

YOU AND YOUR TREATMENT

Danielle, age 22,
11-year Leukemia
(T-ALL) survivor



If children have the ability to ignore all odds and percentages, then maybe we can all learn from them.

When you think about it, what other choice is there but to hope?

We have two options, medically and emotionally: give up, or fight like hell.

LANCE ARMSTRONG

YOU AND YOUR TREATMENT

TREATMENT FOR MOST PEDIATRIC CANCERS primarily consists of chemotherapy, surgery, or radiation.

These treatments can be used alone or in combination with one another. Other treatments also used include bone marrow/stem cell transplantation, immunotherapy (using the body's own immune system to fight cancer cells), and differentiating agents (drugs that mature cancer cells).

The choice of treatment is based on the following:

- Type and stage of the tumor
- Whether the tumor responds best to chemotherapy, radiation, or surgery
- Evidence based on results of clinical trials done over the last 20 years

This chapter provides a general understanding of the different cancers that occur in children and their respective treatments (chemotherapy, radiation, surgery, bone marrow/stem cell transplantation), how these treatments work, and what their possible late effects might be. There is also a section devoted to the different tests that doctors perform, first, to diagnose the cancer, and then to follow response.

Finally, included are recommendations for screening and follow-up for the late effects of all the treatments you may have received for your cancer. These are standard guidelines adapted from the 'Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers' published by the Children's Oncology Group (COG).

We hope that this simplified explanation of your treatment will help you better understand your cancer, and that the follow-up guidelines provided will keep you on track for regular visits to your healthcare providers.

You and Your Treatment

1	An Overview of Childhood Cancers <ul style="list-style-type: none">• Childhood Cancer Incidence and Survival• Cancer Staging and Pre-Treatment Evaluation• Important Tests for Diagnosis and Follow-up• Types of Cancers and Recommended Screening• Late Effects Associated with Childhood Cancers
2	Chemotherapy and Related Late Effects
3	Radiation and Related Late Effects
4	Surgery and Related Late Effects
5	Bone Marrow/Stem Cell Transplantation and Related Late Effects

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For all information related to Long-Term Follow-Up Guidelines:

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AN OVERVIEW

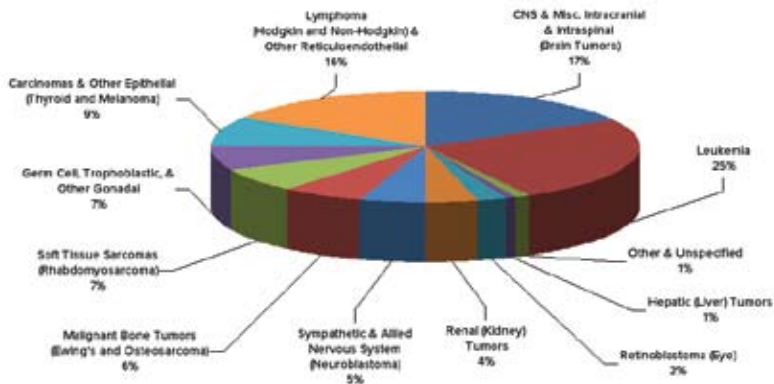
of Childhood Cancers

Childhood Cancer Incidence and Survival

Childhood Cancer Is Rare

- Approximately 12,400 American children and adolescents under the age of 20 were diagnosed with cancer in the year 2000.
- The rate at which new cases develop in children per year (incidence) roughly corresponds to 1:6500 children and adolescents under the age of 20.
- The risk of any individual child developing cancer between birth and 20 years of age is 1:300.
- In most cases, the cause of childhood cancer remains unknown.
- In a fraction of cases, the following factors are known to increase the risk of developing certain childhood cancers:
 - Genetic factors
 - Certain prenatal (before birth) exposures, such as radiation and diethylbestrol (medicine used to prevent miscarriages in pregnant women)
 - Certain postnatal (after birth) exposures, such as radiation and viruses

Distribution of Childhood Cancers (Age 0-19) by International Classification of Childhood Cancers (ICCC) Category, 1975–1995



Source: ACS, 2000. Data from SEER Program, National Cancer Institute

Cancer Staging and Pre-Treatment Evaluation

When cancer is diagnosed, it is important for the oncologist to know where the cancer is and whether the disease has spread from the original site to other parts of the body. This is known as staging—a description of the extent of the cancer within the body.

Why is Staging important?

- Staging helps an oncologist plan the most effective treatment
- Staging helps clinicians exchange information about patients, and gives them a common language for evaluating the results of clinical trials (research studies)
- Staging is used for all solid tumors

Staging Systems:

Staging systems for cancer have evolved over time, and continue to change as scientists learn more about cancer. Although, there are different types of staging systems for different types of tumors, in general, this is what they mean:

- **Stage I** - The cancer is localized or has not spread to other parts of the body.
- **Stage II** - The cancer has spread locally beyond the primary tumor (the site where the cancer started) to tissue or a lymph node close to the primary tumor.
- **Stage III** - Usually means that the tumor is very large and difficult to remove surgically. Surrounding lymph nodes are positive for disease. The tumor may lie above and below the diaphragm (muscle separating chest and abdomen).
- **Stage IV** - The cancer has spread beyond the primary tumor to distant parts of the body. This is known as metastasis.

Determination of Stage:

To determine the stage and treatment of a tumor, a number of pre-treatment diagnostic tests are performed. There is variation for each tumor type, but in general, the following tests and exams are done:

- Audiology Exam
- Blood Tests (CBC, chemistry panel, LDH, uric acid, ESR, ferritin, and other specialized tests depending on the tumor)
- Bone Marrow Aspirate/Biopsy
- Bone Scan
- Creatinine Clearance
- CT Scan
- Echocardiogram
- Electrocardiogram
- Eye Exam with Fundoscopy
- Gallium scan
- MIBG Scan
- MRI
- PET scan
- Pulmonary Function Tests
- Spinal tap (lumbar puncture)
- Tanner Staging
- Tumor biopsy
- Ultrasound
- Urinalysis
- X-ray

Important Tests for Diagnosis and Follow-Up

As part of your long term follow-up screening, you may need to have testing done on a periodic basis. Many of these tests are the same as what you had done before you began treatment. Some of these will be done as a baseline at your first long-term follow-up visit, and then again only as needed.

Audiogram



An audiogram is a picture of your hearing that is reflected on a graph that shows the softest sounds a person can hear at different pitches or frequencies. It provides accurate diagnosis of most hearing problems.

It is used to identify the presence of hearing loss, as well as the cause.

Blood Tests



- **Hormone studies:** These tests are done to measure hormone levels in your body. For females, these would include estradiol, FSH, and LH; for males, these would include testosterone, FSH and LH.
- **Thyroid studies:** These tests are done to learn how well your thyroid is working and include TSH, Free T4, and T3.
- **Lipid profile:** This measures your total cholesterol, as well as good (HDL) and bad (LDL) cholesterol levels.
- **Kidney profile:** These tests measure how well your kidneys are working and include BUN, creatinine, and electrolytes (blood salts, sugar, and minerals).

- **Liver profile:** These tests measure how well the liver is working and include AST, ALT, LDH, and bilirubin (total, direct, and indirect).
- **CBC:** This measures how well your bone marrow is making white blood cells (to fight infection), red blood cells (to transport oxygen), and platelets (help stop bleeding).

Bone Density Test (Also called a DEXA SCAN)



© UT Austin

A bone density test uses special X-rays to measure how many grams of calcium and other bone minerals are packed into a segment of bone. The higher your mineral content, the denser your bones are. The denser your bones, the stronger they generally are. This means they are less likely to break. Doctors use a bone density test to determine if you have, or are at risk of, osteoporosis (weakened bones). Survivors who received steroids as a part of their cancer treatment are at risk for developing osteoporosis.

Bone Marrow Aspirate/Biopsy



A bone marrow aspirate is a procedure that uses a hollow needle to remove fluid from the body's bone marrow. A bone marrow biopsy is a similar procedure used to remove solid tissue from the bone marrow.

Bone Scan



A bone scan is a test that detects areas of increased or decreased bone metabolism (turnover). The test is performed to identify abnormal processes involving the bone such as tumor, infection, or fracture.

Creatinine Clearance



Creatinine clearance measures the amount of waste product, creatinine, which is found in the blood and urine. This allows for a doctor to determine how well your kidneys are working. The test is usually performed with both a blood and urine sample collected over 24-hours.

CT Scan or CAT scan (Computed axial tomography scan)



A CT scan is a painless imaging technique that uses special x-ray equipment to produce multiple pictures of the inside of the body. A computer then joins these images together in cross-sectional views of the areas being studied. CT scans of internal organs, bones, soft tissues, and blood vessels provide more information than regular x-rays. These images can be printed out or looked at on a computer monitor.

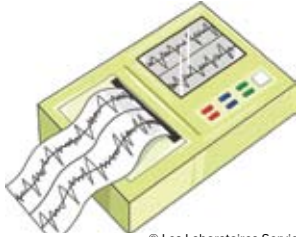
ECHO (Echocardiogram)



© Les Laboratoires Servier

An echo is a type of ultrasound test that uses high frequency sound waves to provide pictures of the structure and components of the heart. An echo measures the size and thickness of the heart chambers, how the heart is handling the pumping of blood through the chambers, and blood flow through the heart valves.

EKG (Electrocardiogram)



© Les Laboratoires Servier

Electrical signals in the heart trigger heartbeats. The signals travel from the top of the heart to the bottom which causes the heart muscle to contract. As the heart contracts, it pumps blood out to the rest of the body. An EKG records the electrical activity of the heart and

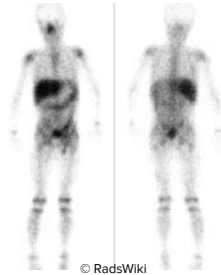
detects and locates the source of heart problems. An EKG translates the electrical activity into line tracings on paper.

Eye Exam with Fundoscopy



A visual acuity exam tests the clearness of vision and the ability of the retina to properly focus and transmit signals to the brain. A fundoscopic exam is a technique that illuminates and provides a magnified image of the back of the eye to observe for abnormalities.

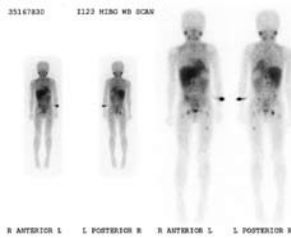
Gallium Scan



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A gallium scan is a type of nuclear medicine test that uses the radioactive dye, gallium citrate, to allow a camera to take pictures of specific tissues of the body. The gallium is usually injected into the arm and then the scan is performed 24 -48 hours later. Due to the chemical nature of gallium, it flows through the blood stream and accumulates at sites of disease and infection, allowing these trouble spots to be highlighted in the scan.

MIBG Scan



© RadsWiki

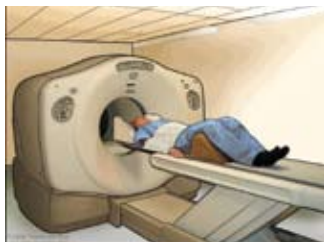
A MIBG scan is a type of nuclear medicine test that uses the radioisotope MIBG to allow a scanner to detect for adrenal gland tumors, such as neuroblastoma. The MIBG radioisotope is usually injected into the patient's arm or central line.

MRI (Magnetic Resonance Imaging)



A painless technique that combines a powerful magnet, radio waves, and sophisticated computers to produce extremely detailed images of your internal organs and tissues *without* exposing you to radiation. Common MRI exams involve the brain, spinal cord, abdomen, and blood vessels. They are very helpful in diagnosing, both disease and injury.

PET Scan (Positron Emission Tomography)



A PET scan is a type of nuclear medicine imaging technique that uses gamma rays to scan the metabolic activity of the human body in a three-dimensional image. While CT and MRI scans provide details about body structure, a PET scan provides

information about function throughout the entire body and can uncover abnormalities that might otherwise go undetected.

■ PET/CT (Positron Emission Tomography and Computed Tomography)

Sometimes these two tests are done together. The PET demonstrates the biological function of the body and the CT scan provides information about the anatomy such as size, shape, and location. When combined, these scanning technologies can help physicians accurately identify and diagnose diseases, such as cancer.

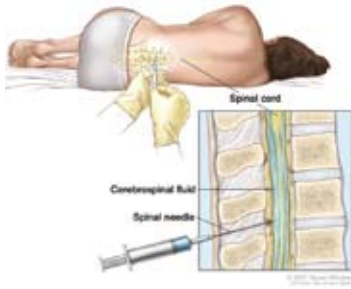
Pulmonary Function Tests



Pulmonary function tests are a group of tests that measure the strength and capacity of the lungs by measuring how well the lungs take in and release air, move oxygen into blood, and oxygenate the rest of the body.

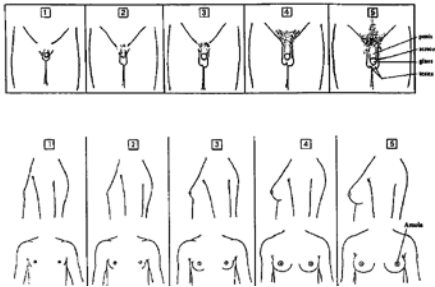
The information from this test is useful in diagnosing certain types of lung problems.

Spinal Tap (Lumbar Puncture)



A spinal tap is a procedure done to remove cerebrospinal fluid from your spinal column in order to test for diseases of the brain and spinal cord, such as multiple sclerosis or leukemia. It is done by placing a needle into the spinal column. It is commonly referred to as an LP.

Tanner Staging



Tanner Staging is an assessment of puberty levels based on the growth of pubic hair in both sexes, genitalia maturity in boys, and breast maturity in girls.

Source: 'Assessment of Nutritional Status in Emergency-Affected Populations.' Woodruff, et al.

Tumor Biopsy



A biopsy is a medical procedure performed to remove tissue or cells from a tumor. These samples are later analyzed under a microscope to make the diagnosis.

Ultrasound



A procedure in which high-energy sound waves (ultrasound) are bounced off internal tissues or organs to make echoes. The echoes form a picture of body tissues called a sonogram. An ultrasound is helpful in looking for tumors.

Urinalysis



Urinalysis is a test to check the color of urine and its contents, such as sugar, protein, blood, and bacteria.

X-Ray



An x-ray is a type of energy beam that can go through the body and onto film, making a picture of areas inside the body.

Types of Cancers and Recommended Screening

- ▶ Bone Tumors
- ▶ Brain Tumors
- ▶ Germ Cell Tumors
- ▶ Histiocytosis*
- ▶ Leukemia
- ▶ Liver Tumors
- ▶ Lymphoma
- ▶ Melanoma
- ▶ Nasopharyngeal Carcinoma
- ▶ Neuroblastoma
- ▶ Retinoblastoma
- ▶ Soft Tissue Sarcomas
- ▶ Thyroid Cancer
- ▶ Wilms' Tumor

*Not usually considered a malignancy

Bone Tumors

- Malignant bone tumors account for 6% of childhood cancers
- Peak incidence is at age 15, which coincides with adolescent growth spurts
- Osteosarcoma and Ewing's Sarcoma Family of Tumors (ESFT's) fall into this category

Ewing's Sarcoma Family of Tumors (ESFT)

What is Ewing's Sarcoma?

- Ewing's sarcoma is a cancerous tumor that develops in the bone or in the tissues outside the bone, called soft tissue.
- Ewing's sarcoma can occur in any bone in the body, but the most common sites are the pelvis (hip), thigh bone (femur), upper arm bone (humerus), and the ribs.
- The Ewing's sarcoma family of tumors also includes other similar soft tissue tumors such as Extrasosseous Ewing's sarcoma (EES) and Peripheral Neuroectodermal Tumor (PNET).

Facts about ESFTs

- ▶ Number of cases/year in the USA is approximately 250
- ▶ It most commonly occurs between the ages of 10 and 20, but younger children and adults can get it too
- ▶ It can occur anytime in childhood, but most commonly occurs during puberty when bones are growing rapidly
- ▶ More common in boys than in girls, and more in Caucasians than in other races
- ▶ No environmental factors have been associated with ESFTs
- ▶ More than 90% of ESFTs have a translocation between chromosomes 11 and 22 called t (11; 22)
- ▶ Five year survival for localized disease is close to 60%

Treatment

Chemotherapy

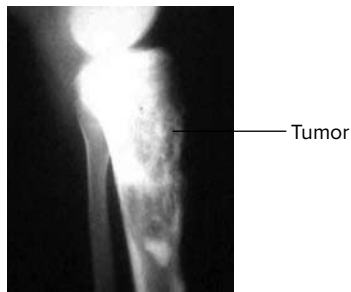
- First given to shrink the tumor as much as possible before surgery
- Given again following surgery to kill any remaining cancer cells that were too small to see during surgery
- Common chemotherapy drugs used for Ewing's Sarcoma:
 - **Frontline drugs:** vincristine, doxorubicin, cyclophosphamide, etoposide, ifosfamide
 - **Relapse or refractory disease:** topotecan, irinotecan, temozolamide, taxotere, monoclonal antibodies

Surgery

- Only if the tumor is at an accessible site and can be removed without a problem
 - Limb salvage surgery
 - Amputation
 - Thoracotomy (removal of tumor from the lungs)

Radiation Therapy

- ESFT'S are very radio-sensitive tumors
- Radiation is usually directed to the tumor site
- Only given to patients whose tumors cannot be removed completely.



End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist.

History & Physical Exam:

1st–4th year: every 3 months

5th year every 6 months

Blood Tests:

1st–4th year: every 3 months

5th year every 6 months

Chest & extremity X-Ray:

every 3 months for 1st-4th year, then every 6 months for 5th year

CT/MRI chest and tumor site:

at end of treatment, and then as indicated

Cardiac Evaluation (Echo/EKG):

at end of treatment and then at 1-5 years depending on anthracycline dose received

Functional evaluation:

1 year off treatment, then at 2.5 years & 5 years

Fertility Evaluation:

1 year off treatment, then as needed

Osteosarcoma

What is Osteosarcoma?

