's Cancer Centers[19]

Survival rates for childhood cancer have risen sharply over the past 20 years. In the United States, more than 75 percent of children with cancer are now alive 5 years after diagnosis, compared with about 60 percent in the mid-1970s. Much of this dramatic improvement is due to the development of improved therapies at children's cancer centers, where the majority of children with cancer have their treatment.

[19] This section has been adapted from the NCI: **http://cis.nci.nih.gov/fact/1_21.htm**.

What Are Children's Cancer Centers?

Children's cancer centers are hospitals or units in hospitals that specialize in the diagnosis and treatment of cancer in children and adolescents. Most children's, or pediatric, cancer centers treat patients up to the age of 20.

Are There Standards for Children's Cancer Centers?

The following groups have established standards for children's cancer centers or programs:

- The National Cancer Institute (NCI)-sponsored Children's Oncology Group (COG), formerly known as the Children's Cancer Group (CCG) and the Pediatric Oncology Group (POG), is a network of children's cancer centers that meet strict quality assurance standards.
- The American Academy of Pediatrics (AAP) published Guidelines for the Pediatric Cancer Center and Role of such Centers in Diagnosis and Treatment in 1986 and 1997.
- The American Society of Pediatric Hematology/Oncology (ASPH/O) established standard requirements for programs treating children with cancer and blood disorders.

These groups agree that a childhood cancer center should be staffed by trained pediatric oncologists (doctors who specialize in childhood cancer) and other specialists who work as a team. Other members of the health professional team usually include pediatric surgeons, specialist surgeons (for instance neurosurgeons and urologic surgeons), radiation oncologists, pathologists, nurses, consulting pediatric specialists, psychiatrists, oncology social workers, nutritionists, and home health care professionals—all with expertise in treating children and adolescents with cancer. Together, these professionals offer comprehensive care.

What Are the Advantages of a Specialized Children's Cancer Center?

Because childhood cancer is relatively rare, it is important to seek treatment in centers that specialize in the treatment of children with cancer. Specialized cancer programs at comprehensive, multidisciplinary cancer centers follow established protocols (step-by-step guidelines for treatment). These protocols are carried out using a team approach. The team of health professionals is involved in designing the appropriate treatment and support program for

the child and the child's family. In addition, these centers participate in specially designed and monitored research studies that help develop more effective treatments and address issues of long-term childhood cancer survival.

Can Children with Cancer Be Treated at the National Cancer Institute?

The Pediatric Oncology Branch (POB) of the National Cancer Institute conducts clinical trials for a wide variety of childhood cancers at the Warren Grant Magnuson Clinical Center, which is located at the National Institutes of Health in Bethesda, Maryland. There is no charge to patients for services provided at the Clinical Center.

Children, teenagers, and young adults with newly diagnosed or recurrent cancer (cancer that has come back) may be referred to the POB. To refer a patient with cancer, the patient's doctor should call the POB's toll-free number at 1–877–624–4878 between the hours of 8:30 a.m. and 5:00 p.m. and ask for the attending physician. The attending physician will discuss the case with the patient's doctor, determine whether the patient is eligibile for treatment at NCI, and help arrange the referral. The POB can also be reached at **http://www-dcs.nci.nih.gov/branches/pedonc/index.html** on the Internet.

POB attending physicians also are available to provide a second opinion about a patient. The patient, family, or physician can contact the POB to arrange for a second opinion. POB staff can offer assistance in cases where a diagnosis is difficult and also can aid in developing an appropriate treatment plan.

Finding a Children's Cancer Center

A family's pediatrician or family doctor often can provide a referral to a comprehensive children's cancer center. Families and health professionals also can call the NCI's Cancer Information Service (CIS) at 1–800–4–CANCER to learn about children's cancer centers that belong to the Children's Cancer Study Group and the Pediatric Oncology Group. All of the cancer centers that participate in these Groups have met strict standards of excellence for childhood cancer care.

Additional Cancer Support Information

In addition to the references above, the NCI has set up guidance Web sites that offers information on issues relating to cancer. These include:

- Facing Forward - A Guide for Cancer Survivors: **http://www.cancer.gov/cancer_information/doc_img.aspx?viewid=cc93a843-6fc0-409e-8798-5c65afc172fe**
- Taking Time: Support for People With Cancer and the People Who Care About Them: **http://www.cancer.gov/cancer_information/doc_img.aspx?viewid=21a46445-a5c8-4fee-95a3-d9d0d665077a**
- When Cancer Recurs: Meeting the Challenge: **http://www.cancer.gov/cancer_information/doc_img.aspx?viewid=9e13d0d2-b7de-4bd6-87da-5750300a0dab**
- Your Health Care Team: Your Doctor Is Only the Beginning: **http://cis.nci.nih.gov/fact/8_10.htm**
- When Someone in Your Family Has Cancer: **http://www.cancer.gov/CancerInformation/whensomeoneinyourfamily**

Vocabulary Builder

The following vocabulary builder provides definitions of words used in this chapter that have not been defined in previous chapters:

Bereavement: Refers to the whole process of grieving and mourning and is associated with a deep sense of loss and sadness. [NIH]

Cervical: Relating to the neck, or to the neck of any organ or structure. Cervical lymph nodes are located in the neck; cervical cancer refers to cancer of the uterine cervix, which is the lower, narrow end (the "neck") of the uterus. [NIH]

Charities: Social welfare organizations with programs designed to assist individuals in times of need. [NIH]

Curative: Tending to overcome disease and promote recovery. [EU]

Hematology: A subspecialty of internal medicine concerned with morphology, physiology, and pathology of the blood and blood-forming tissues. [NIH]

Mammography: The use of x-rays to create a picture of the breast. [NIH]

Neurosurgeon: A doctor who specializes in surgery on the brain, spine, and

other parts of the nervous system. [NIH]

Oncologist: A doctor who specializes in treating cancer. Some oncologists specialize in a particular type of cancer treatment. For example, a radiation oncologist specializes in treating cancer with radiation. [NIH]

Palliative: 1. affording relief, but not cure. 2. an alleviating medicine. [EU]

Pathologist: A doctor who identifies diseases by studying cells and tissues under a microscope. [NIH]

CHAPTER 3. CLINICAL TRIALS AND CHILDHOOD NON-HODGKIN'S LYMPHOMA

Overview

Very few medical conditions have a single treatment. The basic treatment guidelines that your child's physician has discussed with you, or those that you have found using the techniques discussed in Chapter 1, may provide you with all that you will require. For some patients, current treatments can be enhanced with new or innovative techniques currently under investigation. In this chapter, we will describe how clinical trials work and show you how to keep informed of trials concerning childhood non-Hodgkin's lymphoma.

What Is a Clinical Trial?[20]

Clinical trials involve the participation of people in medical research. Most medical research begins with studies in test tubes and on animals. Treatments that show promise in these early studies may then be tried with people. The only sure way to find out whether a new treatment is safe, effective, and better than other treatments for childhood non-Hodgkin's lymphoma is to try it on patients in a clinical trial.

[20] The discussion in this chapter has been adapted from the NIH and the NEI: www.nei.nih.gov/netrials/ctivr.htm.

What Kinds of Clinical Trials Are There?

Clinical trials are carried out in three phases:

- **Phase I.** Researchers first conduct Phase I trials with small numbers of patients and healthy volunteers. If the new treatment is a medication, researchers also try to determine how much of it can be given safely.
- **Phase II.** Researchers conduct Phase II trials in small numbers of patients to find out the effect of a new treatment on childhood non-Hodgkin's lymphoma.
- **Phase III.** Finally, researchers conduct Phase III trials to find out how new treatments for childhood non-Hodgkin's lymphoma compare with standard treatments already being used. Phase III trials also help to determine if new treatments have any side effects. These trials--which may involve hundreds, perhaps thousands, of people--can also compare new treatments with no treatment.

How Is a Clinical Trial Conducted?

Various organizations support clinical trials at medical centers, hospitals, universities, and doctors' offices across the United States. The "principal investigator" is the researcher in charge of the study at each facility participating in the clinical trial. Most clinical trial researchers are medical doctors, academic researchers, and specialists. The "clinic coordinator" knows all about how the study works and makes all the arrangements for your child's visits.

All doctors and researchers who take part in the study on childhood non-Hodgkin's lymphoma carefully follow a detailed treatment plan called a protocol. This plan fully explains how the doctors will treat your child in the study. The "protocol" ensures that all patients are treated in the same way, no matter where they receive care.

Clinical trials are controlled. This means that researchers compare the effects of the new treatment with those of the standard treatment. In some cases, when no standard treatment exists, the new treatment is compared with no treatment. Patients who receive the new treatment are in the treatment group. Patients who receive a standard treatment or no treatment are in the "control" group. In some clinical trials, patients in the treatment group get a new medication while those in the control group get a placebo. A placebo is a harmless substance, a "dummy" pill, that has no effect on childhood non-Hodgkin's lymphoma. In other clinical trials, where a new surgery or device

(not a medicine) is being tested, patients in the control group may receive a "sham treatment." This treatment, like a placebo, has no effect on childhood non-Hodgkin's lymphoma and will not harm your child.

Researchers assign patients "randomly" to the treatment or control group. This is like flipping a coin to decide which patients are in each group. If you choose to have your child participate in a clinical trial, you will not know which group he or she will be appointed to. The chance of any patient getting the new treatment is about 50 percent. You cannot request that your child receive the new treatment instead of the placebo or "sham" treatment. Often, you will not know until the study is over whether your child has been in the treatment group or the control group. This is called a "masked" study. In some trials, neither doctors nor patients know who is getting which treatment. This is called a "double masked" study. These types of trials help to ensure that the perceptions of the participants or doctors will not affect the study results.

Natural History Studies

Unlike clinical trials in which patient volunteers may receive new treatments, natural history studies provide important information to researchers on how childhood non-Hodgkin's lymphoma develops over time. A natural history study follows patient volunteers to see how factors such as age, sex, race, or family history might make some people more or less at risk for childhood non-Hodgkin's lymphoma. A natural history study may also tell researchers if diet, lifestyle, or occupation affects how a medical condition develops and progresses. Results from these studies provide information that helps answer questions such as: How fast will a medical condition usually progress? How bad will the condition become? Will treatment be needed?

What Is Expected of Your Child in a Clinical Trial?

Not everyone can take part in a clinical trial for a specific medical condition. Each study enrolls patients with certain features or eligibility criteria. These criteria may include the type and stage of the condition, as well as, the age and previous treatment history of the patient. You or your child's doctor can contact the sponsoring organization to find out more about specific clinical trials and their eligibility criteria. If you would like your child to participate in a clinical trial, your child's doctor must contact one of the trial's

investigators and provide details about his or her diagnosis and medical history.

When participating in a clinical trial, your child may be required to have a number of medical tests. Your child may also need to take medications and/or undergo surgery. Depending upon the treatment and the examination procedure, your child may be required to receive inpatient hospital care. He or she may have to return to the medical facility for follow-up examinations. These exams help find out how well the treatment is working. Follow-up studies can take months or years. However, the success of the clinical trial often depends on learning what happens to patients over a long period of time. Only patients who continue to return for follow-up examinations can provide this important long-term information.

Recent Trials on Childhood Non-Hodgkin's Lymphoma

The National Institutes of Health and other organizations sponsor trials on various medical conditions. Because funding for research goes to the medical areas that show promising research opportunities, it is not possible for the NIH or others to sponsor clinical trials for every medical condition at all times. The following lists recent trials dedicated to childhood non-Hodgkin's lymphoma.[21] If the trial listed by the NIH is still recruiting, your child may be eligible. If it is no longer recruiting or has been completed, then you can contact the sponsors to learn more about the study and, if published, the results. Further information on the trial is available at the Web site indicated. Please note that some trials may no longer be recruiting patients or are otherwise closed. Before contacting sponsors of a clinical trial, consult with your child's physician who can help you determine if your child might benefit from participation.

- **Antibody Therapy in Treating Patients With Refractory or Relapsed Non-Hodgkin's Lymphoma or Chronic Lymphocytic Leukemia**

  Condition(s): recurrent diffuse small lymphocytic/marginal zone lymphoma; recurrent adult diffuse small cleaved cell lymphoma; recurrent adult lymphoblastic lymphoma; recurrent grade III follicular large cell lymphoma; recurrent adult immunoblastic large cell lymphoma; recurrent adult diffuse small noncleaved cell/Burkitt's lymphoma; recurrent adult diffuse mixed cell lymphoma; recurrent mantle cell lymphoma; refractory chronic lymphocytic leukemia; recurrent adult diffuse large cell lymphoma; recurrent grade I follicular

[21] These are listed at **www.ClinicalTrials.gov**.

small cleaved cell lymphoma; recurrent grade II follicular mixed cell lymphoma

Study Status: This study is currently recruiting patients.

Sponsor(s): National Cancer Institute (NCI); Norris Cotton Cancer Center

Purpose - Excerpt: RATIONALE: Antibodies can locate tumor cells and either kill them or deliver tumor-killing substances to them without harming normal cells. PURPOSE: Phase I trial to study the effectiveness of antibody therapy in treating patients who have refractory or relapsed non-Hodgkin's lymphoma or chronic lymphocytic leukemia.

Phase(s): Phase I

Study Type: Treatment

Contact(s): New Hampshire; Norris Cotton Cancer Center, Lebanon, New Hampshire, 03756-0002, United States; Recruiting; Pamela Ely 603-650-5747. Study chairs or principal investigators: Pamela Ely, Study Chair; Norris Cotton Cancer Center

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00014560;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Antineoplaston Therapy in Treating Patients With Non-Hodgkin's Lymphoma**

  Condition(s): recurrent diffuse small lymphocytic/marginal zone lymphoma; recurrent adult diffuse small cleaved cell lymphoma; recurrent adult lymphoblastic lymphoma; recurrent grade III follicular large cell lymphoma; recurrent adult immunoblastic large cell lymphoma; recurrent adult diffuse small noncleaved cell/Burkitt's lymphoma; recurrent adult diffuse mixed cell lymphoma; recurrent mantle cell lymphoma; recurrent grade I follicular small cleaved cell lymphoma; recurrent grade II follicular mixed cell lymphoma; recurrent adult diffuse large cell lymphoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Burzynski Research Institute

  Purpose - Excerpt: RATIONALE: Antineoplastons are naturally occurring substances found in urine. Antineoplastons may inhibit the growth of cancer cells. PURPOSE: Phase II trial to study the effectiveness of antineoplaston therapy in treating patients who have non-Hodgkin's lymphoma that has not responded to high-dose chemotherapy and bone marrow transplantation .

  Phase(s): Phase II

Study Type: Treatment

Contact(s): Texas; Burzynski Research Institute, Houston, Texas, 77055, United States; Recruiting; Stanislaw R. Burzynski 713-335-5697. Study chairs or principal investigators: Stanislaw R. Burzynski, Study Chair; Burzynski Research Institute

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00003498;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Antineoplaston Therapy in Treating Patients With Recurrent or Refractory High-Grade Stage II, Stage III, or Stage IV Non-Hodgkin's Lymphoma**

  Condition(s): noncontiguous stage II adult immunoblastic large cell lymphoma; recurrent adult lymphoblastic lymphoma; recurrent adult immunoblastic large cell lymphoma; recurrent adult diffuse small noncleaved cell/Burkitt's lymphoma; noncontiguous stage II adult diffuse small noncleaved cell/Burkitt's lymphoma; contiguous stage II adult lymphoblastic lymphoma; contiguous stage II adult immunoblastic large cell lymphoma; stage III adult diffuse small noncleaved cell/Burkitt's lymphoma; stage IV adult diffuse small noncleaved cell/Burkitt's lymphoma; contiguous stage II adult diffuse small noncleaved cell/Burkitt's lymphoma; stage III adult immunoblastic large cell lymphoma; stage IV adult immunoblastic large cell lymphoma; noncontiguous stage II adult lymphoblastic lymphoma; stage III adult lymphoblastic lymphoma; stage IV adult lymphoblastic lymphoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Burzynski Research Institute

  Purpose - Excerpt: RATIONALE: Antineoplastons are naturally-occurring substances found in urine. Antineoplastons may inhibit the growth of cancer cells. PURPOSE: Phase II trial to study the effectiveness of antineoplaston therapy in treating patients with recurrent or refractory high-grade stage II, stage III, or stage IV non-Hodgkin's lymphoma following previous chemotherapy.

  Phase(s): Phase II

  Study Type: Treatment

  Contact(s): Texas; Burzynski Research Institute, Houston, Texas, 77055, United States; Recruiting; Stanislaw R. Burzynski 713-335-5697. Study chairs or principal investigators: Stanislaw R. Burzynski, Study Chair; Burzynski Research Institute

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00003501;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **BAY 59-8862 in Treating Patients With Refractory Non-Hodgkin's Lymphoma**

  Condition(s): recurrent adult lymphoblastic lymphoma; recurrent grade III follicular large cell lymphoma; recurrent adult immunoblastic large cell lymphoma; recurrent adult diffuse small noncleaved cell/Burkitt's lymphoma; recurrent adult diffuse mixed cell lymphoma; recurrent mantle cell lymphoma; recurrent adult diffuse large cell lymphoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Theradex Systems, Incorporated

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop cancer cells from dividing so they stop growing or die. PURPOSE: Phase II trial to study the effectiveness of BAY 59-8862 in treating patients who have refractory non-Hodgkin's lymphoma.

  Phase(s): Phase II

  Study Type: Treatment

  Contact(s): see Web site below

  Web Site:
  http://clinicaltrials.gov/ct/gui/show/NCT00039156;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Biological Therapy Plus Monoclonal Antibody Therapy in Treating Patients With Relapsed or Refractory Non-Hodgkin's Lymphoma**

  Condition(s): recurrent diffuse small lymphocytic/marginal zone lymphoma; recurrent adult diffuse small cleaved cell lymphoma; recurrent adult lymphoblastic lymphoma; recurrent grade III follicular large cell lymphoma; recurrent adult immunoblastic large cell lymphoma; recurrent adult diffuse small noncleaved cell/Burkitt's lymphoma; recurrent adult diffuse mixed cell lymphoma; recurrent mantle cell lymphoma; recurrent adult diffuse large cell lymphoma; recurrent grade I follicular small cleaved cell lymphoma; recurrent grade II follicular mixed cell lymphoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Cancer Institute (NCI); Jonsson Comprehensive Cancer Center

Purpose - Excerpt: RATIONALE: Monoclonal antibodies such as rituximab can locate cancer cells and either kill them or deliver cancer-killing substances to them without harming normal cells. Biological therapies such as CpG 7909 use different ways to stimulate the immune system and stop cancer cells from growing. Combining CpG 7909 with rituximab may kill more cancer cells. PURPOSE: Phase I trial to study the effectiveness of CpG 7909 plus rituximab in treating patients who have relapsed or refractory non-Hodgkin's lymphoma.

Phase(s): Phase I

Study Type: Treatment

Contact(s): California; Jonsson Comprehensive Cancer Center, UCLA, Los Angeles, California, 90095-1781, United States; Recruiting; Christos E. Emmanouilides 310-206-0716. Study chairs or principal investigators: Christos E. Emmanouilides, Study Chair; Jonsson Comprehensive Cancer Center

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00040950;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Chemotherapy and Monoclonal Antibody Therapy in Treating Patients With B-cell Non-Hodgkin's Lymphoma That Has Relapsed Following Peripheral Stem Cell Transplantation**

  Condition(s): recurrent diffuse small lymphocytic/marginal zone lymphoma; recurrent adult diffuse small cleaved cell lymphoma; recurrent adult lymphoblastic lymphoma; recurrent grade III follicular large cell lymphoma; recurrent adult immunoblastic large cell lymphoma; recurrent adult diffuse small noncleaved cell/Burkitt's lymphoma; recurrent adult diffuse mixed cell lymphoma; recurrent mantle cell lymphoma; recurrent adult diffuse large cell lymphoma; Waldenstrom's macroglobulinemia; recurrent grade I follicular small cleaved cell lymphoma; recurrent grade II follicular mixed cell lymphoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Cancer Institute (NCI); Jonsson Comprehensive Cancer Center

  Purpose - Excerpt: RATIONALE: Monoclonal antibodies can locate cancer cells and either kill them or deliver cancer-killing substances to them without harming normal cells. Drugs used in chemotherapy use different ways to stop cancer cells from dividing so they stop growing or die. Combining monoclonal antibody therapy with chemotherapy may kill more cancer cells. PURPOSE: Phase II trial to study the effectiveness

of the monoclonal antibody rituximab plus chemotherapy with vinorelbine in treating patients with B-cell non-Hodgkin's lymphoma that has relapsed following autologous peripheral stem cell transplantation.

Phase(s): Phase II

Study Type: Treatment

Contact(s): California; Jonsson Comprehensive Cancer Center, UCLA, Los Angeles, California, 90095-1781, United States; Recruiting; Mary Carol Territo 310-825-7768. Study chairs or principal investigators: Christos E. Emmanouilides, Study Chair; Jonsson Comprehensive Cancer Center

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00003963;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Combination Chemotherapy Followed by Peripheral Stem Cell Transplantation in Treating Children With Recurrent or Refractory Hodgkin's or Non-Hodgkin's Lymphoma**

  Condition(s): recurrent childhood large cell lymphoma; childhood diffuse large cell lymphoma; recurrent childhood small noncleaved cell lymphoma; recurrent childhood lymphoblastic lymphoma; childhood immunoblastic large cell lymphoma; recurrent/refractory childhood Hodgkin's disease

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Cancer Institute (NCI); Pediatric Oncology Group; Children's Cancer Group

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop cancer cells from dividing so they stop growing or die. Peripheral stem cell transplantation may allow doctors to give higher doses of chemotherapy and kill more cancer cells. PURPOSE: Phase II trial to study the effectiveness of combination chemotherapy followed by peripheral stem cell transplantation in treating children who have recurrent or refractory Hodgkin's disease or non-Hodgkin's lymphoma.

  Phase(s): Phase II

  Study Type: Treatment

  Contact(s): see Web site below

  Web Site:
  http://clinicaltrials.gov/ct/gui/show/NCT00002941;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Combination Chemotherapy in Treating Children or Adolescents With Newly Diagnosed Lymphoblastic Lymphoma**

  Condition(s): stage III childhood lymphoblastic lymphoma; stage IV childhood lymphoblastic lymphoma; stage I childhood lymphoblastic lymphoma; stage II childhood lymphoblastic lymphoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Cancer Institute (NCI); Children's Oncology Group

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop cancer cells from dividing so they stop growing or die. It is not yet known which regimen of combination chemotherapy is most effective for lymphoblastic lymphoma. PURPOSE: Randomized phase III trial to compare the effectiveness of different regimens of combination chemotherapy in treating children or adolescents who have newly diagnosed lymphoblastic lymphoma.

  Phase(s): Phase III

  Study Type: Treatment

  Contact(s): see Web site below

  Web Site:
  http://clinicaltrials.gov/ct/gui/show/NCT00004228;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Combination Chemotherapy in Treating Children With Acute Lymphoblastic Leukemia, Osteosarcoma, or Non-Hodgkin's Lymphoma**

  Condition(s): recurrent childhood large cell lymphoma; recurrent childhood small noncleaved cell lymphoma; recurrent osteosarcoma; recurrent childhood lymphoblastic lymphoma; recurrent childhood acute lymphoblastic leukemia

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Memorial Sloan-Kettering Cancer Center

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop cancer cells from dividing so they stop growing or die. Combining more than one drug may kill more cancer cells. PURPOSE: Phase II trial to study the effectiveness of combination chemotherapy consisting of trimetrexate glucuronate plus leucovorin in treating children who have recurrent acute lymphoblastic leukemia, recurrent osteosarcoma, or refractory non-Hodgkin's lymphoma.

  Phase(s): Phase II

  Study Type: Treatment

Contact(s): New York; Memorial Sloan-Kettering Cancer Center, New York, New York, 10021, United States; Recruiting; Tanya Trippett 212-639-8267. Study chairs or principal investigators: Tanya Trippett, Study Chair; Memorial Sloan-Kettering Cancer Center

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00002738;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Combination Chemotherapy in Treating Children With Non-Hodgkin's Lymphoma**

  Condition(s): stage III childhood lymphoblastic lymphoma; stage IV childhood lymphoblastic lymphoma; stage I childhood lymphoblastic lymphoma; stage II childhood lymphoblastic lymphoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Federation Nationale des Centres de Lutte Contre le Cancer

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop cancer cells from dividing so they stop growing or die. Combining more than one drug may kill more cancer cells. PURPOSE: Phase III trial to study the effectiveness of combination chemotherapy in treating children who have non-Hodgkin's lymphoma.

  Phase(s): Phase III

  Study Type: Treatment

  Contact(s): France; Centre Leon Berard, Lyon, 69373, France; Recruiting; Christophe Bergeron 33-04-78-782642. Study chairs or principal investigators: Christophe Bergeron, Study Chair; Federation Nationale des Centres de Lutte Contre le Cancer

  Web Site:
  http://clinicaltrials.gov/ct/gui/show/NCT00003650;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Combination Chemotherapy Plus Filgrastim in Treating Patients With HIV-Related Non-Hodgkin's Lymphoma**

  Condition(s): AIDS-related diffuse small cleaved cell lymphoma; AIDS-related small noncleaved cell lymphoma; AIDS-related lymphoblastic lymphoma; AIDS-related diffuse mixed cell lymphoma; AIDS-related immunoblastic large cell lymphoma; AIDS-related peripheral/systemic lymphoma; AIDS-related diffuse large cell lymphoma; AIDS-related primary CNS lymphoma

  Study Status: This study is currently recruiting patients.

Sponsor(s): British National Lymphoma Investigation

Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop cancer cells from dividing so they stop growing or die. Combining more than one drug may kill more cancer cells. Colony-stimulating factors such as filgrastim may increase the number of immune cells found in bone marrow or peripheral blood and may help a person's immune system recover from the side effects of chemotherapy. PURPOSE: Phase I/II trial to study the effectiveness of combining filgrastim with combination chemotherapy in treating patients who have HIV -related non-Hodgkin's lymphoma.

Phase(s): Phase I; Phase II

Study Type: Treatment

Contact(s): see Web site below

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00032149;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Combination Chemotherapy Plus Rituximab in Treating Patients With Relapsed Non-Hodgkin's Lymphoma**

  Condition(s): recurrent diffuse small lymphocytic/marginal zone lymphoma; recurrent adult diffuse small cleaved cell lymphoma; recurrent adult lymphoblastic lymphoma; recurrent grade III follicular large cell lymphoma; recurrent adult immunoblastic large cell lymphoma; recurrent adult diffuse small noncleaved cell/Burkitt's lymphoma; recurrent adult diffuse mixed cell lymphoma; recurrent mantle cell lymphoma; recurrent adult diffuse large cell lymphoma; recurrent grade I follicular small cleaved cell lymphoma; recurrent grade II follicular mixed cell lymphoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Cancer Institute (NCI); North Central Cancer Treatment Group

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop cancer cells from dividing so they stop growing or die. Monoclonal antibodies, such as rituximab, can locate cancer cells and either kill them or deliver cancer-killing substances to them without harming normal cells. Combining combination chemotherapy with monoclonal antibody therapy may kill more cancer cells. PURPOSE: Phase II trial to study the effectiveness of combination chemotherapy plus rituximab in treating patients who have relapsed non-Hodgkin's lymphoma.

Phase(s): Phase II

Study Type: Treatment

Contact(s): see Web site below

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00005601;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Combination Chemotherapy Plus Steroid Therapy in Treating Children With Acute Lymphoblastic Leukemia or Lymphoblastic Non-Hodgkin's Lymphoma**

  Condition(s): L2 childhood acute lymphoblastic leukemia; untreated childhood acute lymphoblastic leukemia; stage III childhood lymphoblastic lymphoma; L1 childhood acute lymphoblastic leukemia; acute undifferentiated leukemia; B-cell childhood acute lymphoblastic leukemia; stage IV childhood lymphoblastic lymphoma; T-cell childhood acute lymphoblastic leukemia; stage I childhood lymphoblastic lymphoma; stage II childhood lymphoblastic lymphoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): EORTC Children's Leukemia Cooperative Group

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. Combining more than one drug may kill more tumor cells. It is not yet known which regimen of combination chemotherapy plus steroid therapy is more effective for acute lymphoblastic leukemia or lymphoblastic non-Hodgkin's lymphoma. PURPOSE: Randomized phase III trial to compare the effectiveness of different regimens of combination chemotherapy plus steroid therapy in treating children who have acute lymphoblastic leukemia or lymphoblastic non-Hodgkin's lymphoma.

  Phase(s): Phase III

  Study Type: Treatment

  Contact(s): see Web site below

  Web Site:
  http://clinicaltrials.gov/ct/gui/show/NCT00003728;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Hematopoietic Growth Factor-Treated Bone Marrow to Prevent Neutropenia in Patients Receiving Chemotherapy for Relapsed or Refractory Non-Hodgkin's Lymphoma**

  Condition(s): recurrent diffuse small lymphocytic/marginal zone lymphoma; recurrent adult diffuse small cleaved cell lymphoma; recurrent adult lymphoblastic lymphoma; recurrent grade III follicular large cell lymphoma; recurrent adult immunoblastic large cell lymphoma; recurrent adult diffuse small noncleaved cell/Burkitt's lymphoma; recurrent adult diffuse mixed cell lymphoma; recurrent mantle cell lymphoma; recurrent adult diffuse large cell lymphoma; neutropenia; recurrent grade I follicular small cleaved cell lymphoma; recurrent grade II follicular mixed cell lymphoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Cancer Institute (NCI); Robert H. Lurie Cancer Center

  Purpose - Excerpt: RATIONALE: Giving specific bone marrow cells that have been treated with hematopoietic growth factors may be effective in preventing or controlling neutropenia caused by chemotherapy. PURPOSE: Phase I trial to study the effectiveness of treating specific bone marrow cells with hematopoietic growth factors to reduce neutropenia in patients who have relapsed or refractory non-Hodgkin's lymphoma and who will be treated with high-dose chemotherapy.

  Phase(s): Phase I

  Study Type: Supportive Care, Treatment

  Contact(s): Illinois; Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, Illinois, 60611-3013, United States; Recruiting; Jane N. Winter 312-695-6180. Study chairs or principal investigators: Jane N. Winter, Study Chair; Robert H. Lurie Cancer Center

  Web Site:
  http://clinicaltrials.gov/ct/gui/show/NCT00005787;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Monoclonal Antibody Therapy, Chemotherapy, and Peripheral Stem Cell Transplantation in Treating Patients With Refractory Non-Hodgkin's Lymphoma**

  Condition(s): recurrent diffuse small lymphocytic/marginal zone lymphoma; recurrent adult diffuse small cleaved cell lymphoma; recurrent adult lymphoblastic lymphoma; recurrent grade III follicular large cell lymphoma; recurrent adult immunoblastic large cell lymphoma; recurrent adult diffuse small noncleaved cell/Burkitt's

lymphoma; recurrent adult diffuse mixed cell lymphoma; recurrent mantle cell lymphoma; recurrent adult diffuse large cell lymphoma; recurrent grade I follicular small cleaved cell lymphoma; recurrent grade II follicular mixed cell lymphoma

Study Status: This study is currently recruiting patients.

Sponsor(s): University of California Davis Cancer Center

Purpose - Excerpt: RATIONALE: Monoclonal antibodies can locate cancer cells and either kill them or deliver tumor-killing substances to them without harming normal cells. Drugs used in chemotherapy use different ways to stop cancer cells from dividing so they stop growing or die. Peripheral stem cell transplantation may allow doctors to give higher doses of chemotherapy and kill more cancer cells. PURPOSE: Phase I trial to study the effectiveness of monoclonal antibody therapy, cyclosporine, and paclitaxel followed by peripheral stem cell transplantation in treating patients who have refractory non-Hodgkin's lymphoma.

Phase(s): Phase I

Study Type: Treatment

Contact(s): California; University of California Davis Cancer Center, Sacramento, California, 95817, United States; Recruiting; Robert T. O'Donnell 916-734-3787. Study chairs or principal investigators: Robert T. O'Donnell, Study Chair; University of California Davis Cancer Center

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00008021;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Monoclonal Antibody Therapy, Paclitaxel, and Cyclosporine in Treating Patients With Recurrent or Refractory Non-Hodgkin's Lymphoma**

  Condition(s): recurrent diffuse small lymphocytic/marginal zone lymphoma; recurrent adult diffuse small cleaved cell lymphoma; recurrent adult lymphoblastic lymphoma; recurrent grade III follicular large cell lymphoma; recurrent adult immunoblastic large cell lymphoma; recurrent adult diffuse small noncleaved cell/Burkitt's lymphoma; recurrent adult diffuse mixed cell lymphoma; recurrent mantle cell lymphoma; recurrent adult diffuse large cell lymphoma; recurrent grade I follicular small cleaved cell lymphoma; recurrent grade II follicular mixed cell lymphoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): University of California Davis Cancer Center

Purpose - Excerpt: RATIONALE: Monoclonal antibodies can locate tumor cells and either kill them or deliver tumor-killing substances to them without harming normal cells. Combining monoclonal antibody therapy with cyclosporine and paclitaxel may be an effective treatment for non-Hodgkin's lymphoma. PURPOSE: Phase I trial to study the effectiveness of radiolabeled monoclonal antibody therapy combined with paclitaxel and cyclosporine in treating patients who have recurrent or refractory non-Hodgkin's lymphoma.

Phase(s): Phase I

Study Type: Treatment

Contact(s): California; University of California Davis Cancer Center, Sacramento, California, 95817, United States; Recruiting; Robert T. O'Donnell 916-734-3787. Study chairs or principal investigators: Robert T. O'Donnell, Study Chair; University of California Davis Cancer Center

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00009776;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Oxaliplatin in Treating Patients With Relapsed or Refractory Non-Hodgkin's Lymphoma**

  Condition(s): recurrent diffuse small lymphocytic/marginal zone lymphoma; recurrent adult diffuse small cleaved cell lymphoma; recurrent adult lymphoblastic lymphoma; recurrent grade III follicular large cell lymphoma; recurrent adult immunoblastic large cell lymphoma; recurrent adult diffuse small noncleaved cell/Burkitt's lymphoma; recurrent adult T-cell leukemia/lymphoma; recurrent adult diffuse mixed cell lymphoma; recurrent mantle cell lymphoma; recurrent adult diffuse large cell lymphoma; angioimmunoblastic T-cell lymphoma; Waldenstrom's macroglobulinemia; recurrent grade I follicular small cleaved cell lymphoma; recurrent grade II follicular mixed cell lymphoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Cancer Institute (NCI); M.D. Anderson Cancer Center

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. PURPOSE: Phase II trial to study the effectiveness of oxaliplatin in treating patients who have relapsed or refractory non-Hodgkin's lymphoma .

  Phase(s): Phase II

  Study Type: Treatment

Contact(s): Texas; University of Texas - MD Anderson Cancer Center, Houston, Texas, 77030-4009, United States; Recruiting; Anas Younes 713-792-2860. Study chairs or principal investigators: Anas Younes, Study Chair; M.D. Anderson Cancer Center

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00006473;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Peripheral Stem Transplantation in Treating Patients With Refractory or Relapsed Non-Hodgkin's Lymphoma**

  Condition(s): recurrent diffuse small lymphocytic/marginal zone lymphoma; recurrent adult diffuse small cleaved cell lymphoma; recurrent adult lymphoblastic lymphoma; recurrent grade III follicular large cell lymphoma; graft versus host disease; recurrent adult immunoblastic large cell lymphoma; recurrent childhood small noncleaved cell lymphoma; recurrent adult diffuse small noncleaved cell/Burkitt's lymphoma; recurrent adult diffuse mixed cell lymphoma; recurrent mantle cell lymphoma; recurrent childhood lymphoblastic lymphoma; recurrent adult diffuse large cell lymphoma; recurrent childhood large cell lymphoma; recurrent grade I follicular small cleaved cell lymphoma; recurrent grade II follicular mixed cell lymphoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Cancer Institute (NCI); Fred Hutchinson Cancer Research Center

  Purpose - Excerpt: RATIONALE: Drugs used in chemotherapy use different ways to stop tumor cells from dividing so they stop growing or die. Combining chemotherapy with autologous and allogeneic peripheral stem cell transplantation may allow the doctor to give higher doses of chemotherapy drugs to kill more tumor cells. PURPOSE: Phase I/II trial to study the effectiveness of autologous peripheral stem cell transplantation followed by allogeneic peripheral stem cell transplantation in treating patients who have refractory or relapsed non-Hodgkin's lymphoma.

  Phase(s): Phase I; Phase II

  Study Type: Treatment

  Contact(s): Washington; Fred Hutchinson Cancer Research Center, Seattle, Washington, 98109-1024, United States; Recruiting; David G. Maloney 206-667-5616. Study chairs or principal investigators: David G. Maloney, Study Chair; Fred Hutchinson Cancer Research Center

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00005803;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Radiolabeled Monoclonal Antibody in Treating Patients With Non-Hodgkin's Lymphoma**

  Condition(s): recurrent diffuse small lymphocytic/marginal zone lymphoma; recurrent adult diffuse small cleaved cell lymphoma; recurrent adult lymphoblastic lymphoma; recurrent grade III follicular large cell lymphoma; recurrent adult immunoblastic large cell lymphoma; recurrent adult diffuse small noncleaved cell/Burkitt's lymphoma; recurrent adult diffuse mixed cell lymphoma; recurrent mantle cell lymphoma; recurrent adult diffuse large cell lymphoma; recurrent grade I follicular small cleaved cell lymphoma; recurrent grade II follicular mixed cell lymphoma

  Study Status: This study is currently recruiting patients.

  Sponsor(s): Garden State Cancer Center

  Purpose - Excerpt: RATIONALE: Radiolabeled monoclonal antibodies can locate tumor cells and deliver tumor-killing substances to them without harming normal cells. PURPOSE: Phase I trial to study the effectiveness of radiolabeled monoclonal antibody in treating patients who have relapsed or refractory non-Hodgkin's lymphoma.

  Phase(s): Phase I

  Study Type: Treatment

  Contact(s): New Jersey; Garden State Cancer Center, Belleville, New Jersey, 07103, United States; Recruiting; Jack D. Burton 973-844-7024. Study chairs or principal investigators: Jack D. Burton, Study Chair; Garden State Cancer Center

  Web Site:
  http://clinicaltrials.gov/ct/gui/show/NCT00044941;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

- **Rituximab Plus Combination Chemotherapy in Treating Patients With HIV-Related Non-Hodgkin's Lymphoma**

  Condition(s): AIDS-related diffuse small cleaved cell lymphoma; AIDS-related small noncleaved cell lymphoma; AIDS-related lymphoblastic lymphoma; AIDS-related diffuse mixed cell lymphoma; AIDS-related immunoblastic large cell lymphoma; AIDS-related peripheral/systemic lymphoma; AIDS-related diffuse large cell lymphoma

Study Status: This study is currently recruiting patients.

Sponsor(s): British National Lymphoma Investigation

Purpose - Excerpt: RATIONALE: Monoclonal antibodies such as rituximab can locate tumor cells and either kill them or deliver tumor-killing substances to them without harming normal cells. Drugs used in chemotherapy use different ways to stop cancer cells from dividing so they stop growing or die. Combining rituximab with chemotherapy may kill more cancer cells. PURPOSE: Phase I trial to study the effectiveness of rituximab plus combination chemotherapy in treating patients who have HIV -related non-Hodgkin's lymphoma.

Phase(s): Phase I

Study Type: Treatment

Contact(s): United Kingdom; Chelsea Westminster Hospital, London, SW10 9NH, United Kingdom; Recruiting; Contact Person; United Kingdom, England; St. George's Hospital, London, England, SW17 0QT, United Kingdom; Recruiting; Ruth Pettengell 44 208 725 5454. Study chairs or principal investigators: Ruth Pettengell, Study Chair; British National Lymphoma Investigation

Web Site:
http://clinicaltrials.gov/ct/gui/show/NCT00031902;jsessionid=154E5BA02ECE4CC1EE41815400EA3A1F

Benefits and Risks[22]

What Are the Benefits of Participating in a Clinical Trial?

If you are considering a clinical trial, it is important to realize that your child's participation can bring many benefits:

- A new treatment could be more effective than the current treatment for childhood non-Hodgkin's lymphoma. Although only half of the participants in a clinical trial receive the experimental treatment, if the new treatment is proved to be more effective and safer than the current treatment, then those patients who did not receive the new treatment during the clinical trial may be among the first to benefit from it when the study is over.
- If the treatment is effective, then it may improve your child's health.

[22] This section has been adapted from ClinicalTrials.gov, a service of the National Institutes of Health:
http://www.clinicaltrials.gov/ct/gui/c/a1r/info/whatis?JServSessionIdzone_ct=9jmun6f291.

- Clinical trial patients receive the highest quality of medical care. Experts watch them closely during the study and may continue to follow them after the study is over.
- People who take part in trials contribute to scientific discoveries that may help others with childhood non-Hodgkin's lymphoma. In cases where certain medical conditions run in families, your child's participation may lead to better care or prevention for you and other family members.

The Informed Consent

Once you agree to have your child take part in a clinical trial, you will be asked to sign an "informed consent." This document explains a clinical trial's risks and benefits, the researcher's expectations of you and your child, and your child's rights as a patient.

What Are the Risks?

Clinical trials may involve risks as well as benefits. Whether or not a new treatment will work cannot be known ahead of time. There is always a chance that a new treatment may not work better than a standard treatment. There is also the possibility that it may be harmful. The treatment your child receives may cause side effects that are serious enough to require medical attention.

How Is Your Child's Safety Protected?

Clinical trials can raise fears of the unknown. Understanding the safeguards that protect your child can ease some of these fears. Before a clinical trial begins, researchers must get approval from their hospital's Institutional Review Board (IRB), an advisory group that makes sure a clinical trial is designed to protect your child's safety. During a clinical trial, doctors will closely watch your child to see if the treatment is working and if he or she is experiencing any side effects. All the results are carefully recorded and reviewed. In many cases, experts from the Data and Safety Monitoring Committee carefully monitor each clinical trial and can recommend that a study be stopped at any time. Your child will only be asked to participate in a clinical trial as a volunteer with your informed consent.

What Are Your Child's Rights in a Clinical Trial?

If your child is eligible for a clinical trial, you will be given information to help you decide whether or not you want him or her to participate. You and your child have the right to:

- Information on all known risks and benefits of the treatments in the study.
- Know how the researchers plan to carry out the study, for how long, and where.
- Know what is expected of your child.
- Know any costs involved for you or your child's insurance provider.
- Know before any of your child's medical or personal information is shared with other researchers involved in the clinical trial.
- Talk openly with doctors and ask any questions.

After your child joins a clinical trial, you and your child have the right to:

- Leave the study at any time. Participation is strictly voluntary.
- Receive any new information about the new treatment.
- Continue to ask questions and get answers.
- Maintain your child's privacy. Your child's name will not appear in any reports based on the study.
- Know whether your child participated in the treatment group or the control group (once the study has been completed).

What Questions Should You Ask before Your Child Participates in a Clinical Trial?

Questions you should ask when deciding whether or not to enroll your child in a clinical trial include the following:

- What is the purpose of the clinical trial?
- What are the standard treatments for childhood non-Hodgkin's lymphoma? Why do researchers think the new treatment may be better? What is likely to happen to my child with or without the new treatment?
- What tests and treatments will my child need? Will my child need surgery? Medication? Hospitalization?
- How long will the treatment last? How often will my child have to come back for follow-up exams?

- What are the treatment's possible benefits to my child's condition? What are the short- and long-term risks? What are the possible side effects?
- Will the treatment be uncomfortable? Will it make my child sick? If so, for how long?
- How will my child's health be monitored?
- Where will my child need to go for the clinical trial?
- How much will it cost to participate in the study? What costs are covered by the study? How much will my child's health insurance cover?
- Who will be in charge of my child's care?
- Will taking part in the study affect my child's daily life?
- How does my child feel about taking part in a clinical trial? Will other family members benefit from my child's contributions to new medical knowledge?

Clinical Trials and Insurance Coverage[23]

As you consider enrolling your child in a clinical trial, you will face the critical issue of how to cover the costs of care. Even if you have health insurance, your coverage may not include some or all of the patient care costs associated with a clinical trial. This is because some health plans define clinical trials as "experimental" or "investigational" procedures.

Because lack of coverage for these costs can keep prospective participants from enrolling in trials, the National Cancer Institute is working with major health plans and managed care groups to find solutions. In the meantime, there are strategies that may help you deal with cost and coverage barriers. This section answers frequently asked questions about insurance coverage for clinical trial participation and directs you to additional information resources.

The material here is mainly concerned with treatment clinical trials, since other types of trials (prevention, screening, etc.) are newer and generally not covered by health insurance at all. However, this guide may become more relevant for prevention and other types of trials as these trials grow more common.

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[23] Adapted from the NCI:
http://www.cancer.gov/clinical_trials/doc_header.aspx?viewid=1d92be79-8748-4bda-8005-2a56d332463b.

If you do not have any health insurance, you may find this section helpful for understanding some of the costs that trials involve.

What Costs Do Trials Involve? Who Is Usually Responsible for Paying Them?

There are two types of costs associated with a trial: patient care costs and research costs. Patient care costs fall into two categories:

- Usual care costs, such as doctor visits, hospital stays, clinical laboratory tests, x-rays, etc., which occur whether you are participating in a trial or receiving standard treatment. These costs have usually been covered by a third-party health plan, such as Medicare or private insurance.
- Extra care costs associated with clinical trial participation, such as the additional tests that may or may not be fully covered by the clinical trial sponsor and/or research institution.

The sponsor and the participant's health plan need to resolve coverage of these costs for particular trials.

Research costs are those associated with conducting the trial, such as data collection and management, research physician and nurse time, analysis of results, and tests purely performed for research purposes. Such costs are usually covered by the sponsoring organization, such as NCI or a pharmaceutical company.

Criteria Used by Health Plans to Make Reimbursement Decisions about Trials

Health insurance companies and managed care companies decide which health care services they will pay for by developing coverage policy regarding the specific services. In general, the most important factor determining whether something is covered is a health plan's judgment as to whether the service is established or investigational. Health plans usually designate a service as established if there is a certain amount of scientific data to show that it is safe and effective. If the health plan does not think that such data exist in sufficient quantity, the plan may label the service as investigational.

Health care services delivered within the setting of a clinical trial are very often categorized as investigational and not covered. This is because the health plan thinks that the major reason to perform the clinical trial is that there is not enough data to establish the safety and effectiveness of the service being studied. Thus, for some health plans, any mention of the fact that your child is involved in a clinical trial results in a denial of payment.

Your health plan may define specific criteria that a trial must meet before extending coverage, such as the following:

Sponsorship

Some plans may only cover costs of trials sponsored by organizations whose review and oversight of the trial is careful and scientifically rigorous, according to standards set by the health plan.

Trial Phase and Type

Some plans may cover patient care costs only for the clinical trials they judge to be "medically necessary" on a case-by-case basis. Trial phase may also affect coverage; for example, while a plan may be willing to cover costs associated with Phase III trials, which include treatments that have already been successful with a certain number of people, the plan may require some documentation of effectiveness before covering a Phase I or II trial.

While health plans are interested in efforts to improve prevention and screening, they currently seem less likely to have a review process in place for these trials. Therefore, it may be more difficult to get coverage for the care costs associated with them.

Some plans, especially smaller ones, will not cover any costs associated with a clinical trial. Policies vary widely, but in most cases your best bet is to have your child's doctor initiate discussions with the health plan.

Cost "Neutrality"

Some health plans may limit coverage to trials they consider cost-neutral (i.e., not significantly more expensive than the treatments considered standard).

Lack of Standard Therapy

Some plans limit coverage of trials to situations in which no standard therapy is available.

Facility and Personnel Qualifications

A health plan may require that the facility and medical staff meet specific qualifications to conduct a trial involving unique services, especially intensive therapy such as a bone marrow transplant (high-dose chemotherapy with bone marrow/ stem cell rescue).

Increasing the Likelihood of Insurance Coverage for Trials[24]

There are several steps you can follow to deal with coverage issues up front when deciding to enroll your child in a clinical trial. Along the way, enlist the help of family members and your child's doctor or other health professionals. You may find the following checklist useful:

Understand the Costs Associated with the Trial

Ask your child's doctor or the trial's contact person about the costs that must be covered by you or your health plan. Are these costs significantly higher than those associated with standard care? Also, inquire about the experience of other patients in the trial. Have their plans paid for their care? Have there been any persistent problems with coverage? How often have the trial's administrators been successful in getting plans to cover patient care costs?

Understand Your Health Plan

Be sure you know what's in your policy; request and carefully review the actual contract language. If there's a specific exclusion for "experimental treatment," look closely at the policy to see how the plan defines such treatment and under what conditions it might be covered. If it is not clearly defined, call the plan's customer service line, consult their Web site, and/or write to them. Ask for specific information about clinical trials coverage.

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[24] This section has been adapted from the NCI:
http://www.cancer.gov/clinical_trials/doc_header.aspx?viewid=1d92be79-8748-4bda-8005-2a56d332463b&docid=0df4397a-eccb-465f-bd33-a89e7a708c46.

Work Closely with Your Child's Doctor

Talk with the doctor about the paperwork he or she submits to your health plan. If there have been problems with coverage in the past, you might ask the doctor or the hospital to send an information package to the plan that includes studies supporting the procedure's safety, benefits, and medical appropriateness. This package might include:

- Publications from peer-reviewed literature about the proposed therapy that demonstrate patient benefits;
- A letter that uses the insurance contract's own language to explain why the treatment, screening method, or preventive measure should be covered;
- Letters from researchers that explain the clinical trial;
- Support letters from patient advocacy groups.

Be sure to keep your own copy of any materials that the doctor sends to your health plan for future reference.

Work Closely with Your Company's Benefits Manager

This person may be helpful in enlisting the support of your employer to request coverage for your child by the health plan.

Give Your Health Plan a Deadline

Ask the hospital or cancer center to set a target date for the therapy. This will help to ensure that coverage decisions are made promptly.

Know Your Child's Rights[25]

A number of state governments are addressing the question of whether insurance companies ought to cover the costs associated with patients' participation in clinical trials. Lack of such coverage is a significant barrier to many patients who might otherwise benefit from enrolling in a trial. Lack of coverage also makes it harder for researchers to successfully conduct trials that could improve prevention and treatment options. Information on State initiatives and legislation concerning cancer-related clinical trials is available

[25] Adapted from Cancer.gov: **http://www.cancer.gov/ClinicalTrials/insurancelaws**.

at **http://www.cancer.gov/ClinicalTrials/insurancelaws**. By conducting your own research and learning about your child's rights, you may increase the likelihood that your insurance company will cover the costs of a trial.

If Your Insurance Claim Is Denied after the Trial Has Begun

If a claim is denied, read your policy to find out what steps you can follow to make an appeal. In "What Cancer Survivors Need to Know about Health Insurance", the National Coalition for Cancer Survivorship suggests that you and your doctor demonstrate to the health plan that:

- The therapy in the trial is not just a research study, but also a valid procedure that benefits patients;
- Your child's situation is similar to that of other patients who are participating in clinical trials as part of a covered benefit;
- Possible complications have been anticipated and can be handled effectively.

You also may wish to contact your state insurance counseling hotline or insurance department for more help, or write your state insurance commissioner describing the problem.

Where Else Can I Turn for Assistance?

It's never easy to deal with financial issues when a loved one faces cancer. Unfortunately, costs can present a significant barrier to clinical trials participation. The range of insurance issues and health plan contracts makes it impossible to deal with all of them here. You may wish to consult this partial list of publications, organizations, and Web sites for more information:

Publications

What Cancer Survivors Need to Know about Health Insurance
National Coalition of Cancer Survivorship
1010 Wayne Avenue, 5th floor
Silver Spring, MD 20910
(301) 650-8868
http://www.cansearch.org/

Cancer Treatments Your Insurance Should Cover
The Association of Community Cancer Centers
11600 Nebel Street, Suite 201
Rockville, MD 20852
(301) 984-9496
http://www.accc-cancer.org/main2001.shtml

The Managed Care Answer Guide
Patient Advocate Foundation
739 Thimble Shoals Boulevard, Suite 704
Newport News, VA 23606
(757) 873-6668
E-mail: **ndepaf@pinn.net**

1998 Guide to Health Insurance for People with Medicare, The Medicare Handbook
Medicare Helpline: 1-800-444-4606
Health Care Financing Administration: **http://www.hcfa.gov/**
New Medicare site: **http://www.medicare.gov/**

Assistance Programs

Candlelighters Childhood Cancer Foundation
Ombudsman Program
910 Woodmont Avenue, #4607
Bethesda, MD 20814
(301) 657-8401; 1-800-366-2223 (toll-free)
E-mail: **info@candlelighters.org**
http://www.candlelighters.org
The Ombudsman Program helps families of children with cancer and survivors of childhood cancer resolve a range of problems, including insurance coverage difficulties. Local groups appoint a Parent Advocate who works with the treatment center on behalf of families.

Medical Care Management Corporation
5272 River Road, Suite 650
Bethesda, MD 20816-1405
(301) 652-1818
email: mcman@mcman.com
http://www.mcman.com/
Working for a range of clients, including health plans, employers, and patients, MCMC conducts independent, objective reviews of high-

technology medical care cases to assist in decision-making. While it does charge for its services, MCMC also offers a volunteer program for those who cannot afford to pay.

More Information Resources

OncoLink
A service of the University of Pennsylvania Cancer Center.
http://www.oncolink.com/
In addition to general cancer information, this web site features a section on financial information for patients. Among the topics: viatical settlements, life insurance, a glossary of financial and medical terms, and news about billing and insurance.

American Association of Health Plans
1129 20th Street, NW, Suite 600
Washington, DC 20036-3421
(202) 778-3200
http://www.aahp.org/
The Web site section "For Consumers" includes a fact sheet on clinical research that describes various health plans' efforts to support research initiatives and collaborate with academic health centers and universities.

Health Insurance Association of America
555 13th Street, NW
Washington, DC 20004
(202) 824-1600

- Home page: **http://www.hiaa.org/**
- Consumer Information: **http://www.hiaa.org/consumer/**
- Insurance Counseling Hotlines by State: **http://www.hiaa.org/consumer/insurance_counsel.cfm**
- State Insurance Departments: **http://www.hiaa.org/consumer/state_insurance.cfm**

Government Initiatives to Expand Insurance Coverage for Trials[26]

The good news is that there has been a recent effort in the U.S. to assure clinical trials coverage, with NCI involved in several new initiatives as described below:

NCI-Department of Defense Agreement

An innovative 1996 agreement between NCI and the Department of Defense (DoD) has given thousands of DoD cancer patients more options for care and greater access to state-of-the-art treatments. Patients who are beneficiaries of TRICARE/CHAMPUS, the DoD's health program, are covered for NCI-sponsored Phase II and Phase III clinical treatment trials. NCI and DoD are refining a system that allows physicians and patients to determine quickly what current trials meet their needs and where they are taking place.

NCI-Department of Veterans Affairs Agreement

A 1997 agreement with the Department of Veterans Affairs provides coverage for eligible veterans of the armed services to participate in NCI-sponsored prevention, diagnosis, and treatment studies nationwide. For additional information, see the VA/DoD Beneficiaries Digest Page at **http://www.va.gov/cancer.htm**.

Midwest Health Plans Agreement

Some NCI Cooperative Groups have reached agreements with several insurers in Wisconsin and Minnesota to provide more than 200,000 people with coverage. The coverage is designated for patient care costs if they participate in a cooperative group-sponsored trial.

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[26] Adapted from the NCI:
http://www.cancer.gov/clinical_trials/doc_header.aspx?viewid=1d92be79-8748-4bda-8005-2a56d332463b&docid=d8092601-daf9-4794-8536-3be2712eb6b9.

Pediatric Cancer Care Network

This network, a cooperative agreement among the Children's Cancer Group, the Pediatric Oncology Group, and the Blue Cross Blue Shield System Association (BCBS) nationwide, will ensure that children of BCBS subscribers receive care at designated centers of cancer care excellence and may promote the enrollment of children in Cooperative Group clinical trials.

Keeping Current on Clinical Trials

Various government agencies maintain databases on trials. The U.S. National Institutes of Health, through the National Library of Medicine, has developed ClinicalTrials.gov to provide the public and physicians with current information about clinical research across the broadest number of medical conditions.

The site was launched in February 2000 and currently contains approximately 5,700 clinical studies in over 59,000 locations worldwide, with most studies being conducted in the United States. ClinicalTrials.gov receives about 2 million hits per month and hosts approximately 5,400 visitors daily. To access this database, simply go to their Web site (**www.clinicaltrials.gov**) and search by "childhood non-Hodgkin's lymphoma" (or synonyms).

While ClinicalTrials.gov is the most comprehensive listing of NIH-supported clinical trials available, not all trials are in the database. The database is updated regularly, so clinical trials are continually being added. The following is a list of specialty databases affiliated with the National Institutes of Health that offer additional information on trials:

- For clinical studies at the Warren Grant Magnuson Clinical Center located in Bethesda, Maryland, visit their Web site:
  http://clinicalstudies.info.nih.gov/
- For clinical studies conducted at the Bayview Campus in Baltimore, Maryland, visit their Web site:
  http://www.jhbmc.jhu.edu/studies/index.html
- For cancer trials, visit the National Cancer Institute:
  http://cancertrials.nci.nih.gov/

General References

The following references describe clinical trials and experimental medical research. They have been selected to ensure that they are likely to be available from your local or online bookseller or university medical library. These references are usually written for healthcare professionals, so you may consider consulting with a librarian or bookseller who might recommend a particular reference. The following includes some of the most readily available references (sorted alphabetically by title; hyperlinks provide rankings, information and reviews at Amazon.com):

- **A Guide to Patient Recruitment: Today's Best Practices & Proven Strategies** by Diana L. Anderson; Paperback - 350 pages (2001), CenterWatch, Inc.; ISBN: 1930624115; **http://www.amazon.com/exec/obidos/ASIN/1930624115/icongroupinterna**
- **A Step-By-Step Guide to Clinical Trials** by Marilyn Mulay, R.N., M.S., OCN; Spiral-bound - 143 pages Spiral edition (2001), Jones & Bartlett Pub; ISBN: 0763715697; **http://www.amazon.com/exec/obidos/ASIN/0763715697/icongroupinterna**
- **The CenterWatch Directory of Drugs in Clinical Trials** by CenterWatch; Paperback - 656 pages (2000), CenterWatch, Inc.; ISBN: 0967302935; **http://www.amazon.com/exec/obidos/ASIN/0967302935/icongroupinterna**
- **The Complete Guide to Informed Consent in Clinical Trials** by Terry Hartnett (Editor); Paperback - 164 pages (2000), PharmSource Information Services, Inc.; ISBN: 0970153309; **http://www.amazon.com/exec/obidos/ASIN/0970153309/icongroupinterna**
- **Dictionary for Clinical Trials** by Simon Day; Paperback - 228 pages (1999), John Wiley & Sons; ISBN: 0471985961; **http://www.amazon.com/exec/obidos/ASIN/0471985961/icongroupinterna**
- **Extending Medicare Reimbursement in Clinical Trials** by Institute of Medicine Staff (Editor), et al; Paperback 1st edition (2000), National Academy Press; ISBN: 0309068886; **http://www.amazon.com/exec/obidos/ASIN/0309068886/icongroupinterna**
- **Handbook of Clinical Trials** by Marcus Flather (Editor); Paperback (2001), Remedica Pub Ltd; ISBN: 1901346293; **http://www.amazon.com/exec/obidos/ASIN/1901346293/icongroupinterna**

Vocabulary Builder

The following vocabulary builder gives definitions of words used in this chapter that have not been defined in previous chapters:

506U78: An anticancer drug that belongs to the family of drugs called antimetabolites. [NIH]

Antibody: A type of protein made by certain white blood cells in response to a foreign substance (antigen). Each antibody can bind to only a specific antigen. The purpose of this binding is to help destroy the antigen. Antibodies can work in several ways, depending on the nature of the antigen. Some antibodies destroy antigens directly. Others make it easier for white blood cells to destroy the antigen. [NIH]

Antineoplastons: Substances isolated from normal human blood and urine being tested as a type of treatment for some tumors and AIDS. [NIH]

Chronic: A disease or condition that persists or progresses over a long period of time. [NIH]

CNS: Central nervous system. The brain and spinal cord. [NIH]

Cyclosporine: A drug used to help reduce the risk of rejection of organ and bone marrow transplants by the body. It is also used in clinical trials to make cancer cells more sensitive to anticancer drugs. [NIH]

Filgrastim: A colony-stimulating factor that stimulates the production of neutrophils (a type of white blood cell). It is a cytokine that belongs to the family of drugs called hematopoietic (blood-forming) agents. Also called granulocyte colony-stimulating factor (G-CSF). [NIH]

Grade: The grade of a tumor depends on how abnormal the cancer cells look under a microscope and how quickly the tumor is likely to grow and spread. Grading systems are different for each type of cancer. [NIH]

Graft: Healthy skin, bone, or other tissue taken from one part of the body and used to replace diseased or injured tissue removed from another part of the body. [NIH]

HIV: Human immunodeficiency virus, the cause of acquired immunodeficiency syndrome (AIDS). [NIH]

Leucovorin: A drug used to protect normal cells from high doses of the anticancer drug methotrexate. It is also used to increase the antitumor effects of fluorouracil and tegafur-uracil, an oral treatment alternative to intravenous fluorouracil. [NIH]

Leukemia: Cancer of blood-forming tissue. [NIH]

Lymphocytic: Referring to lymphocytes, a type of white blood cell. [NIH]

Myelogenous: Produced by, or originating in, the bone marrow. [NIH]

Neutropenia: An abnormal decrease in the number of neutrophils, a type of white blood cell. [NIH]

Osteosarcoma: A cancer of the bone that affects primarily children and adolescents. Also called osteogenic sarcoma. [NIH]

Oxaliplatin: An anticancer drug that belongs to the family of drugs called platinum compounds. [NIH]

Paclitaxel: An anticancer drug that belongs to the family of drugs called mitotic inhibitors. [NIH]

Radiolabeled: Any compound that has been joined with a radioactive substance. [NIH]

Randomized: Describes an experiment or clinical trial in which animal or human subjects are assigned by chance to separate groups that compare different treatments. [NIH]

Refractory: Not readily yielding to treatment. [EU]

Regimen: A treatment plan that specifies the dosage, the schedule, and the duration of treatment. [NIH]

Remission: A decrease in or disappearance of signs and symptoms of cancer. In partial remission, some, but not all, signs and symptoms of cancer have disappeared. In complete remission, all signs and symptoms of cancer have disappeared, although there still may be cancer in the body. [NIH]

Rituximab: A type of monoclonal antibody used in cancer detection or therapy. Monoclonal antibodies are laboratory-produced substances that can locate and bind to cancer cells. [NIH]

Screening: Checking for disease when there are no symptoms. [NIH]

Trimetrexate: A nonclassical folic acid inhibitor through its inhibition of the enzyme dihydrofolate reductase. It is being tested for efficacy as an antineoplastic agent and as an antiparasitic agent against Pneumocystis carinii pneumonia in AIDS patients. Myelosuppression is its dose-limiting toxic effect. [NIH]

Urine: Fluid containing water and waste products. Urine is made by the kidneys, stored in the bladder, and leaves the body through the urethra. [NIH]

Vinorelbine: An anticancer drug that belongs to the family of plant drugs called vinca alkaloids. [NIH]

PART II: ADDITIONAL RESOURCES AND ADVANCED MATERIAL

ABOUT PART II

In Part II, we introduce you to additional resources and advanced research on childhood non-Hodgkin's lymphoma. All too often, parents who conduct their own research are overwhelmed by the difficulty in finding and organizing information. The purpose of the following chapters is to provide you an organized and structured format to help you find additional information resources on childhood non-Hodgkin's lymphoma. In Part II, as in Part I, our objective is not to interpret the latest advances on childhood non-Hodgkin's lymphoma or render an opinion. Rather, our goal is to give you access to original research and to increase your awareness of sources you may not have already considered. In this way, you will come across the advanced materials often referred to in pamphlets, books, or other general works. Once again, some of this material is technical in nature, so consultation with a professional familiar with childhood non-Hodgkin's lymphoma is suggested.

CHAPTER 4. STUDIES ON CHILDHOOD NON-HODGKIN'S LYMPHOMA

Overview

Every year, academic studies are published on childhood non-Hodgkin's lymphoma or related conditions. Broadly speaking, there are two types of studies. The first are peer reviewed. Generally, the content of these studies has been reviewed by scientists or physicians. Peer-reviewed studies are typically published in scientific journals and are usually available at medical libraries. The second type of studies is non-peer reviewed. These works include summary articles that do not use or report scientific results. These often appear in the popular press, newsletters, or similar periodicals.

In this chapter, we will show you how to locate peer-reviewed references and studies on childhood non-Hodgkin's lymphoma. We will begin by discussing research that has been summarized and is free to view by the public via the Internet. We then show you how to generate a bibliography on childhood non-Hodgkin's lymphoma and teach you how to keep current on new studies as they are published or undertaken by the scientific community.

The National Library of Medicine: PubMed

One of the quickest and most comprehensive ways to find academic studies in both English and other languages is to use PubMed, maintained by the National Library of Medicine. The advantage of PubMed over previously mentioned sources is that it covers a greater number of domestic and foreign

references. It is also free to the public.[27] If the publisher has a Web site that offers full text of its journals, PubMed will provide links to that site, as well as to sites offering other related data. User registration, a subscription fee, or some other type of fee may be required to access the full text of articles in some journals.

To generate your own bibliography of studies dealing with childhood non-Hodgkin's lymphoma, simply go to the PubMed Web site at **www.ncbi.nlm.nih.gov/pubmed**. Type "childhood non-Hodgkin's lymphoma" (or synonyms) into the search box, and click "Go." The following is the type of output you can expect from PubMed for "childhood non-Hodgkin's lymphoma" (hyperlinks lead to article summaries):

- **Acquired immunodeficiency syndrome presenting as childhood non-Hodgkin's lymphoma.**
  Author(s): Lee WS, Chan TL, Koh MT, Ariffin WA, Lin HP.
  Source: Singapore Med J. 2001 November; 42(11): 530-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11876380&dopt=Abstract

- **Analysis of ploidy and proliferative activity in childhood non-Hodgkin's lymphoma (NHL) and Hodgkin's disease (HD).**
  Author(s): Coad NA, Jones TJ, Muir KR, Parkes SE, Smith K, Raafat F, Mann JR.
  Source: Pediatric Pathology & Laboratory Medicine : Journal of the Society for Pediatric Pathology, Affiliated with the International Paediatric Pathology Association. 1997 November-December; 17(6): 893-902.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9353829&dopt=Abstract

- **Childhood non-Hodgkin's lymphoma in the five Nordic countries. A five-year population-based study from the Nordic Society of Pediatric Hematology and Oncology.**
  Author(s): Marky I, Schmiegelow K, Perkkio M, Jonsson OG, Storm-Mathiesen I, Gustafsson G, Kreuger A, Langmark F.

[27] PubMed was developed by the National Center for Biotechnology Information (NCBI) at the National Library of Medicine (NLM) at the National Institutes of Health (NIH). The PubMed database was developed in conjunction with publishers of biomedical literature as a search tool for accessing literature citations and linking to full-text journal articles at Web sites of participating publishers. Publishers that participate in PubMed supply NLM with their citations electronically prior to or at the time of publication.

Source: Journal of Pediatric Hematology/Oncology : Official Journal of the American Society of Pediatric Hematology/Oncology. 1995 May; 17(2): 163-6.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7749767&dopt=Abstract

- **Childhood non-Hodgkin's lymphoma: an immunophenotypic analysis.**
  Author(s): Shah SH, Muzaffar S, Pervez S, Hassan SH.
  Source: J Pak Med Assoc. 2000 March; 50(3): 89-91.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10795468&dopt=Abstract

- **Childhood non-Hodgkin's lymphoma--results of treatment with ALL high-risk protocol.**
  Author(s): Chu HY, Shu SG, Law KL, Chi CS.
  Source: Zhonghua Min Guo Xiao Er Ke Yi Xue Hui Za Zhi. 1993 March-April; 34(2): 118-24.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8372667&dopt=Abstract

- **Childhood non-Hodgkin's lymphomas in the United Kingdom.**
  Author(s): Reid MM.
  Source: Journal of Clinical Pathology. 1997 August; 50(8): 709. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9301562&dopt=Abstract

- **Could cisplatin as a front-line treatment in childhood non-Hodgkin's lymphoma be a promising therapy?**
  Author(s): Papadopoulou AL, Moschovi M, Panagopoulou-Cristaki M, Anagnostou-Keramida D, Van Vliet-Constantinidou C, Botsonis A, Tsangaris GT, Tzortzatou-Stathopoulou F.
  Source: Pediatric Hematology and Oncology. 1999 July-August; 16(4): 341-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10407871&dopt=Abstract

- **Distinct patterns of chromosome abnormalities characterize childhood non-Hodgkin's lymphoma.**
  Author(s): Mikraki V, Jhanwar SC, Filippa DA, Wollner N, Chaganti RS.

Source: British Journal of Haematology. 1992 January; 80(1): 15-20.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1536806&dopt=Abstract

- **Gastric involvement in childhood non-Hodgkin's lymphoma: a case report.**
  Author(s): Bakir T, Gumustekin E, Bozalioglu H, Tezic T, Ozoran Y.
  Source: Turk J Pediatr. 1991 January-March; 33(1): 43-7. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1844175&dopt=Abstract

- **Growth and growth hormone secretion after treatment for childhood non-Hodgkin's lymphoma.**
  Author(s): Samuelsson BO, Marky I, Rosberg S, Albertsson-Wikland K.
  Source: Medical and Pediatric Oncology. 1997 January; 28(1): 27-34.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8950333&dopt=Abstract

- **Limiting therapy for limited childhood non-Hodgkin's lymphoma.**
  Author(s): Magrath I.
  Source: The New England Journal of Medicine. 1997 October 30; 337(18): 1304-6. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9345082&dopt=Abstract

- **Microcephaly and childhood non-Hodgkin's lymphoma.**
  Author(s): Dluzniewska A, Tredowska-Skoczen D, Armata J, Tacik J.
  Source: Archives of Disease in Childhood. 1995 November; 73(5): 480-1. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8554375&dopt=Abstract

- **Primary subconjunctival lymphoma: an unusual presentation of childhood non-Hodgkin's lymphoma.**
  Author(s): Karadeniz C, Bilgic S, Ruacan S, Sarialioglu F, Buyukpamukcu M, Akyuz C, Dogan A.
  Source: Medical and Pediatric Oncology. 1991; 19(3): 204-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2023568&dopt=Abstract

- **Treatment of childhood non-Hodgkin's lymphoma.**
  Author(s): Lin ST.
  Source: Acta Paediatr Taiwan. 2000 July-August; 41(4): 175-6. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11021000&dopt=Abstract

- **Treatment results of the TPOG-NHL92 protocols for childhood non-Hodgkin's lymphomas in Taiwan: a report from the Taiwan Pediatric Oncology Group (TPOG)**
  Author(s): Yang CP, Hung JJ, Jaing TH, Lin KH, Lin DT, Lu MY, Liang DC, Chen SH, Liu HC, Hsiao CC, Shu SG, Chen JS, Chang TT, Chiou SS, Hsieh YL, Lin MT, Lee MT, Peng CT, Cheng SN, Chen RL, Chen BW, Lin KS.
  Source: Acta Paediatr Taiwan. 2000 July-August; 41(4): 193-204.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11021005&dopt=Abstract

- **Absence of somatic hypermutation of immunoglobulin heavy chain variable region genes in precursor B-lymphoblastic lymphoma: a study of four cases in childhood and adolescence.**
  Author(s): Hojo H, Sasaki Y, Nakamura N, Abe M.
  Source: Am J Clin Pathol. 2001 November; 116(5): 673-82.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11710683&dopt=Abstract

- **Acute lymphoblastic leukemia and the lymphoblastic lymphomas of childhood.**
  Author(s): Head DR, Behm FG.
  Source: Semin Diagn Pathol. 1995 November; 12(4): 325-34. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8578027&dopt=Abstract

- **Childhood T-cell lymphoblastic lymphoma--does early resolution of mediastinal mass predict for final outcome? The United Kingdom Children's Cancer Study Group (UKCCSG).**
  Author(s): Shepherd SF, A'Hern RP, Pinkerton CR.
  Source: British Journal of Cancer. 1995 September; 72(3): 752-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7669589&dopt=Abstract

- **Cutaneous involvement in children with acute lymphoblastic leukemia or lymphoblastic lymphoma. The Children's Leukemia Cooperative Group of the European Organization of Research and Treatment of Cancer (EORTC).**
  Author(s): Millot F, Robert A, Bertrand Y, Mechinaud F, Laureys G, Ferster A, Brock P, Rohrlich P, Mazingue F, Plantaz D, Plouvier E, Pacquement H, Behar C, Rialland X, Chantraine JM, Guilhot F, Otten J.
  Source: Pediatrics. 1997 July; 100(1): 60-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9200360&dopt=Abstract

- **Intensive ALL-type therapy without local radiotherapy provides a 90% event-free survival for children with T-cell lymphoblastic lymphoma: a BFM group report.**
  Author(s): Reiter A, Schrappe M, Ludwig WD, Tiemann M, Parwaresch R, Zimmermann M, Schirg E, Henze G, Schellong G, Gadner H, Riehm H.
  Source: Blood. 2000 January 15; 95(2): 416-21.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10627444&dopt=Abstract

- **Max protein expression is associated with survival of children with lymphoblastic lymphoma.**
  Author(s): Yuza Y, Kawakami M, Takagi K, Yamazaki Y, Urashima M.
  Source: Pediatrics International : Official Journal of the Japan Pediatric Society. 1999 December; 41(6): 637-40.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10618883&dopt=Abstract

- **Precursor B-cell lymphoblastic lymphoma presenting as an orbital mass.**
  Author(s): Alford MA, Nerad JA, Conlan RM, Comito M, Giller RH.
  Source: Orbit (Amsterdam, Netherlands). 1999 March; 18(1): 17-24.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12048694&dopt=Abstract

- **Randomized trial of r-metHu granulocyte colony-stimulating factor in an intensive treatment for T-cell leukemia and advanced-stage lymphoblastic lymphoma of childhood: a Pediatric Oncology Group pilot study.**
  Author(s): Laver J, Amylon M, Desai S, Link M, Schwenn M, Mahmoud H, Shuster J.