- Osteosarcoma is a bone cancer that develops in cells called osteoblasts
- Most common bone tumor
- Most common site for osteosarcoma is in the bones around the knee, usually:
 - at the end of the thigh bone (femur) closest to the knee, or
 - the upper end of the shin bone (tibia) closest to the knee
- The second most common site is at the end of the upper arm bone (humerus), near the shoulder
- Other less common sites include the pelvis (hip), jaw, and ribs
- 20% of children with osteosarcoma already have metastases (cancer spread to other parts of the body, usually the lungs) at the time of diagnosis

Facts about Osteosarcoma

- ▶ There are about 370 new cases diagnosed each year
- ▶ Peak incidence for osteosarcoma occurs between the ages of 10 and 25 years
- ▶ There appears to be an association between the disease and rapid bone growth during the adolescent growth spurt
- ▶ Boys are twice as likely as girls to develop osteosarcoma
- ▶ Slightly more common in Caucasians than in African-Americans
- ▶ Patients with the inherited form of retinoblastoma (tumor of the eye) or Li- Fraumeni syndrome (a rare, inherited disorder) have a higher risk of developing osteosarcoma
- ▶ Radiation is the only known environmental risk factor associated with osteosarcoma
- ▶ Five year survival is close to 65% for localized disease

Treatment

Chemotherapy

- First given to shrink the tumor as much as possible before surgery.
- It is given again following surgery to kill any remaining cancer cells in the body.
- Common chemotherapy drugs used for Osteosarcoma:
 - **Frontline drugs:** doxorubicin, high dose methotrexate with leucovorin rescue, cisplatin, ifosfamide
 - Biological response modifier called MTP-PE (used in patients with localized disease to treat microscopic disease that may be present in the lungs)
 - **Relapse or refractory disease:** topotecan, aerosolized GM-CSF, etoposide, irinotecan, carboplatin, monoclonal antibodies (trastuzumab, anti IGF-1 receptor)

Surgery

- An integral part of treatment for this tumor.
 - Limb salvage surgery
 - Amputation
 - Rotationplasty
 - Thoracotomy (removal of tumor from the lungs in patients with metastatic disease)

Radiation Therapy

- Usually no role in Osteosarcoma
- Targeted radiation may be used for pain control in advanced, refractory disease



Courtesy of
Martin Malawer, MD, FACS

End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist.

History & Physical Exam:

1st year: every 2-3 months
2nd year: every 3-4 months
3rd–4th year: every 6 months
5th–10th year: every 12 months

Blood Tests:

1st–2nd year: every 6 weeks–3months
3rd–4th year: every 2–4 months
5th–10th year: every 6 months

Chest & extremity X-Ray:

every 3 months for 1st year, every 6 months for 2nd–3rd year, every year for 10 years

CT Chest/MRI:

every 4–6 months for first 3 years or as indicated

Cardiac Evaluation (Echo/EKG):

at end of treatment and then at 1-5 years depending on anthracycline dose received

Hearing Test:

end of treatment, 2.5 years or as indicated

Functional evaluation (physical therapy evaluation):

1 year off treatment, then at 2.5 years & 5 years

Fertility Evaluation:

1 year off treatment, then as needed

Brain Tumors

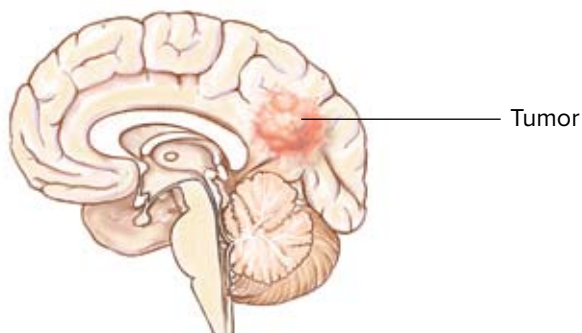
What are Brain Tumors?

Childhood brain tumors make up the second largest group of cancers in children. They are a diverse group of diseases characterized by the abnormal growth of tissue contained within the skull.

Brain tumors can arise from any part of the brain and may be benign (without cancer cells) or malignant (contain cancer cells).

Understanding the basic anatomy of the brain will help in understanding brain tumors. The brain is divided into three main sections: the cerebrum, the brainstem and the cerebellum.

- **Cerebrum:** (supratentorial area or the upper brain) refers to the front of the brain. It is responsible for our emotions, as well as learning, vision, touch, hearing, and reasoning abilities
- **Brainstem:** refers to the midline or middle of the brain and is responsible for eye movement, relaying sensory messages, feelings of hunger, breathing, heart function, swallowing, and coughing
- **Cerebellum:** (infratentorial area or the lower brain) refers to the back of the brain and is responsible for coordination of muscle movement and balance



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Benign and Malignant Brain Tumors

- Arise from abnormal cells that have grown in the brain
- A benign tumor does not contain cancer cells
 - It usually dies if removed, though it can reoccur
 - It can cause similar symptoms to a malignant tumor depending on its size and location, and where it can damage vital brain function
- A malignant tumor contains cancer cells
 - It can grow rapidly and invade the surrounding tissue

Facts about Brain Tumors

- ▶ Primary brain tumors are the most common solid tumors in children and adolescents
- ▶ There are about 2250 new cases diagnosed in the USA each year
- ▶ Since there are many different types of brain tumors, the number of children in each group is small
- ▶ Occur more often in boys than in girls, and more often in Caucasians than African-Americans
- ▶ Children who received radiation therapy to the head as part of another treatment are at increased risk for developing a brain tumor
- ▶ Children or adolescents with certain rare genetic diseases are at greater risk for brain tumors
- ▶ Symptoms of a brain tumor depend mostly on its location
- ▶ 5-year survival rates have improved over time to 67%

Types of Brain Tumors

There are many types of brain tumors.

Children between the ages of 1 and 12 are more likely to develop a brain tumor in the lower half of the brain. After puberty, most tumors are found in the upper brain.

Brain tumors are named for the type of cell from which they grow and their location in the brain. The most common brain tumors found in children are as follows:

Astrocytoma

- More than 1/2 the tumors in children and adults belong to this group
- The tumors arise from star-shaped cells called astrocytes which form the supportive system of the brain
- Low-grade astrocytomas grow slowly and most patients with these tumors do well
- High-grade astrocytomas grow rapidly and are more difficult to treat

Medulloblastomas

- A very fast growing malignant tumor usually located in the cerebellum
- More common in boys than in girls
- More common in children between 4 and 8 years

Ependymomas

- These tumors grow on the inner surface of the brain and spinal cord
- They are often benign
- Ependymomas of the brain are commonly seen in children under 10 years of age

- Ependymomas of the spinal cord are seen in children over the age of 12 years

Brain Stem Gliomas

- Slow or fast growing tumors categorized based on their tissue of origin
- They occur in both boys and girls equally
- Commonly seen between the ages of 5 and 10 years

Optic Nerve Gliomas

- These tumors occur along the optic nerves, optic chiasma and hypothalamus

Craniopharyngioma

- A benign tumor that occurs at the base of the brain.
- May be associated with hormone problems

Treatment of Brain Tumors

Treatment for brain tumors depends on:

- Location of the tumor
- Grade of the tumor
- In general, the higher the grade, the more aggressive the treatment

Treatment primarily consists of a combination of surgery, radiation, and chemotherapy.

Surgery

- This is usually the first step and often one of the most important parts of treatment for brain tumors
- The goal is to remove as much of the tumor as possible while keeping the brain working
- Surgery is needed to obtain a biopsy to figure out the type of brain tumor

- It is also performed to place a shunt to drain fluid from the brain
- Best results are obtained if the entire tumor can be surgically removed. This may not always be possible because:
 - The tumor may be in a location difficult to reach
 - The tumor may have grown into other structures around it
 - Removing the tumor may damage vital areas in the brain

Chemotherapy

The use of chemotherapy varies from tumor to tumor based on:

- The age of the child
 - in children < 3 years of age, it may be used to slow growth of the tumor till radiation can be given
- Sensitivity of the tumor to chemotherapy
 - medulloblastoma is extremely sensitive to chemotherapy
 - brain stem gliomas and ependymomas do not respond well to chemotherapy
- **Frontline drugs:** vincristine, cisplatin, carboplatin, etoposide, temozolamide, cyclophosphamide, CCNU, mephalan, steroids
- **Relapse or refractory disease:** high dose chemotherapy with drugs such as carboplatin, cisplatin, ifosfamide followed by stem cell rescue

Radiation Therapy

- Using high-energy radiation from x-rays to kill cancer cells and shrink tumors is the choice of treatment for many brain tumors
- Radiation usually comes from a machine outside the body (external radiation therapy)
- It is generally given in many doses (fractions) over a period of days or weeks
- The duration of treatment and dose depends on:
 - Age of the child
 - Location of the tumor in the brain
 - Type of tumor

- For some brain tumors, radiation may be given in several small doses per day (hyperfractionated radiation therapy)
- In most cases, radiation is directed to the tumor itself, sparing the surrounding healthy tissue as much as possible
- In very aggressive brain tumors, the tumor site and the whole brain and spine may also be radiated to destroy any cancer cells hiding in those areas
- As brain growth usually occurs in the first few years of life, an effort is always made to postpone or avoid radiation in children less than 3 years of age
- Doses of radiation vary from 1800 cGy to more than 5000 cGy, depending on the tumor
- In order to decrease toxicity, an effort is underway to decrease the dose of radiation and/or employ more targeted radiation

Bone Marrow Transplant/Peripheral Blood Stem Cell Transplants

- Used in relapsed or high risk brain tumors
- High dose chemotherapy is followed by the transplant

Additional Treatment

In addition to chemotherapy, radiation, and surgery, children with brain tumors may need the following:

- Steroids (to treat and prevent swelling in the brain)
- Anti-seizure medications (to prevent seizures)
- ‘Ventriculoperitoneal shunt,’ also called VP shunt (a surgically implanted reservoir that helps to decrease pressure in the brain)
- Rehabilitation: speech, physical, and occupational therapy to regain and re-learn lost motor and speech skills.

End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist.

History & Physical Exam:

1st year: every 3 months
2nd year: every 6 months
3rd–5th year: every 12 months

Blood Tests:

1st year: every 3 months
2nd year: every 6 months
3rd–5th year: every 6–12 months

CT/MRI of original tumor:

every 3 months for 1 yr, every 6 months for year 2, then yearly for 3 years

Hearing tests:

end of treatment then at 3 years

Creatinine clearance:

3 months, then yearly, only if abnormal

Endocrine evaluation:

every 6 months for 2 years, then annually

Neuropsychometric evaluation:

at 3 years

Germ Cell Tumors

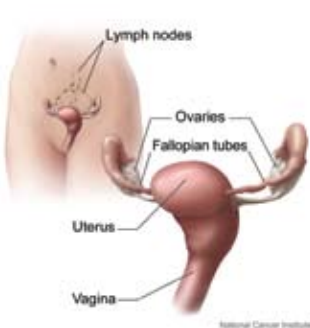
What is a Germ Cell Tumor?

Germ cells are reproductive cells that develop into testicles in males and ovaries in females. Germ cell tumors develop from these testicular or ovarian cells.

Sometimes these cells travel to other areas of the body, such as the brain, chest, abdomen, pelvis, or sacrococcygeal region (area at the end of the spine). In the chest and abdomen, they turn into a rare type of cancer called 'extra-gonadal germ cell tumor'.

Facts about Germ Cell Tumors

- ▶ Account for 7% of all childhood cancers
- ▶ Most germ cell tumors are benign (not cancerous) e.g. teratomas
- ▶ Some may be malignant (cancerous) e.g. some testicular and ovarian tumors
- ▶ More common in adolescents over the age of 15; very rare in children
- ▶ Children and adolescents present with different types of germ cell tumors
- ▶ 5-year survival rates range between 75–94%



Treatment of Germ Cell Tumors

- Usually a combination of surgery and chemotherapy
- Treatment depends on the location of the tumor and age of the child

Surgery

- Usually a complete resection is attempted.
- Surgery may be the only treatment some germ cell tumors need

Chemotherapy

- Not all germ cell tumors need chemotherapy
- **Frontline drugs:** etoposide, cisplatin , bleomycin, carboplatin
- **Relapse drugs:** ifosfamide, etoposide, vinblastine, carboplatin

Radiation

- Limited role in germ cell tumors

High Dose Chemotherapy Followed by Stem Cell Rescue

- In trials for relapsed tumors

End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist.

History & Physical Exam:

1st year: monthly for 6 months, then every 3 months
2nd year: every 6 months
3rd–5th year: every 12 months

Blood Tests:

1st–2nd year: monthly for 6 months, then every 3–6 months
3rd–5th year: every 12 months

CT/MRI of original tumor:

3 months, 6 months, 1 year, 2 years

Chest XRay:

3 months, 6 months, 1 year, 2 years

Hearing tests:

end of treatment, 1 year, 2 years

Pulmonary function tests:

end of treatment, 2 years, 5 years

Creatinine clearance:

3 months, then yearly, only if abnormal

Histiocytosis

What is Histiocytosis?

- A histiocyte is a type of white blood cell that helps destroy certain foreign materials and fight infection
- Histiocytosis is a rare blood disease that is caused by an excess of histiocytes
- These cells cluster together and can attack the skin, bones, lung, liver, spleen, gums, ears, eyes, lymph nodes, bone marrow, and/or the central nervous system
- The most common form is Langerhans cell histiocytosis in which certain cells called Langerhans cells are identified under an electron microscope

Facts about Histiocytosis

- ▶ Histiocytosis is usually seen in children under age 10, and adults of all ages
- ▶ Histiocytosis affects 1 in 200,000 children born each year in the United States
- ▶ Approximately 1,200 new cases are diagnosed each year
- ▶ The cause of histiocytosis is unknown—it may be triggered by an unusual reaction of the immune system from something commonly found in the environment
- ▶ Histiocytosis is not a known infection or cancer
- ▶ Histiocytosis is not known to be hereditary or communicable
- ▶ Histiocytosis is poorly understood and frequently misdiagnosed—it is so rare that there has been limited research into its cause and treatment

Types of Histiocytosis

There are three types of histiocytosis:

■ Class I histiocytosis (Langerhans' cell histiocytosis)

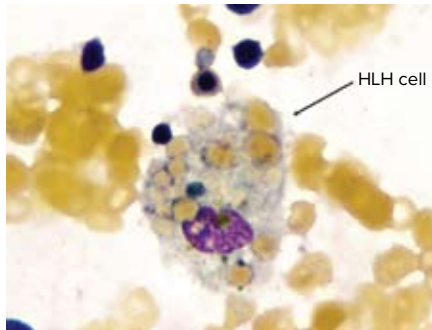
- Most common type of histiocytosis
- Langerhans' cells are found in lesions

■ Class II histiocytosis

- Very rare disorder, also called Hemophagocytic Lymphohistiocytosis (HLH)
- May be familial (runs in the family) or infection associated

■ Class III histiocytosis

- This includes malignant histiocytosis, monocytic leukemia, true histiocytic sarcoma



Treatment for Histiocytosis

In some ways, histiocytosis is similar to cancer and, therefore, has historically been treated by oncologists with chemotherapy and radiation therapy.

Because it so poorly understood, numerous treatment methods have been tried over the years.

- Class I or Langerhans' histiocytosis is treated with a combination of:
 - Etoposide (VP16 or Vepesid)
 - Vinblastine
 - 6-MP
 - Methotrexate
 - Bone marrow transplants are sometimes recommended for children with severe, unresponsive disease.
 - Low-dose radiation may be used for bone involvement; dose ranges from 500-800 cGy.
- Class II histiocytosis or HLH is treated with a combination of:
 - Dexamethasone
 - Etoposide
 - Cyclosporine
 - Bone marrow transplantation is recommended for familial HLH
- Class III or malignant histiocytosis is treated with chemotherapy.
 - **Induction drugs:** vincristine, prednisone, cyclophosphamide and doxorubicin
 - **Maintenance drugs:** vincristine, cyclophosphamide, and doxorubicin

End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist.

- ▶ Complete evaluation at end of treatment with physical exam, blood tests, and relevant x-rays and scans
- ▶ Further follow-up depending on stage of disease

Leukemia

What is Leukemia?

- Leukemia is cancer of the blood cells
- It is the most common childhood cancer, accounting for 25% of all cancers occurring before the age of 20
- It starts in the bone marrow, the soft spongy center of the bone where blood cells are made.

What Happens in Leukemia?

In a healthy person, the bone marrow makes three main types of blood cells:

- **White blood cells:** help the body fight infection.
- **Red blood cells:** carry oxygen from the lungs to all parts of the body
- **Platelets:** help the blood clot

In leukemia, the bone marrow starts to make a lot of abnormal or immature white blood cells, called 'leukemia blasts'. They have an unusual shape and cannot do the work of normal white blood cells. Leukemia cells grow faster than normal cells, and don't stop growing when they should. This explains why the disease is called leukemia which literally means "white blood."

Over time, leukemia cells crowd out the normal blood cells. As a result, healthy, normal cells can no longer be produced. As the red blood cells decrease, the person becomes anemic; with low platelets, one can bleed or bruise excessively; and as there are not enough healthy white cells, there is risk of infection.

Leukemia cells can spread to the blood, lymph nodes, liver, spleen and bones causing swelling or pain.

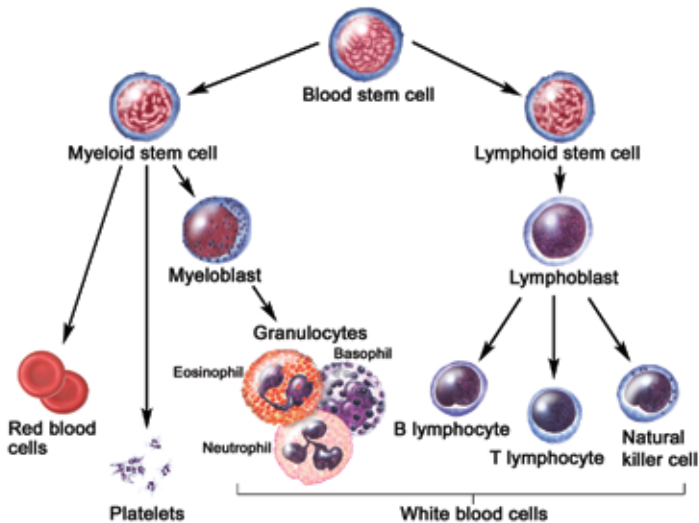
Different Types of Leukemia

The type of leukemia you have depends on:

- The type of white blood cell that is involved (lymphoid or myeloid)
- Whether the leukemia is developing slowly (chronic) or rapidly (acute).