Source: Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology. 1998 February; 16(2): 522-6.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9469336&dopt=Abstract

- **T-cell lymphoblastic lymphoma of the lower jaw in a young child: a case report.**
  Author(s): Wolvius EB, van der Valk P, Baart JA, Schouten-van Meeteren NY, van der Waal I.
  Source: Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics. 1996 October; 82(4): 434-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8899783&dopt=Abstract

- **Translocation (10;12)(q24;q15) in a T-cell lymphoblastic lymphoma with myeloid hyperplasia.**
  Author(s): Sano K, Goji J, Kosaka Y, Nakamura H, Nakamura F, Tatsumi E.
  Source: Cancer Genetics and Cytogenetics. 1998 September; 105(2): 168-71.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9723036&dopt=Abstract

Vocabulary Builder

Alleles: Mutually exclusive forms of the same gene, occupying the same locus on homologous chromosomes, and governing the same biochemical and developmental process. [NIH]

Chromosome: Part of a cell that contains genetic information. Except for sperm and eggs, all human cells contain 46 chromosomes. [NIH]

Cisplatin: An anticancer drug that belongs to the family of drugs called platinum compounds. [NIH]

Cytarabine: An anticancer drug that belongs to the family of drugs called antimetabolites. [NIH]

Cytogenetics: A branch of genetics which deals with the cytological and molecular behavior of genes and chromosomes during cell division. [NIH]

Granulocyte: A type of white blood cell that fights bacterial infection. Neutrophils, eosinophils, and basophils are granulocytes. [NIH]

Hyperplasia: An abnormal increase in the number of cells in an organ or tissue. [NIH]

Immunodeficiency: The decreased ability of the body to fight infection and disease. [NIH]

Immunoglobulin: A protein that acts as an antibody. [NIH]

Molecular: Of, pertaining to, or composed of molecules : a very small mass of matter. [EU]

Oral: By or having to do with the mouth. [NIH]

Orbital: Pertaining to the orbit (= the bony cavity that contains the eyeball). [EU]

Paediatric: Of or relating to the care and medical treatment of children; belonging to or concerned with paediatrics. [EU]

Ploidy: The number of sets of chromosomes in a cell or an organism. For example, haploid means one set and diploid means two sets. [NIH]

Precursor: Something that precedes. In biological processes, a substance from which another, usually more active or mature substance is formed. In clinical medicine, a sign or symptom that heralds another. [EU]

Radiology: The use of radiation (such as x-rays) or other imaging technologies (such as ultrasound and magnetic resonance imaging) to diagnose or treat disease. [NIH]

Radiotherapy: The treatment of disease by ionizing radiation. [EU]

Secretion: 1. the process of elaborating a specific product as a result of the activity of a gland; this activity may range from separating a specific substance of the blood to the elaboration of a new chemical substance. 2. any substance produced by secretion. [EU]

Somatic: 1. pertaining to or characteristic of the soma or body. 2. pertaining to the body wall in contrast to the viscera. [EU]

Subconjunctival: Situated or occurring beneath the conjunctiva. [EU]

Virus: Submicroscopic organism that causes infectious disease. In cancer therapy, some viruses may be made into vaccines that help the body build an immune response to, and kill, tumor cells. [NIH]

CHAPTER 5. PHYSICIAN GUIDELINES AND DATABASES

Overview

Doctors and medical researchers rely on a number of information sources to help children with childhood non-Hodgkin's lymphoma. Many will subscribe to journals or newsletters published by their professional associations or refer to specialized textbooks or clinical guides published for the medical profession. In this chapter, we focus on databases and Internet-based guidelines created or written for this professional audience.

NIH Guidelines

For the more common medical conditions, the National Institutes of Health publish guidelines that are frequently consulted by physicians. Publications are typically written by one or more of the various NIH Institutes. For physician guidelines, commonly referred to as "clinical" or "professional" guidelines, you can visit the following Institutes:

- Office of the Director (OD); guidelines consolidated across agencies available at **http://www.nih.gov/health/consumer/conkey.htm**
- National Institute of General Medical Sciences (NIGMS); fact sheets available at **http://www.nigms.nih.gov/news/facts/**
- National Library of Medicine (NLM); extensive encyclopedia (A.D.A.M., Inc.) with guidelines: **http://www.nlm.nih.gov/medlineplus/healthtopics.html**
- National Cancer Institute (NCI); guidelines available at **http://cancernet.nci.nih.gov/pdq/pdq_treatment.shtml**

In this chapter, we begin by reproducing one such guideline for childhood non-Hodgkin's lymphoma:

What Is Childhood Non-Hodgkin's Lymphoma?[28]

This treatment information summary on childhood non-Hodgkin's lymphoma (NHL) is an overview of prognosis, diagnosis, classification, and treatment. The National Cancer Institute created the PDQ database to increase the availability of new treatment information and its use in treating patients. Information and references from the most recently published literature are included after review by pediatric oncology specialists.

Cancer in children and adolescents is rare. Children and adolescents with cancer should be referred to medical centers that have a multidisciplinary team of cancer specialists with experience treating the cancers that occur during childhood and adolescence. This multidisciplinary team incorporates the skills of the primary care physician, pediatric surgical subspecialists, radiation oncologists, pediatric medical oncologists/hematologists, rehabilitation specialists, pediatric nurse specialists, social workers, and others in order to ensure that children receive treatment, supportive care, and rehabilitation that will achieve optimal survival and quality of life. Guidelines for pediatric cancer centers and their role in the treatment of children with cancer have been outlined by the American Academy of Pediatrics.[29] At these pediatric cancer centers, there are clinical trials available for most of the types of cancer that occur in children and adolescents, and the opportunity to participate in these trials is offered to most patients/families. Clinical trials for children and adolescents with cancer are generally designed to compare potentially better therapy with therapy that is currently accepted as standard. The majority of the progress made in identifying curative therapies for childhood cancers have been achieved through clinical trials. Information about ongoing clinical trials is available from the NCI (**http://cancer.gov/clinical_trials/**).

Lymphoma (Hodgkin's and non-Hodgkin's) is the third most common childhood malignancy, and non-Hodgkin's lymphoma (NHL) accounts for

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[28] The following guidelines appeared on the NCI website on Aug 26, 2002. The text was last modified Jul, 2002. The text has been adapted for this sourcebook.

[29] Sanders J, Glader B, Cairo M, et al.: Guidelines for the pediatric cancer center and role of such centers in diagnosis and treatment. American Academy of Pediatrics Section Statement Section on Hematology/Oncology. Pediatrics 99(1): 139-141, 1997.

approximately 7% of cancers in children less than 20 years of age.[30] In the United States, there are about 800 new cases of NHL diagnosed each year. Incidence is approximately 10 per 1,000,000. Although there is no sharp age peak, NHL occurs most commonly in the second decade of life, and occurs less frequently in children less than 3 years of age. NHL is the most frequent malignancy in children with AIDS, and it often occurs before the age of 4 years in those who have vertical transmission of the virus.[31] Screening for HIV should be considered for all children with NHL.[32]

More than 70% of children and adolescents with NHL will survive at least 5 years with modern chemotherapy although outcome is variable depending on a number of factors.[33] The most important prognostic determinant, given optimal therapy, is the extent of disease at diagnosis as determined by pretreatment staging. Patients with a single extra-abdominal/extrathoracic tumor and those with totally resected intra-abdominal tumor have an excellent prognosis (a 5-year survival rate of approximately 90%), regardless of histology. Patients with extensive intrathoracic or intra-abdominal disease and patients with bone marrow or central nervous system involvement at diagnosis require intensified therapy.[34] These therapies have improved the outcome for patients with advanced stage disease.

Information about ongoing clinical trials is available from the NCI (**http://cancer.gov/clinical_trials/**).

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[30] Percy CL, Smith MA, Linet M, et al.: Lymphomas and reticuloendothelial neoplasms. In: Ries LA, Smith MA, Gurney JG, et al., eds.: Cancer Incidence and Survival Among Children and Adolescents: United States SEER Program 1975-1995. Bethesda, Md: National Cancer Institute, SEER Program, NIH Pub.No. 99-4649, 1999, pp 35-50.
Sandlund JT, Downing JR, Crist WM: Non-Hodgkin's lymphoma in childhood. New England Journal of Medicine 334(19): 1238-1248, 1996.

[31] Evans JA, Gibb DM, Holland FJ, et al.: Malignancies in UK children with HIV infection acquired from mother to child transmission. Archives of Disease in Childhood 76(4): 330-333, 1997.

[32] McClain KL, Joshi VV, Murphy SB: Cancers in children with HIV infection. Hematology/Oncology Clinics of North America 10(5): 1189-1201, 1996.
Serraino D, Franceschi S: Kaposi's sarcoma and non-Hodgkin's lymphomas in children and adolescents with AIDS. AIDS 10(6): 643-647, 1996.

[33] Pinkerton CR: The continuing challenge of treatment for non-Hodgkin's lymphoma in children. British Journal of Haematology 107(2): 220-234, 1999.

[34] Percy CL, Smith MA, Linet M, et al.: Lymphomas and reticuloendothelial neoplasms. In: Ries LA, Smith MA, Gurney JG, et al., eds.: Cancer Incidence and Survival Among Children and Adolescents: United States SEER Program 1975-1995. Bethesda, Md: National Cancer Institute, SEER Program, NIH Pub.No. 99-4649, 1999, pp 35-50.

Cellular Classification and Clinical Presentation

In children, non-Hodgkin's lymphomas (NHLs) are distinct from the more common forms of lymphomas in adults. While lymphomas in adults are more commonly of low or intermediate grade, almost all that occur in children are high grade and can be classified into 1 of 4 categories:

- Burkitt's and Burkitt's-like lymphoma/small noncleaved B cell lymphoma;
- Lymphoblastic lymphomas;
- Diffuse large cell lymphomas (b,t,null); and
- Anaplastic large cell lymphoma. Other types of lymphomas occur rarely in children.

Each type of childhood NHL is associated with distinctive molecular biological characteristics which are outlined in the following table. The Revised European-American Lymphoma Classification (REAL) and the World Health Organization Classification (WHO)[35] are the most current NHL classifications utilized and are shown below. The working formulation is also listed for reference below. The WHO Classification applies the principles of the REAL Classification and focuses on the specific type of lymphoma for therapy purposes. The remainder of the categories, for the most part, do not pertain to pediatric NHL and are not shown.

[35] Harris NL, Jaffe ES, Diebold J, et al.: World Health Organization classification of neoplastic diseases of the hematopoietic and lymphoid tissues: report of the Clinical Advisory Committee meeting--Airlie House, Virginia, November 1997. Journal of Clinical Oncology 17(12): 3835-3849, 1999.

Table 1: Major histopathological categories of non-Hodgkin's lymphoma in children and adolescents.*

Category WHO Classification/ Updated REAL	Category (Working Formulation)	Immunophenotype	Clinical Presentation	Chromosomal Translocation	Genes Affected
Burkitt's and Burkitt's like lymphomas	ML small non-cleaved cell	Mature B cell	Intraabdominal (sporadic) jaw (endemic)	t(8;14)(q24; q32), t(2;8) (p11;q24), t(8;22)(q24; q11)	C-MYC, IgH, IgK, Ig1**
Lymphoblastic lymphoma, Precursor T/leukemia	Lymphoblastic convoluted and non-convoluted	T cell Pre B-cell	Mediastinal, bone marrow Skin, bone	MTS1/p16ink4a Deletion TAL1 t(1;14)(p34; q11), t(11;14) (p13;q11)	TAL1 TCRao*** RHOMB1, HOX11
Diffuse large B-cell lymphoma	ML large cell	Mature B cell Maybe CD30+	Nodal, abdomen, bone, primary CNS, mediastinal	Not well characterized in children	
Anaplastic large cell lymphoma, systemic	ML immunoblastic or ML large	CD30+ (Ki+) T cell or null cell	Variable	t(2;5)(p23; q35)	ALK, NMP
Anaplastic large cell lymphoma, cutaneous		CD30+ (Ki- usually) T cell	Skin only Single or multiple lesions	Lacks t(2;5)	

ML = Malignant lymphoma
* Adapted from Percy, Smith, Linet, et al.[36]
l** = lambda
ao*** = alpha omega

Lymphoblastic Lymphoma

Lymphoblastic lymphomas, which make up approximately 30% of childhood NHL, are predominantly tumors of thymocyte (T-cell) origin. Nearly 75% of patients with lymphoblastic lymphoma have an anterior mediastinal mass, and may present with symptoms of dyspnea, wheezing, stridor, dysphagia, or swelling of the head and neck. Pleural effusions may be present and involvement of lymph nodes, usually above the diaphragm,

[36] Percy CL, Smith MA, Linet M, et al.: Lymphomas and reticuloendothelial neoplasms. In: Ries LA, Smith MA, Gurney JG, et al., eds.: Cancer Incidence and Survival Among Children and Adolescents: United States SEER Program 1975-1995. Bethesda, Md: National Cancer Institute, SEER Program, NIH Pub.No. 99-4649, 1999, pp 35-50.

may be a prominent feature. There may also be involvement of bone, skin, bone marrow, central nervous system (CNS), abdominal organs (but rarely bowel), and occasionally other sites such as lymphoid tissue of Waldeyer's ring and testis. Abdominal involvement is rare; most patients who present with an abdominal mass have small noncleaved cell or large cell lymphoma. Localized lymphoblastic lymphomas may occur in lymph nodes, bone, subcutaneous tissue, etc. Lymphoblastic lymphoma within the mediastinum is not considered localized disease.

Involvement of the bone marrow may lead to confusion as to whether the patient has lymphoma with bone marrow involvement or leukemia. Traditionally, patients with greater than 25% marrow blasts are considered to have leukemia, and those with less than 25% marrow blasts are considered to have lymphoma. It is not yet clear whether these arbitrary definitions are biologically distinct or relevant for treatment design.

Lymphoblastic lymphomas are usually positive for the enzyme terminal deoxynucleotidyl transferase (TdT) and have a T-cell immunophenotype. About 10% to 15% of lymphoblastic lymphomas have non-T immunologic characteristics (for example, common acute lymphocytic leukemia antigen [CD10]-positive precursor B-cell phenotype).[37] Chromosomal abnormalities are not well characterized in patients with lymphoblastic lymphoma.

Small Noncleaved Cell Lymphoma (Burkitt's and Non-Burkitt's)

This category accounts for 40% to 50% of childhood NHL and exhibits consistent clinical behavior. Up to 90% of these tumors are intra-abdominal. Other sites of involvement include testis, lymphoid tissue of Waldeyer's ring, nasal sinuses, bone, peripheral lymph nodes, skin, bone marrow, and CNS. Small noncleaved cell lymphomas are of B-cell origin; they usually express surface immunoglobulin, the large majority bearing immunoglobulin M (IgM) of either kappa or lambda light chain subtype. TdT is negative, and a variety of additional B-cell markers are usually present. Almost all childhood B-cell lymphomas express cALLa (CD10). About 25% contain Epstein-Barr virus genomes. These tumors also express a characteristic chromosomal translocation, usually t(8;14) and more rarely t(8;22) or t(2;8). Each of these translocations juxtaposes the c-myc gene to immunoglobulin locus regulatory elements, resulting in the inappropriate expression of c-myc, a gene involved in cellular proliferation.

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[37] Neth O, Seidemann K, Jansen P, et al.: Precursor B-cell lymphoblastic lymphoma in childhood and adolescence: clinical features, treatment, and results in trials NHL-BFM 86 and 90. Medical and Pediatric Oncology 35(1): 20-27, 2000.

Large Cell Lymphoma (LCL)

This is a heterogeneous group of tumors accounting for approximately 20% to 25% of childhood NHL. While the pathological types of LCL as described in the REAL and WHO classification are anaplastic large cell and diffuse large cell, treatment decisions in pediatric LCLs are based on immunophenotype. There are separate treatments for patients with diffuse large B-cell lymphoma and those with T-lineage (or null cell lineage) anaplastic large cell lymphoma. The treatment for the rare, nonanaplastic T-cell lymphomas is not defined.

B lineage LCL has been divided into tumors of germinal center origin (large cleaved and large noncleaved) and immunoblastic lymphoma, but this distinction has proved difficult to make and is no longer of clinical significance. Biologically, B-cell LCL occasionally is similar to small noncleaved cell lymphomas both with respect to immunophenotyping and chromosomal abnormalities (e.g., presence of an (8;14) translocation). It may present clinically like the small noncleaved lymphomas, although it is most often localized, frequently involves the mediastinum[38], less often involves the bone marrow or CNS, and is associated with superior survival.[39]

T-lineage LCL can be divided into the CD30 (Ki-1)-positive anaplastic LCL[40] and other peripheral T-cell lymphomas, although it is not clear that these represent distinct entities. While the predominant immunophenotype of the anaplastic LCLs is T-cell, null-cell types have also been described. More than 90% of anaplastic LCLs are CD30-positive and have the nonrandom translocation (2;5)(p23;q35) leading to the expression of the fusion protein NPM ALK. Clinically, anaplastic LCL has a broad range of presentations, including involvement of lymph nodes and a variety of extranodal sites, particularly skin, bone, and, less often, gastrointestinal tract, lung, pleura, and muscle. Involvement of the CNS and bone marrow is uncommon. These

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[38] Lones MA, Perkins SL, Sposto R, et al.: Large-cell lymphoma arising in the mediastinum in children and adolescents is associated with an excellent outcome: A Children's Cancer Group report. Journal of Clinical Oncology 18(22): 3845-3853, 2000.

[39] Hutchison RE, Berard CW, Shuster JJ, et al.: B-cell lineage confers a favorable outcome among children and adolescents with large-cell lymphoma: a Pediatric Oncology Group study. Journal of Clinical Oncology 13(8): 2023-2032, 1995.

[40] Hutchison RE, Berard CW, Shuster JJ, et al.: B-cell lineage confers a favorable outcome among children and adolescents with large-cell lymphoma: a Pediatric Oncology Group study. Journal of Clinical Oncology 13(8): 2023-2032, 1995.

Sandlund JT, Pui CH, Santana VM, et al.: Clinical features and treatment outcome for children with CD30+ large-cell non-Hodgkin's lymphoma. Journal of Clinical Oncology 12(5): 895-898, 1994.

tumors are often associated with systemic symptoms (e.g., fever, weight loss) and a prolonged waxing and waning course.

Stage Information

Several different staging schemes exist; none is perfect. The most widely used staging scheme is that of the St. Jude Children's Research Hospital, which separates patients with limited disease (i.e., a single mass with or without regional node involvement) from those with extensive thoracic or intra-abdominal tumor (stage III). Patients with completely excised primary gastrointestinal disease as their only site of involvement are usually classified as stage II and have an excellent prognosis. Patients with bone marrow and central nervous system (CNS) disease have the worst prognosis and are classified as stage IV. Treatment decisions are based on both histology and clinical stage.[41] The staging scheme used at the St. Jude Children's Research Hospital is presented below (slightly modified). The Children's Cancer Group designations of limited and extensive disease correspond closely to stages I/II and stages III/IV, respectively.

Stage I Childhood NHL

In stage I non-Hodgkin's lymphoma, a single tumor or nodal area outside of the abdomen and mediastinum is present.

Stage II Childhood NHL

In stage II non-Hodgkin's lymphoma, disease extent is a single tumor with regional node involvement, two or more tumors or nodal areas on one side of the diaphragm, or a primary gastrointestinal tract tumor (resected) with or without regional node involvement.

Stage III Childhood NHL

Stage III non-Hodgkin's lymphoma includes tumors or lymph node areas on both sides of the diaphragm, any primary intrathoracic or extensive intra-abdominal disease, or any paraspinal or epidural tumors.

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[41] Murphy SB, Fairclough DL, Hutchison RE, et al.: Non-Hodgkin's lymphomas of childhood: an analysis of the histology, staging, and response to treatment of 338 cases at a single institution. Journal of Clinical Oncology 7(2): 186-193, 1989.

Stage IV Childhood NHL

Stage IV non-Hodgkin's lymphoma includes patients with bone marrow or CNS disease regardless of other sites of involvement. Bone marrow involvement has been defined as 5% malignant cells in an otherwise normal bone marrow with normal peripheral blood counts and smears. Patients with lymphoblastic lymphoma with greater than 25% malignant cells in the bone marrow are usually considered to have leukemia and may be appropriately treated on leukemia clinical trials. Central nervous system (CNS) disease in lymphoblastic lymphoma is defined similarly to criteria used for acute lymphocytic leukemia, i.e., WBC greater than or equal to 5/microliter with malignant cells. For small noncleaved or large cell lymphoma however, the definition of CNS disease is any malignant cell regardless of cell count.

Treatment Option Overview

Many of the improvements in survival in childhood cancer have been made using combinations of known and/or new agents that have attempted to improve on the best available, accepted therapy. Clinical trials in pediatrics are designed to compare potentially better therapy with therapy that is currently accepted as standard. This comparison may be done in a randomized study of 2 treatment arms or by evaluating a single new treatment and comparing the results with those previously obtained with standard therapy.

All children with non-Hodgkin's lymphoma (NHL) should be considered for entry into a clinical trial. Treatment planning by a multidisciplinary team of cancer specialists with experience treating tumors of childhood is strongly recommended to determine, coordinate, and implement treatment to achieve optimal survival. Children with NHL should be referred for treatment by a multidisciplinary team of pediatric oncologists at an institution with experience in treating pediatric cancers. Information about ongoing clinical trials is available from the NCI (**http://cancer.gov/clinical_trials/**).

NHL in children is generally considered to be widely disseminated from the outset, even when apparently localized; as a result, combination chemotherapy is recommended for all patients.[42] There are 2 potentially life-threatening clinical situations that are often seen in children with NHL:

[42] Sandlund JT, Downing JR, Crist WM: Non-Hodgkin's lymphoma in childhood. New England Journal of Medicine 334(19): 1238-1248, 1996.

superior vena cava syndrome (or mediastinal tumor with airway obstruction), most often seen in lymphoblastic lymphoma; and tumor lysis syndrome, most often seen in small noncleaved cell NHL. These emergent situations should be anticipated in children with NHL and addressed immediately.

Patients with large mediastinal masses are at risk of cardiac or respiratory arrest during general anesthesia or heavy sedation.[43] Due to the risks of general anesthesia or heavy sedation, a careful physiologic and radiographic evaluation of the patient should be carried out and the least invasive procedure should be used to establish the diagnosis of lymphoma.[44] Bone marrow aspirate and biopsy should always be performed early in the work up of these patients. If a pleural effusion is present, a cytologic diagnosis is frequently possible using thoracentesis. In those children who present with peripheral adenopathy, a lymph node biopsy under local anesthesia and in an upright position may be possible.[45] In situations in which the above diagnostic procedures are not fruitful, consideration of a CT guided core needle biopsy should be contemplated. This procedure can frequently be carried out using light sedation and local anesthesia before proceeding to more invasive procedures. Mediastinoscopy, anterior mediastinotomy or thoracoscopy are the procedures of choice when other diagnostic modalities fail to establish the diagnosis. A formal thoracotomy is rarely if ever indicated for the diagnosis or treatment of childhood lymphoma. Occasionally it will not be possible to perform a diagnostic operative procedure because of the risk of general anesthesia or heavy sedation. In these situations, preoperative treatment with steroids or localized radiation therapy should be considered. Since preoperative treatment may affect the ability to obtain an accurate tissue diagnosis, a diagnostic biopsy should be obtained as soon as the risk of general anesthesia or heavy sedation are thought to be alleviated.

Tumor lysis syndrome results from rapid breakdown of malignant cells resulting in a number of metabolic abnormalities, most notably hyperuricemia, hyperkalemia, and hyperphosphatemia. Hyperhydration

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[43] Azizkhan RG, Dudgeon DL, Buck JR, et al.: Life-threatening airway obstruction as a complication to the management of mediastinal masses in children. Journal of Pediatric Surgery 20(6): 816-822, 1985.

[44] King DR, Patrick LE, Ginn-Pease ME, et al.: Pulmonary function is compromised in children with mediastinal lymphoma. Journal of Pediatric Surgery 32(2): 294-300, 1997.
Shamberger RC, Holzman RS, Griscom NT, et al.: Prospective evaluation by computed tomography and pulmonary function tests of children with mediastinal masses. Surgery 118(3): 468-471, 1995.

[45] Prakash UBS, Abel MD, Hubmayr RD: Mediastinal mass and tracheal obstruction during general anesthesia. Mayo Clinic Proceedings 63: 1004-1011, 1988.

and allopurinol or rasburicase (urate oxidase) are essential components of therapy in all but patients with the most limited disease.[46] A strategy used in Europe is to treat patients with an initial "pre-phase" consisting of low-dose cyclophosphamide and vincristine, but this does not obviate the need for allopurinol and hydration. Gastrointestinal bleeding, obstruction, and (rarely) perforation may occur. Hyperuricemia and tumor lysis syndrome, particularly when associated with ureteral obstruction, frequently result in life-threatening complications. Patients with NHL should be managed only in institutions having pediatric tertiary care facilities.

Certain pediatric NHL clinical trials are based on immunophenotype while others are based on histopathology. Children with limited disease have an excellent prognosis when treated with chemotherapy. Radiation is not used as front-line therapy for children. Radiation therapy can serve an ancillary role, i.e., as emergency treatment for involvement of the nervous system, for testicular involvement, or when there is a severe mass effect, as in superior vena caval compression or airway obstruction. Even in these circumstances, the use of radiation therapy is being questioned.[47]

The designations in PDQ that treatments are "standard" or "under clinical evaluation" are not to be used as a basis for reimbursement determinations.

Stage I and II Childhood Lymphoblastic Lymphoma

While results of 65% to 70% event-free survival are observed with differing approaches to treatment of children with limited stage lymphoblastic lymphoma, several regimens have produced excellent response rates. Overall survival is greater than 80% with aggressive leukemia-like therapy.[48]

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[46] Pui CH, Mahmoud HH, Wiley JM, et al.: Recombinant urate oxidase for the prophylaxis or treatment of hyperuricemia in patients with leukemia or lymphoma. Journal of Clinical Oncology 19(3): 697-704, 2001.

[47] Dalle JH, Mechinaud F, Michon J, et al.: Testicular disease in childhood B-cell non-Hodgkin's lymphoma: the French Society of Pediatric Oncology experience. Journal of Clinical Oncology 19(9): 2397-2403, 2001.

[48] Link MP, Shuster JJ, Donaldson SS, et al.: Treatment of children and young adults with early-stage non-Hodgkin's lymphoma. New England Journal of Medicine 337(18): 1259-1266, 1997.

Magrath IT, Janus C, Edwards BK, et al.: An effective therapy for both undifferentiated (including Burkitt's) lymphomas and lymphoblastic lymphomas in children and young adults. Blood 63(5): 1102-1111, 1984.

Anderson JR, Jenkin RD, Wilson JF, et al.: Long-term follow-up of patients treated with COMP or LSA2L2 therapy for childhood non-Hodgkin's lymphoma: a report of CCG-551 from the Childrens Cancer Group. Journal of Clinical Oncology 11(6): 1024-1032, 1993.

A clinical trial to address duration of therapy compared 9 weeks of CHOP chemotherapy with 9 weeks of CHOP chemotherapy plus 24 weeks of maintenance therapy. The 24-week maintenance therapy improved relapse-free survival in patients with localized lymphoblastic NHL.[49]

Central nervous system prophylaxis should be given to all patients with primary tumors of the head and neck. Intrathecal methotrexate alone has been shown to be effective without cranial irradiation.

Standard treatment options:

- Vincristine, doxorubicin, cyclophosphamide, prednisone, mercaptopurine, methotrexate.[50]
- CHOP plus MTX (NCI-POB-7704): cyclophosphamide, doxorubicin, vincristine, prednisone, alternating with infusional methotrexate.[51]
- COMP: cyclophosphamide, vincristine, methotrexate, prednisone.[52]

Stage III and IV Childhood Lymphoblastic Lymphoma

Patients with stage III or IV lymphoblastic non-Hodgkin's lymphoma have long-term survival rates from 75% to 90% as reported by the German Cooperative Group (BFM).[53] Because of the complexities of optimal

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Hvizdala EV, Berard C, Callihan T, et al.: Lymphoblastic lymphoma in children--a randomized trial comparing LSA2-L2 with the A-COP+ therapeutic regimen: a Pediatric Oncology Group study. Journal of Clinical Oncology 6(1): 26-33, 1988.

[49] Link MP, Shuster JJ, Donaldson SS, et al.: Treatment of children and young adults with early-stage non-Hodgkin's lymphoma. New England Journal of Medicine 337(18): 1259-1266, 1997.

[50] Link MP, Shuster JJ, Donaldson SS, et al.: Treatment of children and young adults with early-stage non-Hodgkin's lymphoma. New England Journal of Medicine 337(18): 1259-1266, 1997.

[51] Magrath IT, Janus C, Edwards BK, et al.: An effective therapy for both undifferentiated (including Burkitt's) lymphomas and lymphoblastic lymphomas in children and young adults. Blood 63(5): 1102-1111, 1984.

[52] Anderson JR, Jenkin RD, Wilson JF, et al.: Long-term follow-up of patients treated with COMP or LSA2L2 therapy for childhood non-Hodgkin's lymphoma: a report of CCG-551 from the Childrens Cancer Group. Journal of Clinical Oncology 11(6): 1024-1032, 1993.

[53] Grenzebach J, Schrappe M, Ludwig WD, et al.: Favorable outcome for children and adolescents with T-cell lymphoblastic lymphoma with an intensive ALL-type therapy without local radiotherapy. Annals of Hematology 80(Suppl 3): B73-B76, 2001.

Patte C, Kalifa C, Flamant F, et al.: Results of the LMT81 protocol, a modified LSA2L2 protocol with high dose methotrexate, on 84 children with non-B-cell (lymphoblastic) lymphoma. Medical and Pediatric Oncology 20(2): 105-113, 1992.

therapeutic regimens, and the possibility of toxic side effects, patients should be offered the opportunity to enter into a clinical trial. Information about ongoing clinical trials is available from the NCI (**http://cancer.gov/clinical_trials**).

Central nervous system (CNS) prophylaxis should be given to all patients with stage III and IV lymphoblastic lymphoma, even if CNS disease is not detectable at presentation. Intrathecal methotrexate alone has been shown to be effective without cranial irradiation. Involvement of the CNS is unusual at presentation, but in this circumstance, radiation should be considered. CNS involvement is defined as 5 or more white cells/cubic millimeter with cytologically identifiable blasts present on a cytospin preparation in a nontraumatic tap.

Involvement of the bone marrow may lead to confusion as to whether the patient has lymphoma or leukemia. Traditionally, patients with greater than 25% marrow blasts are classified as having leukemia and those with less than 25% marrow blasts are classified as having lymphoma. It is not yet clear whether these arbitrary definitions are biologically distinct or relevant for treatment design. All effective therapies for advanced stage lymphoblastic non-Hodgkin's lymphoma have been derived from regimens designed for the treatment of acute lymphoblastic leukemia.

Mediastinal radiation is not necessary for patients with mediastinal masses except in the emergency treatment of superior vena caval obstruction or airway obstruction, where low-dose radiation is sometimes employed. Refer to the Treatment Option Overview section for more information on such complications.

Standard treatment options:

- BFM-NHL 90: prednisone, dexamethasone, vincristine, daunorubicin, doxorubicin, L-asparaginase, cyclophosphamide, cytarabine, methotrexate, 6-mercaptopurine, 6-thioguanine, CNS irradiation.[54]
- LMTB1: LSA2L2 regimen supplemented by 10 courses of high-dose methotrexate.[55]

Tubergen DG, Krailo MD, Meadows AT, et al.: Comparison of treatment regimens for pediatric lymphoblastic non-Hodgkin's lymphoma: a Childrens Cancer Group study. Journal of Clinical Oncology 13(6): 1368-1376, 1995.

[54] Grenzebach J, Schrappe M, Ludwig WD, et al.: Favorable outcome for children and adolescents with T-cell lymphoblastic lymphoma with an intensive ALL-type therapy without local radiotherapy. Annals of Hematology 80(Suppl 3): B73-B76, 2001.

Recurrent Childhood Lymphoblastic Lymphoma

The prognosis for the child with recurrent or progressive lymphoblastic non-Hodgkin's lymphoma is poor. The selection of further treatment depends on many factors including the site of recurrence and prior treatment, as well as individual patient considerations. There is no established approach to therapy, and intensive regimens including bone marrow transplantation should be considered. Radiation therapy may have a role in treating patients who have not had a complete response to therapy.

Treatment options:

- Allogeneic bone marrow transplantation.[56]
- Treatment with a different and previously unused regimen for lymphoblastic disease (see treatment options for stage III/IV lymphoblastic disease).
- DECAL: (Dexamethasone, Etoposide, Cisplatin, Cytarabine, L-asparaginase)[57]
- Clinical trials.[58] Information about ongoing clinical trials is available from the NCI (**http://cancer.gov/clinical_trials/**).

Patients whose disease progresses during treatment on a salvage regimen carry an exceptionally poor prognosis and should be considered for entry on clinical trials.

Stage I and II Childhood Small Noncleaved Cell Lymphoma

Because of the excellent prognosis (greater than 90% survival) for patients with limited disease (i.e., localized to a single extra-abdominal, extrathoracic

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[55] Patte C, Kalifa C, Flamant F, et al.: Results of the LMT81 protocol, a modified LSA2L2 protocol with high dose methotrexate, on 84 children with non-B-cell (lymphoblastic) lymphoma. Medical and Pediatric Oncology 20(2): 105-113, 1992.

[56] Appelbaum FR, Sullivan KM, Buckner CD, et al.: Treatment of malignant lymphoma in 100 patients with chemotherapy, total body irradiation, and marrow transplantation. Journal of Clinical Oncology 5(9): 1340-1347, 1987.

[57] Kobrinsky NL, Sposto R, Shah NR, et al.: Outcomes of treatment of children and adolescents with recurrent non-Hodgkin's lymphoma and Hodgkin's disease with dexamethasone, etoposide, cisplatin, cytarabine, and L-asparaginase, maintenance chemotherapy, and transplantation: Study CCG-5912. Journal of Clinical Oncology 19(9): 2390-2396, 2001.

[58] Gentet JC, Patte C, Quintana E, et al.: Phase II study of cytarabine and etoposide in children with refractory or relapsed non-Hodgkin's lymphoma: a study of the French Society of Pediatric Oncology. Journal of Clinical Oncology 8(4): 661-665, 1990.

tumor site), less intensive therapy is under evaluation as a potentially effective way to avoid unnecessary toxicity for these patients while achieving cure rates similar to those obtained with more prolonged treatment. In a randomized study comparing a short course (6 months) with a more prolonged course (18 months) of COMP therapy, results suggest that patients with localized small noncleaved cell lymphoma have comparable outcomes with either treatment.[59] The Pediatric Oncology Group has conducted a trial of 9 weeks versus 24 weeks of additional therapy and has reported no advantage to 24 weeks of treatment in patients with small noncleaved histology.[60]

Intrathecal methotrexate is indicated in patients with head and neck disease, but the rarity of central nervous system (CNS) recurrence in patients with totally excised intra-abdominal tumor in the absence of other disease sites has led some investigators to omit CNS prophylaxis in such patients.

Treatment options:

- COMP: cyclophosphamide, vincristine, methotrexate, prednisone.[61]
- CHOP: doxorubicin, cyclophosphamide, vincristine, prednisone.[62]
- CHOP plus MTX (NCI-POB-7704): cyclophosphamide, doxorubicin, vincristine, prednisone, alternating with infusional methotrexate.[63]
- NHL-BFM 90: prednisone, dexamethasone, vincristine, doxorubicin, cyclophosphamide, ifosfamide, etoposide, cytarabine, methotrexate.[64]
- French LMB-89: high-dose cyclophosphamide, vincristine, prednisone, doxorubicin.[65]

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[59] Meadows AT, Sposto R, Jenkin RD, et al.: Similar efficacy of 6 and 18 months of therapy with four drugs (COMP) for localized non-Hodgkin's lymphoma of children: a report from the Children's Cancer Study Group. Journal of Clinical Oncology 7(1): 92-99, 1989.

[60] Link MP, Shuster JJ, Donaldson SS, et al.: Treatment of children and young adults with early-stage non-Hodgkin's lymphoma. New England Journal of Medicine 337(18): 1259-1266, 1997.

[61] Meadows AT, Sposto R, Jenkin RD, et al.: Similar efficacy of 6 and 18 months of therapy with four drugs (COMP) for localized non-Hodgkin's lymphoma of children: a report from the Children's Cancer Study Group. Journal of Clinical Oncology 7(1): 92-99, 1989.