The most common types of childhood leukemia are:

- Acute Lymphoblastic Leukemia (ALL)
- Acute Myeloid Leukemia (AML)
- Chronic Myeloid Leukemia (CML)



Acute Lymphoblastic Leukemia (ALL)

Facts about ALL

- ▶ ALL is a cancer of the lymphocytes (a type of white blood cell)
- ▶ ALL accounts for almost 80% of all childhood leukemias
- ▶ It occurs at all ages, from birth to adulthood; peak incidence is between 2-6 years of age
- ▶ Approximately 2400 children are diagnosed with ALL every year in the US
- ▶ It is more common in Caucasians than African-Americans, and in boys more than girls
- ▶ The 5-year survival rate for ALL is 80%

Risk Factors for ALL

- Having a brother or sister with leukemia
- Being white or Hispanic
- Being exposed to X-rays before birth
- Being exposed to radiation
- Past treatment with chemotherapy or other drugs that weaken the immune system
- Having certain genetic disorders, such as Down Syndrome

Types of ALL

- B-Cell ALL
- T-Cell ALL

Treatment of ALL

- Treatment of ALL is combination chemotherapy. Radiation is only used in certain cases
- It is determined by an analysis of numerous clinical and biologic features, based on which, a child is considered 'standard risk' or 'high risk' and treatment tailored accordingly

■ To determine the risk level of the patient, the following factors are considered:

- Initial white blood count
- Age at diagnosis
- Presence of CNS leukemia
- Presence or absence of certain chromosomal translocations in the leukemia cells [t;(9;22), t;(12;21), t;(1;19), t;(4;11)]
- How quickly the child goes into remission

Chemotherapy

- Systemic chemotherapy (given by mouth or IV)
- Intrathecal chemotherapy (given into the spinal fluid) to prevent spread of ALL to the brain and to treat if ALL is in the brain or spinal cord

Treatment of ALL is typically divided into 4 phases:

- Induction:
 - Intensive chemotherapy is used to kill as many leukemia cells as possible and put the patient into remission.
 - Frontline drugs: prednisone, dexamethasone, vincristine, asparaginase, daunorubicin, cyclophosphamide, ara-C and methotrexate
 - Methotrexate and ara-C are used to prevent or treat ALL in the brain and spinal cord
- CNS Prophylaxis:
 - Intrathecal chemotherapy or high dose systemic chemotherapy is given to kill any leukemia cells hiding in the brain or spinal cord.
 - Sometimes, radiation is given for this reason as well.
 - Frontline drugs: methotrexate, ara-C, hydrocortisone
- Consolidation /Intensification:
 - This begins once remission occurs and there is no sign of leukemia
 - Attempts to destroy any remaining leukemia cells
 - Usually involves a combination of many high-dose chemotherapy drugs

- Frontline drugs: methotrexate, ara-C, 6-mercaptopurine, cyclophosphamide, ara-C, asparaginase, vincristine, 6-thioguanine, doxorubicin, prednisone, dexamethasone, etoposide

■ Maintenance:

- Chemotherapy is given for two or more years in an attempt to continue killing any residual leukemia and to cure the patient
- Consists of daily low-dose chemotherapy with pulses of other agents and periodic intrathecal therapy
- Frontline drugs: 6-mercaptopurine, methotrexate, vincristine, dexamethasone, prednisone

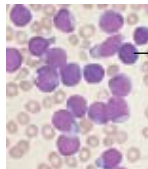
Radiation

Radiation therapy is only used in ALL in certain circumstances:

- CNS prophylaxis: to prevent spread of leukemia cells to the brain or spinal cord in certain leukemias or in high risk patients
- Children who present with leukemia in the brain or spinal fluid at diagnosis, get cranial and spinal radiation

Relapse or Refractory ALL

- Treatment depends on timing of relapse, number of relapses and response to re-treatment
- Chemotherapy combinations using the same or different drugs
- Bone marrow transplantation is recommended for children who do not respond to conventional chemotherapy or are considered poor-risk.



Leukemia Blast

End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist.

History & Physical Exam:

1st year:	every month
2nd year:	every 2 months
3rd year:	every 3 months
4th year:	every 6 months
5th year:	every 6 to 12 months

Blood Tests:

1st year:	every month
2nd year:	every 2 months
3rd year:	every 3 months
4th year:	every 6 months
5th year:	every 6 to 12 months

Serum Markers (ALT):

1st year: every 2 months until normal

Bone Marrow Aspirate/Biopsy:

end of treatment, then as clinically needed

Spinal tap (Lumbar Puncture):

end of treatment, then as clinically indicated

Cardiac Evaluation (Echo/EKG):

end of treatment, then as recommended at 1–5 years, depending on anthracycline dose received

Neuropsychological Evaluation:

during the 1st year off treatment

Acute Myeloid Leukemia (AML)

Facts about AML

- ▶ AML is a cancer of the granulocytes (a type of white blood cell)
- ▶ AML accounts for approximately 20% of all leukemias
- ▶ Diagnosis is higher under the age of 2, then decreases until 9 years of age; increases again in adolescence
- ▶ Approximately 500 children in the USA are diagnosed with AML each year
- ▶ Occurs equally in all ethnic groups, boys and girls are equally affected
- ▶ The 5 year survival rate for AML is less than 50%

Risk Factors for AML:

- Children with certain genetic syndromes are at higher risk of developing AML than other children:
 - Fanconi anemia
 - Kostmann syndrome
 - Bloom syndrome
 - Down syndrome
- Having a brother or sister, especially a twin, with leukemia
- Being exposed to cigarette smoke or alcohol before birth.
- Having a history of myelodysplastic syndrome (also called pre-leukemia) or aplastic anemia
- Past treatment with chemotherapy or radiation therapy
- Being exposed to ionizing radiation or chemicals such as benzene

Types of AML

There are eight different sub-types of AML based on cell shape and chemical properties

- M0 – M7
- M4 sub-types are more common in children < 2 years in age
- M3 subtype has the best survival. It is treated with retinoic acid (ATRA) and chemotherapy

Treatment of AML

Treatment of AML is intensive and is done in phases:

Induction

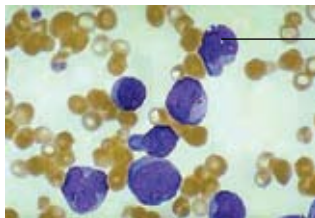
- This is the first phase of treatment. Its purpose is to kill the leukemia cells in the blood and bone marrow. This puts the leukemia into remission
- Front-line treatment: ara-C, daunorubicin, etoposide (common), dexamethasone, 6-thioguanine, idarubicin
- Intrathecal therapy: ara-C, methotrexate
- Monoclonal antibody – gemtuzemab (in clinical trials only)

Consolidation/Intensification

- This is the second phase of treatment. It begins once the leukemia is in remission. The purpose of this phase is to kill any remaining leukemia cells that may not be active but could begin to re-grow and cause a relapse
- Front-line treatment: high dose ara-C, etoposide, asparaginase, doxorubicin or a matched sibling transplant in selected cases

Relapse and Refractory AML

- Drugs used: ara-C, fludarabine, idarubicin, mitoxantrone, etoposide, asparaginase
- Monoclonal antibody – gemtuzemab (in clinical trials only)
- Bone marrow transplantation



Leukemia Blast

End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist.

History & Physical Exam:

1st year:	every month
2nd year:	every 2 months
3rd year:	every 3 months
4th year:	every 6 months
5th year:	every 6 to 12 months

Blood Tests:

1st year:	every 3 months
2nd year:	every 3 months
3rd year:	every 6 months
4th year:	every 6 months
5th year:	every 6 months

Bone Marrow Aspirate/Biopsy:

end of treatment, then as clinically needed

Spinal tap (Lumbar Puncture):

end of treatment, then as clinically indicated

Cardiac Evaluation (Echo/EKG):

- end of treatment and then at 1–5 years depending on anthracycline dose received
- Downs Syndrome patients will need a cardiac evaluation annually for 5 years, then as needed

Chronic Myeloid Leukemia (CML)

In CML, too many bone marrow stem cells develop into a type of white blood cell called granulocytes. Some of these bone marrow stem cells never become mature white blood cells. These are called blasts. Over time, the granulocytes and blasts crowd out the red blood cells and platelets in the bone marrow.

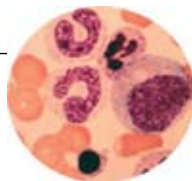
Facts about CML

- ▶ CML is rare in children
- ▶ Accounts for 2–3% of all childhood leukemias
- ▶ Most CML carry a genetic abnormality t;(9:22), also called Philadelphia chromosome
- ▶ Risk factors for CML are the same as for other myeloid leukemias diagnosed each year in USA

Types of CML

- Adult CML
 - Occurs in adolescents and adults
 - It has 3 phases: chronic phase, accelerated phase, blastic phase
 - Patients present with very high white cell counts at diagnosis
 - Frontline treatment: imatinib (Gleevac), dasatinib, ara-C, hydroxyurea, busulphan, related Bone marrow transplantation
- Juvenile CML
 - Is also called chronic myelomonocytic leukemia
 - Mostly occurs in infants
 - Treatment is usually Bone marrow transplantation

CML cells ———



End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist.

History & Physical Exam:

1st year:	every month
2nd year:	every 2 months
3rd year:	every 3 months
4th year:	every 6 months
5th year:	every 6 months

Blood Tests:

1st year:	every 3 months
2nd year:	every 3 months
3rd year:	every 6 months
4th year:	every 6 months
5th year:	every 6 months

Bone Marrow Aspirate/Biopsy:

end of treatment, then as clinically needed in first 2 years

Cardiac Evaluation (Echo/EKG):

end of treatment and then at 1–5 years depending on anthracycline dose received.

Liver Tumors (Hepatic)

What is a Hepatic Tumor?

- Hepatic tumors are cancerous tumors that grow in the liver
- Hepatocytes are the primary cells of the liver. For unknown reasons, a change occurs in these cells and they begin to grow abnormally and form a mass in the liver

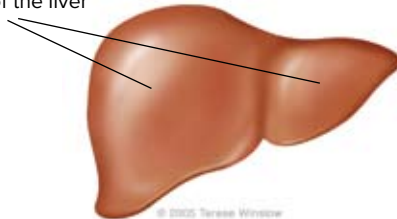
The two most common types of liver cancer are:

- Hepatoblastoma: make up more than 2/3 of all liver tumors
 - More common in younger children < 18 months of age
- Hepatocellular carcinoma: seen most often in older children and adolescents

Facts about Hepatic Tumors

- ▶ Account for 1% of all childhood cancers
- ▶ Boys are affected more than girls
- ▶ About 32 cases in teens are diagnosed each year in the U.S.
- ▶ Children infected with Hepatitis B or Hepatitis C are more likely to develop hepatocellular carcinoma
- ▶ Common areas of metastasis include the lungs, bone marrow, and lymph nodes
- ▶ 5 year survival rates are 54% for all liver tumors (higher for hepatoblastoma at 63%)

Lobes of the liver



Treatment of Hepatic Tumors

Treatment for liver tumors involves surgery, chemotherapy, radiation and liver transplantation, alone or in combination

Surgery

- Usually the most important upfront treatment necessary for liver tumors
- The goal is to remove the entire tumor
- Large portions of the liver can be removed because liver cells can grow back quickly
- In cases where the tumor is too large to be taken out, or involve more than one area of the liver, surgery may have to be done after shrinking the tumor with chemotherapy
- Surgery is also used for biopsy of the tumor

Chemotherapy

- Used to shrink the tumor before surgery and afterwards to kill any remaining cancer cells that were too small to be seen during surgery
- Chemotherapy may be given systemically (by IV) or regionally (directly given to the liver)
- Frontline drugs: cisplatin, vincristine, 5-fluorouracil, doxorubicin, etoposide and ifosfamide may also be used for advanced cases

Liver Transplantation

- Another option for selected patients with liver cancer

Radiation

- A rarely used option for treatment

End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist.

History & Physical Exam:

1st year	every month
2nd–3rd year	every 2 months
3rd–4th year	every 3 months
5th year	every 6 months

Blood Tests (include liver function tests and AFP):

1st year	every month x 6 months, then every 2 months
2nd–4th year	every 3 months
5th year	every 6 months

CT/MRI Abdomen:

every 4-6 months for first 3 years

Cardiac Evaluation (Echo/EKG):

end of treatment and then at 1–5 years depending on anthracycline dose received

Hearing Test:

end of treatment, once a year for 4 years

GFR (kidney function test):

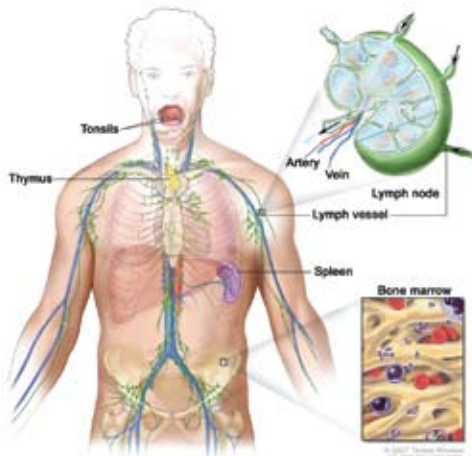
once a year x 4 years

Lymphomas

- Lymphoma means cancer of the lymphatic system, a part of the immune system
- There are two main types of lymphoma:
 - Hodgkin lymphoma
 - Non-Hodgkin's lymphoma
- Lymphomas account for 16% of all childhood cancers
- The risk of developing lymphoma increases with age

What is the Lymphatic System?

- The lymphatic system is made up of a network of thin tubes that run throughout the body, these tubes are called lymph vessels
- Lymph is a clear, colorless, watery liquid that travels through the lymph vessels and carries lymphocytes (a specific type of white cells that protect the body against infection and growth of tumors)
- Interspersed alongside this lymph vessel network are the 'lymph nodes' that make and store lymphocytes
- Lymph nodes are present all over the body: in the neck, armpit, groin, abdomen, and pelvis
- The lymphatic system also includes other important organs such as the liver, spleen, thymus, tonsils, and the bone marrow



Hodgkin Lymphoma

- Hodgkin lymphoma is an abnormal growth of cancer cells in the lymphatic system
- It occurs in both children and adults
- The hallmark of Hodgkin lymphoma is the Reed Sternberg cell, which has a characteristic owl's eye' appearance under the microscope

Facts about Hodgkin Lymphoma

- ▶ Hodgkin lymphoma was first described in 1832 by Dr. Thomas Hodgkin
- ▶ It makes up about 6% of all childhood cancers
- ▶ Most commonly diagnosed in the second decade of life, uncommon in children less than ten years of age
- ▶ The incidence of Hodgkin lymphoma continues to increase during the early teen and adolescent years
- ▶ Under the age of 10, it is more common in boys than in girls
- ▶ Risk factors for Hodgkin lymphoma in the USA include:
 - Being between the ages of 5 and 14 years
 - Having a brother or sister with Hodgkin's disease
 - Having had an infection with the EBV virus (the "mono" virus)
- ▶ Approximately 90–95% children with Hodgkin lymphoma can be cured today

Stages of Hodgkin Lymphoma

- **Stage I** – Cancer is limited to a single lymph node region
- **Stage II** – Cancer is found in two or more lymph node regions on the same side of the diaphragm (the breathing muscle that separates the chest from the abdomen)
- **Stage III** – Cancer is found in lymph nodes on both sides of the diaphragm
- **Stage IV** – There is widespread disease found not only in the lymph tissue, but in other areas as well, such as the bone marrow, liver, lungs, skin, or central nervous system
- Each stage can be further classified as A or B, based on symptoms of fever, night sweats, or weight loss

Types of Hodgkin Lymphoma

There are two types of childhood Hodgkin lymphoma:

- Classical Hodgkin lymphoma
 - Lymphocyte-rich classical Hodgkin lymphoma
 - Nodular sclerosis Hodgkin lymphoma
 - Mixed cellularity Hodgkin lymphoma
 - Lymphocyte-depleted Hodgkin lymphoma
- Nodular lymphocyte predominant Hodgkin lymphoma

Treatment for Hodgkin Lymphoma

Specific treatment for Hodgkin lymphoma depends on the stage of the disease, age of the child, and type of disease.

Therapy may include (alone or in combination):

- Chemotherapy
- Radiation therapy
 - Most patients receive a combination of chemotherapy with low-dose involved-field radiation therapy (LD-IFRT)
- High-dose chemotherapy with stem cell rescue
- Surgery

Chemotherapy

- Usually consists of a combination of different chemotherapy agents
- Is usually risk-adapted (lesser treatment for low stages)
- **Frontline drugs:** cyclophosphamide, procarbazine, vincristine and/or vinblastine, prednisone or dexamethasone, doxorubicin, bleomycin, dacarbazine, etoposide, methotrexate, cytosine arabinoside, mechlorethamine
- **Relapse or refractory disease:** cytarabine, carboplatin, cisplatin, ifosfamide, etoposide, vinorelbine, gemcitabine, vinblastine

Radiation Therapy

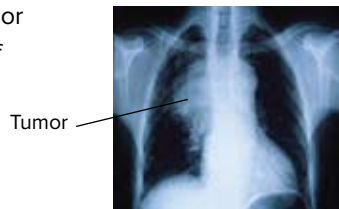
- LD-IFRT involves the use of meticulous and judiciously designed radiation fields
 - To achieve local control of disease
 - To minimize damage to normal tissue
- Care is taken to shield normal tissue as much as possible
 - Shielding of the breast during chest radiation
 - Shielding of the ovaries during groin radiation
- Usual dose of radiation used is between 1500 – 2500 cGy

High Dose Chemotherapy with Stem Cell Rescue

- Used in patients who have relapsed or continue to have disease in spite of treatment
- Usually the patient's own stem cells are given back following treatment with intensive chemotherapy and radiation

Surgery

- Generally used for biopsy of the tumor
- Rarely used to reduce the amount of disease



End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist.