[62] Link MP, Shuster JJ, Donaldson SS, et al.: Treatment of children and young adults with early-stage non-Hodgkin's lymphoma. New England Journal of Medicine 337(18): 1259-1266, 1997.

[63] Magrath IT, Janus C, Edwards BK, et al.: An effective therapy for both undifferentiated (including Burkitt's) lymphomas and lymphoblastic lymphomas in children and young adults. Blood 63(5): 1102-1111, 1984.

[64] Reiter A, Schrappe M, Tiemann M, et al.: Improved treatment results in childhood B-cell neoplasms with tailored intensification of therapy: a report of the Berlin-Frankfurt-Munster Group Trial NHL-BFM 90. Blood 94(10): 3294-3306, 1999.

Stage III and IV Childhood Small Noncleaved Cell Lymphoma

Patients with stage III and IV small noncleaved cell (SNCC) (Burkitt's and non-Burkitt's) non-Hodgkin's lymphoma (NHL), including those with extensive intra-abdominal disease have a 80% to 90% long-term survival.[66] Even patients with central nervous system involvement now appear to have an excellent prognosis. Testicular disease at diagnosis does not seem to confer poor prognosis.[67]

Involvement of the bone marrow may lead to confusion as to whether the patient has lymphoma or leukemia. Traditionally, patients with greater than 25% marrow blasts are classified as having B-cell leukemia and those with less than 25% marrow blasts are classified as having lymphoma. It is not clear whether these arbitrary definitions are biologically distinct or relevant for treatment design, but there is no question that patients with "acute B-cell leukemia" should be treated with protocols designed for SNCC lymphomas.[68]

Tumor lysis syndrome is often present at diagnosis or after initiation of treatment. This emergent clinical situation should be anticipated and addressed prior to starting treatment. Refer to the Treatment Option Overview section for more information. Since tumor lysis syndrome frequently results in life-threatening complications, these patients should be managed only in institutions having pediatric tertiary care facilities.

Intrathecal methotrexate should be used in all patients.

Treating children with small noncleaved cell lymphoma with combination chemotherapy has improved results markedly, particularly in patients with extensive disease. The improvement in survival appears to be associated with both the administration of higher dose drugs and the introduction of

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[65] Patte C, Auperin A, Michon J, et al.: The Societe Francaise d'Oncologie Pediatrique LMB89 protocol: highly effective multiagent chemotherapy tailored to the tumor burden and initial response in 561 unselected children with B-cell lymphomas and L3 leukemia. Blood 97(11): 3370-3379, 2001.

[66] Atra A, Imeson JD, Hobson R et al.: Improved outcome in children with advanced stage B-cell non-Hodgkin's lymphoma (B-NHL): results of the United Kingdom Children Cancer Study Group (UKCCSG) 9002 protocol. British Journal of Cancer 82(8): 1396-1402, 2000.

[67] Dalle JH, Mechinaud F, Michon J, et al.: Testicular disease in childhood B-cell non-Hodgkin's lymphoma: the French Society of Pediatric Oncology experience. Journal of Clinical Oncology 19(9): 2397-2403, 2001.

[68] Anderson JR, Jenkin RD, Wilson JF, et al.: Long-term follow-up of patients treated with COMP or LSA2L2 therapy for childhood non-Hodgkin's lymphoma: a report of CCG-551 from the Childrens Cancer Group. Journal of Clinical Oncology 11(6): 1024-1032, 1993.

additional drugs such as cytarabine, epipodophyllotoxins and, in some protocols, ifosfamide.[69] All patients should be considered for entry into a clinical trial.

Rituximab is a mouse/human chimeric antibody targeting the CD20 antigen. Among the lymphomas that occur in children, diffuse large cell NHL (DLCL) and Burkitt's lymphoma both express high levels of CD20.[70] Data from adult clinical trials demonstrated that rituximab is active against B-cell low-grade lymphomas, particularly follicular center cell lymphoma.[71], and is also active against diffuse large cell lymphoma.[72] Rituximab has been safely

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[69] Schwenn MR, Blattner SR, Lynch E, et al.: HiC-COM: a 2-month intensive chemotherapy regimen for children with stage III and IV Burkitt's lymphoma and B-cell acute lymphoblastic leukemia. Journal of Clinical Oncology 9(1): 133-138, 1991.
Patte C, Auperin A, Michon J, et al.: The Societe Francaise d'Oncologie Pediatrique LMB89 protocol: highly effective multiagent chemotherapy tailored to the tumor burden and initial response in 561 unselected children with B-cell lymphomas and L3 leukemia. Blood 97(11): 3370-3379, 2001.
Reiter A, Schrappe M, Tiemann M, et al.: Improved treatment results in childhood B-cell neoplasms with tailored intensification of therapy: a report of the Berlin-Frankfurt-Munster Group Trial NHL-BFM 90. Blood 94(10): 3294-3306, 1999.
Reiter A, Schrappe M, Ludwig W, et al.: Favorable outcome of B-cell acute lymphoblastic leukemia in childhood: a report of three consecutive studies of the BFM Group. Blood 80(10): 2471-2478, 1992.
Brecher M, Murphy SB, Bowman P, et al.: Results of Pediatric Oncology Group (POG) 8616: a randomized trial of two forms of therapy for stage III diffuse, small non-cleaved cell lymphoma in children. Proceedings of the American Society of Clinical Oncology 11: A-1167, 340, 1992.
Adde M, Shad A, Venzon D, et al.: Additional chemotherapy agents improve treatment outcome for children and adults with advanced B-cell lymphomas. Seminars in Oncology 25(2 suppl 4): 33-39, 1998.
Cecalupo A, Finlay J, Hutchison R, et al.: Pattern of relapse and relation to dose intensity in children with advanced small non-cleaved cell lymphoma (SNCCL) and acute B-lymphoid leukemia (B-ALL): a report of the Childrens Cancer Study Group trial CCG-552. Proceedings of the American Society of Clinical Oncology 10: A-1012, 289, 1991.
Bowman WP, Shuster JJ, Cook B, et al.: Improved survival for children with B-cell acute lymphoblastic leukemia and stage IV small noncleaved-cell lymphoma: a Pediatric Oncology Group study. Journal of Clinical Oncology 14(4): 1252-1261, 1996.
[70] Gregory CD, Tursz T, Edwards CF, et al.: Identification of a subset of normal B cells with a Burkitt's lymphoma (BL)-like phenotype. Journal of Immunology 139(1): 313-318, 1987.
Jennings CD, Foon KA: Recent advances in flow cytometry: application to the diagnosis of hematologic malignancy. Blood 90(8): 2863-2892, 1997.
[71] McLaughlin P, Grillo-Lopez AJ, Link BK, et al.: Rituximab chimeric anti-CD20 monoclonal antibody therapy for relapsed indolent lymphoma: half of patients respond to a four-dose treatment program. Journal of Clinical Oncology 16(8): 2825-2833, 1998.
[72] Coiffier B, Haioun C, Ketterer N, et al.: Rituximab (anti-CD20 monoclonal antibody) for the treatment of patients with relapsing or refractory aggressive lymphoma: a multicenter phase II study. Blood 92(6): 1927-1932, 1998.

combined with standard CHOP chemotherapy,[73] with no substantial increase in toxicity above that associated with CHOP chemotherapy alone. A randomized trial in elderly adults with diffuse large cell lymphoma comparing CHOP to CHOP plus rituximab demonstrated significantly higher event-free survival (EFS) and survival rates for patients receiving rituximab plus chemotherapy.[74] Rituximab has also been safely combined in an adult study with an intensive chemotherapy regimen used to treat Burkitt's lymphoma.[75] A Children's Oncology Group pilot study (ANHL01P1) is evaluating rituximab in combination with an intensive chemotherapy regimen based upon the French LMB-89 protocol.

Standard treatment options:

- French LMB-89: high-dose cyclophosphamide, high-dose methotrexate/leucovorin, cytarabine, vincristine, prednisone, doxorubicin.[76]
- Modified "Total B": cyclophosphamide, doxorubicin, vincristine, methotrexate, cytarabine.[77]
- NHL-BFM 90: prednisone, dexamethasone, vincristine, doxorubicin, cyclophosphamide, etoposide, ifosfamide, cytarabine, methotrexate.[78]
- NCI-89-C-0041F: cyclophosphamide, vincristine, doxorubicin, methotrexate (Codox-M) alternating with cytarabine, etoposide, and ifosfamide (IVAC).[79]

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[73] Czuczman M, Grillo-Lopez AJ, White CA, et al.: Rituximab/CHOP chemoimmunotherapy in patients (PTS) with low grade lymphoma (LG/F NHL): progression free survival (PFS) after three years (median) follow-up. Blood 94(10 pt 2): A-432, 99a, 1999.
Vose JM, Link BK, Grossbard ML, et al.: Phase II study of rituximab in combination with CHOP chemotherapy in patients with previously untreated intermediate- or high-grade non-Hodgkin's lymphoma (NHL). Blood 94(10 pt 2): A-388, 89a, 1999.

[74] Coiffier B, Lepage E, Briere J, et al.: CHOP chemotherapy plus rituximab compared with CHOP alone in elderly patients with diffuse large-B-cell lymphoma. New England Journal of Medicine 346(4): 235-242, 2002.

[75] Thomas DA, Cortes J, Giles FJ, et al.: Rituximab and hyper-CVAD for adult Burkitt's (BL) or Burkitt's-like (BLL) leukemia or lymphoma. Blood 98(11 pt 1): A-3342, 804a, 2001.

[76] Patte C, Auperin A, Michon J, et al.: The Societe Francaise d'Oncologie Pediatrique LMB89 protocol: highly effective multiagent chemotherapy tailored to the tumor burden and initial response in 561 unselected children with B-cell lymphomas and L3 leukemia. Blood 97(11): 3370-3379, 2001.

[77] Bowman WP, Shuster JJ, Cook B, et al.: Improved survival for children with B-cell acute lymphoblastic leukemia and stage IV small noncleaved-cell lymphoma: a Pediatric Oncology Group study. Journal of Clinical Oncology 14(4): 1252-1261, 1996.

[78] Reiter A, Schrappe M, Tiemann M, et al.: Improved treatment results in childhood B-cell neoplasms with tailored intensification of therapy: a report of the Berlin-Frankfurt-Munster Group Trial NHL-BFM 90. Blood 94(10): 3294-3306, 1999.

Treatment options under clinical evaluation:

- ANHL01P1: addition of rituximab to French LMB-89-based therapy.

Information about ongoing clinical trials is available from the NCI (**http://cancer.gov/clinical_trials/**).

Recurrent Childhood Small Noncleaved Cell Lymphoma

The prognosis for the child with recurrent or progressive small noncleaved cell (SNCC) lymphoma is poor.[80] The selection of further treatment depends on many factors including the site of recurrence and prior treatment, as well as individual patient considerations.

For patients who have relapsed after the completion of front-line therapy, an aggressive treatment strategy should be considered. For patients who have progressive disease or who recurred while receiving front-line therapy, clinical trials are appropriate and may be the best treatment option.

Standard treatment options:

- High-dose cytarabine with other agents, particularly etoposide and ifosfamide.[81]
- Allogeneic or autologous bone marrow transplantation.[82]

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[79] Adde M, Shad A, Venzon D, et al.: Additional chemotherapy agents improve treatment outcome for children and adults with advanced B-cell lymphomas. Seminars in Oncology 25(2 suppl 4): 33-39, 1998.

[80] Philip T, Hartmann O, Pinkerton R, et al.: Curability of relapsed childhood B-cell non-Hodgkin's lymphoma after intensive first line therapy: a report from the French Society of Pediatric Oncology. Blood 81(1): 2003-2006, 1993.

Atra A, Gerrard M, Hobson R, et al.: Outcome of relapsed or refractory childhood B-cell acute lymphoblastic leukaemia and B-cell non-Hodgkin's lymphoma treated with the UKCCSG 9003/9002 protocols. British Journal of Haematology 112(4): 965-968, 2001.

[81] Gentet JC, Patte C, Quintana E, et al.: Phase II study of cytarabine and etoposide in children with refractory or relapsed non-Hodgkin's lymphoma: a study of the French Society of Pediatric Oncology. Journal of Clinical Oncology 8(4): 661-665, 1990.

Magrath I, Adde M, Sandlund J, et al.: Ifosfamide in the treatment of high-grade recurrent non-Hodgkin's lymphomas. Hematological Oncology 9: 267-274, 1991.

Kobrinsky NL, Sposto R, Shah NR, et al.: Outcomes of treatment of children and adolescents with recurrent non-Hodgkin's lymphoma and Hodgkin's disease with dexamethasone, etoposide, cisplatin, cytarabine, and L-asparaginase, maintenance chemotherapy, and transplantation: Study CCG-5912. Journal of Clinical Oncology 19(9): 2390-2396, 2001.

[82] Philip T, Hartmann O, Pinkerton R, et al.: Curability of relapsed childhood B-cell non-Hodgkin's lymphoma after intensive first line therapy: a report from the French Society of Pediatric Oncology. Blood 81(1): 2003-2006, 1993.

- Treatment using regimens listed under stage III or IV SNCC lymphoma.

Treatment options under clinical evaluation:

- ADVL0013: A phase I study of rituximab followed by yttrium90 ibritumomab tiuxetan.

Information about ongoing clinical trials is available from the NCI (**http://cancer.gov/clinical_trials/**).

Stage I and II Childhood Large Cell Lymphoma

Stage I and II Diffuse Large B-Cell Lymphoma

The outlook for children with localized large cell lymphoma is excellent with an expected long-term survival of approximately 90%.[83] The treatment approach in the past has been the same as that for other types of non-Hodgkin's lymphoma.

Treatment consists of a short course of combination chemotherapy combined with central nervous system prophylaxis for only those patients with head and neck primaries. Radiation therapy has not been shown to improve survival.

Treatment options:

- COMP: cyclophosphamide, vincristine, methotrexate, prednisone.[84]
- CHOP: cyclophosphamide, doxorubicin, vincristine, prednisone.[85]
- French LMB 89: High dose cyclophosphamide, vincristine, prednisone, doxorubicin.[86]

Ladenstein R, Pearce R, Hartmann O, et al.: High-dose chemotherapy with autologous bone marrow rescue in children with poor-risk Burkitt's lymphoma: a report from the European Lymphoma Bone Marrow Transplantation Registry. Blood 90(8): 2921-2930, 1997.

[83] Link MP, Donaldson SS, Berard CW, et al.: Results of treatment of childhood localized non-Hodgkin's lymphoma with combination chemotherapy with or without radiotherapy. New England Journal of Medicine 322(17): 1169-1174, 1990.

[84] Meadows AT, Sposto R, Jenkin RD, et al.: Similar efficacy of 6 and 18 months of therapy with four drugs (COMP) for localized non-Hodgkin's lymphoma of children: a report from the Children's Cancer Study Group. Journal of Clinical Oncology 7(1): 92-99, 1989.

[85] Link MP, Donaldson SS, Berard CW, et al.: Results of treatment of childhood localized non-Hodgkin's lymphoma with combination chemotherapy with or without radiotherapy. New England Journal of Medicine 322(17): 1169-1174, 1990.

[86] Patte C, Auperin A, Michon J, et al.: The Societe Francaise d'Oncologie Pediatrique LMB89 protocol: highly effective multiagent chemotherapy tailored to the tumor burden and initial

- NHL-BFM 90 regimen: Alternating courses of chemotherapy containing dexamethasone, ifosfamide, methotrexate, cytarabine, etoposide +/- vincristine and dexamethasone, cyclophosphamide, methotrexate, doxorubicin +/- vincristine. The number of courses is determined by the extent of resection and by the histology (diffuse large B-cell versus anaplastic large cell).[87]

Stage I and II Anaplastic Large Cell Lymphoma

The outlook for children with localized anaplastic large cell lymphoma is excellent with an expected long-term survival of approximately 90%.[88] The treatment approach in the past has been the same as that for other types of non-Hodgkin's lymphoma.

Treatment consists of a short course of combination chemotherapy combined with central nervous system prophylaxis for only those patients with head and neck primaries. Radiation therapy has not been shown to improve survival.

Treatment options:

- COMP: cyclophosphamide, vincristine, methotrexate, prednisone.[89]
- CHOP: cyclophosphamide, doxorubicin, vincristine, prednisone.[90]
- French LMB 89: High dose cyclophosphamide, vincristine, prednisone, doxorubicin.[91]

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response in 561 unselected children with B-cell lymphomas and L3 leukemia. Blood 97(11): 3370-3379, 2001.

[87] Reiter A, Schrappe M, Tiemann M, et al.: Improved treatment results in childhood B-cell neoplasms with tailored intensification of therapy: a report of the Berlin-Frankfurt-Munster Group Trial NHL-BFM 90. Blood 94(10): 3294-3306, 1999.
Seidemann K, Tiemann M, Schrappe M, et al.: Short-pulse B-non-Hodgkin lymphoma-type chemotherapy is efficacious treatment for pediatric anaplastic large cell lymphoma: a report of the Berlin-Frankfurt-Munster Group Trial NHL-BFM 90. Blood 97(12): 3699-3706, 2001.

[88] Link MP, Donaldson SS, Berard CW, et al.: Results of treatment of childhood localized non-Hodgkin's lymphoma with combination chemotherapy with or without radiotherapy. New England Journal of Medicine 322(17): 1169-1174, 1990.

[89] Meadows AT, Sposto R, Jenkin RD, et al.: Similar efficacy of 6 and 18 months of therapy with four drugs (COMP) for localized non-Hodgkin's lymphoma of children: a report from the Children's Cancer Study Group. Journal of Clinical Oncology 7(1): 92-99, 1989.

[90] Link MP, Donaldson SS, Berard CW, et al.: Results of treatment of childhood localized non-Hodgkin's lymphoma with combination chemotherapy with or without radiotherapy. New England Journal of Medicine 322(17): 1169-1174, 1990.

[91] Patte C, Auperin A, Michon J, et al.: The Societe Francaise d'Oncologie Pediatrique LMB89 protocol: highly effective multiagent chemotherapy tailored to the tumor burden and initial

- NHL-BFM 90 regimen: Alternating courses of chemotherapy containing dexamethasone, ifosfamide, methotrexate, cytarabine, etoposide +/- vincristine and dexamethasone, cyclophosphamide, methotrexate, doxorubicin +/- vincristine. The number of courses is determined by the extent of resection and by the histology (diffuse large B-cell versus anaplastic large cell).[92]

Stage III and IV Childhood Large Cell Lymphoma

Stage III and IV Diffuse Large B-Cell Lymphoma

Patients with stage III and IV large cell lymphoma (LCL) have a 60% to 80% chance of long-term survival. B-cell lineage and LCL arising in the mediastinum confer a more favorable outcome.[93]

Treatment in the past has generally been the same as that of other types of non-Hodgkin's lymphoma (NHL) of the same stage. Newer approaches are emphasizing therapeutic strategies specifically for LCL.[94]

Rituximab is a mouse/human chimeric antibody targeting the CD20 antigen. Among the lymphomas that occur in children, diffuse large cell NHL (DLCL) and Burkitt's lymphoma both express high levels of CD20.[95] Data from adult clinical trials demonstrated that rituximab is active against B-cell

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response in 561 unselected children with B-cell lymphomas and L3 leukemia. Blood 97(11): 3370-3379, 2001.

[92] Reiter A, Schrappe M, Tiemann M, et al.: Improved treatment results in childhood B-cell neoplasms with tailored intensification of therapy: a report of the Berlin-Frankfurt-Munster Group Trial NHL-BFM 90. Blood 94(10): 3294-3306, 1999.
Seidemann K, Tiemann M, Schrappe M, et al.: Short-pulse B-non-Hodgkin lymphoma-type chemotherapy is efficacious treatment for pediatric anaplastic large cell lymphoma: a report of the Berlin-Frankfurt-Munster Group Trial NHL-BFM 90. Blood 97(12): 3699-3706, 2001.

[93] Hutchison RE, Berard CW, Shuster JJ, et al.: B-cell lineage confers a favorable outcome among children and adolescents with large-cell lymphoma: a Pediatric Oncology Group study. Journal of Clinical Oncology 13(8): 2023-2032, 1995.
Lones MA, Perkins SL, Sposto R, et al.: Large-cell lymphoma arising in the mediastinum in children and adolescents is associated with an excellent outcome: A Children's Cancer Group report. Journal of Clinical Oncology 18(22): 3845-3853, 2000.

[94] Laver JH, Mahmoud H, Pick TE, et al.: Results of a randomized phase III trial in children and adolescents with advanced stage diffuse large cell non Hodgkin's lymphoma: a Pediatric Oncology Group study. Leukemia and Lymphoma 42(3): 399-405, 2001.

[95] Gregory CD, Tursz T, Edwards CF, et al.: Identification of a subset of normal B cells with a Burkitt's lymphoma (BL)-like phenotype. Journal of Immunology 139(1): 313-318, 1987.
Jennings CD, Foon KA: Recent advances in flow cytometry: application to the diagnosis of hematologic malignancy. Blood 90(8): 2863-2892, 1997.

low-grade lymphomas, particularly follicular center cell lymphoma.[96], and is also active against diffuse large cell lymphoma.[97] Rituximab has been safely combined with standard CHOP chemotherapy[98], with no substantial increase in toxicity above that associated with CHOP chemotherapy alone. A randomized trial in elderly adults with diffuse large cell lymphoma comparing CHOP to CHOP plus rituximab demonstrated significantly higher event-free survival (EFS) and survival rates for patients receiving rituximab plus chemotherapy.[99] Rituximab has also been safely combined in an adult study with an intensive chemotherapy regimen used to treat Burkitt's lymphoma.[100] A Children's Oncology Group pilot study (ANHL01P1) is evaluating rituximab in combination with an intensive chemotherapy regimen based upon the French LMB-89 protocol.

Standard treatment options:

- APO: doxorubicin, prednisone, vincristine, methotrexate.[101]
- CHOP: vincristine, doxorubicin, cyclophosphamide, prednisone.[102]
- NHL-BFM 90: vincristine, doxorubicin, prednisone, cyclophosphamide, dexamethasone, etoposide, ifosfamide, cytarabine, methotrexate, vindesine.[103]

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[96] McLaughlin P, Grillo-Lopez AJ, Link BK, et al.: Rituximab chimeric anti-CD20 monoclonal antibody therapy for relapsed indolent lymphoma: half of patients respond to a four-dose treatment program. Journal of Clinical Oncology 16(8): 2825-2833, 1998.

[97] Coiffier B, Haioun C, Ketterer N, et al.: Rituximab (anti-CD20 monoclonal antibody) for the treatment of patients with relapsing or refractory aggressive lymphoma: a multicenter phase II study. Blood 92(6): 1927-1932, 1998.

[98] Czuczman M, Grillo-Lopez AJ, White CA, et al.: Rituximab/CHOP chemoimmunotherapy in patients (PTS) with low grade lymphoma (LG/F NHL): progression free survival (PFS) after three years (median) follow-up. Blood 94(10 pt 2): A-432, 99a, 1999.

Vose JM, Link BK, Grossbard ML, et al.: Phase II study of rituximab in combination with CHOP chemotherapy in patients with previously untreated intermediate- or high-grade non-Hodgkin's lymphoma (NHL). Blood 94(10 pt 2): A-388, 89a, 1999.

[99] Coiffier B, Lepage E, Briere J, et al.: CHOP chemotherapy plus rituximab compared with CHOP alone in elderly patients with diffuse large-B-cell lymphoma. New England Journal of Medicine 346(4): 235-242, 2002.

[100] Thomas DA, Cortes J, Giles FJ, et al.: Rituximab and hyper-CVAD for adult Burkitt's (BL) or Burkitt's-like (BLL) leukemia or lymphoma. Blood 98(11 pt 1): A-3342, 804a, 2001.

[101] Laver JH, Mahmoud H, Pick TE, et al.: Results of a randomized phase III trial in children and adolescents with advanced stage diffuse large cell non Hodgkin's lymphoma: a Pediatric Oncology Group study. Leukemia and Lymphoma 42(3): 399-405, 2001.

[102] Hvizdala EV, Berard C, Callihan T, et al.: Nonlymphoblastic lymphoma in children - histology and stage-related response to therapy: a Pediatric Oncology Group study. Journal of Clinical Oncology 9(7): 1189-1195, 1991.

[103] Seidemann K, Tiemann M, Schrappe M, et al.: Short-pulse B-non-Hodgkin lymphoma-type chemotherapy is efficacious treatment for pediatric anaplastic large cell lymphoma: a

- French LMB 89: High-dose cyclophosphamide, high-dose methotrexate/leucovorin, cytarabine, vincristine, prednisone, doxorubicin.[104]

Treatment options under clinical evaluation:

- ANHL01P1: Addition of rituximab to French LMB-89-based therapy.

Stage III and IV Anaplastic Large Cell Lymphoma

Patients with stage III and IV Ki+ anaplastic large cell lymphoma have an event-free survival of approximately 70% to 75%.[105] Treatment in the past has generally been the same as other types of non-Hodgkin's lymphoma of the same stage. Newer approaches are testing the addition of vinblastine to a CHOP-based regimen.[106]

Standard treatment options:

- APO: doxorubicin, prednisone, vincristine, methotrexate.[107]
- CHOP: vincristine, doxorubicin, cyclophosphamide, prednisone.[108]

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report of the Berlin-Frankfurt-Munster Group Trial NHL-BFM 90. Blood 97(12): 3699-3706, 2001.

[104] Patte C, Auperin A, Michon J, et al.: The Societe Francaise d'Oncologie Pediatrique LMB89 protocol: highly effective multiagent chemotherapy tailored to the tumor burden and initial response in 561 unselected children with B-cell lymphomas and L3 leukemia. Blood 97(11): 3370-3379, 2001.

[105] Seidemann K, Tiemann M, Schrappe M, et al.: Short-pulse B-non-Hodgkin lymphoma-type chemotherapy is efficacious treatment for pediatric anaplastic large cell lymphoma: a report of the Berlin-Frankfurt-Munster Group Trial NHL-BFM 90. Blood 97(12): 3699-3706, 2001.

Murphy SB: Pediatric lymphomas: recent advances and commentary on Ki-1-positive anaplastic large-cell lymphomas of childhood. Annals of Oncology 5(Suppl 1): s31-s33, 1994.

Massimino M, Gasparini M, Giardini R: Ki-1 (CD30) anaplastic large-cell lymphoma in children. Annals of Oncology 6(9): 915-920, 1995.

[106] Brugieres L, Quartier P, Le Deley MC, et al.: Relapses of childhood anaplastic large-cell lymphoma: treatment results in a series of 41 children--a report from the French Society of Pediatric Oncology. Annals of Oncology 11(1): 53-58, 2000.

[107] Laver JH, Mahmoud H, Pick TE, et al.: Results of a randomized phase III trial in children and adolescents with advanced stage diffuse large cell non Hodgkin's lymphoma: a Pediatric Oncology Group study. Leukemia and Lymphoma 42(3): 399-405, 2001.

[108] Hvizdala EV, Berard C, Callihan T, et al.: Nonlymphoblastic lymphoma in children - histology and stage-related response to therapy: a Pediatric Oncology Group study. Journal of Clinical Oncology 9(7): 1189-1195, 1991.

- NHL-BFM 90: vincristine, doxorubicin, prednisone, cyclophosphamide, dexamethasone, etoposide, ifosfamide, cytarabine, methotrexate, vindesine.[109]

Recurrent Childhood Large Cell Lymphoma

Recurrent Diffuse Large B-Cell Lymphoma

The prognosis for the child with recurrent or progressive large cell lymphoma (LCL) is poor. An aggressive treatment strategy including stem cell transplantation should be considered for LCL patients who have relapsed after the completion of front-line therapy.[110] Radiation may have a role in treating patients who have not had a complete response to therapy.

Rituximab is a mouse/human chimeric antibody targeting the CD20 antigen. Data from adult clinical trials have demonstrated that rituximab is active against recurrent diffuse large B-cell lymphoma.[111] Rituximab has been safely combined with standard lymphoma chemotherapy regimens with no substantial increase in toxicity above that associated with the chemotherapy alone.[112] A randomized trial in elderly adults with newly diagnosed diffuse large B-cell lymphoma comparing standard CHOP therapy to CHOP plus rituximab demonstrated significantly higher event-free survival (EFS) and survival rates for patients receiving rituximab plus chemotherapy.[113] Rituximab has also been combined with ifosfamide, carboplatin, and etoposide (ICE) in adults with recurrent high-grade B-cell lymphomas[114], and

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[109] Seidemann K, Tiemann M, Schrappe M, et al.: Short-pulse B-non-Hodgkin lymphoma-type chemotherapy is efficacious treatment for pediatric anaplastic large cell lymphoma: a report of the Berlin-Frankfurt-Munster Group Trial NHL-BFM 90. Blood 97(12): 3699-3706, 2001.

[110] Gordon BG, Warkentin PI, Weisenburger DD, et al.: Bone marrow transplantation for peripheral T-cell lymphoma in children and adolescents. Blood 80(11): 2938-2942, 1992.

[111] Coiffier B, Haioun C, Ketterer N, et al.: Rituximab (anti-CD20 monoclonal antibody) for the treatment of patients with relapsing or refractory aggressive lymphoma: a multicenter phase II study. Blood 92(6): 1927-1932, 1998.

[112] Vose JM, Link BK, Grossbard ML, et al.: Phase II study of rituximab in combination with CHOP chemotherapy in patients with previously untreated intermediate- or high-grade non-Hodgkin's lymphoma (NHL). Blood 94(10 pt 2): A-388, 89a, 1999.
Czuczman M, Grillo-Lopez AJ, White CA, et al.: Rituximab/CHOP chemoimmunotherapy in patients (PTS) with low grade lymphoma (LG/F NHL): progression free survival (PFS) after three years (median) follow-up. Blood 94(10 pt 2): A-432, 99a, 1999.

[113] Coiffier B, Lepage E, Briere J, et al.: CHOP chemotherapy plus rituximab compared with CHOP alone in elderly patients with diffuse large-B-cell lymphoma. New England Journal of Medicine 346(4): 235-242, 2002.

[114] Kewalramiani T, Zelenetz A, Bertino J, et al.: Rituximab significantly increases the complete response rate in patients with relapsed or primary refractory DLBCL receiving ICE as second-line therapy. Blood 98(11 pt 2): A-1459, 346a, 2001.

this four drug regimen has high levels of activity. As diffuse large B-cell lymphoma in the pediatric population most commonly occurs among 15-19 year olds[115], the experience with rituximab in the treatment of adults with recurrent disease may be applicable to this older pediatric population, but currently should be considered experimental.

For patients who have progressive disease or who recurred while receiving front-line therapy, clinical trials are appropriate and may be the best treatment option.

Standard treatment options:

- Allogeneic or autologous bone marrow transplantation.[116]
- Treatment using regimens tested under stage III or IV small noncleaved cell lymphoma.
- DECAL: (Dexamethasone, Etoposide, Cisplatin, Cytarabine, L-asparaginase)[117]

Treatment options under clinical evaluation:

- ADVL0013: A phase I study of rituximab followed by yttrium90 ibritumomab tiuxetan

Information about ongoing clinical trials is available from the NCI (**http://cancer.gov/clinical_trials/**).

Recurrent Anaplastic Large Cell Lymphoma

Children with recurrent anaplastic large cell lymphoma have a more optimistic outlook with a second complete remission rate as high as 88% and

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[115] Percy CL, Smith MA, Linet M, et al.: Lymphomas and reticuloendothelial neoplasms. In: Ries LA, Smith MA, Gurney JG, et al., eds.: Cancer Incidence and Survival Among Children and Adolescents: United States SEER Program 1975-1995. Bethesda, Md: National Cancer Institute, SEER Program, NIH Pub.No. 99-4649, 1999, pp 35-50.

[116] Gordon BG, Warkentin PI, Weisenburger DD, et al.: Bone marrow transplantation for peripheral T-cell lymphoma in children and adolescents. Blood 80(11): 2938-2942, 1992.
Appelbaum FR, Sullivan KM, Buckner CD, et al.: Treatment of malignant lymphoma in 100 patients with chemotherapy, total body irradiation, and marrow transplantation. Journal of Clinical Oncology 5(9): 1340-1347, 1987.

[117] Kobrinsky NL, Sposto R, Shah NR, et al.: Outcomes of treatment of children and adolescents with recurrent non-Hodgkin's lymphoma and Hodgkin's disease with dexamethasone, etoposide, cisplatin, cytarabine, and L-asparaginase, maintenance chemotherapy, and transplantation: Study CCG-5912. Journal of Clinical Oncology 19(9): 2390-2396, 2001.

three year event-free survival and overall survival rates of 44% and 69% respectively.[118]

An aggressive treatment strategy including stem cell transplantation should be considered for patients who have relapsed on front-line therapy and have chemosensitive disease.[119] Vinblastine given weekly has been found effective in securing long-term remissions in patients that have experienced relapse.[120] Radiation may have a role in treating patients who have not had a complete response to therapy.

For patients who have progressive disease or who recurred while receiving front-line therapy, clinical trials are appropriate and may be the best treatment option.

Treatment options:

- Allogeneic or autologous bone marrow transplantation.[121]
- Treatment using regimens tested under stage III or IV small non-cleaved cell lymphoma.
- DECAL:(Dexamethasone, Etoposide, Cisplatin, Cytarabine, L-asparaginase)[122]
- Clinical trials: Information about ongoing clinical trials is available from the NCI (**http://cancer.gov/clinical_trials/**)

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[118] Brugieres L, Quartier P, Le Deley MC, et al.: Relapses of childhood anaplastic large-cell lymphoma: treatment results in a series of 41 children--a report from the French Society of Pediatric Oncology. Annals of Oncology 11(1): 53-58, 2000.

[119] Gordon BG, Warkentin PI, Weisenburger DD, et al.: Bone marrow transplantation for peripheral T-cell lymphoma in children and adolescents. Blood 80(11): 2938-2942, 1992.

[120] Brugieres L, Quartier P, Le Deley MC, et al.: Relapses of childhood anaplastic large-cell lymphoma: treatment results in a series of 41 children--a report from the French Society of Pediatric Oncology. Annals of Oncology 11(1): 53-58, 2000.

[121] Gordon BG, Warkentin PI, Weisenburger DD, et al.: Bone marrow transplantation for peripheral T-cell lymphoma in children and adolescents. Blood 80(11): 2938-2942, 1992.
Appelbaum FR, Sullivan KM, Buckner CD, et al.: Treatment of malignant lymphoma in 100 patients with chemotherapy, total body irradiation, and marrow transplantation. Journal of Clinical Oncology 5(9): 1340-1347, 1987.

[122] Kobrinsky NL, Sposto R, Shah NR, et al.: Outcomes of treatment of children and adolescents with recurrent non-Hodgkin's lymphoma and Hodgkin's disease with dexamethasone, etoposide, cisplatin, cytarabine, and L-asparaginase, maintenance chemotherapy, and transplantation: Study CCG-5912. Journal of Clinical Oncology 19(9): 2390-2396, 2001.

NIH Databases

In addition to the various Institutes of Health that publish professional guidelines, the NIH has designed a number of databases for professionals.[123] Physician-oriented resources provide a wide variety of information related to the biomedical and health sciences, both past and present. The format of these resources varies. Searchable databases, bibliographic citations, full text articles (when available), archival collections, and images are all available. The following are referenced by the National Library of Medicine:[124]

- **Bioethics:** Access to published literature on the ethical, legal and public policy issues surrounding healthcare and biomedical research. This information is provided in conjunction with the Kennedy Institute of Ethics located at Georgetown University, Washington, D.C.: **http://www.nlm.nih.gov/databases/databases_bioethics.html**
- **HIV/AIDS Resources:** Describes various links and databases dedicated to HIV/AIDS research: **http://www.nlm.nih.gov/pubs/factsheets/aidsinfs.html**
- **NLM Online Exhibitions:** Describes "Exhibitions in the History of Medicine": **http://www.nlm.nih.gov/exhibition/exhibition.html**. Additional resources for historical scholarship in medicine: **http://www.nlm.nih.gov/hmd/hmd.html**
- **Biotechnology Information:** Access to public databases. The National Center for Biotechnology Information conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information for the better understanding of molecular processes affecting human health and disease: **http://www.ncbi.nlm.nih.gov/**
- **Population Information:** The National Library of Medicine provides access to worldwide coverage of population, family planning, and related health issues, including family planning technology and programs, fertility, and population law and policy: **http://www.nlm.nih.gov/databases/databases_population.html**
- **Cancer Information:** Access to caner-oriented databases: **http://www.nlm.nih.gov/databases/databases_cancer.html**

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[123] Remember, for the general public, the National Library of Medicine recommends the databases referenced in MEDLINE*plus* (**http://medlineplus.gov/** or **http://www.nlm.nih.gov/medlineplus/databases.html**).

[124] See **http://www.nlm.nih.gov/databases/databases.html**.