History & Physical Exam:

1st year: every 3 months
2nd–3rd year: every 6 months
4th–10th year: every 12 months

Blood Tests:

1st year: every 3 months
2nd–3rd year: every 6 months
4th–10th year: every 12 months

Chest X-Ray:

every 4 months for 1st year, every 6 months for 2nd-3rd year, every year for 10 years

CT neck, chest, abdomen, pelvis, Gallium Scan/PET:

at 4 months, at 1 year, then as clinically indicated

Cardiac Evaluation (Echo/EKG):

end of treatment and then at 1–5 years depending on anthracycline dose received

Pulmonary Function Tests:

end of treatment, then at 1 year, 3, 5, 10 and 20 years

DEXA Scan, Endocrine and Fertility Evaluation:

1, 3, 5, 10 and 20 years

Second Malignancy Evaluation:

1, 3, 5, 10 and 20 years

Non-Hodgkin's Lymphoma (NHL)

What is Non-Hodgkin's Lymphoma?

- NHL is a cancer of the immune or lymphatic system
- With some exceptions, it is a generalized disease
- The pattern of spread mimics the migration pattern of normal lymphoid cells
- It occurs in both children and adults
- The incidence of NHL increases with age

Facts about Non-Hodgkin's Lymphoma

- ▶ It's the third most common type of childhood cancer
- ▶ Approximately, 800 children under the age of 20 are diagnosed with NHL every year in the USA
- ▶ Boys are 3 times more likely than girls to develop it
- ▶ Most cases occur in children between the ages of 5 and 15 years
- ▶ NHL rarely occurs in very young children
- ▶ It can start in any part of the body where there is lymphoid tissue, and then spread to almost any organ or tissue in the body, including the liver, bone marrow, and spleen
- ▶ There is an increased risk in children diagnosed with AIDS or those who have weakened immune systems
- ▶ The five-year survival rate for childhood NHL is over 70%

Types of Non-Hodgkin's Lymphoma:

The specific type of lymphoma is determined by how the cells look under a microscope.

There are three major types of childhood non-Hodgkin lymphoma:

- **B-cell NHL:**
 - B-cell origin
 - Accounts for 40-50% of NHL
 - Includes: Burkitt and Burkitt-like lymphoma, Burkitt leukemia
- **Lymphoblastic lymphoma:**
 - Predominantly T-cell origin
 - Accounts for 30% of childhood NHL
- **Large cell lymphoma:**
 - Can be of B or T cell lineage
 - Accounts for 20-25% childhood NHL
 - Includes: Diffuse large B-cell lymphoma and Anaplastic large cell lymphoma

Stages of Non-Hodgkin's lymphoma

- **Stage I** – Single tumor site in one area; no disease in the chest or abdomen
- **Stage II** – Single tumor that may involve local lymph nodes, two or more lymph nodes, or tumor areas on the same side of the diaphragm (breathing muscles that separate the chest from the abdomen); or a primary tumor in the intestinal tract
- **Stage III** – Several tumors above and below the diaphragm, two or more lymph node areas above and/or below the diaphragm, chest tumors, large abdominal tumors, or all tumors near the brain or spine
- **Stage IV** – Any of the above with a tumor involving the central nervous system or bone marrow
- **Recurrent** – Cancer has returned after treatment
- **NHL can also be classified as localized or disseminated**
 - Localized NHL usually includes Stages I and II
 - Disseminated NHL included Stages III and IV

Treatment of Non-Hodgkin's Lymphoma

- Treatment for all NHL is based on the type and clinical stage of the tumor
- Since NHL grows and spreads quickly, treatment is aggressive
- The main treatment for non-Hodgkin's lymphoma is combination chemotherapy
- Surgery and radiation have small roles in selected cases only
- Most children and adolescents with non-Hodgkin's lymphoma do not get radiation therapy
- High dose chemotherapy with stem cell rescue is used in relapsed cases
- Monoclonal antibody therapy is in clinical trials at this time

Chemotherapy

- A combination of different chemotherapy agents is used in NHL treatment
 - Systemically (through the IV)
 - Intrathecally (into the spinal fluid)
- **Frontline drugs:** Vincristine, prednisone, doxorubicin, methotrexate, cyclophosphamide, cytarabine, etoposide, 6-mercaptopurine, asparaginase
- **Relapse or refractory disease:** cisplatin, etoposide, asparaginase, dexamethasone, cytarabine , ifosfamide, carboplatin

Radiation therapy

- Limited role in childhood NHL
- Used in emergency situations for tumors in the chest that cause difficulty breathing or compression of big blood vessels
- Used in patients with lymphoma in the spinal fluid and brain (not all cases)

Surgery

- Used to obtain a biopsy of the tumor
- Used for complications related to chemotherapy treatment or tumor

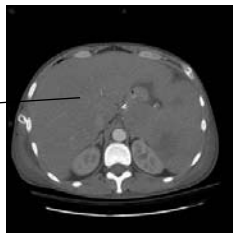
High Dose Chemotherapy with Stem Cell Rescue

- Used in patients who have relapsed or continue to have disease in spite of treatment
- Usually the patient's own stem cells are given back following treatment with intensive chemotherapy

Monoclonal Antibody Treatment

- It is a cancer treatment that uses antibodies made in the laboratory from a single type of immune system cell
- These antibodies can identify substances on cancer cells or normal substances that may help cancer cells grow
- The antibodies attach to the substances and kill the cancer cells, block their growth, or keep them from spreading
- Monoclonal antibodies are given through an IV and may be used alone or to carry drugs, toxins or radioactive material directly to cancer cells
- Rituximab is an anti-CD20 antibody currently in trial for relapsed and advanced NHL

Lymphoma
of liver



End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist

History & Physical Exam:

1st–2nd year: every 1–2 months
3rd–4th year: every 3–6 months
5th year: every 12 months

Blood Tests:

1st–2nd year: every 1–2 months
3rd–4th year: every 3–6 months
5th year: every 12 months

CT neck, chest, abdomen, pelvis, Gallium Scan/PET:

3 months, 6 months, 1 year, then as clinically indicated

Cardiac Evaluation (Echo/EKG):

end of treatment and then at 1–5 years depending on anthracycline dose received

Fertility Evaluation:

end of treatment, at puberty, every 2 years post puberty

Melanoma

What is Melanoma?

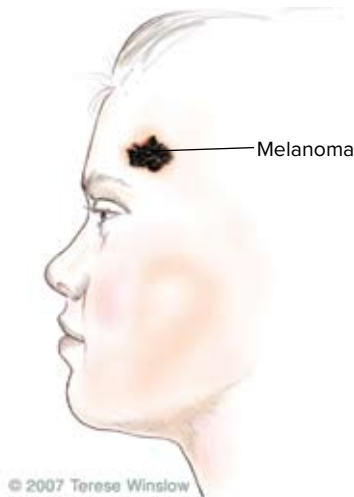
- Melanoma is a malignant form of skin cancer that occurs in cells called melanocytes, which produce pigments that give the skin its color
- Melanoma usually appears as an irregular brown, black, and/or red spot, or as an existing mole that begins to change color, size, or shape

Facts about Melanoma

- ▶ Melanoma is the most common skin cancer in children
- ▶ Children and adolescents represent 1% of all melanoma cases diagnosed in the United States each year
- ▶ Melanoma is most often diagnosed in children 10 years or older, but can occur in younger children
- ▶ Melanoma may be congenital (present at birth)
 - Children with hereditary immunodeficiencies have an increased lifetime risk of developing melanoma
- ▶ It is slightly more common in girls than boys
- ▶ The most common causes of skin cancer of any type include:
 - exposure to the ultraviolet (UV) portion of sunlight
 - radiation exposure
 - immunodeficiency
 - immunosuppression
- ▶ The person who is most likely to develop a melanoma is easily sunburned, has poor tanning ability, and generally has light hair, blue eyes, and pale skin
- ▶ Melanoma in children is similar to that of adults in relation to symptoms, description, and spread
- ▶ 5-year survival rate for melanoma is 92%

Stages of Melanoma

- **Stage 0** – cancer is found only in the outer layer of skin cells (epidermis)
- **Stage I** – cancer is found in the epidermis and
 - may or may not have spread to the upper part of the inner layer of skin (dermis)
 - is no more than 2 mm thick
 - may or may not have ulceration
- **Stage II** – the melanoma is anywhere from 1 - 4 mm thick, with or without ulceration, or the melanoma is more than 4 mm thick with ulceration
- **Stage III** – the cancer can be any thickness, with or without ulceration, and has spread to 1 or more lymph nodes or into the nearby lymph system
- **Stage IV** – the tumor may be any thickness, with or without ulceration, and has spread to other places in the body



Treatment for Melanoma

Surgery

- Primary treatment for patients with stage 0 or 1 melanoma
- For more advanced stages, surgery depends on the size, site, level of invasion, and extent of spread of the tumor

Biologic therapy

- If the melanoma has not spread beyond the lymph nodes, adjuvant biologic therapy (treatment that boosts the immune system to destroy cancer cells), in the form of alpha interferon, may be given

Chemotherapy

- If the melanoma has spread beyond the lymph nodes, treatment may include a combination of chemotherapy and biologic therapy—chemotherapy alone has not been found to be useful

Vaccine therapy

- Currently in clinical trials

End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist.

- ▶ Complete evaluation at end of treatment with physical exam, blood tests, and relevant x-rays and scans
- ▶ Further follow-up depending on stage of tumor

Nasopharyngeal Carcinoma (NPC)

What is Nasopharyngeal Carcinoma?

- The nasopharynx is the upper and back part of the pharynx (throat) behind the nose
 - The pharynx is a hollow tube that starts behind the nose and ends at the top of the trachea (windpipe) and esophagus (the tube that goes from the throat to the stomach)
- Nasopharyngeal cancer is a disease in which cancer cells form in the tissues of the nasopharynx

Facts about Nasopharyngeal Carcinoma

- ▶ Nasopharyngeal carcinoma represents about one-third of all cancers of the upper airways
- ▶ In the United States, approximately 1 in 100,000 persons younger than age 20 are diagnosed with Nasopharyngeal carcinoma
- ▶ This disease most often occurs in children between 10 and 15 years old
- ▶ There is a higher frequency of this tumor in North African and Southeast Asian populations
- ▶ Nasopharyngeal carcinoma may occur in association with Epstein-Barr virus (EBV), the virus associated with mononucleosis (sometimes known as “mono”)
- ▶ This cancer most frequently spreads to lymph nodes in the neck, which may alert the patient, parent, or physician to the presence of the tumor



Treatment

Radiation

- High-dose radiation therapy alone may have a role in the management of low-stage nasopharyngeal carcinoma
- Chemotherapy combined with high-dose radiation therapy to the primary tumor site and the neck is the most effective way to treat nasopharyngeal carcinoma

Chemotherapy

Drug combinations that have been used in children with nasopharyngeal carcinoma include:

- BEP (bleomycin, epirubicin, and cisplatin)
- PF (cisplatin, fluorouracil)
- PMB (cisplatin, methotrexate, and bleomycin)

Surgery:

- Limited role in the management of nasopharyngeal carcinoma since the disease is usually considered unresectable (unable to remove) because of extensive local spread
- The principle role of surgery is to obtain a biopsy of the tumor of the involved lymph node or primary site

Treatments under Clinical Evaluation:

- New radiation therapy techniques such as intensity-modulated radiation therapy
- Biologic therapy

End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist.

- ▶ Complete evaluation at end of treatment with physical exam, blood tests, and relevant x-rays and scans
- ▶ Further follow-up depending on stage of tumor

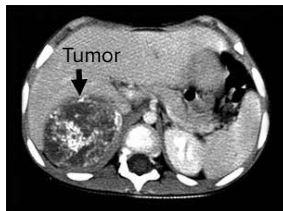
Neuroblastoma

Sympathetic and Allied Nervous System Tumors

- These are tumors of the sympathetic nervous system (network of nerves that carry messages from the brain to all parts of the body)
- The sympathetic nervous system is responsible for the way the body reacts to emotions and other stresses in the environment
- Cancers in this category account for 5% of all childhood cancers
- These are the most common cancers diagnosed in the first year of life
- Neuroblastoma accounts for almost all the cases of cancer in this category

What is Neuroblastoma?

- Neuroblastoma is a solid cancerous tumor, in which malignant (cancer) cells form in nerve tissue of the adrenal gland, neck, chest, or spinal cord.
- Neuroblastoma usually begins in the nerve tissue of the adrenal glands:
 - There are two adrenal glands, one on top of each kidney in the back of the upper abdomen
 - The adrenal glands produce important hormones that help control heart rate, blood pressure, blood sugar, and the way the body reacts to stress
 - By the time it is diagnosed, in most cases, the tumor has already spread to the surrounding lymph nodes, liver, lungs, bone, and bone marrow



Facts about Neuroblastoma

- ▶ Two thirds of the children diagnosed with neuroblastoma are younger than 5 years of age
- ▶ The average age at diagnosis is 2 years:
 - 25% of new diagnoses are below the age of 1
 - Only 3% of the patients are older than 10 years at diagnosis
 - The disease is very uncommon in teenagers
- ▶ It is more common in boys than girls
- ▶ There are about 570 cases diagnosed in the U.S. each year
- ▶ The signs and symptoms of neuroblastoma depend on
 - Location of the tumor
 - Whether it has spread to other parts of the body
- ▶ 5-year survival rate for neuroblastoma is approximately 66%

Treatment for Neuroblastoma

The treatment of neuroblastoma is usually a combination of surgery, radiation therapy, chemotherapy, and bone marrow transplantation.

The treatment of neuroblastoma depends on:

- Age at diagnosis
- Where the tumor is in the body
- Stage of disease
- Involvement of lymph nodes
- Biology of tumor
 - The patterns of the tumor cells
 - The number of chromosomes in the tumor cells
 - The number of copies of the N-myc gene in the tumor cells
- Depending on these factors, the tumor biology is said to be favorable or unfavorable
 - Favorable tumor biology means there is a better chance of survival

Based on all these factors, patients are categorized into low-risk, intermediate-risk, and high-risk groups and treatment is tailored accordingly.

Surgery

Surgery is an important component of treatment for neuroblastoma. It is used:

- To obtain a biopsy of the tumor for diagnosis
- For removal of localized tumors
- To remove as much of the tumor as possible in unresectable tumors
- For second-look surgery after chemotherapy

Chemotherapy

- Almost all children with neuroblastoma receive chemotherapy
- It is given to shrink the tumor before surgery, and then again after surgery to kill any remaining cancer cells
- **Frontline drugs:** carboplatin, etoposide, cyclophosphamide, doxorubicin, ifosfamide, cisplatin
- **Relapse or refractory disease:** topotecan, cyclophosphamide, irinotecan

Radiation

Neuroblastoma is very sensitive to radiation therapy. It is used:

- For local control of tumors that cannot be removed by surgery
- As part of total body radiation for bone marrow transplantation
- For control of pain in neuroblastoma that has spread to bone

Bone Marrow/Stem Cell Transplantation

- In addition to chemotherapy, radiation, and surgery, patients considered high-risk also undergo autologous bone marrow/stem cell transplantation following high dose chemotherapy
- Bone marrow/stem cell transplantation is also recommended in relapse situations

Retinoic Acid Treatment

13-cis retinoic acid is a vitamin-like drug that slows the ability of the cancer to make more cancer cells, and changes how these cells look and act.

It is usually given for 6 months to high risk patients after completion of chemotherapy, radiation, surgery, and autologous bone marrow/ stem cell transplant.

Monoclonal Antibody Treatment

Monoclonal antibody treatment is currently in clinical trials for newly diagnosed high risk and relapsed neuroblastoma.

- Anti GD2 Monoclonal antibody

End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist.

History & Physical Exam:

1st year: every month
2nd year: every 2 months
3rd–4th year: every 6 months
5th year: every 12 months

Blood Tests:

1st–2nd year: every 6 weeks–2 months
3rd–4th year: every 6 months
5th year: every 12 months

Catecholamines (VMA, HVA) and Urinalysis:

end of treatment, every 4 months for 1 year, every 6 months for 2nd year, then yearly

CT/MRI of tumor:

every 4–6 months for 1st 3 years

Cardiac Evaluation (Echo/EKG):

end of treatment and then at 1-5 years depending on anthracycline dose received

Hearing Test:

end of treatment, once a year for 2 years

Bone scan/MIBG:

end of treatment, every 6 months for 2 years

Creatinine clearance:

end of treatment, then 2–4 months until normal

Retinoblastoma

What is Retinoblastoma?

Retinoblastoma is a disease in which malignant (cancer) cells form in the tissues of the retina. The retina is the nerve tissue that lines the inside of the back of the eye. The retina senses light and sends images to the brain via the optic nerve.

When retinoblastoma affects one eye, it is called unilateral retinoblastoma. If both eyes are affected, it is called bilateral retinoblastoma.

Facts about Retinoblastoma

- ▶ It is a relatively uncommon tumor and accounts for 2% of all childhood cancers
- ▶ Each year, in the USA, it affects approximately 300 children and adolescents under the age of 20
- ▶ It occurs equally in both boys and girls
- ▶ It is usually discovered in babies between the ages of 6 and 24 months, though it can be found at older or younger ages
- ▶ 95% of the cases occur in children below the age of 5
- ▶ Retinoblastoma is sometimes caused by a gene mutation that is passed from the parent to the child
 - This is the 'inherited form' and is called hereditary retinoblastoma
 - It occurs at a younger age than retinoblastoma that is not inherited
 - Retinoblastoma that occurs in only one eye is usually not inherited
 - Retinoblastoma that occurs in both eyes is always inherited
 - When hereditary retinoblastoma first occurs in only one eye, there is a chance it will develop later in the other eye
- ▶ Retinoblastoma is usually confined to the eye and rarely spreads to the nearby tissue or other parts of the body
- ▶ 5-year survival rate for retinoblastoma is about 94%

Stages of Retinoblastoma

- **Intraocular:** the cancer is only in the eye and has not spread to the surrounding tissue or other body parts
- **Extraocular:** the cancer has spread beyond the eye

Treatment for Retinoblastoma

- The aim of treatment is to get rid of the cancer and try to preserve sight in the affected eye
- Treatment depends on:
 - Stage of the tumor
 - The likelihood of saving vision in one or both eyes
 - The size and number of tumors
- Early diagnosis and intervention are essential for successful disease outcome

Treatment options include one or a combination of the following:

Enucleation

- Surgery to remove the eye and part of the optic nerve
- Done for large tumors
- Performed when there is very little chance that vision could be saved
- The patient is usually fitted with an artificial eye after the surgery

Radiation therapy

- High-energy x-rays or other types of radiation are used to kill cancer cells or keep them from growing
- In retinoblastoma, different forms of radiation may be used:
 - External radiation therapy – a machine from outside sends radiation towards the tumor
 - Intensity modulated radiation therapy (IMRT)
 - Stereotactic radiation
- Proton beam radiation therapy

- The goal is to give radiation to the tumor while causing less damage to healthy tissue around it
- Internal radiation therapy uses a radioactive substance sealed in needles, seeds, wires, plaques, or catheters that are placed directly into or near the cancer
 - **Plaque radiotherapy:** Radioactive seeds are attached to one side of a disk, called a plaque, and placed directly on the outside wall of the eye near the tumor. The side of the plaque with the seeds on it faces the eyeball, aiming radiation at the tumor. The plaque helps protect other nearby tissue from the radiation.
- The method of radiation used depends on the stage of the retinoblastoma
- 3500–4600 cGy is the dose generally used for radiation

Cryotherapy

- Use of extreme cold to destroy the tumor
- Used for very small, localized tumors

Thermotherapy

- Use of heat to destroy cancer cells

Photocoagulation

- Use of laser light to destroy blood vessels leading to the tumor

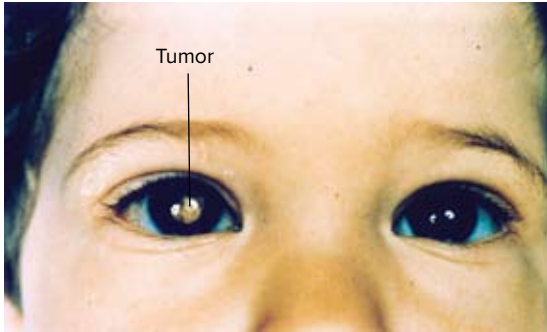
Chemotherapy

- Chemotherapy is used for the treatment of intraocular and extraocular tumors
- A form of chemotherapy called chemoreduction is used to treat localized disease
- Chemoreduction reduces the size of the tumor so it may be treated with local treatment (such as radiation therapy, cryotherapy, photocoagulation, or thermotherapy)
- **Frontline drugs:** carboplatin, etoposide, cisplatin, vincristine, cyclophosphamide, doxorubicin

- Intrathecal therapy with methotrexate, ara-C and hydrocortisone, if there is spread in the brain

New Treatments

- Subtenon chemotherapy is the use of drugs injected through the membrane covering the muscles and nerves at the back of the eyeball
 - This is a type of regional chemotherapy
 - It is usually combined with systemic chemotherapy and local treatment (such as radiation therapy, cryotherapy, photocoagulation, or thermotherapy)
- High dose chemotherapy with stem cell transplant is used for relapsed or refractory tumors



End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist.

History & Physical Exam:

1st year: every 3 months
2nd year: every 6 months
3rd–5th year: every 12 months

Blood Tests:

1st year: every 3 months
2nd year: every 6 months
3rd–5th year: every 12 months

CT/MRI of tumor:

end of treatment, every 6 months for 2 years

Examination Under Anesthesia:

as per treating ophthalmologist. More frequent checks for intraocular retinoblastoma

Performance evaluation:

end of treatment, every 3 months for 1 year, every 6 months for 2 years, then yearly

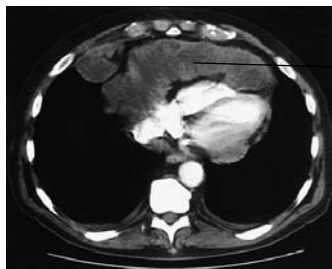
Soft Tissue Sarcomas (STS)

- Cancers that arise in various soft tissues of the body, such as:
 - muscles
 - tendons
 - fibrous tissues
 - fat
 - nerves
 - blood vessels
 - synovial tissue
- Soft tissue sarcomas account for 7% of all childhood cancers
- Rhabdomyosarcoma is the most common soft tissue sarcoma in children under the age of 15
- Other rare soft tissue sarcomas (more common between the ages of 15–19 years):
 - fibrosarcoma
 - neurofibrosarcoma
 - leiomyosarcoma
 - liposarcoma
 - synovial sarcoma
 - hemangiopericytoma
 - alveolar soft parts sarcoma
 - malignant fibrous histiocytoma

Rhabdomyosarcoma

What is Rhabdomyosarcoma?

- Rhabdomyosarcoma is a soft tissue sarcoma of the muscle
- It can start anywhere in the body, however, where the tumor originates is often associated with age at diagnosis
 - Most head and neck tumors occur in children under the age of 8
 - Extremity tumors usually occur in adolescents
 - Rarely, tumors can occur in the genitor-urinary tract, urinary bladder, and prostate in boys and the vagina in girls



Tumor

Facts about Rhabdomyosarcoma

- ▶ It is the most common soft tissue sarcoma found in children
- ▶ In the U.S., approximately 250 children are diagnosed with rhabdomyosarcoma each year
- ▶ 2/3 of the cases occur in children under the age of 6
- ▶ Slightly higher incidence in boys than in girls
- ▶ Patients with Li- Fraumeni syndrome (a rare, inherited disorder), neurofibromatosis, or Beckwith-Weidemann syndrome have a higher risk of developing rhabdomyosarcoma
- ▶ There are no known environmental factors associated with rhabdomyosarcoma

Different Types of Rhabdomyosarcoma

- Embryonal:
 - Accounts for 60–70% of all rhabdomyosarcomas
 - Commonly involves the head, neck, genito-urinary organs (bladder, prostate, testes, vagina).
- Botryoid:
 - Accounts for 10% of all rhabdomyosarcomas
 - Type of embryonal rhabdomyosarcoma
 - Commonly seen in the genitor-urinary region (bladder, vagina)
 - Most often seen in infants
- Alveolar:
 - Account for about 15% of all rhabdomyosarcomas
 - Most likely to develop in the extremities (arms and legs) or in the trunk of the body.
 - More common in adolescents.
 - Are associated with the chromosomal translocation t (2;13)

Treatment for Rhabdomyosarcoma

Surgery

All patients with rhabdomyosarcoma get surgery:

- Initial biopsy of the tumor to make a diagnosis
- All or part of the tumor is removed, as soon as possible after diagnosis, to reduce disease
- Second-look surgery after finishing chemotherapy to remove any remaining disease

Chemotherapy

All children with rhabdomyosarcoma get chemotherapy. It is given following surgery to kill any remaining cancer cells in the body.

Common chemotherapy drugs used for Rhabdomyosarcoma:

- **Frontline drugs:** vincristine, dactinomycin, cyclophosphamide, doxorubicin, ifosfamide, etoposide
- **Relapse or refractory disease:** topotecan, irinotecan, carboplatin, gemcitabine, autologous bone marrow transplant, immunotherapy, and biological modifiers (being investigated)

Radiation therapy

- Very important component of treatment for Rhabdomyosarcoma
- Not needed if tumor has been completely removed
- Usually given approximately 9 weeks after starting chemotherapy
- Some patients with tumor in the skull, spinal cord, or around the eye may need it at the beginning of treatment

Other Soft Tissue Sarcomas

What are Other Soft Tissue Sarcomas?

- These are the cancers that arise in soft tissue anywhere in the body
- They are also called the ‘non-rhabdomyosarcoma STS’
- They account for about 3% of all cancers in children
- They can originate from tendons, blood vessels, nerves, fat, muscles, or synovia (lining around the joints)
- Other rare soft tissue sarcomas (more common between the ages of 15–19 years):
 - fibrosarcoma
 - neurofibrosarcoma
 - leiomyosarcoma
 - liposarcoma
 - synovial sarcoma
 - hemangiopericytoma
 - alveolar soft parts sarcoma
 - malignant fibrous histiocytoma

Synovial sarcoma

- The most common sarcoma after rhabdomyosarcoma
- Usually seen in children over the age of 10 years
- Most commonly seen in the thigh or knee, followed by the arm and hand, head, neck, and trunk

Malignant peripheral nerve sheath tumor

- Also known as malignant schwannoma or neurofibrosarcoma
- Very aggressive cancer
- Makes up 5-10% of all non rhabdomyosarcoma STS
- Usually occurs in patients with neurofibromatosis
- Commonly seen in the upper and lower limbs

Fibrosarcoma

- STS frequently seen in children less than one year of age
- Has two incidence peaks:
 - infants and children less than five years of age
 - children between ten and fifteen years of age

- Most children have localized disease
- Usually occurs in the upper and lower limbs
- Infants respond better to treatment than older children

Malignant fibrous histiocytoma

- Usually seen in the trunk and lower limbs
- Rarely may present in the kidney, scalp, or upper limbs

Other rare STS usually seen in older children and teenagers

- Leiomyosarcoma
- Alveolar soft parts sarcoma
- Liposarcoma
- Hemangiopericytoma

Treatment for Other Soft Tissue Sarcomas

- Surgical removal of as much of the tumor as possible is the treatment of choice for all non rhabdomyosarcoma STS
- This is usually followed by radiation therapy
- Chemotherapy is usually only used to try and shrink a large tumor before surgery
- Most children are given treatment similar to that used for rhabdomyosarcomas
- How well a child does depends on how much of the tumor could be removed with surgery

End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist.

History & Physical Exam:

1st year: every 3 months
2nd–3rd year: every 4 months
4th year: every 6 months
5th–10th year: every 12 months

Blood Tests:

1st year: every 3 months
2nd–3rd year: every 4 months
4th year: every 6 months
5th–10th year: every 12 months

Urinalysis:

every 3–6 months for 1 yr, every 6 months for 2nd year, then yearly for 10 years (in selected patients)

CT/MRI of primary tumor:

every 3 months for 1 year, every 4 months for year 2, every 6 months for years 3 and 4

Chest X-Ray:

every 3 months for 1 year, every 4 months for year 2, every 6 months for years 3 and 4

Other specific testing:

based on site of primary tumor

Thyroid Cancer

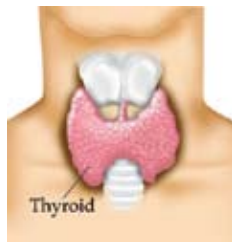
Thyroid cancer is a disease where malignant (cancerous) cells form in the thyroid gland. The thyroid is an important organ at the base of the throat responsible for making hormones that help control heart rate, blood pressure, body temperature, and weight.

Risk Factors for Thyroid Cancer

- Being between 25 and 65 years old
- Being female
- Being exposed to radiation to the head and neck as a child
 - The cancer may occur as soon as 5 years after exposure
- Having a history of goiter (enlarged thyroid)
- Having a family history of thyroid disease or thyroid cancer
- Having certain genetic conditions such as familial medullary thyroid cancer
- Being of Asian descent

Types of Thyroid Cancer

- Papillary thyroid cancer
 - Most common type of thyroid cancer
- Medullary thyroid cancer
- Follicular thyroid cancer
- Anaplastic thyroid cancer



Treatment of Thyroid Cancer

Four types of standard treatment are used:

Surgery

The most common treatment for thyroid cancer, usually involving one of the following procedures:

- **Lobectomy:** removal of the lobe in which thyroid cancer is found
- **Biopsies** of lymph nodes in the area may be done to see if they contain cancer
- **Near-total thyroidectomy:** removal of all but a very small part of the thyroid
- **Total thyroidectomy:** removal of the whole thyroid
- **Lymphadenectomy:** removal of lymph nodes in the neck that contain cancer

Radiation therapy

- This includes radioactive iodine therapy
- Radiation therapy may be given after surgery to kill any thyroid cancer cells that were not removed
- Follicular and papillary thyroid cancers are sometimes treated with radioactive iodine (RAI) therapy

Chemotherapy

- Only used in advanced cases
- **Frontline drugs:** doxorubicin, cisplatin

Thyroid Hormone Therapy

- In the treatment of thyroid cancer, drugs may be given to prevent the body from making thyroid-stimulating hormone (TSH), a hormone that can increase the chance that thyroid cancer will grow or recur
- As thyroid cancer treatment kills thyroid cells, the thyroid is not able to make enough thyroid hormone
 - Patients are given thyroid hormone replacement pills

End of Treatment Follow-up

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- ▶ Complete evaluation at end of treatment with physical exam, blood tests, and relevant x-rays and scans
- ▶ Further follow-up depending on stage of tumor

Wilms' Tumor and Other Kidney Tumors

What is Wilms' Tumor?

Wilm's tumor and other childhood kidney tumors are diseases in which malignant (cancer) cells form in the tissues of the kidney.

- The kidneys are bean-shaped organs located on the right and left side of your backbone
- These organs filter blood, make urine, and help your body get rid of waste

Facts about Wilms' Tumor

- ▶ Kidney tumors account for 4% of all childhood malignancies
- ▶ Wilms' tumor accounts for about 90% of all kidney cancers that occur in children and adolescents
- ▶ About 490 cases are diagnosed each year
- ▶ Most cases of Wilms' tumor are found in children under 5 years old
- ▶ Usually occurs in only one kidney, but it can occur in both kidneys
- ▶ 5-year survival rates for Wilm's tumor are more than 90%



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Certain genetic syndromes or birth defects may increase the risk of developing Wilms' tumor:

- WAGR (Wilms' tumor, aniridia, ambiguous genitalia, and mental retardation) syndrome
- Beckwith-Weidemann Syndrome
- Hemihypertrophy
- Denys-Drash syndrome
- Hypospadias

Other Kidney Tumors

- **Clear cell sarcoma** of the kidney is a type of kidney tumor that may spread to the lung, bone, brain, and soft tissue
- **Rhabdoid tumor** of the kidney is a type of cancer that occurs mostly in children under age 2. It grows and spreads quickly, often to the lungs and brain
- **Neuroepithelial tumors** of the kidney are rare and usually occur in young adults. They grow and spread quickly
- **Renal cell carcinoma** occurs rarely in children. The tumor can spread to the lungs, bones, liver, and lymph nodes
- **Mesoblastic nephroma** is a tumor of the kidney that is usually diagnosed within the first 3 months of life. It may also be found during an ultrasound before birth. Mesoblastic nephroma occurs more often in males than females

Stages of Wilms' Tumor

- Wilms' tumor is staged using a National Wilms' Tumor Study Group staging system
- Staging is based on certain characteristics of the cancer cells and whether the cancer has spread outside the kidney
- Staging the tumor is necessary because decisions for treatment are based on this information

Treatment for Wilms' Tumor

Wilms' tumor treatment consists of surgery, chemotherapy, and/or radiation.

Surgery

- Is usually done first
- The goal is to remove as much of the tumor as possible, while sparing the kidney
- How much of the kidney (part or whole) is removed depends on the position of the tumor and how big the tumor is

Chemotherapy

- All children/adolescents with Wilms' tumor receive chemotherapy as part of treatment
- It is given after surgery to kill any remaining tumor that is still there, as well as cancer cells that were too small to see
- **Frontline drugs:** vincristine, dactinomycin, doxorubicin
- **Relapse or advanced disease:** cyclophosphamide, etoposide, ifosfamide, carboplatin

Radiation

- This is usually reserved for patients with more advanced disease

High Dose Chemotherapy and Stem Cell Rescue

- This is an option that could be used for patients who do not respond to standard treatment or relapse after treatment is completed

End of Treatment Follow-up

This is a follow-up plan for the first 5 years (in some cases, 10 years) you are off treatment. It should be used as a guideline only, and is not a substitute for the specific follow-up schedule designated by your oncologist.

History & Physical Exam:

1st–2nd year: every 3 months
3rd–4th year: every 6 months
5th–10th year: every 12 months

Blood Tests:

1st–2nd year: every 3–6 months
3rd–4th year: every 6 months
5th–10th year: every 12 months

Urinalysis:

every 3 months for 1 yr, every 6 months for 2nd year, then yearly for 10 years

CT chest and abdomen:

3–6 months for 2 years (high risk patients) then as clinically indicated for 5 years

Ultrasound abdomen, Chest X-Ray:

3–6 months for 1-4 years, then as needed

Cardiac Evaluation (Echo/EKG):

end of treatment and then at 1-5 years depending on anthracycline dose received

Late Effects Associated with Childhood Cancers

Cancer	Potential Late Effects
Leukemia	<ul style="list-style-type: none"> ▶ Cognitive effects (e.g., learning disabilities) ▶ Abnormal growth and maturation ▶ Heart problems ▶ Second cancers ▶ Hepatitis C (effects of blood transfusion) ▶ Weakness, fatigue ▶ Obesity ▶ Osteoporosis ▶ Avascular necrosis of bone ▶ Dental problems ▶ Cataracts
Brain Cancer	<ul style="list-style-type: none"> ▶ Neurologic and cognitive effects (e.g., learning disabilities) ▶ Abnormal growth and maturation ▶ Hearing loss ▶ Kidney damage ▶ Hepatitis C ▶ Infertility ▶ Vision problems ▶ Second cancers
Hodgkin's Disease	<ul style="list-style-type: none"> ▶ Adhesions and intestinal obstruction (if spleen removed) ▶ Decreased resistance to infection (potential for life-threatening sepsis) ▶ Abnormal growth and maturation ▶ Hypothyroidism (effect of neck radiation) ▶ Salivary gland malfunctioning (effect of jawbone irradiation) ▶ Lung damage ▶ Heart problems ▶ Infertility ▶ Hepatitis C ▶ Second cancers (e.g., breast cancer in females)
Non-Hodgkin's Lymphoma	<ul style="list-style-type: none"> ▶ Bone Problems (Osteopenia/Osteoporosis) ▶ Cognitive Effects ▶ Heart Complications ▶ Hepatitis C ▶ Infertility

Late Effects Associated with Childhood Cancers (cont.)