- **Profiles in Science:** Offering the archival collections of prominent twentieth-century biomedical scientists to the public through modern digital technology: **http://www.profiles.nlm.nih.gov/**
- **Chemical Information:** Provides links to various chemical databases and references: **http://sis.nlm.nih.gov/Chem/ChemMain.html**
- **Clinical Alerts:** Reports the release of findings from the NIH-funded clinical trials where such release could significantly affect morbidity and mortality: **http://www.nlm.nih.gov/databases/alerts/clinical_alerts.html**
- **Space Life Sciences:** Provides links and information to space-based research (including NASA): **http://www.nlm.nih.gov/databases/databases_space.html**
- **MEDLINE:** Bibliographic database covering the fields of medicine, nursing, dentistry, veterinary medicine, the healthcare system, and the pre-clinical sciences: **http://www.nlm.nih.gov/databases/databases_medline.html**
- **Toxicology and Environmental Health Information (TOXNET):** Databases covering toxicology and environmental health: **http://sis.nlm.nih.gov/Tox/ToxMain.html**
- **Visible Human Interface:** Anatomically detailed, three-dimensional representations of normal male and female human bodies: **http://www.nlm.nih.gov/research/visible/visible_human.html**

While all of the above references may be of interest to physicians who study and treat childhood non-Hodgkin's lymphoma, the following are particularly noteworthy.

The Combined Health Information Database

A comprehensive source of information on clinical guidelines written for professionals is the Combined Health Information Database. You will need to limit your search to "Brochure/Pamphlet," "Fact Sheet," or "Information Package" and childhood non-Hodgkin's lymphoma using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find associations, use the drop boxes at the bottom of the search page where "You may refine your search by." For the publication date, select "All Years," select your preferred language, and the format option "Fact Sheet." By making these selections and typing "childhood non-Hodgkin's lymphoma" (or synonyms) into the

"For these words:" box above, you will only receive results on fact sheets dealing with childhood non-Hodgkin's lymphoma.

The NLM Gateway[125]

The NLM (National Library of Medicine) Gateway is a Web-based system that lets users search simultaneously in multiple retrieval systems at the U.S. National Library of Medicine (NLM). It allows users of NLM services to initiate searches from one Web interface, providing "one-stop searching" for many of NLM's information resources or databases.[126] One target audience for the Gateway is the Internet user who is new to NLM's online resources and does not know what information is available or how best to search for it. This audience may include physicians and other healthcare providers, researchers, librarians, students, and, increasingly, parents and the public.[127] To use the NLM Gateway, simply go to the search site at **http://gateway.nlm.nih.gov/gw/Cmd**. Type "childhood non-Hodgkin's lymphoma" (or synonyms) into the search box and click "Search." The results will be presented in a tabular form, indicating the number of references in each database category.

Results Summary

Category	Items Found
Journal Articles	350473
Books / Periodicals / Audio Visual	2584
Consumer Health	294
Meeting Abstracts	2575
Other Collections	87
Total	356013

[125] Adapted from NLM: **http://gateway.nlm.nih.gov/gw/Cmd?Overview.x**.

[126] The NLM Gateway is currently being developed by the Lister Hill National Center for Biomedical Communications (LHNCBC) at the National Library of Medicine (NLM) of the National Institutes of Health (NIH).

[127] Other users may find the Gateway useful for an overall search of NLM's information resources. Some searchers may locate what they need immediately, while others will utilize the Gateway as an adjunct tool to other NLM search services such as PubMed® and MEDLINEplus®. The Gateway connects users with multiple NLM retrieval systems while also providing a search interface for its own collections. These collections include various types of information that do not logically belong in PubMed, LOCATORplus, or other established NLM retrieval systems (e.g., meeting announcements and pre-1966 journal citations). The Gateway will provide access to the information found in an increasing number of NLM retrieval systems in several phases.

HSTAT[128]

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.[129] HSTAT's audience includes healthcare providers, health service researchers, policy makers, insurance companies, consumers, and the information professionals who serve these groups. HSTAT provides access to a wide variety of publications, including clinical practice guidelines, quick-reference guides for clinicians, consumer health brochures, evidence reports and technology assessments from the Agency for Healthcare Research and Quality (AHRQ), as well as AHRQ's Put Prevention Into Practice.[130] Simply search by "childhood non-Hodgkin's lymphoma" (or synonyms) at the following Web site: **http://text.nlm.nih.gov**.

Coffee Break: Tutorials for Biologists[131]

Some parents may wish to have access to a general healthcare site that takes a scientific view of the news and covers recent breakthroughs in biology that may one day assist physicians in developing treatments. To this end, we recommend "Coffee Break," a collection of short reports on recent biological discoveries. Each report incorporates interactive tutorials that demonstrate how bioinformatics tools are used as a part of the research process. Currently, all Coffee Breaks are written by NCBI staff.[132] Each report is about 400 words and is usually based on a discovery reported in one or more articles from recently published, peer-reviewed literature.[133] This site has

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[128] Adapted from HSTAT: **http://www.nlm.nih.gov/pubs/factsheets/hstat.html**.

[129] The HSTAT URL is **http://hstat.nlm.nih.gov/**.

[130] Other important documents in HSTAT include: the National Institutes of Health (NIH) Consensus Conference Reports and Technology Assessment Reports; the HIV/AIDS Treatment Information Service (ATIS) resource documents; the Substance Abuse and Mental Health Services Administration's Center for Substance Abuse Treatment (SAMHSA/CSAT) Treatment Improvement Protocols (TIP) and Center for Substance Abuse Prevention (SAMHSA/CSAP) Prevention Enhancement Protocols System (PEPS); the Public Health Service (PHS) Preventive Services Task Force's *Guide to Clinical Preventive Services*; the independent, nonfederal Task Force on Community Services *Guide to Community Preventive Services*; and the Health Technology Advisory Committee (HTAC) of the Minnesota Health Care Commission (MHCC) health technology evaluations.

[131] Adapted from **http://www.ncbi.nlm.nih.gov/Coffeebreak/Archive/FAQ.html**.

[132] The figure that accompanies each article is frequently supplied by an expert external to NCBI, in which case the source of the figure is cited. The result is an interactive tutorial that tells a biological story.

[133] After a brief introduction that sets the work described into a broader context, the report focuses on how a molecular understanding can provide explanations of observed biology and lead to therapies for diseases. Each vignette is accompanied by a figure and hypertext

new articles every few weeks, so it can be considered an online magazine of sorts, and intended for general background information. Access the Coffee Break Web site at **http://www.ncbi.nlm.nih.gov/Coffeebreak/**.

Other Commercial Databases

In addition to resources maintained by official agencies, other databases exist that are commercial ventures addressing medical professionals. Here are a few examples that may interest you:

- **CliniWeb International:** Index and table of contents to selected clinical information on the Internet; see **http://www.ohsu.edu/cliniweb/**.
- **Image Engine:** Multimedia electronic medical record system that integrates a wide range of digitized clinical images with textual data stored in the University of Pittsburgh Medical Center's MARS electronic medical record system; see the following Web site: **http://www.cml.upmc.edu/cml/imageengine/imageEngine.html**.
- **Medical World Search:** Searches full text from thousands of selected medical sites on the Internet; see **http://www.mwsearch.com/**.
- **MedWeaver:** Prototype system that allows users to search differential diagnoses for any list of signs and symptoms, to search medical literature, and to explore relevant Web sites; see **http://www.med.virginia.edu/~wmd4n/medweaver.html**.
- **Metaphrase:** Middleware component intended for use by both caregivers and medical records personnel. It converts the informal language generally used by caregivers into terms from formal, controlled vocabularies; see the following Web site: **http://www.lexical.com/Metaphrase.html**.

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links that lead to a series of pages that interactively show how NCBI tools and resources are used in the research process.

The Genome Project and Childhood Non-Hodgkin's Lymphoma

With all the discussion in the press about the Human Genome Project, it is only natural that physicians, researchers, and parents want to know about how human genes relate to childhood non-Hodgkin's lymphoma. In the following section, we will discuss databases and references used by physicians and scientists who work in this area.

Online Mendelian Inheritance in Man (OMIM)

The Online Mendelian Inheritance in Man (OMIM) database is a catalog of human genes and genetic disorders authored and edited by Dr. Victor A. McKusick and his colleagues at Johns Hopkins and elsewhere. OMIM was developed for the World Wide Web by the National Center for Biotechnology Information (NCBI).[134] The database contains textual information, pictures, and reference information. It also contains copious links to NCBI's Entrez database of MEDLINE articles and sequence information.

To search the database, go to **http://www.ncbi.nlm.nih.gov/Omim/searchomim.html**. Type "childhood non-Hodgkin's lymphoma" (or synonyms) in the search box, and click "Submit Search." If too many results appear, you can narrow the search by adding the word "clinical." Each report will have additional links to related research and databases. By following these links, especially the link titled "Database Links," you will be exposed to numerous specialized databases that are largely used by the scientific community. These databases are overly technical and seldom used by the general public, but offer an abundance of information. The following is an example of the results you can obtain from the OMIM for childhood non-Hodgkin's lymphoma:

- **Ataxia-telangiectasia**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?208900

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[134] Adapted from **http://www.ncbi.nlm.nih.gov/**. Established in 1988 as a national resource for molecular biology information, NCBI creates public databases, conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information--all for the better understanding of molecular processes affecting human health and disease.

- **Cartilage-hair Hypoplasia**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?250250
- **Tumor Protein P53**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?191170
- **Usher Syndrome, Type Iia; Ush2a**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?276901

Genes and Disease (NCBI - Map)

The Genes and Disease database is produced by the National Center for Biotechnology Information of the National Library of Medicine at the National Institutes of Health. This Web site categorizes each disorder by the system of the body associated with it. Go to **http://www.ncbi.nlm.nih.gov/disease/**, and browse the system pages to have a full view of important conditions linked to human genes. Since this site is regularly updated, you may wish to re-visit it from time to time. The following systems and associated disorders are addressed:

- **Cancer:** Uncontrolled cell division.
  Examples: Breast And Ovarian Cancer, Burkitt lymphoma, chronic myeloid leukemia, colon cancer, lung cancer, malignant melanoma, multiple endocrine neoplasia, neurofibromatosis, p53 tumor suppressor, pancreatic cancer, prostate cancer, Ras oncogene, RB: retinoblastoma, von Hippel-Lindau syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Cancer.html**

Entrez

Entrez is a search and retrieval system that integrates several linked databases at the National Center for Biotechnology Information (NCBI). These databases include nucleotide sequences, protein sequences, macromolecular structures, whole genomes, and MEDLINE through PubMed. Entrez provides access to the following databases:

- **PubMed:** Biomedical literature (PubMed),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed**
- **Nucleotide Sequence Database (Genbank):**
  Web site:
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Nucleotide
- **Protein Sequence Database:**
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Protein**
- **Structure:** Three-dimensional macromolecular structures,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Structure**
- **Genome:** Complete genome assemblies,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Genome**
- **PopSet:** Population study data sets,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Popset**
- **OMIM:** Online Mendelian Inheritance in Man,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM**
- **Taxonomy:** Organisms in GenBank,
  Web site:
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Taxonomy
- **Books:** Online books,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=books**
- **ProbeSet:** Gene Expression Omnibus (GEO),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **3D Domains:** Domains from Entrez Structure,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **NCBI's Protein Sequence Information Survey Results:**
  Web site: **http://www.ncbi.nlm.nih.gov/About/proteinsurvey/**

To access the Entrez system at the National Center for Biotechnology Information, go to **http://www.ncbi.nlm.nih.gov/entrez/**, and then select the database that you would like to search. The databases available are listed in

the drop box next to "Search." In the box next to "for," enter "childhood non-Hodgkin's lymphoma" (or synonyms) and click "Go."

Jablonski's Multiple Congenital Anomaly/Mental Retardation (MCA/MR) Syndromes Database[135]

This online resource can be quite useful. It has been developed to facilitate the identification and differentiation of syndromic entities. Special attention is given to the type of information that is usually limited or completely omitted in existing reference sources due to space limitations of the printed form.

At the following Web site you can also search across syndromes using an index: **http://www.nlm.nih.gov/mesh/jablonski/syndrome_toc/toc_a.html.** You can search by keywords at this Web site: **http://www.nlm.nih.gov/mesh/jablonski/syndrome_db.html**.

The Genome Database[136]

Established at Johns Hopkins University in Baltimore, Maryland in 1990, the Genome Database (GDB) is the official central repository for genomic mapping data resulting from the Human Genome Initiative. In the spring of 1999, the Bioinformatics Supercomputing Centre (BiSC) at the Hospital for Sick Children in Toronto, Ontario assumed the management of GDB. The Human Genome Initiative is a worldwide research effort focusing on structural analysis of human DNA to determine the location and sequence of the estimated 100,000 human genes. In support of this project, GDB stores and curates data generated by researchers worldwide who are engaged in the mapping effort of the Human Genome Project (HGP). GDB's mission is to provide scientists with an encyclopedia of the human genome which is continually revised and updated to reflect the current state of scientific knowledge. Although GDB has historically focused on gene mapping, its focus will broaden as the Genome Project moves from mapping to sequence, and finally, to functional analysis.

To access the GDB, simply go to the following hyperlink: **http://www.gdb.org/**. Search "All Biological Data" by "Keyword." Type

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[135] Adapted from the National Library of Medicine: **http://www.nlm.nih.gov/mesh/jablonski/about_syndrome.html**.

[136] Adapted from the Genome Database: **http://gdbwww.gdb.org/gdb/aboutGDB.html#mission**.

"childhood non-Hodgkin's lymphoma" (or synonyms) into the search box, and review the results. If more than one word is used in the search box, then separate each one with the word "and" or "or" (using "or" might be useful when using synonyms). This database is extremely technical as it was created for specialists. The articles are the results which are the most accessible to non-professionals and often listed under the heading "Citations." The contact names are also accessible to non-professionals.

Specialized References

The following books are specialized references written for professionals interested in childhood non-Hodgkin's lymphoma (sorted alphabetically by title; hyperlinks provide rankings, information, and reviews at Amazon.com):

- **Advanced and Critical Care Oncology Nursing: Managing Primary Complications** by Cynthia C. Chernecky (Editor), et al; Paperback - 736 pages (September 18, 1997), W B Saunders Co; ISBN: 0721668607; **http://www.amazon.com/exec/obidos/ASIN/0721668607/icongroupinterna**
- **Atlas of Pediatric Physical Diagnosis** by Basil J. Zitelli, Holly W. Davis (Editor); Hardcover, 3rd edition (March 1997), Mosby-Year Book; ISBN: 0815199309; **http://www.amazon.com/exec/obidos/ASIN/0815199309/icongroupinterna**
- **Cancer: Etiology, Diagnosis, and Treatment** by Walter J. Burdette; Paperback - 287 pages, 1st edition (January 15, 1998), McGraw Hill Text; ISBN: 0070089922; **http://www.amazon.com/exec/obidos/ASIN/0070089922/icongroupinterna**
- **Cancer Management: A Multidisciplinary Approach: Medical, Surgical & Radiation** by Richard Pazdur (Editor), et al; Paperback - 982 pages, 5th edition (June 15, 2001), Publisher Research & Representation, Inc.; ISBN: 1891483080; **http://www.amazon.com/exec/obidos/ASIN/1891483080/icongroupinterna**
- **The Child with Cancer: Family-Centered Care in Practice** by Helen Langton (Editor); Paperback - 404 pages; 1st edition (January 15, 2000), W B Saunders Co; ISBN: 0702023000; **http://www.amazon.com/exec/obidos/ASIN/0702023000/icongroupinterna**
- **Familial Cancer and Prevention: Molecular Epidemiology: A New Strategy Toward Cancer Control** by Joji Utsunomiya (Editor), et al; Hardcover (April 1999), Wiley-Liss; ISBN: 0471249378; **http://www.amazon.com/exec/obidos/ASIN/0471249378/icongroupinterna**

- **The 5-Minute Pediatric Consult** by M. William Schwartz (Editor); Hardcover - 1050 pages, 2nd edition (January 15, 2000), Lippincott, Williams & Wilkins; ISBN: 0683307444; **http://www.amazon.com/exec/obidos/ASIN/0683307444/icongroupinterna**
- **Fundamentals of Cancer Epidemiology** by Philip C. Nasca, Ph.D. (Editor), Pastides Harris, Ph.D., MPH (Editor); Hardcover - 368 pages, 1st edition (February 15, 2001), Aspen Publishers, Inc.; ISBN: 0834217767; **http://www.amazon.com/exec/obidos/ASIN/0834217767/icongroupinterna**
- **Helping Cancer Patients Cope: A Problem-Solving Approach** by Arthur M. Nezu (Editor), et al; Hardcover - 314 pages (December 15, 1998), American Psychological Association (APA); ISBN: 1557985332; **http://www.amazon.com/exec/obidos/ASIN/1557985332/icongroupinterna**
- **Nelson Textbook of Pediatrics** by Richard E. Behrman (Editor), et al; Hardcover - 2414 pages, 16th edition (January 15, 2000), W B Saunders Co; ISBN: 0721677673; **http://www.amazon.com/exec/obidos/ASIN/0721677673/icongroupinterna**
- **Quantitative Estimation and Prediction of Human Cancer Risks (Iarc Scientific Publications, 131)** by Suresh H. Moolgavkar (Editor), et al; Paperback (September 1999), Oxford University Press; ISBN: 9283221311; **http://www.amazon.com/exec/obidos/ASIN/9283221311/icongroupinterna**
- **Textbook of Cancer Epidemiology** by ADAMI, et al; Hardcover - 385 pages, 1st edition (July 15, 2002), Oxford University Press; ISBN: 0195109694; **http://www.amazon.com/exec/obidos/ASIN/0195109694/icongroupinterna**

Vocabulary Builder

Abdominal: Having to do with the abdomen, which is the part of the body between the chest and the hips that contains the pancreas, stomach, intestines, liver, gallbladder, and other organs. [NIH]

Adenopathy: Large or swollen lymph glands. [NIH]

Allopurinol: A drug that lowers high levels of uric acid (a byproduct of metabolism) in the blood caused by some cancer treatments. [NIH]

Anaplastic: A term used to describe cancer cells that divide rapidly and bear little or no resemblance to normal cells. [NIH]

Anesthesia: Loss of feeling or awareness. Local anesthetics cause loss of feeling in a part of the body. General anesthetics put the person to sleep. [NIH]

Antigen: Any substance which is capable, under appropriate conditions, of

inducing a specific immune response and of reacting with the products of that response, that is, with specific antibody or specifically sensitized T-lymphocytes, or both. Antigens may be soluble substances, such as toxins and foreign proteins, or particulate, such as bacteria and tissue cells; however, only the portion of the protein or polysaccharide molecule known as the antigenic determinant (q.v.) combines with antibody or a specific receptor on a lymphocyte. Abbreviated Ag. [EU]

Asparaginase: An anticancer drug that is an enzyme. [NIH]

Aspirate: Fluid withdrawn from a lump, often a cyst, or a nipple. [NIH]

Ataxia: Loss of muscle coordination. [NIH]

Biopsy: The removal of cells or tissues for examination under a microscope. When only a sample of tissue is removed, the procedure is called an incisional biopsy or core biopsy. When an entire tumor or lesion is removed, the procedure is called an excisional biopsy. When a sample of tissue or fluid is removed with a needle, the procedure is called a needle biopsy or fine-needle aspiration. [NIH]

Blasts: Immature blood cells. [NIH]

Bowel: The long tube-shaped organ in the abdomen that completes the process of digestion. There is both a small and a large bowel. Also called the intestine. [NIH]

Carboplatin: An anticancer drug that belongs to the family of drugs called platinum compounds. [NIH]

Cardiac: Having to do with the heart. [NIH]

Chromosomal: Pertaining to chromosomes. [EU]

Confusion: Disturbed orientation in regard to time, place, or person, sometimes accompanied by disordered consciousness. [EU]

Cranial: Pertaining to the cranium, or to the anterior (in animals) or superior (in humans) end of the body. [EU]

Cyclophosphamide: An anticancer drug that belongs to the family of drugs called alkylating agents. [NIH]

Daunorubicin: An anticancer drug that belongs to the family of drugs called antitumor antibiotics. [NIH]

Dexamethasone: A synthetic steroid (similar to steroid hormones produced naturally in the adrenal gland). Dexamethasone is used to treat leukemia and lymphoma and may be used to treat some of the problems caused by other cancers and their treatment. [NIH]

Doxorubicin: An anticancer drug that belongs to the family of drugs called antitumor antibiotics. It is an anthracycline. [NIH]

Dysphagia: Difficulty in swallowing. [EU]

Dyspnea: Difficult, painful breathing or shortness of breath. [NIH]

Effusion: The escape of fluid into a part or tissue, as an exudation or a transudation. [EU]

Endemic: Present or usually prevalent in a population or geographical area at all times; said of a disease or agent. Called also endemial. [EU]

Enzyme: A protein that speeds up chemical reactions in the body. [NIH]

Etoposide: An anticancer drug that is a podophyllotoxin derivative and belongs to the family of drugs called mitotic inhibitors. [NIH]

Gastrointestinal: Refers to the stomach and intestines. [NIH]

Hematologist: A doctor who specializes in treating diseases of the blood. [NIH]

Hyperuricemia: A buildup of uric acid (a byproduct of metabolism) in the blood; a side effect of some anticancer drugs. [NIH]

Hypoplasia: Incomplete development or underdevelopment of an organ or tissue. [EU]

Ifosfamide: An anticancer drug that belongs to the family of drugs called alkylating agents. [NIH]

Immunophenotyping: Process of classifying cells of the immune system based on structural and functional differences. The process is commonly used to analyze and sort T-lymphocytes into subsets based on CD antigens by the technique of flow cytometry. [NIH]

Invasive: 1. having the quality of invasiveness. 2. involving puncture or incision of the skin or insertion of an instrument or foreign material into the body; said of diagnostic techniques. [EU]

Lesion: An area of abnormal tissue change. [NIH]

Lymphoid: Referring to lymphocytes, a type of white blood cell. Also refers to tissue in which lymphocytes develop. [NIH]

Malignancy: A cancerous tumor that can invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Malignant: Cancerous; a growth with a tendency to invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Mediastinoscopy: A procedure in which a tube is inserted into the chest to view the organs in the area between the lungs and nearby lymph nodes. The tube is inserted through an incision above the breastbone. This procedure is usually performed to get a tissue sample from the lymph nodes on the right side of the chest. [NIH]

Mediastinum: The area between the lungs. The organs in this area include the heart and its large blood vessels, the trachea, the esophagus, the bronchi, and lymph nodes. [NIH]

Mercaptopurine: An anticancer drug that belongs to the family of drugs called antimetabolites. [NIH]

Methotrexate: An anticancer drug that belongs to the family of drugs called antimetabolites. [NIH]

Millimeter: A measure of length. A millimeter is approximately 26-times smaller than an inch. [NIH]

Perforation: 1. the act of boring or piercing through a part. 2. a hole made through a part or substance. [EU]

Phenotype: The outward appearance of the individual. It is the product of interactions between genes and between the genotype and the environment. This includes the killer phenotype, characteristic of YEASTS. [NIH]

Physiologic: Having to do with the functions of the body. When used in the phrase "physiologic age," it refers to an age assigned by general health, as opposed to calendar age. [NIH]

Prednisone: Belongs to the family of drugs called steroids and is used to treat several types of cancer and other disorders. Prednisone also inhibits the body's immune response. [NIH]

Preoperative: Preceding an operation. [EU]

Progressive: Advancing; going forward; going from bad to worse; increasing in scope or severity. [EU]

Recurrence: The return of cancer, at the same site as the original (primary) tumor or in another location, after the tumor had disappeared. [NIH]

Resected: Surgical removal of part of an organ. [NIH]

Resection: Removal of tissue or part or all of an organ by surgery. [NIH]

Sporadic: Neither endemic nor epidemic; occurring occasionally in a random or isolated manner. [EU]

Steroids: Drugs used to relieve swelling and inflammation. [NIH]

Subcutaneous: Beneath the skin. [NIH]

Telangiectasia: The permanent enlargement of blood vessels, causing redness in the skin or mucous membranes. [NIH]

Testicular: Pertaining to a testis. [EU]

Testis: Either of the paired male reproductive glands that produce the male germ cells and the male hormones. [NIH]

Thioguanine: An anticancer drug that belongs to the family of drugs called antimetabolites. [NIH]

Thoracentesis: Removal of fluid from the pleural cavity through a needle inserted between the ribs. [NIH]

Thoracoscopy: The use of a thin, lighted tube (called an endoscope) to

examine the inside of the chest. [NIH]

Thoracotomy: An operation to open the chest. [NIH]

Toxic: Having to do with poison or something harmful to the body. Toxic substances usually cause unwanted side effects. [NIH]

Toxicity: The quality of being poisonous, especially the degree of virulence of a toxic microbe or of a poison. [EU]

Vinblastine: An anticancer drug that belongs to the family of plant drugs called vinca alkaloids. It is a mitotic inhibitor. [NIH]

Vincristine: An anticancer drug that belongs to the family of plant drugs called vinca alkaloids. [NIH]

Vindesine: An anticancer drug that belongs to the family of plant drugs called vinca alkaloids. [NIH]

PART III. APPENDICES

ABOUT PART III

Part III is a collection of appendices on general medical topics relating to childhood non-Hodgkin's lymphoma and related conditions.

APPENDIX A. RESEARCHING YOUR CHILD'S MEDICATIONS

Overview

There are a number of sources available on new or existing medications which could be prescribed to treat childhood non-Hodgkin's lymphoma. While a number of hard copy or CD-Rom resources are available to parents and physicians for research purposes, a more flexible method is to use Internet-based databases. In this chapter, we will begin with a general overview of medications. We will then proceed to outline official recommendations on how you should view your child's medications. You may also want to research medications that your child is currently taking for other conditions as they may interact with medications for childhood non-Hodgkin's lymphoma. Research can give you information on the side effects, interactions, and limitations of prescription drugs used in the treatment of childhood non-Hodgkin's lymphoma. Broadly speaking, there are two sources of information on approved medications: public sources and private sources. We will emphasize free-to-use public sources.

Your Child's Medications: The Basics[137]

The Agency for Health Care Research and Quality has published extremely useful guidelines on the medication aspects of childhood non-Hodgkin's lymphoma. Giving your child medication can involve many steps and decisions each day. The AHCRQ recommends that parents take part in treatment decisions. Do not be afraid to ask questions and talk about your concerns. By taking a moment to ask questions, your child may be spared from possible problems. Here are some points to cover each time a new medicine is prescribed**:**

- Ask about all parts of your child's treatment, including diet changes, exercise, and medicines.
- Ask about the risks and benefits of each medicine or other treatment your child might receive.
- Ask how often you or your child's doctor will check for side effects from a given medication.

Do not hesitate to tell the doctor about preferences you have for your child's medicines. You may want your child to have a medicine with the fewest side effects, or the fewest doses to take each day. You may care most about cost. Or, you may want the medicine the doctor believes will work the best. Sharing your concerns will help the doctor select the best treatment for your child.

Do not be afraid to "bother" the doctor with your questions about medications for childhood non-Hodgkin's lymphoma. You can also talk to a nurse or a pharmacist. They can help you better understand your child's treatment plan. Talking over your child's options with someone you trust can help you make better choices. Specifically, ask the doctor the following:

- The name of the medicine and what it is supposed to do.
- How and when to give your child the medicine, how much, and for how long.
- What food, drinks, other medicines, or activities your child should avoid while taking the medicine.
- What side effects your child may experience, and what to do if they occur.
- If there are any refills, and how often.
- About any terms or directions you do not understand.

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[137] This section is adapted from AHCRQ: **http://www.ahcpr.gov/consumer/ncpiebro.htm**.

- What to do if your child misses a dose.
- If there is written information you can take home (most pharmacies have information sheets on prescription medicines; some even offer large-print or Spanish versions).

Do not forget to tell the doctor about all the medicines your child is currently taking (not just those for childhood non-Hodgkin's lymphoma). This includes prescription medicines and the medicines that you buy over the counter. When talking to the doctor, you may wish to prepare a list of medicines your child is currently taking including why and in what forms. Be sure to include the following information for each:

- Name of medicine
- Reason taken
- Dosage
- Time(s) of day

Also include any over-the-counter medicines, such as:

- Laxatives
- Diet pills
- Vitamins
- Cold medicine
- Aspirin or other pain, headache, or fever medicine
- Cough medicine
- Allergy relief medicine
- Antacids
- Sleeping pills
- Others (include names)

Learning More about Your Child's Medications

Because of historical investments by various organizations and the emergence of the Internet, it has become rather simple to learn about the medications the doctor has recommended for childhood non-Hodgkin's lymphoma. One such source is the United States Pharmacopeia. In 1820, eleven physicians met in Washington, D.C. to establish the first compendium of standard drugs for the United States. They called this compendium the "U.S. Pharmacopeia (USP)." Today, the USP is a non-profit organization consisting of 800 volunteer scientists, eleven elected officials, and 400

representatives of state associations and colleges of medicine and pharmacy. The USP is located in Rockville, Maryland, and its home page is located at **www.usp.org**. The USP currently provides standards for over 3,700 medications. The resulting USP DI® Advice for the Patient® can be accessed through the National Library of Medicine of the National Institutes of Health. The database is partially derived from lists of federally approved medications in the Food and Drug Administration's (FDA) Drug Approvals database.[138]

While the FDA database is rather large and difficult to navigate, the Phamacopeia is both user-friendly and free to use. It covers more than 9,000 prescription and over-the-counter medications. To access this database, simply type the following hyperlink into your Web browser: **http://www.nlm.nih.gov/medlineplus/druginformation.html**. To view examples of a given medication (brand names, category, description, preparation, proper use, precautions, side effects, etc.), simply follow the hyperlinks indicated within the United States Pharmacopoeia (USP). It is important to read the disclaimer by the USP (**http://www.nlm.nih.gov/medlineplus/drugdisclaimer.html**) before using the information provided.

Commercial Databases

In addition to the medications listed in the USP above, a number of commercial sites are available by subscription to physicians and their institutions. You may be able to access these sources from your local medical library or your child's doctor's office.

Reuters Health Drug Database

The Reuters Health Drug Database can be searched by keyword at the hyperlink: **http://www.reutershealth.com/frame2/drug.html**.

Mosby's GenRx

Mosby's GenRx database (also available on CD-Rom and book format) covers 45,000 drug products including generics and international brands. It

[138] Though cumbersome, the FDA database can be freely browsed at the following site: **www.fda.gov/cder/da/da.htm**.

provides information on prescribing and drug interactions. Information can be obtained at the following hyperlink: **http://www.genrx.com/Mosby/PhyGenRx/group.html**.

Physicians Desk Reference

The Physicians Desk Reference database (also available in CD-Rom and book format) is a full-text drug database. The database is searchable by brand name, generic name or by indication. It features multiple drug interactions reports. Information can be obtained at the following hyperlink: **http://physician.pdr.net/physician/templates/en/acl/psuser_t.htm**.

Other Web Sites

A number of additional Web sites discuss drug information. As an example, you may like to look at **www.drugs.com** which reproduces the information in the Pharmacopeia as well as commercial information. You may also want to consider the Web site of the Medical Letter, Inc. which allows users to download articles on various drugs and therapeutics for a nominal fee: **http://www.medletter.com/**.

Drug Development and Approval

The following Web sites can be valuable resources when conducting research on the development and approval of new cancer drugs:

- FDA Home Page: Search for drugs currently in development or those which have been recently approved by the FDA.
  http://redir.nci.nih.gov/cgi-bin/redir.pl?section=Cancerinfo&destURI=http://www.fda.gov/
- Cancer Liaison Program: Answers questions from the public about drug approval processes, cancer clinical trials, and access to investigational therapies.
  http://redir.nci.nih.gov/cgi-bin/redir.pl?section=Cancerinfo&destURI=http://www.fda.gov/oashi/cancer/cancer.html
- Center for Drug Evaluation and Research
  http://redir.nci.nih.gov/cgi-bin/redir.pl?section=Cancerinfo&destURI=http://www.fda.gov/cder/

- Drug Approvals by Cancer Indications (Alphabetical List)
  http://redir.nci.nih.gov/cgi-bin/redir.pl?section=Cancerinfo&destURI=http://www.fda.gov/oashi/cancer/cdrugalpha.html
- Drug Approvals by Cancer Indications (Cancer Type)
  http://redir.nci.nih.gov/cgi-bin/redir.pl?section=Cancerinfo&destURI=http://www.fda.gov/oashi/cancer/cdrugind.html
- Electronic Orange Book of Approved Drug Products
  http://redir.nci.nih.gov/cgi-bin/redir.pl?section=Cancerinfo&destURI=http://www.fda.gov/cder/ob/default.htm
- Guidance Documents for Industry: Contains an archive of documents describing FDA policies on specific topics.
  http://redir.nci.nih.gov/cgi-bin/redir.pl?section=Cancerinfo&destURI=http://www.fda.gov/cder/guidance/index.htm
- Industry Collaboration: Provides information to industry on the process for getting new drugs into clinical trials.
  http://ctep.cancer.gov/industry/index.html
- Investigator's Handbook: Provides information to investigators on specific procedures related to clinical trial development.
  http://ctep.cancer.gov/handbook/index.html
- Questions and Answers About NCI's Natural Products Branch: A fact sheet that describes the functions of this branch, which collects and analyzes specimens of plant, marine, and microbial origin for possible anticancer properties.
  http://cis.nci.nih.gov/fact/7_33.htm

Understanding the Approval Process for New Cancer Drugs[139]

Since June 1996, about 80 new cancer-related drugs, or new uses for drugs already on the market, have been approved by the U.S. Food and Drug Administration (FDA), the division of the U.S. Department of Health and Human Services charged with ensuring the safety and effectiveness of new drugs before they can go on the market. (The FDA maintains an annotated

[139] Adapted from the NCI:
http://www.cancer.gov/clinical_trials/doc_header.aspx?viewid=d94cbfac-e478-4704-9052-d8e8a3372b56.

online list of drugs approved for use with cancer since 1996.) Some of these drugs treat cancer, some alleviate pain and other symptoms, and, in one case, reduce the risk of invasive cancer in people who are considered high-risk. The FDA relied on the results of clinical trials in making every one of these approvals. Without reliable information about a drug's effects on humans, it would be impossible to approve any drug for widespread use.

When considering a new drug, the FDA faces two challenges:

- First, making sure that the drug is safe and effective before it is made widely available;
- Second, ensuring that drugs which show promise are made available as quickly as possible to the people they can help.

To deal with these challenges, the FDA maintains a rigorous review process but also has measures in place to make some drugs available in special cases. This aim of this section is to acquaint you with the drug approval process and point you to other resources for learning more about it.

The Role of the Federal Drug Administration (FDA)

Approval is only one step in the drug development process. In fact, the FDA estimates that, on average, it takes eight and a half years to study and test a new drug before it can be approved for the general public. That includes early laboratory and animal testing, as well as the clinical trials that evaluate the drugs in humans. The FDA plays a key role at three main points in this process:

- Determining whether or not a new drug shows enough promise to be given to people in clinical trials
- Once clinical trials begin, deciding whether or not they should continue, based on reports of efficacy and adverse reactions
- When clinical trials are completed, deciding whether or not the drug can be sold to the public and what its label should say about directions for use, side effects, warnings, and the like.

To make these decisions, the FDA must review studies submitted by the drug's sponsor (usually the manufacturer), evaluate any adverse reports from preclinical studies and clinical trials (that is, reports of side effects or complications), and review the adequacy of the chemistry and manufacturing. This process is lengthy, but it is meant to ensure that only beneficial drugs with acceptable side effects will make their way into the

hands of the public. At the same time, recent legislative mandates and streamlined procedures within the FDA have accelerated the approval of effective drugs, especially for serious illnesses such as cancer. In addition, specific provisions make some drugs available to patients with special needs even before the approval process is complete.

From Lab to Patient Care

By law, the Food and Drug Administration (FDA) must review all test results for new drugs to ensure that products are safe and effective for specific uses. "Safe" does not mean that the drug is free of possible adverse side effects; rather, it means that the potential benefits have been determined to outweigh any risks. The testing process begins long before the first person takes the drug, with preliminary research and animal testing.

If a drug proves promising in the lab, the drug company or sponsor must apply for FDA approval to test it in clinical trials involving people. For drugs, the application, called an Investigational New Drug (IND) Application, is sent through the Center for Drug Evaluation and Research's (CDER) IND Review Process; for biological agents, the IND is sent to the Center for Biologics Evaluation and Research (CBER). Once the IND is approved by CDER or CBER, clinical trials can begin.

If the drug makes it through the clinical trials process—that is, the studies show that it is superior to current drugs—the manufacturer must submit a New Drug Application (NDA) or (for biological agents) a Biologics License Application (BLA) to the FDA. (Biological agents, such as serums, vaccines, and cloned proteins, are manufactured from substances taken from living humans or animals.) This application must include:

- The exact chemical makeup of the drug or biologic and the mechanisms by which it is effective
- Results of animal studies
- Results of clinical trials
- How the drug or biologic is manufactured, processed, and packaged
- Quality control standards
- Samples of the product in the form(s) in which it is to be administered.

Once the FDA receives the NDA or BLA from the manufacturer or developer, the formal New Drug Application Review Process or Biologics/Product License Application Review Process begins.

For an overview of the entire process from start to finish, see the CDER's visual representation of The New Drug Development Process: Steps from Test Tube to New Drug Application Review, which is available for public viewing at the following Web address: **http://www.fda.gov/cder/handbook/develop.htm**.

Speed versus Safety in the Approval Process

The FDA's current goal is that no more than ten months will pass between the time that a complete application is submitted and the FDA takes action on it. But the process is not always smooth. Sometimes FDA's external advisory panels call for additional research or data. In other cases, the FDA staff asks for more information or revised studies. Some new drug approvals have taken as little as 42 days; other more difficult NDAs have spent years in the approval process.

Setting Priorities

The order in which NDAs are assessed by the FDA is determined by a classification system designed to give priority to drugs with the greatest potential benefits. All drugs that offer significant medical advances over existing therapies for any disease are considered "priority" drugs in the approval process. NDAs for cancer treatment drugs are reviewed for this status primarily by the Division of Oncology Drug Products in the FDA's Center for Drug Evaluation and Research (CDER). For Biologic License Applications (vaccines, blood products, and medicines made from animal products), the Center for Biologics Evaluation and Research (CBER) provides additional regulation and oversight.

Expert Advice

The FDA relies on a system of independent advisory committees, made up of professionals from outside the agency, for expert advice and guidance in making sound decisions about drug approval. Each committee meets as needed to weigh available evidence and assess the safety, effectiveness, and appropriate use of products considered for approval. In addition, these

committees provide advice about general criteria for evaluation and scientific issues not related to specific products. The Oncologic Drugs Advisory Committee (ODAC) meets regularly to provide expert advice on cancer-related treatments and preventive drugs.

Each committee is composed of representatives from the research science and medical fields. At least one member on every advisory committee must represent the consumer perspective.

Final Approval

As the FDA looks at all the data submitted and the results of its own review, it applies two benchmark questions to each application for drug approval:

- Do the results of well-controlled studies provide substantial evidence of effectiveness?
- Do the results show the product is safe under the conditions of use in the proposed labeling? In this context, "safe" means that potential benefits have been determined to outweigh any risks.

Continued Vigilance

The FDA's responsibility for new drug treatments does not stop with final approval. The Office of Compliance in the Center for Drug Evaluation and Research (CDER) implements and tracks programs to make sure manufacturers comply with current standards and practice regulations. CDER's Office of Drug Marketing, Advertising, and Communication monitors new drug advertising to make sure it is truthful and complete. At the Center for Biologic Evaluation and Research, biologics are followed with the same vigilance after approval. And through a system called MedWatch, the FDA gets feedback from health professionals and consumers on how the new drugs are working, any adverse reactions, and potential problems in labeling and dosage.

Online FDA Resources

The following information from the FDA should help you better understand the drug approval process:

- Center for Drug Evaluation and Research: **http://www.fda.gov/cder/handbook**

- From Test Tube to Patient: New Drug Development in the U.S. – a special January 1995 issue of the magazine FDA Consumer:
  http://www.fda.gov/fdac/special/newdrug/ndd_toc.html
- Milestones in U.S. Food and Drug Law History:
  http://www.fda.gov/opacom/backgrounders/miles.html
- Drug Approvals for Cancer Indications:
  http://www.fda.gov/oashi/cancer/cdrug.html

Getting Drugs to Patients Who Need Them

Clinical trials provide the most important information used by the FDA in determining whether a new drug shows "substantial evidence of effectiveness," or whether an already-approved drug can be used effectively in new ways (for example, to treat or prevent other types of cancer, or at a different dosage). The FDA must certify that a drug has shown promise in laboratory and animal trials before human testing can begin. The trials process includes three main stages and involves continuous review, which ensures that the sponsor can stop the study early if major problems develop or unexpected levels of treatment benefit are found. As with all clinical trials, benefits and risks must be carefully weighed by the researchers conducting the study and the patients who decide to participate.

Not everyone is eligible to participate in a clinical trial. Some patients do not fit the exact requirements for studies, some have rare forms of cancer for which only a limited number of studies are underway, and others are too ill to participate. Working with the NCI and other sponsors, the FDA has established special conditions under which a patient and his or her physician can apply to receive cancer drugs that have not yet been through the approval process. In the past, these special case applications for new drugs were grouped under the name "compassionate uses." More recently, such uses have expanded to include more patients and more categories of investigational drugs.

Access to Investigational Drugs

The process of new drug development has many parts. In the United States, until a drug has been approved by the FDA, it can generally be obtained only through several mechanisms: enrollment in a clinical trial studying the drug, an expanded access program or special exemption/compassionate use programs. For more information about investigational drugs, see "Questions

and Answers: Access to Investigational Drugs" at **http://www.cancer.gov/cancer_information/doc_img.aspx?viewid=74b62d84-e135-451f-9bc9-d54358ede947**.

"Group C" Drugs

In the 1970s, researchers from the NCI became concerned about the lag between the date when an investigational drug was found to have anti-tumor activity and the time that drug became available on the market. Working with the FDA, the NCI established the "Group C" classification to allow access to drugs with reproducible activity. Group C drugs are provided to properly trained physicians who have registered using a special form to assure that their patient qualifies under guideline protocols for the drug. Each Group C drug protocol specifies patient eligibility, reporting methodology, and drug use. Not only does Group C designation (now called Group C/Treatment INDs) speed new drugs to patients who need them most, but the process also allows the NCI to gather important information on the safety as well as activity of the drugs in the settings in which they will be most used after final FDA approval. Drugs are placed in the Group C category by agreement between the FDA and the NCI. Group C drugs are always provided free of charge, and the Health Care Financing Administration provides coverage for care associated with Group C therapy.

Treatment INDs

In 1987, the FDA began authorizing the use of new drugs still in the development process to treat certain seriously ill patients. In these cases, the process is referred to as a treatment investigational new drug application (Treatment IND). Clinical trials of the new drug must already be underway and have demonstrated positive results that are reproducible. The FDA sets guidelines about what constitutes serious and life-threatening illnesses, how much must already be known about a drug's side effects and benefits, and where physicians can obtain the drug for treatment. For many seriously ill patients, the risks associated with taking a not-yet-completely proven drug are outweighed by the possible benefits.

Accelerated Approval

"Accelerated approval" is the short-hand term for the FDA's new review system which, in the 1990s, has been used to ensure rapid approval while at

the same time putting new safeguards into place. Accelerated approval is based on "surrogate endpoint" judgments: FDA can grant marketing approval to drugs and treatments that, according to certain indicators, prove they are likely to have beneficial effects on a disease or condition, even before such direct benefits have been shown clinically. Accelerated approval does NOT mean that additional clinical trials are not needed or that FDA stops gathering information about the effects of the drug; a follow-up study is required to demonstrate activity by more conventional endpoints.

Contraindications and Interactions (Hidden Dangers)

Some of the medications mentioned in the previous discussions can be problematic for children with childhood non-Hodgkin's lymphoma--not because they are used in the treatment process, but because of contraindications, or side effects. Medications with contraindications are those that could react with drugs used to treat childhood non-Hodgkin's lymphoma or potentially create deleterious side effects in patients with childhood non-Hodgkin's lymphoma. You should ask the physician about any contraindications, especially as these might apply to other medications that your child may be taking for common ailments.

Drug-drug interactions occur when two or more drugs react with each other. This drug-drug interaction may cause your child to experience an unexpected side effect. Drug interactions may make medications less effective, cause unexpected side effects, or increase the action of a particular drug. Some drug interactions can even be harmful to your child.

Be sure to read the label every time you give your child a nonprescription or prescription drug, and take the time to learn about drug interactions. These precautions may be critical to your child's health. You can reduce the risk of potentially harmful drug interactions and side effects with a little bit of knowledge and common sense.

Drug labels contain important information about ingredients, uses, warnings, and directions which you should take the time to read and understand. Labels also include warnings about possible drug interactions. Further, drug labels may change as new information becomes avaiable. This is why it's especially important to read the label every time you give your child a medication. When the doctor prescribes a new drug, discuss all over-the-counter and prescription medications, dietary supplements, vitamins, botanicals, minerals and herbals your child takes. Ask your pharmacist for

the package insert for each drug prescribed. The package insert provides more information about potential drug interactions.

A Final Warning

At some point, you may hear of alternative medications from friends, relatives, or in the news media. Advertisements may suggest that certain alternative drugs can produce positive results for childhood non-Hodgkin's lymphoma. Exercise caution--some of these drugs may have fraudulent claims, and others may actually hurt your child. The Food and Drug Administration (FDA) is the official U.S. agency charged with discovering which medications are likely to improve the health of patients with childhood non-Hodgkin's lymphoma. The FDA warns to watch out for[140]:

- Secret formulas (real scientists share what they know)
- Amazing breakthroughs or miracle cures (real breakthroughs don't happen very often; when they do, real scientists do not call them amazing or miracles)
- Quick, painless, or guaranteed cures
- If it sounds too good to be true, it probably isn't true.

If you have any questions about any kind of medical treatment, the FDA may have an office near you. Look for their number in the blue pages of the phone book. You can also contact the FDA through its toll-free number, 1-888-INFO-FDA (1-888-463-6332), or on the World Wide Web at **www.fda.gov**.

General References

In addition to the resources provided earlier in this chapter, the following general references describe medications (sorted alphabetically by title; hyperlinks provide rankings, information and reviews at Amazon.com):

- **Antifolate Drugs in Cancer Therapy (Cancer Drug Discovery and Development)** by Ann L. Jackman (Editor); Hardcover: 480 pages; (March 1999), Humana Press; ISBN: 0896035964; **http://www.amazon.com/exec/obidos/ASIN/0896035964/icongroupinterna**
- **Consumers Guide to Cancer Drugs** by Gail M. Wilkes, et al; Paperback - 448 pages, 1st edition (January 15, 2000), Jones & Bartlett Publishing; ISBN:

[140] This section has been adapted from **http://www.fda.gov/opacom/lowlit/medfraud.html**.

0763711705;
http://www.amazon.com/exec/obidos/ASIN/0763711705/icongroupinterna

- **Patient Education Guide to Oncology Drugs (Book with CD-ROM)** by Gail M. Wilkes, et al; CD-ROM - 447 pages, 1st edition (January 15, 2000), Jones & Bartlett Publishing; ISBN: 076371173X;
http://www.amazon.com/exec/obidos/ASIN/076371173X/icongroupinterna
- **The Role of Multiple Intensification in Medical Oncology** by M. S. Aapro (Editor), D. Maraninchi (Editor); Hardcover (June 1998), Springer Verlag; ISBN: 3540635432;
http://www.amazon.com/exec/obidos/ASIN/3540635432/icongroupinterna

Vocabulary Builder

The following vocabulary builder gives definitions of words used in this chapter that have not been defined in previous chapters:

Aspirin: A drug that reduces pain, fever, inflammation, and blood clotting. Aspirin belongs to the family of drugs called nonsteroidal anti-inflammatory agents. It is also being studied in cancer prevention. [NIH]

Preclinical: Before a disease becomes clinically recognizable. [EU]

Serum: The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed. [NIH]

APPENDIX B. RESEARCHING ALTERNATIVE MEDICINE

Overview[141]

Research indicates that the use of complementary and alternative therapies is increasing. A large-scale study published in the November 11, 1998, issue of the Journal of the American Medical Association found that CAM use among the general public increased from 34 percent in 1990 to 42 percent in 1997.

Several surveys of CAM use by cancer patients have been conducted with small numbers of patients. One study published in the February 2000 issue of the journal *Cancer* reported that 37 percent of 46 patients with prostate cancer used one or more CAM therapies as part of their cancer treatment. These therapies included herbal remedies, old-time remedies, vitamins, and special diets. A larger study of CAM use in patients with different types of cancer was published in the July 2000 issue of the Journal of Clinical Oncology . That study found that 83 percent of 453 cancer patients had used at least one CAM therapy as part of their cancer treatment. The study included CAM therapies such as special diets, psychotherapy, spiritual practices, and vitamin supplements. When psychotherapy and spiritual practices were excluded, 69 percent of patients had used at least one CAM therapy in their cancer treatment.

In this chapter, we will begin by giving you a broad perspective on complementary and alternative therapies. Next, we will introduce you to official information sources on CAM relating to childhood non-Hodgkin's lymphoma. Finally, at the conclusion of this chapter, we will provide a list of readings on childhood non-Hodgkin's lymphoma from various authors. We will begin, however, with the National Center for Complementary and

[141]Adapted from the NCI: **http://cis.nci.nih.gov/fact/9_14.htm**

Alternative Medicine's (NCCAM) overview of complementary and alternative medicine.

What Is CAM?[142]

Complementary and alternative medicine (CAM) covers a broad range of healing philosophies, approaches, and therapies. Generally, it is defined as those treatments and healthcare practices which are not taught in medical schools, used in hospitals, or reimbursed by medical insurance companies. Many CAM therapies are termed "holistic," which generally means that the healthcare practitioner considers the whole person, including physical, mental, emotional, and spiritual health. Some of these therapies are also known as "preventive," which means that the practitioner educates and treats the person to prevent health problems from arising, rather than treating symptoms after problems have occurred.

People use CAM treatments and therapies in a variety of ways. Therapies are used alone (often referred to as alternative), in combination with other alternative therapies, or in addition to conventional treatment (sometimes referred to as complementary). Complementary and alternative medicine, or "integrative medicine," includes a broad range of healing philosophies, approaches, and therapies. Some approaches are consistent with physiological principles of Western medicine, while others constitute healing systems with non-Western origins. While some therapies are far outside the realm of accepted Western medical theory and practice, others are becoming established in mainstream medicine.

Complementary and alternative therapies are used in an effort to prevent illness, reduce stress, prevent or reduce side effects and symptoms, or control or cure disease. Some commonly used methods of complementary or alternative therapy include mind/body control interventions such as visualization and relaxation, manual healing including acupressure and massage, homeopathy, vitamins or herbal products, and acupuncture.

Should you wish to explore non-traditional types of treatment, be sure to discuss all issues concerning treatments and therapies with your child's healthcare provider, whether a physician or practitioner of complementary and alternative medicine. Competent healthcare management requires that the practitioner know of all conventional and alternative therapies that your child is taking.

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[142] Adapted from the NCCAM: **http://nccam.nih.gov/nccam/fcp/faq/index.html#what-is**.

The decision to use complementary and alternative treatments is an important one. Consider before selecting an alternative therapy, the safety and effectiveness of the therapy or treatment, the expertise and qualifications of the healthcare practitioner, and the quality of delivery. These topics should be considered when selecting any practitioner or therapy.

What Are the Domains of Alternative Medicine?[143]

The list of CAM practices changes continually. The reason being is that these new practices and therapies are often proved to be safe and effective, and therefore become generally accepted as "mainstream" healthcare practices. Today, CAM practices may be grouped within five major domains: (1) alternative medical systems, (2) mind-body interventions, (3) biologically-based treatments, (4) manipulative and body-based methods, and (5) energy therapies. The individual systems and treatments comprising these categories are too numerous to list in this sourcebook. Thus, only limited examples are provided within each.

Alternative Medical Systems

Alternative medical systems involve complete systems of theory and practice that have evolved independent of, and often prior to, conventional biomedical approaches. Many are traditional systems of medicine that are practiced by individual cultures throughout the world, including a number of venerable Asian approaches.

Traditional oriental medicine emphasizes the balance or disturbances of qi (pronounced chi) or vital energy in health and illness, respectively. Traditional oriental medicine consists of a group of techniques and methods including acupuncture, herbal medicine, oriental massage, and qi gong (a form of energy therapy). Acupuncture involves stimulating specific anatomic points in the body for therapeutic purposes, usually by puncturing the skin with a thin needle.

Ayurveda is India's traditional system of medicine. Ayurvedic medicine (meaning "science of life") is a comprehensive system of medicine that places equal emphasis on body, mind, and spirit. Ayurveda strives to restore the innate harmony of the individual. Some of the primary Ayurvedic

[143] Adapted from the NCCAM: **http://nccam.nih.gov/nccam/fcp/classify/index.html**.

treatments include diet, exercise, meditation, herbs, massage, exposure to sunlight, and controlled breathing.

Other traditional healing systems have been developed by the world's indigenous populations. These populations include Native American, Aboriginal, African, Middle Eastern, Tibetan, and Central and South American cultures. Homeopathy and naturopathy are also examples of complete alternative medicine systems.

Homeopathic medicine is an unconventional Western system that is based on the principle that "like cures like," i.e., that the same substance that in large doses produces the symptoms of an illness, in very minute doses cures it. Homeopathic health practitioners believe that the more dilute the remedy, the greater its potency. Therefore, they use small doses of specially prepared plant extracts and minerals to stimulate the body's defense mechanisms and healing processes in order to treat illness.

Naturopathic medicine is based on the theory that a medical condition is the manifestation of alterations in the processes by which the body naturally heals itself and emphasizes health restoration rather than treatment for the condition itself. Naturopathic physicians employ an array of healing practices, including the following: diet and clinical nutrition, homeopathy, acupuncture, herbal medicine, hydrotherapy (the use of water in a range of temperatures and methods of applications), spinal and soft-tissue manipulation, physical therapies (such as those involving electrical currents, ultrasound, and light), therapeutic counseling, and pharmacology.

Mind-Body Interventions

Mind-body interventions employ a variety of techniques designed to facilitate the mind's capacity to affect bodily function and symptoms. Only a select group of mind-body interventions having well-documented theoretical foundations are considered CAM. For example, patient education and cognitive-behavioral approaches are now considered "mainstream." On the other hand, complementary and alternative medicine includes meditation, certain uses of hypnosis, dance, music, and art therapy, as well as prayer and mental healing.

Biological-Based Therapies

This category of CAM includes natural and biological-based practices, interventions, and products, many of which overlap with conventional medicine's use of dietary supplements. This category includes herbal, special dietary, orthomolecular, and individual biological therapies.

Herbal therapy employs an individual herb or a mixture of herbs for healing purposes. An herb is a plant or plant part that produces and contains chemical substances that act upon the body. Special diet therapies, such as those proposed by Drs. Atkins, Ornish, Pritikin, and Weil, are believed to prevent and/or control illness as well as promote health. Orthomolecular therapies aim to treat medical conditions with varying concentrations of chemicals such as magnesium, melatonin, and mega-doses of vitamins. Biological therapies include, for example, the use of laetrile and shark cartilage to treat cancer and the use of bee pollen to treat autoimmune and inflammatory conditions.

Manipulative and Body-Based Methods

This category includes methods that are based on manipulation and/or movement of the body. For example, chiropractors focus on the relationship between structure and function, primarily pertaining to the spine, and how that relationship affects the preservation and restoration of health. Chiropractors use manipulative therapy as an integral treatment tool.

In contrast, osteopaths place particular emphasis on the musculoskeletal system and practice osteopathic manipulation. Osteopaths believe that all of the body's systems work together and that disturbances in one system may have an impact upon function elsewhere in the body. Massage therapists manipulate the soft tissues of the body to normalize those tissues.

Energy Therapies

Energy therapies focus on energy fields originating within the body (biofields) or those from other sources (electromagnetic fields). Biofield therapies are intended to affect energy fields (the existence of which is not yet experimentally proven) that surround and penetrate the human body. Some forms of energy therapy manipulate biofields by applying pressure and/or manipulating the body by placing the hands in or through these fields. Examples include Qi gong, Reiki and Therapeutic Touch.

Qi gong is a component of traditional oriental medicine that combines movement, meditation, and regulation of breathing to enhance the flow of vital energy (qi) in the body, improve blood circulation, and enhance immune function. Reiki, the Japanese word representing Universal Life Energy, is based on the belief that, by channeling spiritual energy through the practitioner, the spirit is healed and, in turn, heals the physical body. Therapeutic Touch is derived from the ancient technique of "laying-on of hands." It is based on the premises that the therapist's healing force affects recovery and that healing is promoted when the body's energies are in balance. By passing their hands over the patient, these healers identify energy imbalances.

Bioelectromagnetic-based therapies involve the unconventional use of electromagnetic fields to treat illnesses or manage pain. These therapies are often used to treat asthma, cancer, and migraine headaches. Types of electromagnetic fields which are manipulated in these therapies include pulsed fields, magnetic fields, and alternating current or direct current fields.

How Are Complementary and Alternative Approaches Evaluated?[144]

It is important that the same scientific evaluation which is used to assess conventional approaches be used to evaluate complementary and alternative therapies. A number of medical centers are evaluating complementary and alternative therapies by developing clinical trials (research studies with people) to test them.

Conventional approaches to cancer treatment have generally been studied for safety and effectiveness through a rigorous scientific process, including clinical trials with large numbers of patients. Often, less is known about the safety and effectiveness of complementary and alternative methods. Some of these complementary and alternative therapies have not undergone rigorous evaluation. Others, once considered unorthodox, are finding a place in cancer treatment—not as cures, but as complementary therapies that may help patients feel better and recover faster. One example is acupuncture. According to a panel of experts at a National Institutes of Health (NIH) Consensus Conference in November 1997, acupuncture has been found to be effective in the management of chemotherapy-associated nausea and vomiting and in controlling pain associated with surgery. Some approaches, such as laetrile, have been studied and found ineffective or potentially harmful.

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[144]Adapted from the NCI: **http://cis.nci.nih.gov/fact/9_14.htm**

NCI-Sponsored Clinical Trials in Complementary and Alternative Medicine

The NCI is currently sponsoring several clinical trials (research studies with patients) that study complementary and alternative treatments for cancer. Current trials include enzyme therapy with nutritional support for the treatment of inoperable pancreatic cancer, shark cartilage therapy for the treatment of non-small cell lung cancer, and studies of the effects of diet on prostate and breast cancers. Some of these trials compare alternative therapies with conventional treatments, while others study the effects of complementary approaches used in addition to conventional treatments. Patients who are interested in taking part in these or any clinical trials should talk with their doctor.

More information about clinical trials sponsored by the NCI can be obtained from NCCAM (http://nccam.nih.gov, 1-888-644-6226), OCCAM (http://occam.nci.nih.gov), and the NCI's Cancer Information Service (CIS) (http://cis.nci.nih.gov, 1-800-4-CANCER).

Questions to Ask Your Child's Healthcare Provider about CAM

When considering complementary and alternative therapies, ask your child's healthcare provider the following questions:

- What benefits can be expected from this therapy?
- What are the risks associated with this therapy?
- Do the known benefits outweigh the risks?
- What side effects can be expected?
- Will the therapy interfere with conventional treatment?
- Is this therapy part of a clinical trial? If so, who is sponsoring the trial?
- Will the therapy be covered by health insurance?
- How can patients and their health care providers learn more about complementary and alternative therapies?

Levels of Evidence for Human Studies of CAM for Cancer[145]

A classification system has been developed by the National Cancer Institute's PDQ Adult Treatment Editorial Board to allow the ranking of human cancer treatment studies according to statistical strength of the study design and scientific strength of the treatment outcomes (i.e., endpoints) measured. This classification system has been adapted to allow the ranking of human studies of complementary and alternative medicine treatments for cancer. The purpose of classifying studies in this way is to assist readers in evaluating the strength of the evidence associated with particular treatments. However, not all human studies are classified. Only those reporting a therapeutic endpoint(s), such as tumor response, improvement in survival, or measured improvement in quality of life, are considered. In addition, anecdotal reports and individual case reports are not classified because important clinical details are often missing, the evidence from them is generally considered weak, and there is an increased probability that similar results (either positive or negative) will not be obtained with other patients. Furthermore, reports of case series are excluded when the description of clinical findings is so incomplete as to hinder proper assessment and interpretation.

Finding CAM References on Childhood Non-Hodgkin's Lymphoma

Having read the previous discussion, you may be wondering which complementary or alternative treatments might be appropriate for childhood non-Hodgkin's lymphoma. For the remainder of this chapter, we will direct you to a number of official sources which can assist you in researching studies and publications. Some of these articles are rather technical, so some patience may be required.

National Center for Complementary and Alternative Medicine

The National Center for Complementary and Alternative Medicine (NCCAM) of the National Institutes of Health (**http://nccam.nih.gov**) has created a link to the National Library of Medicine's databases to allow parents to search for articles that specifically relate to childhood non-

[145] For more information, visit the NCI's Web page dedicated to this topic: **http://www.cancer.gov/cancer_information/doc.aspx?viewid=47595A5D-AD15-4F7D-BAE6-DEA914E6C153**

Hodgkin's lymphoma and complementary medicine. To search the database, go to the following Web site: **www.nlm.nih.gov/nccam/camonpubmed.html**. Select "CAM on PubMed." Enter "childhood non-Hodgkin's lymphoma" (or synonyms) into the search box. Click "Go." The following references provide information on particular aspects of complementary and alternative medicine (CAM) that are related to childhood non-Hodgkin's lymphoma:

- **A new therapy schedule for pediatric non-Hodgkin lymphoma toxicity with preliminary results.**
  Author(s): Meadows AT, Jenkin RD, Anderson J, Chilcote R, Coccia P, Exelby P, Kushner J, Leikin S, Siegel S, Wilson JF, Hammond D.
  Source: Medical and Pediatric Oncology. 1980; 8(1): 15-24.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7003336&dopt=Abstract

- **A new treatment protocol for childhood non-Hodgkin's lymphoma: preliminary evaluation.**
  Author(s): de Andrea ML, de Camargo B, Melaragno R.
  Source: Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology. 1990 April; 8(4): 666-71.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2179479&dopt=Abstract

- **A novel treatment of childhood lymphoblastic non-Hodgkin's lymphoma: early and intermittent use of teniposide plus cytarabine.**
  Author(s): Dahl GV, Rivera G, Pui CH, Mirro J Jr, Ochs J, Kalwinsky DK, Abromowitch M, Look AT, Murphy SB.
  Source: Blood. 1985 November; 66(5): 1110-4.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3840395&dopt=Abstract

- **A rare entity among childhood malignant lymphomas (large anaplastic T-cell Ki-1 +).**
  Author(s): Ulukutlu L, Hitzig W, Maurer R.
  Source: Turk J Pediatr. 1992 January-March; 34(1): 37-41. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1509528&dopt=Abstract

- **Activity of cyclosporins as resistance modifiers in primary cultures of human haematological and solid tumours.**
  Author(s): Fridborg H, Jonsson B, Nygren P, Csoka K, Nilsson K, Oberg G, Kristensen J, Bergh J, Tholander B, Olsen L, et al.

Source: British Journal of Cancer. 1994 July; 70(1): 11-7.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8018519&dopt=Abstract

- **Anaplastic large cell lymphoma in childhood: analysis of 72 patients treated on The United Kingdom Children's Cancer Study Group chemotherapy regimens.**
  Author(s): Williams DM, Hobson R, Imeson J, Gerrard M, McCarthy K, Pinkerton CR.
  Source: British Journal of Haematology. 2002 June; 117(4): 812-20. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12060115&dopt=Abstract

- **APO therapy for malignant lymphoma of large cell "histiocytic" type of childhood: analysis of treatment results for 29 patients.**
  Author(s): Weinstein HJ, Lack EE, Cassady JR.
  Source: Blood. 1984 August; 64(2): 422-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6378276&dopt=Abstract

- **CD30(+) anaplastic large-cell lymphoma in children: analysis of 82 patients enrolled in two consecutive studies of the French Society of Pediatric Oncology.**
  Author(s): Brugieres L, Deley MC, Pacquement H, Meguerian-Bedoyan Z, Terrier-Lacombe MJ, Robert A, Pondarre C, Leverger G, Devalck C, Rodary C, Delsol G, Hartmann O.
  Source: Blood. 1998 November 15; 92(10): 3591-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9808552&dopt=Abstract

- **Childhood abdominal lymphoma in two brothers.**
  Author(s): Pevzner S, Leef F.
  Source: Isr J Med Sci. 1973 July; 9(7): 914-7. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=4732928&dopt=Abstract

- **Childhood anaplastic large cell lymphoma Ki-1/CD30: clinicopathologic features of 19 cases.**
  Author(s): Rubie H, Gladieff L, Robert A, Gaubert I, Huguet F, Rochaix P, Pein F, Michel G, Hoerni B, Sommelet D, et al.

Source: Medical and Pediatric Oncology. 1994; 22(3): 155-61.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8272005&dopt=Abstract

- **Childhood Ki-1 lymphoma: presentation as a buttock mass.**
  Author(s): Winter SS, Duncan MH, Foucar E, McConnell TS, Cartwright KC.
  Source: The American Journal of Pediatric Hematology/Oncology. 1991 Fall; 13(3): 334-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1724356&dopt=Abstract

- **Childhood non-Hodgkin's lymphoma in Egypt: preliminary results of treatment with a new ifosfamide-containing regimen.**
  Author(s): Gad-el-Mawla N, Hussein MH, Abdel-Hadi S, el-Taneer O, Adde M, Magrath I.
  Source: Cancer Chemotherapy and Pharmacology. 1989; 24 Suppl 1: S20-3.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2758567&dopt=Abstract

- **Childhood non-Hodgkin's lymphoma. The results of a randomized therapeutic trial comparing a 4-drug regimen (COMP) with a 10-drug regimen (LSA2-L2).**
  Author(s): Anderson JR, Wilson JF, Jenkin DT, Meadows AT, Kersey J, Chilcote RR, Coccia P, Exelby P, Kushner J, Siegel S, Hammond D.
  Source: The New England Journal of Medicine. 1983 March 10; 308(10): 559-65.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6338381&dopt=Abstract

- **Childhood non-Hodgkin's lymphoma--a study of 17 cases in Israel.**
  Author(s): Aghai E, Hulu N, Virag I, Kende G, Ramot B.
  Source: Cancer. 1974 May; 33(5): 1411-6. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=4362957&dopt=Abstract

- **Current trends in childhood acute lymphocytic leukemia and non-hodgkin's lymphoma.**
  Author(s): Castleberry RP.

Source: Ala J Med Sci. 1981 July; 18(3): 243-8. No Abstract Available.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6945058&dopt=Abstract

- **Disseminated nonlymphoblastic lymphoma of childhood: a Childrens Cancer Group study, CCG-552.**
  Author(s): Finlay JL, Anderson JR, Cecalupo AJ, Hutchinson RJ, Kadin ME, Kjeldsberg CR, Provisor AJ, Woods WG, Meadows AT.
  Source: Medical and Pediatric Oncology. 1994; 23(6): 453-63.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7935170&dopt=Abstract

- **Effective multi-agent chemotherapy for advanced abdominal lymphoma and FAB L3 leukemia of childhood.**
  Author(s): Toogood IR, Tiedemann K, Stevens M, Smith PJ.
  Source: Medical and Pediatric Oncology. 1993; 21(2): 103-10.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8433675&dopt=Abstract

- **Epipodophyllotoxins in the treatment of childhood cancer.**
  Author(s): Rivera GK, Pui CH, Santana VM, Pratt CB, Crist WM.
  Source: Cancer Chemotherapy and Pharmacology. 1994; 34 Suppl: S89-95. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8070034&dopt=Abstract

- **Etoposide: twenty years later.**
  Author(s): Hainsworth JD, Greco FA.
  Source: Annals of Oncology : Official Journal of the European Society for Medical Oncology / Esmo. 1995 April; 6(4): 325-41. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7619747&dopt=Abstract

- **Evaluation of the LSA2L2 protocol for treatment of childhood non-Hodgkin's lymphoma. A report from the Polish Children's Leukemia/Lymphoma Study Group.**
  Author(s): Boguslawska-Jaworska J, Koscielniak E, Sroczynska M, Sonta-Jakimczyk D, Armata J, Balwierz W, Ciepielewska D, Kaczmarek-Kanold M, Ochocka M, Radwanska U, et al.

Source: The American Journal of Pediatric Hematology/Oncology. 1984 Winter; 6(4): 363-70.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6549496&dopt=Abstract

- **Factors of prognostic importance in childhood non-Hodgkin's lymphoma treated with two modified LSA2-L2 protocols. A multivariate analysis approach.**
  Author(s): de Andrea ML, de Camargo B, Correa Alves A, Machado JC, Franco EL.
  Source: Cancer. 1988 July 15; 62(2): 240-50.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3383125&dopt=Abstract

- **Favorable outcome for children and adolescents with T-cell lymphoblastic lymphoma with an intensive ALL-type therapy without local radiotherapy.**
  Author(s): Grenzebach J, Schrappe M, Ludwig WD, Parwaresch R, Zimmermann M, Gadner H, Riehm H, Reiter A.
  Source: Annals of Hematology. 2001; 80 Suppl 3: B73-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11757713&dopt=Abstract

- **Granulocyte colony-stimulating factor in induction treatment of children with non-Hodgkin's lymphoma: a randomized study of the French Society of Pediatric Oncology.**
  Author(s): Patte C, Laplanche A, Bertozzi AI, Baruchel A, Frappaz D, Schmitt C, Mechinaud F, Nelken B, Boutard P, Michon J.
  Source: Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology. 2002 January 15; 20(2): 441-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11786572&dopt=Abstract

- **Hemophagocytic syndrome in Epstein-Barr virus-associated T-lymphoproliferative disorders: disease spectrum, pathogenesis, and management.**
  Author(s): Su IJ, Wang CH, Cheng AL, Chen RL.
  Source: Leukemia & Lymphoma. 1995 November; 19(5-6): 401-6. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8590839&dopt=Abstract

- **High-dose cyclophosphamide-high-dose methotrexate with coordinated intrathecal therapy for advanced nonlymphoblastic lymphoma of childhood: results of a Pediatric Oncology Group study.**
  Author(s): Sullivan MP, Brecher M, Ramirez I, Ragab A, Hvizdala E, Pullen J, Shuster J, Berard C, Crist W, Vietti T.
  Source: The American Journal of Pediatric Hematology/Oncology. 1991 Fall; 13(3): 288-95.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1793154&dopt=Abstract

- **High-dose methotrexate and continuous infusion Ara-C in children's non-Hodgkin's lymphoma: phase II studies and their use in further protocols.**
  Author(s): Patte C, Bernard A, Hartmann O, Kalifa C, Flamant F, Lemerle J.
  Source: Pediatric Hematology and Oncology. 1986; 3(1): 11-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3153214&dopt=Abstract

- **High-dose methotrexate therapy (6-8 g/m2) in childhood malignancies: clinical tolerability and pharmacokinetics.**
  Author(s): Slordal L, Kolmannskog S, Moe PJ, Prytz PS, Aarbakke J.
  Source: Pediatric Hematology and Oncology. 1987; 4(1): 33-42.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3152911&dopt=Abstract

- **Ifosfamide/carboplatin/etoposide (ICE) for recurrent malignant solid tumors of childhood: a Pediatric Oncology Group Phase I/II study.**
  Author(s): Kung FH, Desai SJ, Dickerman JD, Goorin AM, Harris MB, Inoue S, Krischer JP, Murphy SB, Pratt CB, Toledano S, et al.
  Source: Journal of Pediatric Hematology/Oncology : Official Journal of the American Society of Pediatric Hematology/Oncology. 1995 August; 17(3): 265-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7620926&dopt=Abstract

- **Ifosfamide/carboplatin/etoposide (ICE), an effective salvaging therapy for recurrent malignant non-Hodgkin lymphoma of childhood: a Pediatric Oncology Group phase II study.**
  Author(s): Kung FH, Harris MB, Krischer JP.

Source: Medical and Pediatric Oncology. 1999 March; 32(3): 225-6. No Abstract Available.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10064193&dopt=Abstract

- **Improved treatment results in childhood B-cell neoplasms with tailored intensification of therapy: A report of the Berlin-Frankfurt-Munster Group Trial NHL-BFM 90.**
  Author(s): Reiter A, Schrappe M, Tiemann M, Ludwig WD, Yakisan E, Zimmermann M, Mann G, Chott A, Ebell W, Klingebiel T, Graf N, Kremens B, Muller-Weihrich S, Pluss HJ, Zintl F, Henze G, Riehm H.
  Source: Blood. 1999 November 15; 94(10): 3294-306.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10552938&dopt=Abstract

- **Improved treatment results of non-Hodgkin's lymphoma in children: a report from the Children's Cancer and Leukemia Study Group of Japan.**
  Author(s): Shimizu H, Kikuchi M, Takaue Y, Utsumi J, Takeda T, Fujimoto T.
  Source: International Journal of Hematology. 1995 February; 61(2): 85-96.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7734716&dopt=Abstract

- **Indications for and benefits of intensive therapies in treatment of childhood cancers.**
  Author(s): Lampkin BC, Wong KY.
  Source: Cancer. 1986 July 15; 58(2 Suppl): 481-7. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3521834&dopt=Abstract

- **Long-term follow-up of patients treated with COMP or LSA2L2 therapy for childhood non-Hodgkin's lymphoma: a report of CCG-551 from the Childrens Cancer Group.**
  Author(s): Anderson JR, Jenkin RD, Wilson JF, Kjeldsberg CR, Sposto R, Chilcote RR, Coccia PF, Exelby PR, Siegel S, Meadows AT, et al.
  Source: Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology. 1993 June; 11(6): 1024-32.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8501488&dopt=Abstract

- **Poor-risk non-lymphoblastic lymphoma of childhood: results of an intensive pilot study.**
  Author(s): Finlay JL, Trigg ME, Link MP, Frierdich S.
  Source: Medical and Pediatric Oncology. 1989; 17(1): 29-38.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2913472&dopt=Abstract

- **Precursor B-cell lymphoblastic lymphoma in childhood and adolescence: clinical features, treatment, and results in trials NHL-BFM 86 and 90.**
  Author(s): Neth O, Seidemann K, Jansen P, Mann G, Tiemann M, Ludwig WD, Riehm H, Reiter A.
  Source: Medical and Pediatric Oncology. 2000 July; 35(1): 20-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10881003&dopt=Abstract

- **Ten years' experience with LSA2-L2 therapy for childhood advanced lymphoblastic lymphoma.**
  Author(s): Katz JA, Hvizdala E, Shuster J, Falletta JM, Schwenn M, Murphy SB.
  Source: Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology. 1993 October; 11(10): 2054-5. No Abstract Available.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8410135&dopt=Abstract

- **Teniposide plus cytarabine as intensification therapy and in continuation therapy for advanced nonlymphoblastic lymphomas of childhood.**
  Author(s): Maluf PT, Odone Filho V, Cristofani LM, Britto JL, Almeida MT, Pontes E, Maksoud JG, Manissadjian A.
  Source: Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology. 1994 September; 12(9): 1963-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8083717&dopt=Abstract

- **Therapy for childhood non-Hodgkin's lymphomas, nonlymphoblastic type. Review of recent studies and current recommendations.**
  Author(s): Nachman J.