Bone Tumor	<ul style="list-style-type: none"> ▶ Amputation/disfigurement ▶ Functional, activity limitations ▶ Damage to soft tissues and underlying bones (radiation may cause scarring, swelling, or inhibit growth) ▶ Heart problems ▶ Hearing loss ▶ Kidney damage ▶ Second cancers ▶ Hepatitis C ▶ Fertility problems
Wilm's Tumor	<ul style="list-style-type: none"> ▶ Heart problems ▶ Kidney damage ▶ Damage to soft tissues and underlying bones (radiation may cause scarring, swelling, or inhibit growth) ▶ Second cancers ▶ Fertility problems ▶ Scoliosis
Neuroblastoma	<ul style="list-style-type: none"> ▶ Heart problems ▶ Damage to soft tissues and underlying bones (radiation may cause scarring, swelling, or inhibit growth) ▶ Neurocognitive effects ▶ Hearing loss ▶ Hepatitis C ▶ Second cancers ▶ Kidney damage
Soft-Tissue Sarcoma	<ul style="list-style-type: none"> ▶ Amputation/disfigurement ▶ Functional, activity limitations ▶ Heart problems ▶ Damage to soft tissues and underlying bones (radiation may cause scarring, swelling, or inhibit growth) ▶ Second cancers ▶ Hepatitis C ▶ Kidney damage ▶ Cataracts ▶ Infertility ▶ Neurocognitive effects

Source: 'Childhood Cancer Survivorship: Improving Care and Quality of Life.' Institute of Medicine. Adapted with permission.

CHEMOTHERAPY

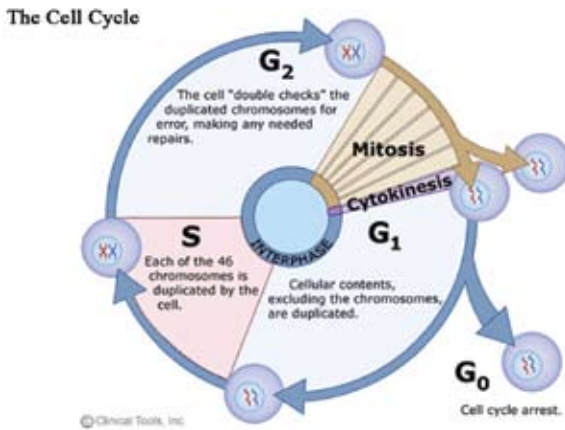
and Related Late Effects

How Does Chemotherapy Work?

IN ORDER TO UNDERSTAND HOW CHEMOTHERAPY works, it is important to first be familiar with how cells divide and multiply.

The cell cycle, or cell-division cycle, is the series of steps that takes place in order for the cell to replicate. These events can be divided into two main parts—Interphase and Mitosis:

- **Interphase:** During this phase the cell grows, accumulates nutrients needed for mitosis, and doubles its DNA. Interphase consists of four stages:



- **G₀** = Stage 1 A resting phase that follows mitosis
- **G₁** = Stage 2 Cell growth and preparation for cell division
- **S** = Stage 3 DNA is replicated within the cell chromosome
- **G₂** = Stage 4 Preparation for mitosis

■ **Mitosis:** During this phase, the cell undergoes nuclear division.

Mitosis consists of one main phase:

- **M = Mitosis** Series of steps during which the cell splits itself into two separate cells, often called “daughter cells”.

Certain chemotherapy drugs are cell specific and are effective only during a certain stage of the cell cycle. For example:

- Methotrexate is an antimetabolite; antimetabolites kill cancer cells during the S phase of the cell cycle.
- Cyclophosphamide is an alkylating agent; alkylating agents are non-phase specific, meaning they kill cancer cells at any point in the cell cycle.

We now understand through scientific studies that optimal treatment is achieved by combining various chemotherapy agents that work in different parts of the cell cycle.

Types of Chemotherapy

- ▶ Alkylating Agents
 - Heavy Metals
- ▶ Antimetabolites
- ▶ Antitumor Antibiotics
 - Anthracyclines
- ▶ Corticosteroids
- ▶ Enzymes
- ▶ Plant Products



Periwinkle Plant:
Plant from which the
chemotherapy drug,
Vincristine, is produced.

Alkylating Agents

Alkylating agents are a category of chemotherapy drugs that are used for treating certain types of cancer. Alkylating agents include the following:

Alkylating Agents	
▶ Busulfan	▶ Carmustine (BCNU)
▶ Chlorambucil	▶ Thiotepa
▶ Cyclophosphamide (Cytosan)	▶ Mechlorethamine (Nitrogen Mustard)
▶ Lomustine (CCNU)	▶ Temozolomide
▶ Melphalan	▶ Procarbazine
▶ Ifosfamide	▶ Dacarbazine

How Do They Work?

Alkylating agents have been used for cancer treatment since the 1940s and are one of the oldest and most commonly used forms of chemotherapy.

Alkylating agents work by damaging DNA within the cell. This directly affects DNA function. When DNA is damaged, cancer cells can no longer divide and reproduce; eventually the cells die.

Alkylating agents are not phase specific, which means they work in all stages of the cell cycle. They are, therefore, used to treat a large number of cancers, such as non-Hodgkin's lymphoma, Hodgkin lymphoma, solid tumors, leukemias, breast cancer, ovarian cancer, and lung cancer. Specific alkylating agents, such as Carmustine and Lomustine, are also useful in treating brain tumors and malignant melanomas.

Alkylating agents, when used over long periods of times, may cause infertility and other reproductive complications, as well as increase the risk for secondary cancers.

Recommended Late Effects Screening for all *Alkylating Agents*

- Reproductive Assessment for Boys*
 - Physical exam to monitor Tanner Staging
 - Hormone blood work (testosterone/FSH/LH) starting at 11 or 12 years of age, and then yearly until puberty is complete*
 - Yearly urinalysis
 - Sperm analysis (optional)
 - Yearly CBC check for 10 to 15 years after treatment with alkylating agents

* Any detected abnormalities should be referred to an endocrinologist (hormonal specialist), urologist (specialist in male reproductive organs), and fertility specialist.

What does this mean for me?

Alkylating agents may affect the male reproductive system. One possible effect is testosterone deficiency, where the testicles are unable to produce enough of the male hormone, testosterone. Testosterone is needed for males to begin and maintain puberty development. If testosterone deficiency occurs, male hormones prescribed by a doctor may be given to develop and maintain male function.

For more information, please visit www.survivorshipguidelines.org and select "Male Health Issues"

■ Reproductive Assessment for Girls*

- Physical exam to monitor Tanner Staging and menstrual history
- Hormone blood work (FSH/LH/estradiol) at 10 years of age, and then yearly until puberty is complete*
- Yearly urinalysis
- Gynecologic exam/Pap test at 18 years of age, and then yearly (or once sexually active)
- Yearly CBC check for 10 to 15 years after treatment with alkylating agents

* Any detected abnormalities should be referred to an endocrinologist (hormonal specialist), gynecologist or fertility specialist.

What does this mean for me?

Alkylating agents can sometimes damage the ovaries, reducing the reserve supply of eggs. Damage to the ovaries can affect puberty, menstruation, and fertility. Hormonal therapy may be needed if the ovaries are failing to function, and this is best managed by an endocrinologist.

For more information, please visit www.survivorshipguidelines.org and select “Female Health Issues”

Specific Late Effects Screening for *Busulfan, Carmustine, Lomustine*

- Yearly pulmonary exam
- Chest x-ray at initial long-term follow-up visit, and then repeated only as needed
- Pulmonary function tests at initial long-term follow-up visit, and then repeated only as needed for worsening lung function.
- Yearly eye exams (visual acuity and fundoscopic exam) for patients treated with Busulfan

What does this mean for me?

The lungs are one of the most important organs in the body, and occasionally some alkylating agents, such as Busulfan, Carmustine, and Lomustine, may have adverse effects on lung function. The use of these drugs may result in difficulty breathing, scarring of the lungs, or lung inflammation. This can also lead to heart complications as blood does not properly get the oxygen it needs. It is important to have regular checkups with a physician, routine chest x-rays, and pulmonary function exams. It is critical for patients at risk to practice health-promoting behavior- the most important of which is DO NOT SMOKE. Smoking, or even being around someone who smokes, greatly increases the risk of lung complications. Regular physical exercise can also help in developing strong, healthy lungs.

Busulfan in pediatric cancer patients may also increase the risk of cataracts. A cataract is a clouding of the eye lens which can result in vision problems, sensitivity to light, or fading of colors. Cataracts can be easily treated surgically by replacing the cloudy lens with an artificial one. It is still important to wear sunglasses outside and avoid bright light emitting objects such as fireworks

For more information, please visit www.survivorshipguidelines.org and select select "Pulmonary Health" or "Cataracts"

Heavy Metals

Heavy Metals (Non-Classical Alkylating Agents)

▶ Cisplatin

▶ Carboplatin

How Do They Work?

Heavy metals are chemotherapy drugs that fall under the class of platinum. Platinum derived drugs have been found to be useful in treating cancer for the past 150 years, but only in the last 30 years has clinical use been incorporated.

Heavy metals can act during any stage of the cell cycle. They work by interfering with the structure of DNA. This change in structure effectively alters the genes of the cancer cells and stops them from undergoing proper DNA formation and function.

They are used for treatment of osteosarcoma, brain tumors, relapsed lymphomas and solid tumors, and testicular and lung cancers. The use of heavy metals may lead to hearing complications, as well as increase the risk of peripheral nerve damage and kidney toxicity.

Recommended Late Effects Screening for all *Heavy Metals*

- Yearly history and physical exam, including the otoscopic exam (ear exam)
- Complete audiogram or BAER test at initial long-term follow-up visit and then according to the following guidelines:
 - If hearing loss is observed, yearly hearing tests are needed
 - For patients who have also received cranial/ear radiation
 - yearly tests should be performed for 5 years
 - if younger than age 10, continue every year until 10 years of age, and then every 5 years

- Yearly urinalysis
- Yearly neurological exam to test for neuropathy until 2 to 3 years after treatment, and then yearly only if symptoms persist
- Fasting lipid profile at initial long-term follow-up visit and then as per United States Preventative Task Force Recommendations

What does this mean for me?

Heavy metals may affect hearing by damaging the inner ear, which can lead to sensori-neural hearing loss. What this means is that sound waves are still processed by the ear, but cannot be properly converted into nerve signals and sent to the brain. Hearing loss can lead to problems in communication and may result in difficulty at school. Various options such as hearing aids and cochlear implants exist to help treat hearing loss. Therefore, it is important to be regularly monitored by a physician.

Heavy metals can also harm the kidneys. This can result in swelling (especially of the legs and ankles), high blood pressure, and low red blood cell count. It is important to remember to drink plenty of fluids and be regularly monitored by a physician.

Neuropathy is damage to the peripheral nerve cells, which is sometimes a side effect of heavy metals. This may result in pain or a tingling sensation in the hands and feet, muscle weakness, or increased sensitivity, but these effects may be controllable through physical therapy and pain management.

For more information, please visit www.survivorshipguidelines.org and select "Hearing Loss" or "Kidney Health"

Antimetabolites

Antimetabolites are a category of chemotherapy drugs that are used for treating certain types of cancer. Antimetabolites include the following:

Antimetabolites	
▶ Methotrexate	▶ Mercaptopurine (6-MP)
▶ Cytarabine	▶ Thioguanine (6-TG)

How Do They Work?

Antimetabolites work by interfering with the production of DNA and RNA in cancer cells. They “trick” the cells by looking like certain vitamins and amino acids that cancer cells need in order to reproduce. Once they enter the cells, the antimetabolites block the cells from growing. New cancer DNA is not formed and cancer cell division and multiplication cannot occur. Once the cells are unable to grow, they eventually die.

Antimetabolites are cell specific and are most effective in damaging cancer cells during the “S” stage of the cell cycle.

Antimetabolites are used to treat leukemias, breast cancer, ovarian cancer, tumors of the gastrointestinal tract, as well as other cancers.

Antimetabolites, especially when given intrathecally (in the spinal fluid), or high dose IV, e.g. methotrexate and cytarabine, may cause learning problems as well as bone weakening and kidney damage.

Specific Late Effects Screening for *Cytarabine (Ara-C)*

- Yearly history and physical exam to monitor educational and cognitive development, as well as motor and neurological function
- Neurological and neurocognitive evaluation at initial long-term follow-up visit, and then repeated as needed if evidence of problems
- Cytarabine given intrathecally (IT) or as high dose IV, can cause more problems than when given as low dose.

Specific Late Effects Screening for *Methotrexate*

- Yearly history and physical exam to monitor educational and cognitive development, as well as motor and neurological function
- Neurological and neurocognitive evaluation at initial long-term follow-up visit, and then repeated as needed if evidence of problems
- Bone density test at initial long-term follow-up visit, and then repeated only as needed
- Blood work at initial long-term follow-up visit, and then repeated only as needed
- Yearly urinalysis
- Methotrexate given intrathecally (IT) or as high dose IV, can cause more problems than when given as low dose.

What does this mean for me?

High dose IV Cytarabine and Methotrexate may impair neurocognitive function and affect a child's performance in school. Deficits that may occur include: shortened attention span, slower processing speed, change in behavior, and memory problems. Math and reading are subjects most commonly affected by these changes. It is important for patients at risk to have specialized psychological and learning tests performed by a licensed psychologist, and educational progress carefully monitored by parents. Good communication with school staff and an early understanding of the possible learning problems caused by treatment helps survivors obtain specialized educational adaptations.

Bone formation is an important part of a child's growth. Methotrexate may cause bone weakening and result in disorders such as osteoporosis. Osteoporosis is a condition where bone decay occurs faster than new bone formation occurs, resulting in a weakening of the bone and a greater chance of fractures or injury. Height and spinal curvature can also be affected. If at risk for osteoporosis, it is important to exercise and eat a healthy diet high in calcium and Vitamin D. X-rays and bone scans are useful in early detection of bone complications.

Methotrexate can also have a harmful effect on the kidneys. This can result in swelling (especially of the legs and ankles), high blood pressure, and low red blood cell count. It is important to remember to drink plenty of fluids and be regularly monitored by a physician.

For more information, please visit www.survivorshipguidelines.org and select "Educational Issues," "Bone Health", "Kidney Health", or "Liver Health"

Specific Late Effects Screening for *Mercaptopurine & Thioguanine*

- Yearly physical exam to observe liver health
- Blood work (ALT/AST/Bilirubin) at baseline of long-term follow-up care and then repeated as clinically indicated

What does this mean for me?

Chemotherapy treatment with antimetabolites, such as Mercaptopurine, Thioguanine, and Methotrexate, may lead to complications with the liver, but this usually occurs (if at all), shortly after treatment. The liver keeps the body free of toxins and helps in digestion. Side effects from liver damage include: jaundice, nausea, loss of appetite, dark urine/stools, or scarring and inflammation of the liver. In more serious cases, a condition called veno-occlusive disease may occur, which can lead to renal failure. If at risk, regular blood tests and physical exams by a physician are recommended.

For more information, please visit www.survivorshipguidelines.org and select “Liver Health”

Antitumor Antibiotics

Antitumor antibiotics are a category of chemotherapy drugs that are used for treating certain types of cancer. Antitumor antibiotics include the following:

Antitumor Antibiotics

▶ Bleomycin

▶ Dactinomycin

How Do They Work?

Antitumor antibiotics originate from natural sources, such as the fungus, *Streptomyces*, and release toxic substances which cause fractures in the cancer cell DNA. These breaks in the DNA strands eventually lead to the overall death of the cancer cell.

Antitumor antibiotics are usually used in combination with other chemotherapy agents to treat tumors such as Wilm's tumor, testicular cancer and Hodgkin's lymphoma.

The use of antitumor antibiotics, specifically Bleomycin, may lead to pulmonary complications and lung toxicity several years after treatment.

Specific Late Effects Screening for *Bleomycin*

- Annual history and physical exam with emphasis on respiratory complaints.
- Chest x-ray at first long-term follow-up visit, and then repeated only as needed.
- Pulmonary function tests (PFT's) at first long-term follow-up visit, and then repeated only as needed for worsening lung function.

Note: There are no specific late effects associated with *Dactinomycin*.

What does this mean for me?

The lungs are one of the most important organs in the body, and chemotherapy drugs, such as Bleomycin, may have adverse effects on pulmonary function. Use of high doses of Bleomycin may result in difficulty breathing, lung scarring, or lung inflammation. This can also later lead to heart complications as blood does not properly get the oxygen it needs. It is important to have regular checkups with a physician, chest x-rays, and pulmonary function tests. It is critical for patients at risk to practice health-promoting behavior—the most important of which is **DO NOT SMOKE**. Smoking, or even being around someone who smokes, greatly increases the risk of lung complications. Regular physical exercise can also help in developing strong, healthy lungs.

For more information, please visit www.survivorshipguidelines.org and select “Pulmonary Health” or “Bleomycin Alert”

Anthracyclines

Anthracyclines	
▶ Doxorubicin (Adriamycin)	▶ Epirubicin
▶ Daunorubicin (Daunomycin)	▶ Idarubicin
▶ Mitoxantrone	

How Do They Work?

Anthracyclines work by releasing toxic substances that destroy the cancerous DNA . They also block certain enzymes involved in DNA replication and growth, which eventually leads to the death of the cancer cells.

Like alkylating agents, anthracyclines are not cell stage specific, and so can be used to treat a wide variety of cancers. They are usually actively used in treating leukemias, lymphomas, breast cancer, ovarian cancer, uterine cancer, and lung cancer.

Anthracyclines may result in a condition called cardiomyopathy. This is a type of heart disease in which the heart muscle becomes abnormally large, thick, and stiff. This causes damage to the left ventricle, one of the four chambers of the heart. The left ventricle is responsible for pumping oxygen-rich blood into the rest of the body. When the left ventricle becomes damaged, it is not able to effectively pump blood. This is especially significant when the heart needs to work harder. While exercise is overall very important in keeping the heart healthy, certain strenuous activities such as heavy bench pressing are not recommended for anyone who received anthracyclines.