Source: The American Journal of Pediatric Hematology/Oncology. 1990 Fall; 12(3): 359-66. Review.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2240485&dopt=Abstract

Additional Web Resources

A number of additional Web sites offer encyclopedic information covering CAM and related topics. The following is a representative sample:

- Alternative Medicine Foundation, Inc.: **http://www.herbmed.org/**
- AOL: **http://search.aol.com/cat.adp?id=169&layer=&from=subcats**
- Chinese Medicine: **http://www.newcenturynutrition.com/**
- drkoop.com®: **http://www.drkoop.com/InteractiveMedicine/IndexC.html**
- Family Village: **http://www.familyvillage.wisc.edu/med_altn.htm**
- Google: **http://directory.google.com/Top/Health/Alternative/**
- Healthnotes: **http://www.thedacare.org/healthnotes/**
- Open Directory Project: **http://dmoz.org/Health/Alternative/**
- TPN.com: **http://www.tnp.com/**
- Yahoo.com: **http://dir.yahoo.com/Health/Alternative_Medicine/**
- WebMD®Health: **http://my.webmd.com/drugs_and_herbs**
- WellNet: **http://www.wellnet.ca/herbsa-c.htm**
- WholeHealthMD.com: **http://www.wholehealthmd.com/reflib/0,1529,,00.html**

General References

A good place to find general background information on CAM is the National Library of Medicine. It has prepared within the MEDLINEplus system an information topic page dedicated to complementary and alternative medicine. To access this page, go to the MEDLINEplus site at: **www.nlm.nih.gov/medlineplus/alternativemedicine.html.** This Web site provides a general overview of various topics and can lead to a number of general sources. The following additional references describe, in broad terms, alternative and complementary medicine (sorted alphabetically by

title; hyperlinks provide rankings, information, and reviews at Amazon.com):

- **Alternative Medicine Definitive Guide to Cancer** by W. John Diamond, et al; Hardcover - 1120 pages Package edition (March 18, 1997), Alternativemedicine.Com Books; ISBN: 1887299017; **http://www.amazon.com/exec/obidos/ASIN/1887299017/icongroupinterna**
- **Beating Cancer With Nutrition - Revised** by Patrick Quillin, Noreen Quillin (Contributor); Paperback - 352 pages; Book & CD edition (January 1, 2001), Bookworld Services; ISBN: 0963837281; **http://www.amazon.com/exec/obidos/ASIN/0963837281/icongroupinterna**
- **Cancer: Increasing Your Odds for Survival - A Resource Guide for Integrating Mainstream, Alternative and Complementary Therapies** by David Bognar, Walter Cronkite; Paperback (August 1998), Hunter House; ISBN: 0897932471; **http://www.amazon.com/exec/obidos/ASIN/0897932471/icongroupinterna**
- **Choices in Healing** by Michael Lerner; Paperback - 696 pages; (February 28, 1996), MIT Press; ISBN: 0262621045; **http://www.amazon.com/exec/obidos/ASIN/0262621045/icongroupinterna**
- **The Gerson Therapy: The Amazing Nutritional Program for Cancer and Other Illnesses** by Charlotte Gerson, Morton Walker, D.P.M.; Paperback - 448 pages (October 2001), Kensington Publishing Corp.; ISBN: 1575666286; **http://www.amazon.com/exec/obidos/ASIN/1575666286/icongroupinterna**
- **Natural Compounds in Cancer Therapy** by John C. Boik; Paperback - 520 pages (March 2001), Oregon Medical Press; ISBN: 0964828014; **http://www.amazon.com/exec/obidos/ASIN/0964828014/icongroupinterna**
- **There's No Place Like Hope: A Guide to Beating Cancer in Mind-Sized Bites** by Vickie Girard, Dan Zadra (Editor); Hardcover - 161 pages (April 2001), Compendium Inc.; ISBN: 1888387416; **http://www.amazon.com/exec/obidos/ASIN/1888387416/icongroupinterna**
- **Your Life in Your Hands** by Jane A. Plant, Ph.D; Hardcover - 272 pages (December 13, 2000), St. Martins Press (Trade); ISBN: 0312275617; **http://www.amazon.com/exec/obidos/ASIN/0312275617/icongroupinterna**

For additional information on complementary and alternative medicine, ask your child's doctor or write to:

National Institutes of Health
National Center for Complementary and Alternative Medicine Clearinghouse
P. O. Box 8218
Silver Spring, MD 20907-8218

APPENDIX C. FINDING MEDICAL LIBRARIES

Overview

At a medical library you can find medical texts and reference books, consumer health publications, specialty newspapers and magazines, as well as medical journals. In this appendix, we show you how to quickly find a medical library in your area.

Preparation

Before going to the library, highlight the references mentioned in this sourcebook that you find interesting. Focus on those items that are not available via the Internet, and ask the reference librarian for help with your search. He or she may know of additional resources that could be helpful to you. Most importantly, your local public library and medical libraries have Interlibrary Loan programs with the National Library of Medicine (NLM), one of the largest medical collections in the world. According to the NLM, most of the literature in the general and historical collections of the National Library of Medicine is available on interlibrary loan to any library. NLM's interlibrary loan services are only available to libraries. If you would like to access NLM medical literature, then visit a library in your area that can request the publications for you.[146]

[146] Adapted from the NLM: **http://www.nlm.nih.gov/psd/cas/interlibrary.html**.

Finding a Local Medical Library

The quickest method to locate medical libraries is to use the Internet-based directory published by the National Network of Libraries of Medicine (NN/LM). This network includes 4626 members and affiliates that provide many services to librarians, health professionals, and the public. To find a library in your area, simply visit **http://nnlm.gov/members/adv.html** or call 1-800-338-7657.

Medical Libraries Open to the Public

In addition to the NN/LM, the National Library of Medicine (NLM) lists a number of libraries that are generally open to the public and have reference facilities. The following is the NLM's list plus hyperlinks to each library Web site. These Web pages can provide information on hours of operation and other restrictions. The list below is a small sample of libraries recommended by the National Library of Medicine (sorted alphabetically by name of the U.S. state or Canadian province where the library is located):[147]

- **Alabama:** Health InfoNet of Jefferson County (Jefferson County Library Cooperative, Lister Hill Library of the Health Sciences), **http://www.uab.edu/infonet/**
- **Alabama:** Richard M. Scrushy Library (American Sports Medicine Institute), **http://www.asmi.org/LIBRARY.HTM**
- **Arizona:** Samaritan Regional Medical Center: The Learning Center (Samaritan Health System, Phoenix, Arizona), **http://www.samaritan.edu/library/bannerlibs.htm**
- **California:** Kris Kelly Health Information Center (St. Joseph Health System), **http://www.humboldt1.com/~kkhic/index.html**
- **California:** Community Health Library of Los Gatos (Community Health Library of Los Gatos), **http://www.healthlib.org/orgresources.html**
- **California:** Consumer Health Program and Services (CHIPS) (County of Los Angeles Public Library, Los Angeles County Harbor-UCLA Medical Center Library) - Carson, CA, **http://www.colapublib.org/services/chips.html**
- **California:** Gateway Health Library (Sutter Gould Medical Foundation)
- **California:** Health Library (Stanford University Medical Center), **http://www-med.stanford.edu/healthlibrary/**

[147] Adapted from **http://www.nlm.nih.gov/medlineplus/libraries.html**.

- **California:** Patient Education Resource Center - Health Information and Resources (University of California, San Francisco), **http://sfghdean.ucsf.edu/barnett/PERC/default.asp**
- **California:** Redwood Health Library (Petaluma Health Care District), **http://www.phcd.org/rdwdlib.html**
- **California:** San José PlaneTree Health Library, **http://planetreesanjose.org/**
- **California:** Sutter Resource Library (Sutter Hospitals Foundation), **http://go.sutterhealth.org/comm/resc-library/sac-resources.html**
- **California:** University of California, Davis. Health Sciences Libraries
- **California:** ValleyCare Health Library & Ryan Comer Cancer Resource Center (ValleyCare Health System), **http://www.valleycare.com/library.html**
- **California:** Washington Community Health Resource Library (Washington Community Health Resource Library), **http://www.healthlibrary.org/**
- **Colorado:** William V. Gervasini Memorial Library (Exempla Healthcare), **http://www.exempla.org/conslib.htm**
- **Connecticut:** Hartford Hospital Health Science Libraries (Hartford Hospital), **http://www.harthosp.org/library/**
- **Connecticut:** Healthnet: Connecticut Consumer Health Information Center (University of Connecticut Health Center, Lyman Maynard Stowe Library), **http://library.uchc.edu/departm/hnet/**
- **Connecticut:** Waterbury Hospital Health Center Library (Waterbury Hospital), **http://www.waterburyhospital.com/library/consumer.shtml**
- **Delaware:** Consumer Health Library (Christiana Care Health System, Eugene du Pont Preventive Medicine & Rehabilitation Institute), **http://www.christianacare.org/health_guide/health_guide_pmri_health_info.cfm**
- **Delaware:** Lewis B. Flinn Library (Delaware Academy of Medicine), **http://www.delamed.org/chls.html**
- **Georgia:** Family Resource Library (Medical College of Georgia), **http://cmc.mcg.edu/kids_families/fam_resources/fam_res_lib/frl.htm**
- **Georgia:** Health Resource Center (Medical Center of Central Georgia), **http://www.mccg.org/hrc/hrchome.asp**
- **Hawaii:** Hawaii Medical Library: Consumer Health Information Service (Hawaii Medical Library), **http://hml.org/CHIS/**

- **Idaho:** DeArmond Consumer Health Library (Kootenai Medical Center), **http://www.nicon.org/DeArmond/index.htm**
- **Illinois:** Health Learning Center of Northwestern Memorial Hospital (Northwestern Memorial Hospital, Health Learning Center), **http://www.nmh.org/health_info/hlc.html**
- **Illinois:** Medical Library (OSF Saint Francis Medical Center), **http://www.osfsaintfrancis.org/general/library/**
- **Kentucky:** Medical Library - Services for Patients, Families, Students & the Public (Central Baptist Hospital), **http://www.centralbap.com/education/community/library.htm**
- **Kentucky:** University of Kentucky - Health Information Library (University of Kentucky, Chandler Medical Center, Health Information Library), **http://www.mc.uky.edu/PatientEd/**
- **Louisiana:** Alton Ochsner Medical Foundation Library (Alton Ochsner Medical Foundation), **http://www.ochsner.org/library/**
- **Louisiana:** Louisiana State University Health Sciences Center Medical Library-Shreveport, **http://lib-sh.lsuhsc.edu/**
- **Maine:** Franklin Memorial Hospital Medical Library (Franklin Memorial Hospital), **http://www.fchn.org/fmh/lib.htm**
- **Maine:** Gerrish-True Health Sciences Library (Central Maine Medical Center), **http://www.cmmc.org/library/library.html**
- **Maine:** Hadley Parrot Health Science Library (Eastern Maine Healthcare), **http://www.emh.org/hll/hpl/guide.htm**
- **Maine:** Maine Medical Center Library (Maine Medical Center), **http://www.mmc.org/library/**
- **Maine:** Parkview Hospital, **http://www.parkviewhospital.org/communit.htm#Library**
- **Maine:** Southern Maine Medical Center Health Sciences Library (Southern Maine Medical Center), **http://www.smmc.org/services/service.php3?choice=10**
- **Maine:** Stephens Memorial Hospital Health Information Library (Western Maine Health), **http://www.wmhcc.com/hil_frame.html**
- **Manitoba, Canada:** Consumer & Patient Health Information Service (University of Manitoba Libraries), **http://www.umanitoba.ca/libraries/units/health/reference/chis.html**
- **Manitoba, Canada:** J.W. Crane Memorial Library (Deer Lodge Centre), **http://www.deerlodge.mb.ca/library/libraryservices.shtml**

- **Maryland:** Health Information Center at the Wheaton Regional Library (Montgomery County, Md., Dept. of Public Libraries, Wheaton Regional Library), **http://www.mont.lib.md.us/healthinfo/hic.asp**
- **Massachusetts:** Baystate Medical Center Library (Baystate Health System), **http://www.baystatehealth.com/1024/**
- **Massachusetts:** Boston University Medical Center Alumni Medical Library (Boston University Medical Center), **http://med-libwww.bu.edu/library/lib.html**
- **Massachusetts:** Lowell General Hospital Health Sciences Library (Lowell General Hospital), **http://www.lowellgeneral.org/library/HomePageLinks/WWW.htm**
- **Massachusetts:** Paul E. Woodard Health Sciences Library (New England Baptist Hospital), **http://www.nebh.org/health_lib.asp**
- **Massachusetts:** St. Luke's Hospital Health Sciences Library (St. Luke's Hospital), **http://www.southcoast.org/library/**
- **Massachusetts:** Treadwell Library Consumer Health Reference Center (Massachusetts General Hospital), **http://www.mgh.harvard.edu/library/chrcindex.html**
- **Massachusetts:** UMass HealthNet (University of Massachusetts Medical School), **http://healthnet.umassmed.edu/**
- **Michigan:** Botsford General Hospital Library - Consumer Health (Botsford General Hospital, Library & Internet Services), **http://www.botsfordlibrary.org/consumer.htm**
- **Michigan:** Helen DeRoy Medical Library (Providence Hospital and Medical Centers), **http://www.providence-hospital.org/library/**
- **Michigan:** Marquette General Hospital - Consumer Health Library (Marquette General Hospital, Health Information Center), **http://www.mgh.org/center.html**
- **Michigan:** Patient Education Resouce Center - University of Michigan Cancer Center (University of Michigan Comprehensive Cancer Center), **http://www.cancer.med.umich.edu/learn/leares.htm**
- **Michigan:** Sladen Library & Center for Health Information Resources - Consumer Health Information, **http://www.sladen.hfhs.org/library/consumer/index.html**
- **Montana:** Center for Health Information (St. Patrick Hospital and Health Sciences Center), **http://www.saintpatrick.org/chi/librarydetail.php3?ID=41**

- **National:** Consumer Health Library Directory (Medical Library Association, Consumer and Patient Health Information Section), **http://caphis.mlanet.org/directory/index.html**
- **National:** National Network of Libraries of Medicine (National Library of Medicine) - provides library services for health professionals in the United States who do not have access to a medical library, **http://nnlm.gov/**
- **National:** NN/LM List of Libraries Serving the Public (National Network of Libraries of Medicine), **http://nnlm.gov/members/**
- **Nevada:** Health Science Library, West Charleston Library (Las Vegas Clark County Library District), **http://www.lvccld.org/special_collections/medical/index.htm**
- **New Hampshire:** Dartmouth Biomedical Libraries (Dartmouth College Library), **http://www.dartmouth.edu/~biomed/resources.htmld/conshealth.htmld/**
- **New Jersey:** Consumer Health Library (Rahway Hospital), **http://www.rahwayhospital.com/library.htm**
- **New Jersey:** Dr. Walter Phillips Health Sciences Library (Englewood Hospital and Medical Center), **http://www.englewoodhospital.com/links/index.htm**
- **New Jersey:** Meland Foundation (Englewood Hospital and Medical Center), **http://www.geocities.com/ResearchTriangle/9360/**
- **New York:** Choices in Health Information (New York Public Library) - NLM Consumer Pilot Project participant, **http://www.nypl.org/branch/health/links.html**
- **New York:** Health Information Center (Upstate Medical University, State University of New York), **http://www.upstate.edu/library/hic/**
- **New York:** Health Sciences Library (Long Island Jewish Medical Center), **http://www.lij.edu/library/library.html**
- **New York:** ViaHealth Medical Library (Rochester General Hospital), **http://www.nyam.org/library/**
- **Ohio:** Consumer Health Library (Akron General Medical Center, Medical & Consumer Health Library), **http://www.akrongeneral.org/hwlibrary.htm**
- **Oklahoma:** Saint Francis Health System Patient/Family Resource Center (Saint Francis Health System), **http://www.sfh-tulsa.com/patientfamilycenter/default.asp**

- **Oregon:** Planetree Health Resource Center (Mid-Columbia Medical Center), **http://www.mcmc.net/phrc/**
- **Pennsylvania:** Community Health Information Library (Milton S. Hershey Medical Center), **http://www.hmc.psu.edu/commhealth/**
- **Pennsylvania:** Community Health Resource Library (Geisinger Medical Center), **http://www.geisinger.edu/education/commlib.shtml**
- **Pennsylvania:** HealthInfo Library (Moses Taylor Hospital), **http://www.mth.org/healthwellness.html**
- **Pennsylvania:** Hopwood Library (University of Pittsburgh, Health Sciences Library System), **http://www.hsls.pitt.edu/chi/hhrcinfo.html**
- **Pennsylvania:** Koop Community Health Information Center (College of Physicians of Philadelphia), **http://www.collphyphil.org/kooppg1.shtml**
- **Pennsylvania:** Learning Resources Center - Medical Library (Susquehanna Health System), **http://www.shscares.org/services/lrc/index.asp**
- **Pennsylvania:** Medical Library (UPMC Health System), **http://www.upmc.edu/passavant/library.htm**
- **Quebec, Canada:** Medical Library (Montreal General Hospital), **http://ww2.mcgill.ca/mghlib/**
- **South Dakota:** Rapid City Regional Hospital - Health Information Center (Rapid City Regional Hospital, Health Information Center), **http://www.rcrh.org/education/LibraryResourcesConsumers.htm**
- **Texas:** Houston HealthWays (Houston Academy of Medicine-Texas Medical Center Library), **http://hhw.library.tmc.edu/**
- **Texas:** Matustik Family Resource Center (Cook Children's Health Care System), **http://www.cookchildrens.com/Matustik_Library.html**
- **Washington:** Community Health Library (Kittitas Valley Community Hospital), **http://www.kvch.com/**
- **Washington:** Southwest Washington Medical Center Library (Southwest Washington Medical Center), **http://www.swmedctr.com/Home/**

APPENDIX D. YOUR CHILD'S RIGHTS AND INSURANCE

Overview

Parents face a series of issues related more to the healthcare industry than to their children's medical conditions. This appendix covers two important topics in this regard: your responsibilities and your child's rights as a patient, and how to get the most out of your child's medical insurance plan.

Your Child's Rights as a Patient

The President's Advisory Commission on Consumer Protection and Quality in the Healthcare Industry has created the following summary of your child's rights as a patient.[148]

[148]Adapted from Consumer Bill of Rights and Responsibilities: **http://www.hcqualitycommission.gov/press/cbor.html#head1**.

Information Disclosure

Consumers have the right to receive accurate, easily understood information. Some consumers require assistance in making informed decisions about health plans, health professionals, and healthcare facilities. Such information includes:

- ***Health plans.*** Covered benefits, cost-sharing, and procedures for resolving complaints, licensure, certification, and accreditation status, comparable measures of quality and consumer satisfaction, provider network composition, the procedures that govern access to specialists and emergency services, and care management information.
- ***Health professionals.*** Education, board certification, and recertification, years of practice, experience performing certain procedures, and comparable measures of quality and consumer satisfaction.
- ***Healthcare facilities.*** Experience in performing certain procedures and services, accreditation status, comparable measures of quality, worker, and consumer satisfaction, and procedures for resolving complaints.
- ***Consumer assistance programs.*** Programs must be carefully structured to promote consumer confidence and to work cooperatively with health plans, providers, payers, and regulators. Desirable characteristics of such programs are sponsorship that ensures accountability to the interests of consumers and stable, adequate funding.

Choice of Providers and Plans

Consumers have the right to a choice of healthcare providers that is sufficient to ensure access to appropriate high-quality healthcare. To ensure such choice, the Commission recommends the following:

- ***Provider network adequacy.*** All health plan networks should provide access to sufficient numbers and types of providers to assure that all covered services will be accessible without unreasonable delay -- including access to emergency services 24 hours a day and 7 days a week. If a health plan has an insufficient number or type of providers to provide a covered benefit with the appropriate degree of specialization, the plan should ensure that the consumer obtains the benefit outside the network at no greater cost than if the benefit were obtained from participating providers.
- ***Access to specialists.*** Consumers with complex or serious medical conditions who require frequent specialty care should have direct access

to a qualified specialist of their choice within a plan's network of providers. Authorizations, when required, should be for an adequate number of direct access visits under an approved treatment plan.

- ***Transitional care.*** Consumers who are undergoing a course of treatment for a chronic or disabling condition at the time they involuntarily change health plans or at a time when a provider is terminated by a plan for other than cause should be able to continue seeing their current specialty providers for up to 90 days to allow for transition of care.
- ***Choice of health plans.*** Public and private group purchasers should, wherever feasible, offer consumers a choice of high-quality health insurance plans.

Access to Emergency Services

Consumers have the right to access emergency healthcare services when and where the need arises. Health plans should provide payment when a consumer presents to an emergency department with acute symptoms of sufficient severity--including severe pain--such that a "prudent layperson" could reasonably expect the absence of medical attention to result in placing that consumer's health in serious jeopardy, serious impairment to bodily functions, or serious dysfunction of any bodily organ or part.

Participation in Treatment Decisions

Consumers have the right and responsibility to fully participate in all decisions related to their healthcare. Consumers who are unable to fully participate in treatment decisions have the right to be represented by parents, guardians, family members, or other conservators. Physicians and other health professionals should:

- Provide parents with sufficient information and opportunity to decide among treatment options consistent with the informed consent process.
- Discuss all treatment options with a parent in a culturally competent manner, including the option of no treatment at all.
- Ensure that persons with disabilities have effective communications with members of the health system in making such decisions.
- Discuss all current treatments a consumer may be undergoing.
- Discuss all risks, benefits, and consequences to treatment or nontreatment.

- Give parents the opportunity to refuse treatment for their children and to express preferences about future treatment decisions.
- Discuss the use of advance directives -- both living wills and durable powers of attorney for healthcare -- with parents.
- Abide by the decisions made by parents consistent with the informed consent process.

Health plans, health providers, and healthcare facilities should:

- Disclose to consumers factors -- such as methods of compensation, ownership of or interest in healthcare facilities, or matters of conscience -- that could influence advice or treatment decisions.
- Assure that provider contracts do not contain any so-called "gag clauses" or other contractual mechanisms that restrict healthcare providers' ability to communicate with and advise parents about medically necessary treatment options for their children.
- Be prohibited from penalizing or seeking retribution against healthcare professionals or other health workers for advocating on behalf of their patients.

Respect and Nondiscrimination

Consumers have the right to considerate, respectful care from all members of the healthcare industry at all times and under all circumstances. An environment of mutual respect is essential to maintain a quality healthcare system. To assure that right, the Commission recommends the following:

- Consumers must not be discriminated against in the delivery of healthcare services consistent with the benefits covered in their policy, or as required by law, based on race, ethnicity, national origin, religion, sex, age, mental or physical disability, sexual orientation, genetic information, or source of payment.
- Consumers eligible for coverage under the terms and conditions of a health plan or program, or as required by law, must not be discriminated against in marketing and enrollment practices based on race, ethnicity, national origin, religion, sex, age, mental or physical disability, sexual orientation, genetic information, or source of payment.

Confidentiality of Health Information

Consumers have the right to communicate with healthcare providers in confidence and to have the confidentiality of their individually identifiable healthcare information protected. Consumers also have the right to review and copy their own medical records and request amendments to their records.

Complaints and Appeals

Consumers have the right to a fair and efficient process for resolving differences with their health plans, healthcare providers, and the institutions that serve them, including a rigorous system of internal review and an independent system of external review. A free copy of the Patient's Bill of Rights is available from the American Hospital Association.[149]

Parent Responsibilities

To underscore the importance of finance in modern healthcare as well as your responsibility for the financial aspects of your child's care, the President's Advisory Commission on Consumer Protection and Quality in the Healthcare Industry has proposed that parents understand the following "Consumer Responsibilities."[150] In a healthcare system that protects consumers' rights, it is reasonable to expect and encourage consumers to assume certain responsibilities. Greater involvement by parents in their children's care increases the likelihood of achieving the best outcome and helps support a quality-oriented, cost-conscious environment. Such responsibilities include:

- Take responsibility for maximizing your child's healthy habits.
- Work collaboratively with healthcare providers in developing and carrying out your child's agreed-upon treatment plans.
- Disclose relevant information and clearly communicate wants and needs.

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[149] To order your free copy of the Patient's Bill of Rights, telephone 312-422-3000 or visit the American Hospital Association's Web site: **http://www.aha.org**. Click on "Resource Center," go to "Search" at bottom of page, and then type in "Patient's Bill of Rights." The Patient's Bill of Rights is also available from Fax on Demand, at 312-422-2020, document number 471124.

[150] Adapted from **http://www.hcqualitycommission.gov/press/cbor.html#head1**.

- Use the insurance company's internal complaint and appeal processes to address your concerns.
- Recognize the reality of risks, the limits of the medical science, and the human fallibility of the healthcare professional.
- Be aware of a healthcare provider's obligation to be reasonably efficient and equitable in providing care to the community.
- Become knowledgeable about health plan coverage and options (when available) including all covered benefits, limitations, and exclusions, rules regarding use of network providers, coverage and referral rules, appropriate processes to secure additional information, and the process to appeal coverage decisions.
- Make a good-faith effort to meet financial obligations.
- Abide by administrative and operational procedures of health plans, healthcare providers, and Government health benefit programs.

Choosing an Insurance Plan

There are a number of official government agencies that help consumers understand their healthcare insurance choices.[151] The U.S. Department of Labor, in particular, recommends ten ways to make your health benefits choices work best for your family.[152]

1. Your options are important. There are many different types of health benefit plans. Find out which one your employer offers, then check out the plan, or plans, offered. Your employer's human resource office, the health plan administrator, or your union can provide information to help you match your family's needs and preferences with the available plans. The more information you have, the better your healthcare decisions will be.

2. Reviewing the benefits available. Do the plans offered cover preventive care, well-baby care, vision or dental care? Are there deductibles? Answers to these questions can help determine the out-of-pocket expenses you may face. Cheapest may not always be best. Your goal is high quality health benefits.

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[151] More information about quality across programs is provided at the following AHRQ Web site:
http://www.ahrq.gov/consumer/qntascii/qnthplan.htm.

[152] Adapted from the Department of Labor:
http://www.dol.gov/dol/pwba/public/pubs/health/top10-text.html.

3. Look for quality. The quality of healthcare services varies, but quality can be measured. You should consider the quality of healthcare in deciding among the healthcare plans or options available to your family. Not all health plans, doctors, hospitals and other providers give the highest quality care. Fortunately, there is quality information you can use right now to help you compare your healthcare choices. Find out how you can measure quality. Consult the U.S. Department of Health and Human Services publication "Your Guide to Choosing Quality Health Care" on the Internet at **www.ahcpr.gov/consumer**.

4. Your plan's summary plan description (SPD) provides a wealth of information. Your health plan administrator can provide you with a copy of your plan's SPD. It outlines your family's benefits and your legal rights under the Employee Retirement Income Security Act (ERISA), the federal law that protects your family's health benefits. It should contain information about the coverage of dependents, what services will require a co-pay, and the circumstances under which your employer can change or terminate a health benefits plan. Save the SPD and all other health plan brochures and documents, along with memos or correspondence from your employer relating to health benefits.

5. Assess your benefit coverage as your family status changes. Marriage, divorce, childbirth or adoption, and the death of a spouse are all life events that may signal a need to change your health benefits. You, your spouse and dependent children may be eligible for a special enrollment period under provisions of the Health Insurance Portability and Accountability Act (HIPAA). Even without life-changing events, the information provided by your employer should tell you how you can change benefits or switch plans, if more than one plan is offered. If your spouse's employer also offers a health benefits package, consider coordinating both plans for maximum coverage.

6. Changing jobs and other life events can affect your family's health benefits. Under the Consolidated Omnibus Budget Reconciliation Act (COBRA), you, your covered spouse, and your dependent children may be eligible to purchase extended health coverage under your employer's plan if you lose your job, change employers, get divorced, or upon occurrence of certain other events. Coverage can range from 18 to 36 months depending on your situation. COBRA applies to most employers with 20 or more workers and requires your plan to notify you of your rights. Most plans require eligible individuals to make their COBRA election within 60 days of the plan's notice. Be sure to follow up with your plan sponsor if you don't receive notice, and make sure you respond within the allotted time.

7. HIPAA can also help if you are changing jobs, particularly if you have a medical condition. HIPAA generally limits pre-existing condition exclusions to a maximum of 12 months (18 months for late enrollees). HIPAA also requires this maximum period to be reduced by the length of time you had prior "creditable coverage." You should receive a certificate documenting your prior creditable coverage from your old plan when coverage ends.

8. Plan for retirement. Before you retire, find out what health benefits, if any, extend to you and your spouse during your retirement years. Consult with your employer's human resources office, your union, the plan administrator, and check your SPD. Make sure there is no conflicting information among these sources about the benefits your family will receive or the circumstances under which they can change or be eliminated. With this information in hand, you can make other important choices, like finding out if you are eligible for Medicare and Medigap insurance coverage.

9. Know how to file an appeal if a health benefits claim is denied. Understand how your plan handles grievances and where to make appeals of the plan's decisions. Keep records and copies of correspondence. Check your health benefits package and your SPD to determine who is responsible for handling problems with benefit claims. Contact PWBA for customer service assistance if you are unable to obtain a response to your complaint.

10. You can take steps to improve the quality of the healthcare and the health benefits your family receives. Look for and use things like Quality Reports and Accreditation Reports whenever you can. Quality reports may contain consumer ratings -- how satisfied consumers are with the doctors in their plan, for instance-- and clinical performance measures -- how well a healthcare organization prevents and treats illness. Accreditation reports provide information on how accredited organizations meet national standards, and often include clinical performance measures. Look for these quality measures whenever possible. Consult "Your Guide to Choosing Quality Health Care" on the Internet at **www.ahcpr.gov/consumer**.

Medicaid

Illness strikes both rich and poor families. For low-income families, Medicaid is available to defer the costs of treatment. In the following pages, you will learn the basics about Medicaid as well as useful contact information on how to find more in-depth information.

Medicaid is a joint federal and state program that helps pay medical costs for some people with low incomes and limited resources. Medicaid programs vary from state to state. You can find more information about Medicaid on the HCFA.gov Web site at **http://www.hcfa.gov/medicaid/medicaid.htm**.

Financial Assistance for Cancer Care[153]

Cancer can impose heavy economic burdens. For many parents, a portion of their children's medical expenses is paid by their health insurance plan. For individuals who do not have health insurance or who need financial assistance to cover health care costs, resources are available, including government-sponsored programs and services supported by voluntary organizations.

Parents should discuss any concerns they may have about healthcare costs with the physician, medical social worker, or the business office of their hospital or clinic.

The organizations and resources listed below may offer financial assistance. Organizations that provide publications in Spanish or have Spanish-speaking staff have been identified.

- The American Cancer Society (ACS) office can provide the telephone number of the local ACS office serving your area. The local ACS office may offer reimbursement for expenses related to cancer treatment including transportation, medicine, and medical supplies. The ACS also offers programs that help cancer patients, family members, and friends cope with the emotional challenges they face. Some publications are available in Spanish. Spanish-speaking staff are available. Telephone: 1–800–ACS–2345 (1–800–227–2345). Web site: **http://www.cancer.org**
- The Candlelighters Childhood Cancer Foundation (CCCF) is a nonprofit organization that provides information, peer support, and advocacy through publications, an information clearinghouse, and a network of local support groups. CCCF maintains a list of organizations to which eligible families may apply for financial assistance. Telephone: 1–800–366–CCCF (1–800–366–2223). Web site: **http://www.candlelighters.org**.

Community voluntary agencies and service organizations such as the Salvation Army, Lutheran Social Services, Jewish Social Services, Catholic Charities, and the Lions Club may offer help. These organizations are listed

[153] Adapted from the NCI: **http://cis.nci.nih.gov/fact/8_3.htm**.

in your local phone directory. Some churches and synagogues may provide financial help or services to their members.

Fundraising is another mechanism to consider. Some parents find that friends, family, and community members are willing to contribute financially if they are aware of a difficult situation. Contact your local library for information about how to organize fundraising efforts.

General assistance programs provide food, housing, prescription drugs, and other medical expenses for those who are not eligible for other programs. Funds are often limited. Information can be obtained by contacting your state or local Department of Social Services; this number is found in the local telephone directory.

Hill-Burton is a program through which hospitals receive construction funds from the Federal Government. Hospitals that receive Hill-Burton funds are required by law to provide some services to people who cannot afford to pay for their hospitalization. Information about which facilities are part of this program is available by calling the toll-free number or visiting the Web site shown below. A brochure about the program is available in Spanish. Telephone: 1–800–638–0742. Web site: **http://www.hrsa.gov/osp/dfcr/obtain/consfaq.htm**.

Income Tax Deductions

Medical costs that are not covered by insurance policies sometimes can be deducted from annual income before taxes. Examples of tax deductible expenses might include mileage for trips to and from medical appointments, out-of-pocket costs for treatment, prescription drugs or equipment, and the cost of meals during lengthy medical visits. The local Internal Revenue Service office, tax consultants, or certified public accountants can determine medical costs that are tax deductible. These telephone numbers are available in the local telephone directory. Web site: **http://www.irs.ustreas.gov**.

The Patient Advocate Foundation

The Patient Advocate Foundation (PAF) is a national nonprofit organization that provides education, legal counseling, and referrals to cancer patients and survivors concerning managed care, insurance, financial issues, job discrimination, and debt crisis matters. Telephone: 1–800–532–5274. **Web site: http://www.patientadvocate.org**.

Patient Assistance Programs are offered by some pharmaceutical manufacturers to help pay for medications. To learn whether a specific drug might be available at reduced cost through such a program, talk with a physician or a medical social worker.

The State Children's Health Insurance Program

The State Children's Health Insurance Program (SCHIP) is a Federal-State partnership that offers low-cost or free health insurance coverage to uninsured children of low-wage, working parents. Callers will be referred to the SCHIP program in their state for further information about what the program covers, who is eligible, and the minimum qualifications. Telephone: 1–877–543–7669 (1–877–KIDS–NOW). Web site: **http://www.insurekidsnow.gov**.

Transportation

There are nonprofit organizations that arrange free or reduced cost air transportation for cancer patients going to or from cancer treatment centers. Financial need is not always a requirement. To find out about these programs, talk with a medical social worker. Ground transportation services may be offered or mileage reimbursed through the local ACS or your state or local Department of Social Services.

NORD's Medication Assistance Programs

Finally, the National Organization for Rare Disorders, Inc. (NORD) administers medication programs sponsored by humanitarian-minded pharmaceutical and biotechnology companies to help uninsured or under-insured individuals secure life-saving or life-sustaining drugs.[154] NORD programs ensure that certain vital drugs are available "to those families whose income is too high to qualify for Medicaid but too low to pay for their prescribed medications." The program has standards for fairness, equity, and unbiased eligibility. It currently covers some 14 programs for nine pharmaceutical companies. NORD also offers early access programs for investigational new drugs (IND) under the approved "Treatment INDs" programs of the Food and Drug Administration (FDA). In these programs, a

[154] Adapted from NORD: **http://www.rarediseases.org/cgi-bin/nord/progserv#patient?id=rPIzL9oD&mv_pc=30**.

limited number of individuals can receive investigational drugs that have yet to be approved by the FDA. These programs are generally designed for rare medical conditions. For more information, visit **www.rarediseases.org**.