The effects that may occur from anthracyclines are related to the total dose the patient received. This is very important information and should be written on the patient's late effects summary. The dose a patient received will determine how often an ECHO and EKG needs to be done. This information should be reviewed with the patient's

treating oncologist. The table below gives the recommended schedule.

Recommended Late Effects Screening for all Anthracyclines

- Yearly history, physical exam, blood work, and skin exam until 10 years off treatment
- Side effects such as shortness of breath and ankle swelling are indicators of congestive heart failure and should be checked by the cardiologist
- Women who become pregnant after having received anthracyclines need to have their pregnancy monitored carefully and see a cardiologist
- Cardiac monitoring by ECHO and EKG is necessary at initial long-term follow-up visit and then according to the following table:

Recommended Schedule of Cardiac Screening after Anthracyclines			
Age at Treatment	Chest Radiation	Anthracycline Dose	Recommended Schedule
< 1 year old	Yes	Any	Annually
	No	< 200 mg/m ²	Every 2 years
≥ 200 mg/m ²		Annually	
1-4 years old	Yes	Any	Annually
	No	< 100 mg/m ²	Every 5 years
		≥ 100 to < 300 mg/m ²	Every 2 years
≥ 300 mg/m ²	Annually		
≥ 5 years old	Yes	< 300 mg/m ²	Every 2 years
		≥ 300 mg/m ²	Annually
	No	< 200 mg/m ²	Every 5 years
		≥ 200 to < 300 mg/m ²	Every 2 years
≥ 300 mg/m ²	Annually		
Any age with decrease in serial function			Annually

Source: 'Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers.' Children's Oncology Group. Adapted with permission.

Calculating Total Anthracycline Dose

Anthracycline Drug	Total Dose (mg/m ²)	Equivalent Factor		Total Dose	
Adriamycin		X	1.0	=	
Mitoxantrone		X	2.5	=	
Daunomycin		X	0.75	=	
Idarubicin		X	3.0	=	
Total Cumulative Dose					

Source: 'Transition to Survivorship, What Parents Should Know.' Dana-Farber Cancer Institute, Inc. Adapted with permission.

What does this mean for me?

Anthracyclines may possibly have adverse effects on the heart, even many years after treatment. It is important for patients to be aware of the possible risks in order to be proactive in their health-care. Anthracyclines may weaken heart muscles cells, damage electrical pathways, or obstruct and harm blood vessels. Consequently, problems with heart muscle function/contraction and an atypical heartbeat may result. This can lead to a number of possible symptoms such as, shortness of breath, constant coughing, chest pain, dizziness, lightheadedness, etc. It is vital for patients at risk to have regular heart checkups with their healthcare provider, including any necessary tests such as an ECHO or EKG. Being aware of these risks and taking part in health promoting activities, such as not smoking, eating healthy, and following a moderate exercise plan will help reduce these risks.

Anthracyclines, may also increase the risk for secondary cancers. Anthracyclines can possibly, but rarely, result in secondary acute myeloid leukemia. This usually occurs (if at all) within the first ten years after treatment. It is essential to be closely monitored by a physician and be knowledgeable about possible alerting symptoms, such as excessive fatigue, lumps, blood in urine or stools, etc. Again, taking part in health promoting activities such as using sunscreen, avoiding tobacco and alcohol, and maintaining a healthy diet will help to greatly reduce this risk.

For more information, please visit www.survivorshipguidelines.org and select "Heart Health"

Corticosteroids

Corticosteroids are a category of chemotherapy drugs that are used for treating certain types of cancer. Corticosteroids include the following:

Corticosteroids

▶ Prednisone

▶ Dexamethasone

▶ Hydrocortisone

How Do They Work?

Corticosteroids are man-made chemotherapy drugs that are similar in chemical structure to our own body's naturally produced hormone, cortisol.

Corticosteroids are used with other chemotherapy drugs to maximize the killing of cancer cells. They work by decreasing inflammation and slowing down the immune system, which stops cancer cell growth and eventually destroys them.

Corticosteroids are mostly used in treating leukemia, lymphoma and multiple myeloma.

Corticosteroids may decrease the strength and overall health of bones, and increase the risk of cataracts.

Recommended Late Effects Screening for all *Corticosteroids*

- Yearly history and physical exam with special attention to mobility and the musculoskeletal system
- Bone density evaluation at initial long-term follow-up visit, and then repeated only as needed
- Yearly eye exams (visual acuity and fundoscopic exam) to assess vision problems

What does this mean for me?

Bone formation is an important part of a child's growth. Corticosteroids increase the risk of bone weakening and result in osteoporosis and osteonecrosis. In osteoporosis, the bone decays faster than new bone formation occurs, resulting in a weakening of the bone and a greater chance of fractures or injury. Height and spinal curvature can also be affected. Osteonecrosis is a disorder that causes temporary or permanent loss of blood to the bones. This can severely weaken bones and put joints at high risk for fracture or collapse. If at risk for osteoporosis or osteonecrosis, it is important to take part in health promoting behavior such as regular exercise and a healthy diet high in calcium and Vitamin D. X-rays and bone scans are useful in detecting both disorders.

The use of corticosteroids may also increase the risk of cataracts. A cataract is a clouding of the eye lens, which can result in vision problems, sensitivity to light, or fading of colors. Cataracts can be easily treated surgically by replacing the cloudy lens with an artificial one. It is still important to remember to wear sunglasses outside and avoiding bright light emitting objects such as fireworks.

For more information, please visit www.survivorshipguidelines.org and select "Bone Health", "Osteonecrosis" or "Cataracts"

Enzymes

Enzymes are a category of chemotherapy drugs that are used for treating certain types of cancer. Enzymes include the following:

Enzymes	
▶ Asparaginase	▶ Erwinia asparaginase
▶ E.Coli asparaginase	▶ PEG asparaginase

How Do They Work?

Asparaginase is a bacterial enzyme that provides specific nutrition for leukemia and lymphomas. This enzyme rapidly decreases the circulating pool of asparagine (needed for protein synthesis) by helping convert this amino acid to aspartic acid and ammonia.

Normal tissues respond to this decrease in asparagine by increasing the production of the enzyme, asparagine synthetase. However, leukemia and lymphoma cells cannot increase the production of asparagine synthetase and become dependent on asparagine from outside the cell to continue making protein. In the absence of protein synthesis, these cancer cells can no longer survive.

As a result, asparaginase has a specific anti-leukemia effect.

Note: There are no specific late effects associated with *Asparaginase*.

Plant Products

Plant Products are a category of chemotherapy drugs that are used for treating certain types of cancer. They include:

Plant Products	
Plant Alkaloids	
▶ Vinblastine	▶ Vincristine
Epipodophyllotoxins	
▶ VP-16	▶ VM-26
Taxanes	
▶ Paclitaxel	▶ Docetaxel
Camptothecins	
▶ Topotecan	▶ Irinotecan

Plant Alkaloids

How Do They Work?

Plant alkaloids are chemotherapy drugs that come from the periwinkle plant. They are more specifically labeled ‘vinca alkaloids’.

Plant alkaloids work by either stopping mitosis (process by which cells divide and reproduce) or by inhibiting protein production necessary for cell reproduction. They are most active in the “M” stage of the cell cycle, but can effectively cause cell damage in all stages.

Plant alkaloids are used in treatment of leukemias, but also can be used to treat lymphomas, myeloma, sarcomas and brain tumors.

The use of plant alkaloids may increase the risk of peripheral nerve damage and possibly result in harmful blood vessel contractions called Raynaud’s phenomenon.

Recommended Late Effects Screening for all *Plant Alkaloids*

- Yearly neurological exam to test for neuropathy until 2 to 3 years after treatment, and then yearly only if symptoms persist
- Yearly physical exam of hands and feet to observe for vasospasms

Epipodophyllotoxins

How Do They Work?

Epipodophyllotoxins are cell cycle specific and effectively interfere with the enzyme that is needed for cell replication. Cancer cells are unable to enter the “G1” phase of the cell cycle, and DNA replication is halted in the “S” phase. Both of these effects prevent cancer cells from multiplying properly.

Epipodophyllotoxins are used to treat certain leukemias, lymphomas, sarcomas of the bone and soft tissue, and ovarian cancer.

The use of epipodophyllotoxins may increase the risk of secondary cancers such as acute myeloid leukemia.

Recommended Late Effects Screening for all *Epipodophyllotoxins*

- Yearly history and physical exam until 10 years post-treatment
- Yearly blood work until 10 years post-treatment

What does this mean for me?

Epipodophyllotoxins, may increase the risk for secondary cancers such as acute myeloid leukemia (AML) within the first ten years after treatment. It is essential to be closely monitored by a physician and be knowledgeable about possible alerting symptoms, such as excessive fatigue, lumps, blood in urine or stools, etc. Taking part in health promoting activities such as using sunscreen, avoiding tobacco and alcohol, and maintaining a healthy diet can help to greatly reduce this risk.

For more information, please visit www.survivorshipguidelines.org and select “Reducing the Risk of Secondary Cancers”

Taxanes and Camptothecins

These drugs are only recently being used in the treatment of pediatric cancer. Not enough information is available at this time on their potential late effects.

Recommended Follow-up after Chemotherapy

If Treatment Included Recommended Follow-Up Testing

Actinomycin	<ul style="list-style-type: none"> ▶ Liver function tests
Bleomycin (Blenoxane) Busulfan Lomustine (CCNU) Carmustine (BCNU)	<ul style="list-style-type: none"> ▶ Chest x-ray, PFTs (breathing tests)—baseline, then every 3 to 5 years
Cisplatin (Platinol) Carboplatin	<ul style="list-style-type: none"> ▶ Audiogram (hearing test)—baseline and at 3 and 5 years [if abnormal, follow annually until stable, then every 3 years] ▶ Blood tests: BUN, Cr, Ca, Mg, PO₄—baseline and annually for 5 years, then as indicated ▶ Creatinine clearance—baseline, then every year if abnormal [if normal, then at 5 years]
Cyclophosphamide (Cytosan) Ifosfamide	<ul style="list-style-type: none"> ▶ Blood tests: LH, FSH, estradiol/testosterone—baseline at age 12, then as needed ▶ Semen analysis (males after puberty) ▶ Menstrual history (females) every year after puberty ▶ Urinalysis every year ▶ Creatinine clearance—baseline, then every 5 years ▶ Blood tests: BUN, Cr, Ca, Mg, PO₄—baseline and annually for 5 years, then as indicated
Nitrogen Mustard Lomustine (CCNU) Carmustine (BCNU)	<ul style="list-style-type: none"> ▶ Complete blood count every year ▶ Blood tests: LH, FSH, estradiol/testosterone—baseline at age 12, then as needed ▶ Semen analysis (males after puberty) ▶ Chest x-ray, PFTs (breathing tests)—baseline, then every 3 to 5 years [only if you received BCNU]
Daunorubicin (Daunomycin) Doxorubicin (Adriamycin) Epirubicin Idarubicin	<ul style="list-style-type: none"> ▶ EKG/echocardiogram/chest x-ray—baseline, then every 2 to 5 years depending on risk (higher risk from higher cumulative dose, young age, female, radiation to chest) ▶ Some institutions use a MUGA scan instead of an echocardiogram ▶ Holter monitor (24-hour EKG test) every 2 to 5 years depending on total dose and institution preference ▶ Exercise testing ▶ If pregnant, see an obstetrician who specializes in high-risk care

Recommended Follow-up after Chemotherapy (cont.)

If Treatment Included	Recommended Follow-Up Testing
High-Dose ARA-C (Cytarabine)	<ul style="list-style-type: none"> ▲ Neurologic examination
L-Asparaginase	<ul style="list-style-type: none"> ▲ None, unless associated with acute problems
Intrathecal Medications: <ul style="list-style-type: none"> • Methotrexate • ARA-C • Hydrocortisone 	<ul style="list-style-type: none"> ▲ Neuropsychological testing—baseline, then every 2 years if any learning problems noted ▲ Educational assessment every year
Methotrexate (systemic) 6-MP (6-mercaptopurine) 6-TG (thioguanine)	<ul style="list-style-type: none"> ▲ Liver function tests—baseline, then as needed
Prednisone Dexamethasone (Decadron)	<ul style="list-style-type: none"> ▲ Evaluation for joint pain ▲ Osteoporosis evaluation (bone density) ▲ Growth evaluation ▲ Examination for cataracts
Vincristine (Oncovin)	<ul style="list-style-type: none"> ▲ Neuropathy evaluation
Etoposide (VP-16)	<ul style="list-style-type: none"> ▲ Neurologic examination ▲ Complete blood count every year for 10 years ▲ Counseling about second cancers

Source: Childhood Cancer Survivors: A Practical Guide to Your Future. Patient-Centered Guides, 2006. Adapted with permission.

RADIATION

and Related Late Effects

Radiation Therapy

Also known as, “Radiotherapy,” “Irradiation,” or “X-Ray Therapy”

RADIATION THERAPY IS ONE OF THE MANY COMMON approaches used when treating cancer. It can be used alone, or together with other cancer treatments such as chemotherapy and surgery. The process involves using ionizing radiation (high-energy particles) to target and destroy cancer cells and shrink tumors in the body. Radiation changes the genetic makeup of the cancer cells, effectively rendering them useless with no ability to grow or divide.

Unfortunately, radiation treatment can only be precise to a certain degree, and normal tissue is also affected in the process. In general, this healthy tissue is able to recover and function without incidence. However, when damage to healthy tissue is permanent or irreversible, late effects may result.

The late effects associated with radiation therapy are highly dependent on the location and dose of the radiation given. They can range from cognitive difficulties, to decreased lung function, to issues with fertility, depending on what part of the body received radiation. Higher doses and more wide spread irradiation, such as total body irradiation (TBI), increase the risk for second cancers. These second cancers can arise even 10 years after treatment has ended.

Considering the fact that late effects of radiation therapy are specific to the location and degree of radiation received, it is important to be familiar with the information most pertinent to your situation.

Potential Impact of Radiation on the Body

- ▶ Brain
- ▶ Breast
- ▶ Ear
- ▶ Eye
- ▶ Female Reproductive System
- ▶ Gastrointestinal System/
Liver
- ▶ Heart
- ▶ Lung
- ▶ Male Reproductive System
- ▶ Musculoskeletal System
- ▶ Neck/Thyroid
- ▶ Neuroendocrine System
- ▶ Oral Cavity
- ▶ Spleen
- ▶ Urinary Tract

Late effects of radiation treatment are real! All patients will endure some late effects, but not all of them!

Knowledge is power: educate yourself and be aware of all the late effects. Keep up with the current research in this ever expanding field. For instance, slow cognitive processing is a well known late effect, but there are an enormous amount of strategies and approaches available to help manage the processing deficits. At least one or more of these approaches will work for your child!

Some day in the not too distant future, targeted therapies will dramatically reduce radiation's Late Effects.

—DEB, MOTHER OF KARA, 5-YEAR BRAIN TUMOR SURVIVOR

Potential Impact of Radiation on the Brain

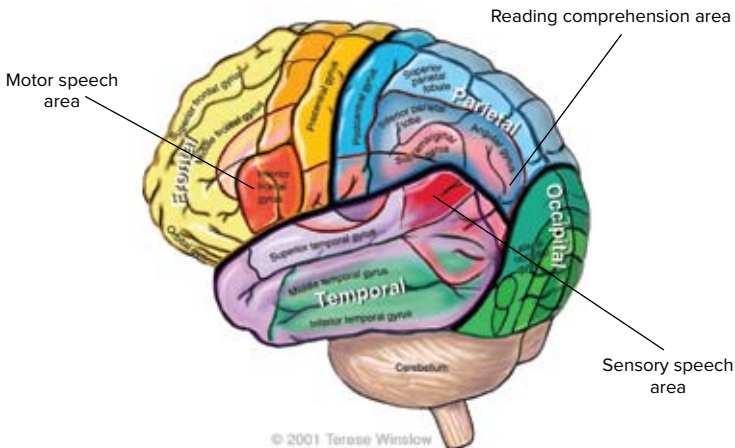
Damage to the Brain

Damage to the brain can occur by radiation treatment to one or more of the following regions:

- | | |
|--------------|--------------------------------|
| ▶ Head/Skull | ▶ Nose |
| ▶ Eye/Orbit | ▶ Total Body Irradiation (TBI) |
| ▶ Ear | |

The tissues of the brain are very susceptible to radiation. The dose and location of radiation, along with the child's sex, age, and individual tolerance, all play a role in how radiation will affect the brain. Children under the age of 2 years are at highest risk for late effects, followed by girls under the age of 5 years. In general, girls are more sensitive to radiation compared to boys.

Radiation damage to the brain can sometimes result in side effects that greatly impact activities in daily life. If treatment involves a vital function area, the patient's educational abilities, behavior, and physical movement may be affected.



Types of Cancers Treated with Radiation that can Impact the Brain

- Brain tumors
- ALL with central nervous system disease
- Retinoblastoma (scatter effects from radiation to the eye socket)
- Rhabdomyosarcoma
- Lymphoma

Possible Late Effects

Radiation Doses Below 2400 cGy

Children with leukemia who receive either 1800 cGy or 2400 cGy whole brain radiation as CNS preventative treatment, fall into this group.

- Educational difficulties, such as:
 - subtle learning difficulties
 - shortened attention span
 - slower processing speeds
 - problems with short-term memory
 - problems in organizing and planning
 - difficulties in math and reading comprehension
 - difficulty with handwriting and spelling
 - diminished IQ
 - changes in behavior
- Inflammation of the sinuses
- Weight gain and obesity
- Reduced thyroid hormone production
- Brain tumor (benign or malignant)

In addition to the late effects mentioned, patients who receive higher doses of radiation may be at risk for these additional problems (depending on location).

Radiation Doses \geq 2400 cGy

- Movement and sensory changes, such as:
 - paralysis
 - gait and balance problems
 - hand-eye coordination problems
 - vision (cataracts) and hearing problems
 - seizures
 - lack of curiosity and interest

Radiation Doses \geq 3000 cGy

- Deformed growth of skull and facial bones

Radiation Doses \geq 4000 cGy

- Stroke
- Brain hemorrhage
- Damaged blood vessels in the brain
- Significant drop in IQ

Children with brain tumors generally receive 3500 cGy to the whole brain with a boost up to 5400 cGy to the tumor bed (where the tumor began). Others receive high-dose radiation directly to the tumor site.