Additional Resources

In addition to the references already listed in this chapter, you may need more information on health insurance, hospitals, or the healthcare system in general. The NIH has set up an excellent guidance Web site that addresses these and other issues. Topics include:[155]

- Health Insurance: **http://www.nlm.nih.gov/medlineplus/healthinsurance.html**
- Health Statistics: **http://www.nlm.nih.gov/medlineplus/healthstatistics.html**
- HMO and Managed Care: **http://www.nlm.nih.gov/medlineplus/managedcare.html**
- Hospice Care: **http://www.nlm.nih.gov/medlineplus/hospicecare.html**
- Medicaid: **http://www.nlm.nih.gov/medlineplus/medicaid.html**
- Medicare: **http://www.nlm.nih.gov/medlineplus/medicare.html**
- Nursing Homes and Long-term Care: **http://www.nlm.nih.gov/medlineplus/nursinghomes.html**
- Patient's Rights, Confidentiality, Informed Consent, Ombudsman Programs, Privacy and Patient Issues: **http://www.nlm.nih.gov/medlineplus/patientissues.html**
- Veteran's Health, Persian Gulf War, Gulf War Syndrome, Agent Orange: **http://www.nlm.nih.gov/medlineplus/veteranshealth.html**

Vocabulary Builder

Cyclosporins: A group of closely related cyclic undecapeptides from the fungi Trichoderma polysporum and Cylindocarpon lucidum. They have some antineoplastic and antifungal action and significant immunosuppressive effects. Cyclosporins have been proposed as adjuvants in tissue and organ transplantation to suppress graft rejection. [NIH]

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[155] You can access this information at: **http://www.nlm.nih.gov/medlineplus/healthsystem.html**.

Haematological: Relating to haematology, that is that branch of medical science which treats of the morphology of the blood and blood-forming tissues. [EU]

Induction: The act or process of inducing or causing to occur, especially the production of a specific morphogenetic effect in the developing embryo through the influence of evocators or organizers, or the production of anaesthesia or unconsciousness by use of appropriate agents. [EU]

Inoperable: Not suitable to be operated upon. [EU]

Intermittent: Occurring at separated intervals; having periods of cessation of activity. [EU]

Nausea: An unpleasant sensation, vaguely referred to the epigastrium and abdomen, and often culminating in vomiting. [EU]

Neoplasm: A new growth of benign or malignant tissue. [NIH]

Non-small cell lung cancer: A group of lung cancers that includes squamous cell carcinoma, adenocarcinoma, and large cell carcinoma. [NIH]

Pharmacokinetics: The activity of drugs in the body over a period of time, including the processes by which drugs are absorbed, distributed in the body, localized in the tissues, and excreted. [NIH]

Psychotherapy: A generic term for the treatment of mental illness or emotional disturbances primarily by verbal or nonverbal communication. [NIH]

Spectrum: A charted band of wavelengths of electromagnetic vibrations obtained by refraction and diffraction. By extension, a measurable range of activity, such as the range of bacteria affected by an antibiotic (antibacterial s.) or the complete range of manifestations of a disease. [EU]

Tumour: 1. swelling, one of the cardinal signs of inflammations; morbid enlargement. 2. a new growth of tissue in which the multiplication of cells is uncontrolled and progressive; called also neoplasm. [EU]

APPENDIX E. TALKING WITH YOUR CHILD ABOUT CANCER

Overview[156]

More children than ever are surviving childhood cancer. Over the last 30 years, survival into adulthood increased from 30 percent to 80 percent. There are new and better drugs and methods to help children deal with the side effects of treatment. And children who have had cancer now have a better quality of life throughout childhood and into adulthood; fewer long-term ill effects follow the treatment.

Yet, in spite of all this good news, cancer is still a serious disease. You are not alone in facing your fears; help is available. A treatment team - doctors, radiation therapists, rehabilitation specialists, dietitians, oncology nurses, and social workers, among others - can help you and your child deal with the disease. They will also help ensure that your child gets the best treatment available with as few ill effects as possible.

Your first question may be, "Should I tell my child about the cancer?" You may want to protect your child, but children usually know when something is wrong. Your child may not be feeling well, may be seeing the doctor often, and may have already had some tests. Your child may notice that you are afraid. No matter how hard you try to keep information about the illness and treatment from your child, others - such as family, friends, and clinic or hospital staff - may inadvertently say things that let your child know about the cancer. In addition, it will upset your child to find out that you were not telling the truth; your child depends on you for honest answers.

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[156] Adapted from the NCI: **http://www.cancer.gov/CancerInformation/youngpeople**.

Why Should I Tell My Child?

Telling your child about his or her cancer is a personal matter, and family, cultural, or religious beliefs will come into play. It is important to be open and honest with your child because children who are not told about their illness often imagine things that are not true. For example, a child may think he or she has cancer as punishment for doing something wrong. Health professionals generally agree that telling children the truth about their illness leads to less stress and guilt. Children who know the truth are also more likely to cooperate with treatment. Finally, talking about cancer often helps to bring the family closer together and makes dealing with the cancer a little easier for everyone.

Parent's Questions

Parents have many questions about talking with their children about the diagnosis. Perhaps you have asked some of these yourself

When Should My Child Be Told?

Because you are probably the best judge of your child's personality and moods, you are the best person to decide when your child should be told. Keep in mind, though, that your child is likely to know early on that something is wrong, so you may want to tell your child soon after the diagnosis. In fact, most parents say it is easiest to tell them then. Waiting days or weeks may give your child time to imagine worse things than the truth and develop fears that may be hard to dispel later. Certainly, it would be easier for your child if he or she is told before treatment starts.

Who Should Tell My Child?

The answer to this question is personal. As a parent, you may feel that it is best for you to tell your child. Some parents, however, find it too painful to do so. Other family members or the treatment team - doctor, nurse, or social worker - may be able to help you. They may either tell your child for you or help you explain the illness.

Thinking about what you are going to say and how to say it will help you feel more relaxed. But how do you decide just what to say? Family and close friends, members of the treatment team, parents of other children who have

cancer, members of support groups (you can find information about them at the end of this booklet), and clergy members can offer ideas.

Who Should Be There?

Your child needs love and support when hearing the diagnosis. Even if the doctor explains the illness, someone your child trusts and depends upon should be present. Having the support of other family members at this time can be very helpful.

What Should My Child Be Told?

How much information and the best way to relate this information depends on your child's age and what your child can understand. Being gentle, open, and honest is usually best.
The following sections describe what most children in various age groups are likely to understand. These guidelines are general; each child is different. Your child may fit into more than one or none of these categories.

Up to 2 Years Old

Children this young do not understand cancer. They understand what they can see and touch. Their biggest concern is what is happening to them right now. They worry most about being away from their parents.

After children are a year old, they think about how things feel and how to control things around them. Very young children are most afraid of medical tests. Many cry, run away, or squirm to try to control what is happening.

Because children begin to think about and understand what is going on around them at about 18 months, it is best to be honest. Be truthful about trips to the hospital and explain procedures that may hurt. You can tell your child that needle sticks will hurt a minute and that it is okay to cry. Being honest lets your child know that you understand and accept his or her feelings and helps your child trust you.

When you can, give your child choices. For example, if a medicine is taken by mouth, you might ask if your child would like it mixed in apple juice, grape juice, or applesauce.

2 to 7 Years Old

When children are between the ages of 2 and 7, they link events to one thing. For example, they usually tie illness to a specific event such as staying in bed or eating chicken soup. Children this age often think their illness is caused by a specific action. Therefore, getting better will "just happen" or will come if they follow a set of rules.

These approaches might help when talking with a child in this age group:

- Explain that treatment is needed so the hurting will go away or so the child can get better and play without getting so tired.
- Explain that the illness or treatment is not punishment for something the child has done, said, or thought.
- Be honest when you explain tests and treatments. Remind the child that all of these things are being done to get rid of the cancer and to help him or her get well.
- Use simple ways to explain the illness. For example, try talking about the cancer as a contest between "good" cells and "bad" cells. Having treatment will help the good cells to be stronger so that they can beat the bad cells.

7 to 12 Years Old

Children ages 7 to 12 are starting to understand links between things and events. For example, a child this age sees his or her illness as a set of symptoms, is less likely to believe that something he or she did caused the illness, understands that getting better comes from taking medicines and doing what the doctor says, and is able to cooperate with treatment.

You can give more details when explaining cancer, but you should still use situations your child may be used to. You might say that the body is made of up different types of cells, and these cells have different jobs to do. Like people, these cells must work together to get the job done. You might describe the cancer cells as "troublemakers" that get in the way of the work of the good cells. Treatment helps to get rid of the troublemakers so that other cells can work well together.

12 Years and Older

Children over 12 years old can often understand complicated relationships between events. They can think about things that have not happened to them. Teenagers tend to think of illness in terms of specific symptoms, such as tiredness, and in terms of limits or changes in their everyday activity. But because they also can understand the reason for their symptoms, you can explain cancer as a disease in which a few cells in the body go "haywire." These "haywire" cells grow more quickly than normal cells, invade other parts of the body, and get in the way of how the body usually works. The goal of treatment is to kill the "haywire" cells. The body can then work normally again, and the symptoms will go away.

Questions Children May Ask

Children are naturally curious about their disease and have many questions about cancer and cancer treatment. Your child will expect you to have answers to most questions. Children may begin to ask questions right after diagnosis or may wait until later. Here are some common questions and some ideas to help you answer them.

Why Me?

A child, like an adult, wonders "Why did I get cancer?" A child may feel that it is his or her fault, that somehow he or she caused the illness. Make it clear that not even the doctors know exactly what caused the cancer. Neither you, your child, nor his or her brothers or sisters did, said, or thought anything that caused the cancer. Stress also that cancer is not contagious, and your child did not "catch" it from someone else.

Will I Get Well?

Children often know about family members or friends who died of cancer. As a result, many children are afraid to ask if they will get well because they fear that the answer will be "no." Thus, you might tell your child that cancer is a serious disease, but that treatment - such as medicine, radiation, or an operation - has helped get rid of cancer in other children, and the doctors and nurses are trying their best to cure your child's cancer, too. Knowing that caring people - such as family, doctors, nurses, counselors, and others -

surround your child and your family may also help him or her feel more secure.

What Will Happen to Me?

When your child is first diagnosed with cancer, many new and scary things will happen. While at the doctor's office, hospital, or clinic, your child may see or play with other children with cancer who may not be feeling well, have lost their hair, or have had limbs removed because of cancer. Your child may wonder, "Will these things happen to me?" Yet, your child may be too afraid to ask questions. It is important to try to get your child to talk about these concerns. Explain ahead of time about the cancer, treatment, and possible side effects. Discuss what the doctor will do to help if side effects occur. You can also explain that there are many different types of cancer and that even when two children have the same cancer, what happens to one child will not always happen to the other.

Children should be told about any changes in their treatment schedule or in the type of treatment they receive. This information helps them prepare for visits to the doctor or hospital. You may want to help your child keep a calendar that shows the days for doctor visits, treatments, or tests. Do not tell younger children about upcoming treatments far ahead of time if it makes them nervous.

Why Do I Have to Take Medicine When I Feel Okay?

With cancer, your child may feel fine much of the time but need to take medicine often. Children do not understand why they have to take medicine when they feel well. You may want to remind your child of the reason for taking the medicine in the first place. For example, a child could be told: "Although you are feeling well, the bad cells are hiding. You must take the medicine for a while longer to find the bad cells and stop them from coming back."

Talking to Your Child with Late-Stage Cancer

During the past several years, health care professionals have become more aware of the needs of children who have late-stage cancer and of their families. For example, attending school half days or even for an hour a day - if possible - may make your child happier. Talking with your child about

death and dying and giving your child as many choices as possible shows your child that you are being open and honest, and shows your support, love, and respect. Paying close attention to changes in your child's behavior may give you important clues as to what your child needs and whether he or she wants to talk about dying. Including all of your children in everyday activities - such as reading, doing homework, or watching a favorite television program or video together - can help keep the family close.

ONLINE GLOSSARIES

The Internet provides access to a number of free-to-use medical dictionaries and glossaries. The National Library of Medicine has compiled the following list of online dictionaries:

- ADAM Medical Encyclopedia (A.D.A.M., Inc.), comprehensive medical reference: **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**
- MedicineNet.com Medical Dictionary (MedicineNet, Inc.): **http://www.medterms.com/Script/Main/hp.asp**
- Merriam-Webster Medical Dictionary (Inteli-Health, Inc.): **http://www.intelihealth.com/IH/**
- Multilingual Glossary of Technical and Popular Medical Terms in Eight European Languages (European Commission) - Danish, Dutch, English, French, German, Italian, Portuguese, and Spanish: **http://allserv.rug.ac.be/~rvdstich/eugloss/welcome.html**
- On-line Medical Dictionary (CancerWEB): **http://www.graylab.ac.uk/omd/**
- Technology Glossary (National Library of Medicine) - Health Care Technology: **http://www.nlm.nih.gov/nichsr/ta101/ta10108.htm**
- Terms and Definitions (Office of Rare Diseases): **http://rarediseases.info.nih.gov/ord/glossary_a-e.html**

Beyond these, MEDLINEplus contains a very user-friendly encyclopedia covering every aspect of medicine (licensed from A.D.A.M., Inc.). The ADAM Medical Encyclopedia Web site address is **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**. ADAM is also available on commercial Web sites such as drkoop.com (**http://www.drkoop.com/**) and Web MD (**http://my.webmd.com/adam/asset/adam_disease_articles/a_to_z/a)**. Topics of interest can be researched by using keywords before continuing elsewhere, as these basic definitions and concepts will be useful in more advanced areas of research. You may choose to print various pages specifically relating to childhood non-Hodgkin's lymphoma and keep them on file.

Online Dictionary Directories

The following are additional online directories compiled by the National Library of Medicine, including a number of specialized medical dictionaries and glossaries:

- Medical Dictionaries: Medical & Biological (World Health Organization): **http://www.who.int/hlt/virtuallibrary/English/diction.htm#Medical**
- MEL-Michigan Electronic Library List of Online Health and Medical Dictionaries (Michigan Electronic Library): **http://mel.lib.mi.us/health/health-dictionaries.html**
- Patient Education: Glossaries (DMOZ Open Directory Project): **http://dmoz.org/Health/Education/Patient_Education/Glossaries/**
- Web of Online Dictionaries (Bucknell University): **http://www.yourdictionary.com/diction5.html#medicine**

CHILDHOOD NON-HODGKIN'S LYMPHOMA GLOSSARY

The following is a complete glossary of terms used in this sourcebook. The definitions are derived from official public sources including the National Institutes of Health [NIH] and the European Union [EU]. After this glossary, we list a number of additional hardbound and electronic glossaries and dictionaries that you may wish to consult.

506U78: An anticancer drug that belongs to the family of drugs called antimetabolites. [NIH]

Abdomen: The part of the body that contains the pancreas, stomach, intestines, liver, gallbladder, and other organs. [NIH]

Abdominal: Having to do with the abdomen, which is the part of the body between the chest and the hips that contains the pancreas, stomach, intestines, liver, gallbladder, and other organs. [NIH]

Adenopathy: Large or swollen lymph glands. [NIH]

Adolescence: The period of life beginning with the appearance of secondary sex characteristics and terminating with the cessation of somatic growth. The years usually referred to as adolescence lie between 13 and 18 years of age. [NIH]

Alleles: Mutually exclusive forms of the same gene, occupying the same locus on homologous chromosomes, and governing the same biochemical and developmental process. [NIH]

Allogeneic: Taken from different individuals of the same species. [NIH]

Allopurinol: A drug that lowers high levels of uric acid (a byproduct of metabolism) in the blood caused by some cancer treatments. [NIH]

Anaplastic: A term used to describe cancer cells that divide rapidly and bear little or no resemblance to normal cells. [NIH]

Anesthesia: Loss of feeling or awareness. Local anesthetics cause loss of feeling in a part of the body. General anesthetics put the person to sleep. [NIH]

Antibiotic: A drug used to treat infections caused by bacteria and other microorganisms. [NIH]

Antibody: A type of protein made by certain white blood cells in response to a foreign substance (antigen). Each antibody can bind to only a specific antigen. The purpose of this binding is to help destroy the antigen. Antibodies can work in several ways, depending on the nature of the antigen. Some antibodies destroy antigens directly. Others make it easier for

white blood cells to destroy the antigen. [NIH]

Antigen: Any substance which is capable, under appropriate conditions, of inducing a specific immune response and of reacting with the products of that response, that is, with specific antibody or specifically sensitized T-lymphocytes, or both. Antigens may be soluble substances, such as toxins and foreign proteins, or particulate, such as bacteria and tissue cells; however, only the portion of the protein or polysaccharide molecule known as the antigenic determinant (q.v.) combines with antibody or a specific receptor on a lymphocyte. Abbreviated Ag. [EU]

Antineoplastons: Substances isolated from normal human blood and urine being tested as a type of treatment for some tumors and AIDS. [NIH]

Asparaginase: An anticancer drug that is an enzyme. [NIH]

Aspirate: Fluid withdrawn from a lump, often a cyst, or a nipple. [NIH]

Aspirin: A drug that reduces pain, fever, inflammation, and blood clotting. Aspirin belongs to the family of drugs called nonsteroidal anti-inflammatory agents. It is also being studied in cancer prevention. [NIH]

Ataxia: Loss of muscle coordination. [NIH]

Autologous: Taken from an individual's own tissues, cells, or DNA. [NIH]

Bereavement: Refers to the whole process of grieving and mourning and is associated with a deep sense of loss and sadness. [NIH]

Biopsy: The removal of cells or tissues for examination under a microscope. When only a sample of tissue is removed, the procedure is called an incisional biopsy or core biopsy. When an entire tumor or lesion is removed, the procedure is called an excisional biopsy. When a sample of tissue or fluid is removed with a needle, the procedure is called a needle biopsy or fine-needle aspiration. [NIH]

Blasts: Immature blood cells. [NIH]

Bowel: The long tube-shaped organ in the abdomen that completes the process of digestion. There is both a small and a large bowel. Also called the intestine. [NIH]

Carboplatin: An anticancer drug that belongs to the family of drugs called platinum compounds. [NIH]

Cardiac: Having to do with the heart. [NIH]

Cell: The individual unit that makes up all of the tissues of the body. All living things are made up of one or more cells. [NIH]

Cervical: Relating to the neck, or to the neck of any organ or structure. Cervical lymph nodes are located in the neck; cervical cancer refers to cancer of the uterine cervix, which is the lower, narrow end (the "neck") of the uterus. [NIH]

Charities: Social welfare organizations with programs designed to assist individuals in times of need. [NIH]

Chemotherapy: Treatment with anticancer drugs. [NIH]

Chromosomal: Pertaining to chromosomes. [EU]

Chromosome: Part of a cell that contains genetic information. Except for sperm and eggs, all human cells contain 46 chromosomes. [NIH]

Chronic: A disease or condition that persists or progresses over a long period of time. [NIH]

Cisplatin: An anticancer drug that belongs to the family of drugs called platinum compounds. [NIH]

CNS: Central nervous system. The brain and spinal cord. [NIH]

Confusion: Disturbed orientation in regard to time, place, or person, sometimes accompanied by disordered consciousness. [EU]

Cranial: Pertaining to the cranium, or to the anterior (in animals) or superior (in humans) end of the body. [EU]

Curative: Tending to overcome disease and promote recovery. [EU]

Cyclophosphamide: An anticancer drug that belongs to the family of drugs called alkylating agents. [NIH]

Cyclosporine: A drug used to help reduce the risk of rejection of organ and bone marrow transplants by the body. It is also used in clinical trials to make cancer cells more sensitive to anticancer drugs. [NIH]

Cyclosporins: A group of closely related cyclic undecapeptides from the fungi Trichoderma polysporum and Cylindocarpon lucidum. They have some antineoplastic and antifungal action and significant immunosuppressive effects. Cyclosporins have been proposed as adjuvants in tissue and organ transplantation to suppress graft rejection. [NIH]

Cytarabine: An anticancer drug that belongs to the family of drugs called antimetabolites. [NIH]

Cytogenetics: A branch of genetics which deals with the cytological and molecular behavior of genes and chromosomes during cell division. [NIH]

Daunorubicin: An anticancer drug that belongs to the family of drugs called antitumor antibiotics. [NIH]

Dexamethasone: A synthetic steroid (similar to steroid hormones produced naturally in the adrenal gland). Dexamethasone is used to treat leukemia and lymphoma and may be used to treat some of the problems caused by other cancers and their treatment. [NIH]

Diaphragm: The thin muscle below the lungs and heart that separates the chest from the abdomen. [NIH]

Doxorubicin: An anticancer drug that belongs to the family of drugs called antitumor antibiotics. It is an anthracycline. [NIH]

Dysphagia: Difficulty in swallowing. [EU]

Dyspnea: Difficult, painful breathing or shortness of breath. [NIH]

Effusion: The escape of fluid into a part or tissue, as an exudation or a transudation. [EU]

Endemic: Present or usually prevalent in a population or geographical area at all times; said of a disease or agent. Called also endemial. [EU]

Enzyme: A protein that speeds up chemical reactions in the body. [NIH]

Epidural: The space between the wall of the spinal canal and the covering of the spinal cord. An epidural injection is given into this space. [NIH]

Etoposide: An anticancer drug that is a podophyllotoxin derivative and belongs to the family of drugs called mitotic inhibitors. [NIH]

Filgrastim: A colony-stimulating factor that stimulates the production of neutrophils (a type of white blood cell). It is a cytokine that belongs to the family of drugs called hematopoietic (blood-forming) agents. Also called granulocyte colony-stimulating factor (G-CSF). [NIH]

Gastrointestinal: Refers to the stomach and intestines. [NIH]

Grade: The grade of a tumor depends on how abnormal the cancer cells look under a microscope and how quickly the tumor is likely to grow and spread. Grading systems are different for each type of cancer. [NIH]

Graft: Healthy skin, bone, or other tissue taken from one part of the body and used to replace diseased or injured tissue removed from another part of the body. [NIH]

Granulocyte: A type of white blood cell that fights bacterial infection. Neutrophils, eosinophils, and basophils are granulocytes. [NIH]

Haematological: Relating to haematology, that is that branch of medical science which treats of the morphology of the blood and blood-forming tissues. [EU]

Hematologist: A doctor who specializes in treating diseases of the blood. [NIH]

Hematology: A subspecialty of internal medicine concerned with morphology, physiology, and pathology of the blood and blood-forming tissues. [NIH]

Histology: The study of tissues and cells under a microscope. [NIH]

HIV: Human immunodeficiency virus, the cause of acquired immunodeficiency syndrome (AIDS). [NIH]

Hyperplasia: An abnormal increase in the number of cells in an organ or

tissue. [NIH]

Hyperuricemia: A buildup of uric acid (a byproduct of metabolism) in the blood; a side effect of some anticancer drugs. [NIH]

Hypoplasia: Incomplete development or underdevelopment of an organ or tissue. [EU]

Ifosfamide: An anticancer drug that belongs to the family of drugs called alkylating agents. [NIH]

Immunization: The induction of immunity. [EU]

Immunodeficiency: The decreased ability of the body to fight infection and disease. [NIH]

Immunoglobulin: A protein that acts as an antibody. [NIH]

Immunophenotyping: Process of classifying cells of the immune system based on structural and functional differences. The process is commonly used to analyze and sort T-lymphocytes into subsets based on CD antigens by the technique of flow cytometry. [NIH]

Induction: The act or process of inducing or causing to occur, especially the production of a specific morphogenetic effect in the developing embryo through the influence of evocators or organizers, or the production of anaesthesia or unconsciousness by use of appropriate agents. [EU]

Inoperable: Not suitable to be operated upon. [EU]

Intermittent: Occurring at separated intervals; having periods of cessation of activity. [EU]

Intrathecal: Describes the fluid-filled space between the thin layers of tissue that cover the brain and spinal cord. Drugs can be injected into the fluid or a sample of the fluid can be removed for testing. [NIH]

Invasive: 1. having the quality of invasiveness. 2. involving puncture or incision of the skin or insertion of an instrument or foreign material into the body; said of diagnostic techniques. [EU]

Lesion: An area of abnormal tissue change. [NIH]

Leucovorin: A drug used to protect normal cells from high doses of the anticancer drug methotrexate. It is also used to increase the antitumor effects of fluorouracil and tegafur-uracil, an oral treatment alternative to intravenous fluorouracil. [NIH]

Leukemia: Cancer of blood-forming tissue. [NIH]

Lymphocytic: Referring to lymphocytes, a type of white blood cell. [NIH]

Lymphoid: Referring to lymphocytes, a type of white blood cell. Also refers to tissue in which lymphocytes develop. [NIH]

Lymphoma: Cancer that arises in cells of the lymphatic system. [NIH]

Malignancy: A cancerous tumor that can invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Malignant: Cancerous; a growth with a tendency to invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Mammography: The use of x-rays to create a picture of the breast. [NIH]

Mediastinoscopy: A procedure in which a tube is inserted into the chest to view the organs in the area between the lungs and nearby lymph nodes. The tube is inserted through an incision above the breastbone. This procedure is usually performed to get a tissue sample from the lymph nodes on the right side of the chest. [NIH]

Mediastinum: The area between the lungs. The organs in this area include the heart and its large blood vessels, the trachea, the esophagus, the bronchi, and lymph nodes. [NIH]

Mercaptopurine: An anticancer drug that belongs to the family of drugs called antimetabolites. [NIH]

Methotrexate: An anticancer drug that belongs to the family of drugs called antimetabolites. [NIH]

Millimeter: A measure of length. A millimeter is approximately 26-times smaller than an inch. [NIH]

Molecular: Of, pertaining to, or composed of molecules : a very small mass of matter. [EU]

Myelogenous: Produced by, or originating in, the bone marrow. [NIH]

Nausea: An unpleasant sensation, vaguely referred to the epigastrium and abdomen, and often culminating in vomiting. [EU]

Neoplasm: A new growth of benign or malignant tissue. [NIH]

Neurosurgeon: A doctor who specializes in surgery on the brain, spine, and other parts of the nervous system. [NIH]

Neutropenia: An abnormal decrease in the number of neutrophils, a type of white blood cell. [NIH]

Non-small cell lung cancer: A group of lung cancers that includes squamous cell carcinoma, adenocarcinoma, and large cell carcinoma. [NIH]

Oncologist: A doctor who specializes in treating cancer. Some oncologists specialize in a particular type of cancer treatment. For example, a radiation oncologist specializes in treating cancer with radiation. [NIH]

Oncology: The study of cancer. [NIH]

Oncology nurse: A nurse who specializes in treating and caring for people who have cancer. [NIH]

Oral: By or having to do with the mouth. [NIH]

Orbital: Pertaining to the orbit (= the bony cavity that contains the eyeball). [EU]

Osteosarcoma: A cancer of the bone that affects primarily children and adolescents. Also called osteogenic sarcoma. [NIH]

Oxaliplatin: An anticancer drug that belongs to the family of drugs called platinum compounds. [NIH]

Paclitaxel: An anticancer drug that belongs to the family of drugs called mitotic inhibitors. [NIH]

Paediatric: Of or relating to the care and medical treatment of children; belonging to or concerned with paediatrics. [EU]

Palliative: 1. affording relief, but not cure. 2. an alleviating medicine. [EU]

Pathologist: A doctor who identifies diseases by studying cells and tissues under a microscope. [NIH]

Pediatrics: A medical specialty concerned with maintaining health and providing medical care to children from birth to adolescence. [NIH]

Perforation: 1. the act of boring or piercing through a part. 2. a hole made through a part or substance. [EU]

Pharmacokinetics: The activity of drugs in the body over a period of time, including the processes by which drugs are absorbed, distributed in the body, localized in the tissues, and excreted. [NIH]

Phenotype: The outward appearance of the individual. It is the product of interactions between genes and between the genotype and the environment. This includes the killer phenotype, characteristic of YEASTS. [NIH]

Physiologic: Having to do with the functions of the body. When used in the phrase "physiologic age," it refers to an age assigned by general health, as opposed to calendar age. [NIH]

Ploidy: The number of sets of chromosomes in a cell or an organism. For example, haploid means one set and diploid means two sets. [NIH]

Polysaccharide: A type of carbohydrate. It contains sugar molecules that are linked together chemically. [NIH]

Preclinical: Before a disease becomes clinically recognizable. [EU]

Precursor: Something that precedes. In biological processes, a substance from which another, usually more active or mature substance is formed. In clinical medicine, a sign or symptom that heralds another. [EU]

Prednisone: Belongs to the family of drugs called steroids and is used to treat several types of cancer and other disorders. Prednisone also inhibits the body's immune response. [NIH]

Preoperative: Preceding an operation. [EU]

Progressive: Advancing; going forward; going from bad to worse; increasing in scope or severity. [EU]

Prophylaxis: An attempt to prevent disease. [NIH]

Psychotherapy: A generic term for the treatment of mental illness or emotional disturbances primarily by verbal or nonverbal communication. [NIH]

Punishment: The application of an unpleasant stimulus or penalty for the purpose of eliminating or correcting undesirable behavior. [NIH]

Radiolabeled: Any compound that has been joined with a radioactive substance. [NIH]

Radiology: The use of radiation (such as x-rays) or other imaging technologies (such as ultrasound and magnetic resonance imaging) to diagnose or treat disease. [NIH]

Radiotherapy: The treatment of disease by ionizing radiation. [EU]

Randomized: Describes an experiment or clinical trial in which animal or human subjects are assigned by chance to separate groups that compare different treatments. [NIH]

Recurrence: The return of cancer, at the same site as the original (primary) tumor or in another location, after the tumor had disappeared. [NIH]

Refractory: Not readily yielding to treatment. [EU]

Regimen: A treatment plan that specifies the dosage, the schedule, and the duration of treatment. [NIH]

Remission: A decrease in or disappearance of signs and symptoms of cancer. In partial remission, some, but not all, signs and symptoms of cancer have disappeared. In complete remission, all signs and symptoms of cancer have disappeared, although there still may be cancer in the body. [NIH]

Resected: Surgical removal of part of an organ. [NIH]

Resection: Removal of tissue or part or all of an organ by surgery. [NIH]

Rituximab: A type of monoclonal antibody used in cancer detection or therapy. Monoclonal antibodies are laboratory-produced substances that can locate and bind to cancer cells. [NIH]

Screening: Checking for disease when there are no symptoms. [NIH]

Secretion: 1. the process of elaborating a specific product as a result of the activity of a gland; this activity may range from separating a specific substance of the blood to the elaboration of a new chemical substance. 2. any substance produced by secretion. [EU]

Serum: The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed. [NIH]

Somatic: 1. pertaining to or characteristic of the soma or body. 2. pertaining to the body wall in contrast to the viscera. [EU]

Spectrum: A charted band of wavelengths of electromagnetic vibrations obtained by refraction and diffraction. By extension, a measurable range of activity, such as the range of bacteria affected by an antibiotic (antibacterial s.) or the complete range of manifestations of a disease. [EU]

Sporadic: Neither endemic nor epidemic; occurring occasionally in a random or isolated manner. [EU]

Staging: Performing exams and tests to learn the extent of the cancer within the body, especially whether the disease has spread from the original site to other parts of the body. [NIH]

Steroids: Drugs used to relieve swelling and inflammation. [NIH]

Subconjunctival: Situated or occurring beneath the conjunctiva. [EU]

Subcutaneous: Beneath the skin. [NIH]

Systemic: Affecting the entire body. [NIH]

Telangiectasia: The permanent enlargement of blood vessels, causing redness in the skin or mucous membranes. [NIH]

Testicular: Pertaining to a testis. [EU]

Testis: Either of the paired male reproductive glands that produce the male germ cells and the male hormones. [NIH]

Thioguanine: An anticancer drug that belongs to the family of drugs called antimetabolites. [NIH]

Thoracentesis: Removal of fluid from the pleural cavity through a needle inserted between the ribs. [NIH]

Thoracoscopy: The use of a thin, lighted tube (called an endoscope) to examine the inside of the chest. [NIH]

Thoracotomy: An operation to open the chest. [NIH]

Toxic: Having to do with poison or something harmful to the body. Toxic substances usually cause unwanted side effects. [NIH]

Toxicity: The quality of being poisonous, especially the degree of virulence of a toxic microbe or of a poison. [EU]

Transplantation: The replacement of an organ with one from another person. [NIH]

Trimetrexate: A nonclassical folic acid inhibitor through its inhibition of the enzyme dihydrofolate reductase. It is being tested for efficacy as an antineoplastic agent and as an antiparasitic agent against Pneumocystis carinii pneumonia in AIDS patients. Myelosuppression is its dose-limiting toxic effect. [NIH]

Tumour: 1. swelling, one of the cardinal signs of inflammations; morbid enlargement. 2. a new growth of tissue in which the multiplication of cells is uncontrolled and progressive; called also neoplasm. [EU]

Urine: Fluid containing water and waste products. Urine is made by the kidneys, stored in the bladder, and leaves the body through the urethra. [NIH]

Vaccine: A substance or group of substances meant to cause the immune system to respond to a tumor or to microorganisms, such as bacteria or viruses. [NIH]

Vinblastine: An anticancer drug that belongs to the family of plant drugs called vinca alkaloids. It is a mitotic inhibitor. [NIH]

Vincristine: An anticancer drug that belongs to the family of plant drugs called vinca alkaloids. [NIH]

Vindesine: An anticancer drug that belongs to the family of plant drugs called vinca alkaloids. [NIH]

Vinorelbine: An anticancer drug that belongs to the family of plant drugs called vinca alkaloids. [NIH]

Virus: Submicroscopic organism that causes infectious disease. In cancer therapy, some viruses may be made into vaccines that help the body build an immune response to, and kill, tumor cells. [NIH]

General Dictionaries and Glossaries

While the above glossary is essentially complete, the dictionaries listed here cover virtually all aspects of medicine, from basic words and phrases to more advanced terms (sorted alphabetically by title; hyperlinks provide rankings, information and reviews at Amazon.com):

- **The Cancer Dictionary** by Roberta Altman, Michael J., Md Sarg; Paperback - 368 pages, 2nd Revised edition (November 1999), Checkmark Books; ISBN: 0816039542; **http://www.amazon.com/exec/obidos/ASIN/0816039542/icongroupinterna**
- **Dictionary of Medical Acronymns & Abbreviations** by Stanley Jablonski (Editor), Paperback, 4th edition (2001), Lippincott Williams & Wilkins Publishers, ISBN: 1560534605, **http://www.amazon.com/exec/obidos/ASIN/1560534605/icongroupinterna**
- **Dictionary of Medical Terms : For the Nonmedical Person (Dictionary of Medical Terms for the Nonmedical Person, Ed 4)** by Mikel A. Rothenberg, M.D, et al, Paperback - 544 pages, 4th edition (2000), Barrons Educational Series, ISBN: 0764112015, **http://www.amazon.com/exec/obidos/ASIN/0764112015/icongroupinterna**

- **A Dictionary of the History of Medicine** by A. Sebastian, CD-Rom edition (2001), CRC Press-Parthenon Publishers, ISBN: 185070368X, **http://www.amazon.com/exec/obidos/ASIN/185070368X/icongroupinterna**
- **Dorland's Illustrated Medical Dictionary (Standard Version)** by Dorland, et al, Hardcover - 2088 pages, 29th edition (2000), W B Saunders Co, ISBN: 0721662544, **http://www.amazon.com/exec/obidos/ASIN/0721662544/icongroupinterna**
- **Dorland's Electronic Medical Dictionary** by Dorland, et al, Software, 29th Book & CD-Rom edition (2000), Harcourt Health Sciences, ISBN: 0721694934, **http://www.amazon.com/exec/obidos/ASIN/0721694934/icongroupinterna**
- **Dorland's Pocket Medical Dictionary (Dorland's Pocket Medical Dictionary, 26th Ed)** Hardcover - 912 pages, 26th edition (2001), W B Saunders Co, ISBN: 0721682812, **http://www.amazon.com/exec/obidos/ASIN/0721682812/icongroupinterna/103-4193558-7304618**
- **Melloni's Illustrated Medical Dictionary (Melloni's Illustrated Medical Dictionary, 4th Ed)** by Melloni, Hardcover, 4th edition (2001), CRC Press-Parthenon Publishers, ISBN: 85070094X, **http://www.amazon.com/exec/obidos/ASIN/85070094X/icongroupinterna**
- **Stedman's Electronic Medical Dictionary Version 5.0 (CD-ROM for Windows and Macintosh, Individual)** by Stedmans, CD-ROM edition (2000), Lippincott Williams & Wilkins Publishers, ISBN: 0781726328, **http://www.amazon.com/exec/obidos/ASIN/0781726328/icongroupinterna**
- **Stedman's Medical Dictionary** by Thomas Lathrop Stedman, Hardcover - 2098 pages, 27th edition (2000), Lippincott, Williams & Wilkins, ISBN: 068340007X, **http://www.amazon.com/exec/obidos/ASIN/068340007X/icongroupinterna**
- **Stedman's Oncology Words** by Beverly J. Wolpert (Editor), Stedmans; Paperback - 502 pages, 3rd edition (June 15, 2000), Lippincott, Williams & Wilkins; ISBN: 0781726549; **http://www.amazon.com/exec/obidos/ASIN/0781726549/icongroupinterna**
- **Tabers Cyclopedic Medical Dictionary (Thumb Index)** by Donald Venes (Editor), et al, Hardcover - 2439 pages, 19th edition (2001), F A Davis Co, ISBN: 0803606540, **http://www.amazon.com/exec/obidos/ASIN/0803606540/icongroupinterna**

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