Screening and Detection

- Baseline (repeat as clinically needed)
 - Neuropsychological evaluation
- Every Year
 - Patient history of cognitive and motor abilities
 - Physical and neurologic exam
- Every 2 Years (overweight and obese patients)
 - Fasting blood glucose
 - Fasting serum insulin
 - Fasting lipid profile
- Every 5 Years (normal weight patients)
 - Fasting blood glucose
 - Fasting serum insulin
 - Fasting lipid profile

Taking Charge!

- ▶ Be proactive in school by:
 - sitting in the front of the classroom
 - modifying testing requirements, such as getting extra time or oral exams
 - getting extra help and tutoring
 - having a classroom helper assigned
 - making a personalized educational plan with your teachers suited to your needs
- ▶ Familiarize yourself with the laws in place to protect your rights to fair education and employment
- ▶ Eat healthy and maintain an exercise plan

For more information, please visit www.survivorshipguidelines.org and select “Educational Issues” or “Diet and Physical Activity”

Potential Impact of Radiation on the Breast

Damage to the Breast

Damage to the breast can occur by radiation treatment to one or more of the following regions:

▶ Neck

▶ Lungs

▶ Chest

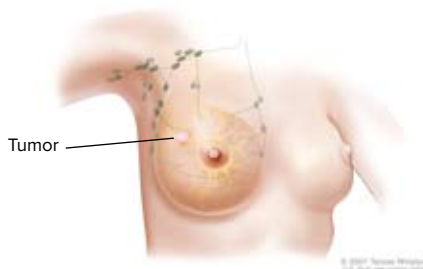
▶ Total Body Irradiation (TBI)

▶ Shoulders

High doses of radiation to the chest and lung may increase the risk for breast cancer later on in life. This does not mean that you will definitely get breast cancer, but simply that you are at higher risk than someone who did not receive radiation. This risk increases 5 to 9 years after treatment, and continues to rise as one ages. As a result, it is important to become familiar with life promoting behaviors and proper monitoring techniques to stay healthy.

Types of Cancers Treated with Radiation that can Impact the Breast

- Hodgkin lymphoma
- Non-Hodgkin's lymphoma
- Sarcomas with primary tumors in the upper extremities and chest (i.e. Ewing's Sarcoma, Rhabdomyosarcoma)
- Sarcomas with metastatic disease in the lungs (i.e. Osteosarcoma, Ewing's Sarcoma, Rhabdomyosarcoma)



Possible Late Effects

Radiation Doses \geq 2000 cGy

- Breast Cancer
- Incomplete growth of breast tissue

Screening and Detection

- Every Month
 - Breast self exam (report any lumps or abnormalities to your healthcare provider)
- Every 6 Months
 - Clinical breast exam after age 25
- Every Year
 - Clinical breast exam until age 25
- Mammogram starting at age 25 or 8 years after receiving radiation

Taking Charge!

- ▶ Maintain a healthy diet rich in fruits and vegetables
- ▶ Exercise at least 30 minutes a day, 5 days a week
- ▶ Avoid cigarettes and alcohol
- ▶ If you have a baby, try to breast feed for at least 4 months

For more information, please visit www.survivorshipguidelines.org and select "Breast Cancer"

Potential Impact of Radiation on the Ear

Damage to the Ear

Damage to the ear can occur by radiation treatment to one or more of the following regions:

▶ Head/Skull

▶ Ear

▶ Nose

Higher doses of radiation may lead to hearing complications. Loss of hearing and damage to the ears can have a long lasting effect on everyday life.

Types of Cancer Treated with Radiation that can Impact the Ear

- Brain tumors
- ALL with central nervous system disease
- Lymphoma involving the brain
- AML with TBI prior to a BMT
- Retinoblastoma
- Nasopharyngeal carcinoma
- Sarcomas with primary tumors to the head, ear or nose (i.e Rhabdomyosarcoma)



Possible Late Effects

Radiation Doses ≥ 3000 cGy

- Hearing loss
- Chronic ear infections
- Ringing in the ear

Yearly Screening and Detection

- History of hearing performance
- Ear exam with an otoscope
- Complete audiogram or BAER test is needed at baseline of long-term follow-up and then according to the following guidelines:
 - if hearing loss is observed, yearly hearing tests are needed
 - for patients who have also received cranial/ear radiation:
 - yearly tests should be performed for 5 years and then every 5 years
 - if younger than age 10, continue every year until 10 years of age

Taking Charge!

- ▶ Discuss with your healthcare provider the best way to protect your hearing
- ▶ Avoid medications that may further damage hearing, such as:
 - Certain antibiotics (gentamicin)
 - Certain diuretics (furosemide)
 - Salicylates (aspirin)
 - Medication for high iron levels
- ▶ Stay away from loud noises, as they can be hazardous to your hearing
- ▶ Avoid in-ear headphones and loud volumes with mp3 players

For more information, please visit www.survivorshipguidelines.org and select "Hearing Loss" or "Educational Issues"

Potential Impact of Radiation on the Eye

Damage to the Eye

Damage to the eye can occur by radiation treatment to one or more of the following regions:

- ▶ Head/Skull
- ▶ Eye/Orbit
- ▶ Total Body Irradiation (TBI)

New and advanced treatments, such as targeted radiation therapy, have resulted in fewer patients diagnosed with Retinoblastoma having to undergo enucleation (removal of the eye). High doses of radiation can cause damage to the eyes, resulting in various late effects.

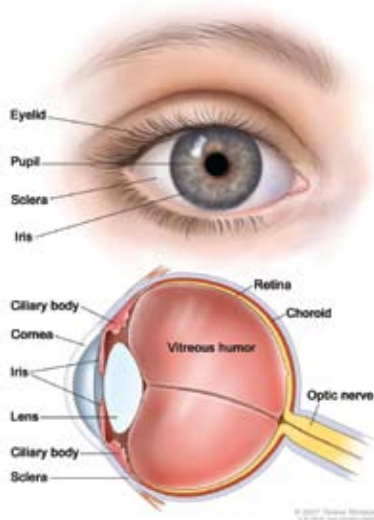
Types of Cancer Treated with Radiation that can Impact the Eye

- Brain tumors
- ALL with central nervous system disease
- AML with TBI prior to a BMT
- Retinoblastoma
- Sarcomas with primary tumors to the head or ear

Possible Late Effects

Lower Radiation Doses

- Cataracts
- Impaired vision



Radiation Doses \geq 3000 cGy

In addition to the late effects mentioned above, patients who receive higher doses of radiation may be at risk for these additional problems:

- Decreased tear production
- Pressure buildup behind the eye (glaucoma)
- Increased dryness and sensitivity (xerophthalmia)
- Blurry or total loss of vision
- Enlarged ocular blood vessels
- Ocular swelling or scarring
- No growth of orbital bone (hypoplasia)
- Sunken eyeball

Screening and Detection

- Every Year
 - History for changes in vision
 - Physical exam with special attention to vision
 - Ophthalmologist evaluation for patients with ocular tumors or treated with \geq 3000 cGy of cranial/orbital/eye radiation
- Every 3–5 Years
 - X-ray of eye and area around the eye
 - Ophthalmologist evaluation for patients without ocular tumors or treated with $<$ 3000 cGy of cranial/orbital/eye radiation

Taking Charge!

It is important to protect your eyes by practicing good safety habits, such as:

- ▶ wearing UV protective sunglasses in bright sunlight
- ▶ wearing proper eye protection when playing certain sports or when working with dangerous equipment or chemicals
- ▶ avoiding fireworks or sharp/protruding toys and objects

For more information, please visit www.survivorshipguidelines.org and select “Cataracts” or “Eye Health”

Potential Impact of Radiation on the Female Reproductive System

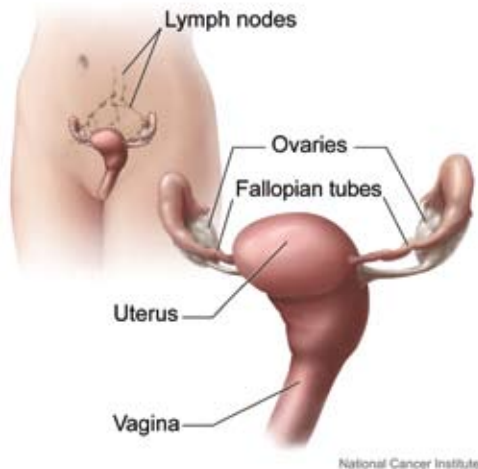
Damage to the Female Reproductive System

Damage to the female reproductive system can occur by radiation treatment to one or more of the following regions:

- | | |
|-----------|--------------------------------|
| ▶ Abdomen | ▶ Spine (middle, lower) |
| ▶ Pelvis | ▶ Total Body Irradiation (TBI) |

The female reproductive system has many organs, all under the control of the pituitary gland in the brain. One of the most important organs are the ovaries, which are responsible for creating the female hormone, estrogen, needed to promote proper physical and sexual growth. Ovaries also contain a girl's limited supply of eggs which are required for fertility. Once an egg is fertilized, it will become implanted into the uterus for further growth.

The late effects of radiation depend heavily on the girl's age at time of treatment and where and how much radiation was given.



Types of Cancers Treated with Radiation that can Impact the Female Reproductive System

- Sarcomas with primary tumor in the abdomen or pelvic area (i.e. Ewing's Sarcoma, Rhabdomyosarcoma)
- Neuroblastoma
- Wilm's tumor
- Germ cell tumors
- Hepatic tumor
- AML with TBI treatment for a BMT
- ALL with central nervous disease
- Hodgkin and Non-Hodgkin's lymphoma

Possible Late Effects

Lower Radiation Doses

- Infertility (higher risk when radiation given directly to ovaries)
- Increased pregnancy risks
- Estrogen deficiency:
 - incomplete or delayed puberty in young girls
 - poor muscle development, weak bones, or heart complications, unless treated with prescribed hormones
- Ovarian failure resulting in stopped egg and hormone production
- Temporary pause of menstruation or premature menopause

Radiation Doses \geq 3500 cGy

In addition to the late effects mentioned above, patients who receive higher doses of radiation may be at risk for these additional problems:

- Vaginal scarring and constriction

Screening and Detection

- Baseline (repeat as clinically needed)
 - Hormone blood work (estradiol/FSH/LH) starting at 10 -12 years of age
- Every Year
 - Patient history and physical exam to document sexual growth (Tanner staging until puberty), function, menstruation, and fertility

Taking Charge!

- ▶ Talk to your doctor about getting prescribed hormones if estrogen deficiency occurs
- ▶ Consult a healthcare provider about possible fertility options such as donor eggs, adoption, and living without a child
- ▶ Discuss with a gynecologist, the possibility of early menopause and consider earlier childbearing, if desired. If children are not desired, continue to use birth control even if menstruation has stopped.
- ▶ Speak with an oncologist about the possible rare genetic risk of passing down your cancer to your children

For more information, please visit www.survivorshipguidelines.org and select "Female Health Issues"

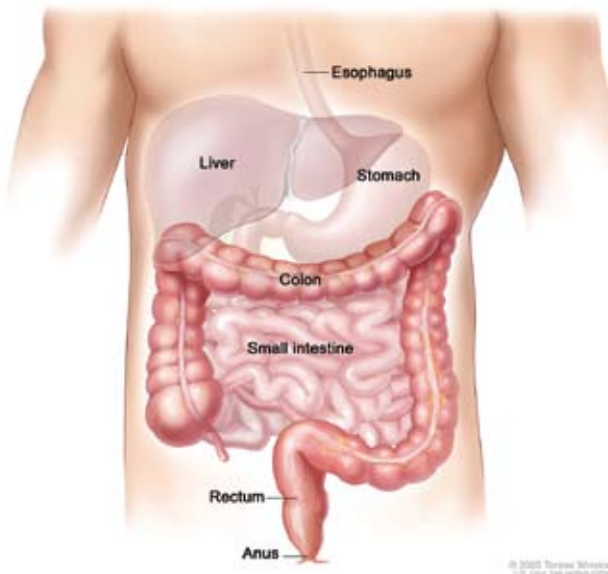
Potential Impact of Radiation on the Gastrointestinal System/Liver

Damage to the Gastrointestinal System/Liver

Damage to the gastrointestinal system/liver can occur by radiation treatment to one or more of the following regions:

- | | |
|-------------------------|-----------|
| ▶ Neck | ▶ Chest |
| ▶ Spine (upper, middle) | ▶ Abdomen |

The gastrointestinal system of the body is an important group of organs responsible for breaking down the food we consume. The breakdown of food provides the needed nutrients for the body to sustain itself and build energy. Depending on the location and dosage, radiation treatment can scar and damage the digestive system and result in late effects.



Types of Cancers Treated with Radiation that can Impact the Gastrointestinal System/Liver

- Wilm's tumor
- Neuroblastoma
- Hepatic tumor
- Germ cell tumor
- Hodgkin lymphoma
- Non-Hodgkin's lymphoma
- Thyroid cancer
- ALL with central nervous system disease
- AML with TBI as treatment for BMT
- Sarcomas with primary tumors in the neck, spine, chest, or abdomen (i.e. Ewing's Sarcoma, Rhabdomyosarcoma)
- Osteosarcoma with lung metastasis
- Nasopharyngeal carcinoma

Possible Late Effects

Radiation Doses \geq 3000 cGy

- Problems swallowing as a result of scarred or constricted esophagus
- Scarring of the liver
- Gallstones
- Blockage of the intestines
- Inflammation of the intestines
 - diarrhea
 - abdominal pain
 - poor absorption of nutrients
- Colorectal cancer

Screening and Detection

- Baseline (repeat as clinically needed)
 - Blood tests (ALT, AST, and Bilirubin)
- Every Year
 - Patient history and physical exam to monitor gastrointestinal, liver, and abdominal health
- Every 5 Years (starting 10 years after radiation or at age 35)
 - Colonoscopy

Taking Charge!

- ▶ Follow healthy eating habits, such as a diet rich in fruits, vegetables, and grains but low on red meat and fatty foods
- ▶ Exercise at least 30 minutes a day, 5 days a week
- ▶ Avoid the use of tobacco products and excessive alcohol
- ▶ Drink plenty of water

For more information, please visit www.survivorshipguidelines.org and select “Gastrointestinal Health,” “Liver Health,” or “Colorectal Cancer”

Potential Impact of Radiation on the Heart

Damage to the Heart

Damage to the heart can occur by radiation treatment to one or more of the following regions:

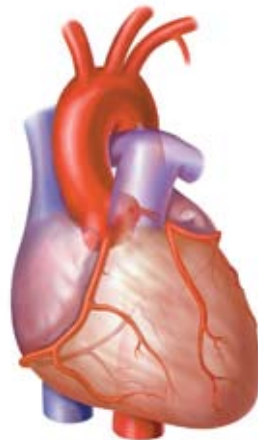
▶ Neck	▶ Shoulders	▶ Abdomen
▶ Chest	▶ Spine (middle)	

The use of radiation may result in damage to the heart muscle, which can lead to later heart complications and cardiac toxicity. The majority of childhood cancer survivors will not develop heart complications as a result of treatment, however, a small percent may. Patients, who received radiation in combination with anthracyclines, need to be particularly monitored for heart related late effects.

Regular checkups and following health promoting habits will help you reduce the risk of heart disease.

Types of Cancer Treated with Radiation that can Impact the Heart

- Hodgkin lymphoma
- Non-Hodgkin's lymphoma
- Sarcomas with primary tumors in the chest, shoulders, spine, or abdomen
- Hepatic Tumors
- Wilm's Tumor
- Germ Cell Tumor
- Neuroblastoma
- ALL with central nervous system disease



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Possible Late Effects

Radiation Doses \geq 3000 cGy

- Congestive heart failure
- Heart disease
- Scarred or rigid heart tissue
- Abnormal heart beat
- Damage to heart muscle, valves, and blood vessels

Screening and Detection

- Baseline (repeat as clinically needed)
 - EKG (including QTc interval evaluation)
 - ECHO
- Every Year
 - Patient history of respiratory function, as well as chest and abdominal symptoms
 - Physical exam
- Every 3–5 Years
 - Fasting glucose and lipid profile

Taking Charge!

- ▶ Avoid excess strain on the heart by activities such as heavy lifting, bench pressing or taking certain drugs
- ▶ Don't smoke
- ▶ Eat a healthy diet with limited fat
- ▶ Maintain an appropriate, healthy body weight

For more information, please visit www.survivorshipguidelines.org and select "Heart Health"

Recommended Frequency of Echocardiogram

Age at Treatment	Radiation Dose	Anthracycline Dose	Recommended Frequency
< 5 years old	Any	None	Every 2 years
		Any	Every Year
≥ 5 years old	< 3000 cGy	None	Every 5 years
	≥ 3000 cGy	None	Every 2 years
	Any	< 300 mg/m ²	Every 2 years
		≥ 300 mg/m ²	Every Year
Any age with serial decrease in function			Every Year

Source: 'Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers.' Children's Oncology Group. Adapted with permission.

Potential Impact of Radiation on the Lung

Damage to the Lung

Damage to the lung can occur by radiation treatment to one or more of the following regions:

▶ Neck

▶ Lungs

▶ Spine (upper, middle)

▶ Total Body Irradiation (TBI)

The lungs are one of the most important organs in the human body and are essential for breathing. Respiration is achieved by regulation of gas exchange within the body via the lungs; ensuring that oxygen is transported into the bloodstream, while carbon dioxide is exhaled out into the atmosphere. Radiation to the chest area may damage the lungs and result in late effects, so it is important to learn good health promoting behaviors to keep them healthy.

Types of Cancer Treated with Radiation that can Impact the Lung

- Hodgkin or Non-Hodgkin's lymphoma
- ALL or AML
- Sarcomas with primary tumors in the upper extremities (i.e. Ewing's Sarcoma, Rhabdomyosarcoma)
- Sarcomas with metastatic disease in the lungs (i.e. Osteosarcoma, Ewing's Sarcoma, Rhabdomyosarcoma)

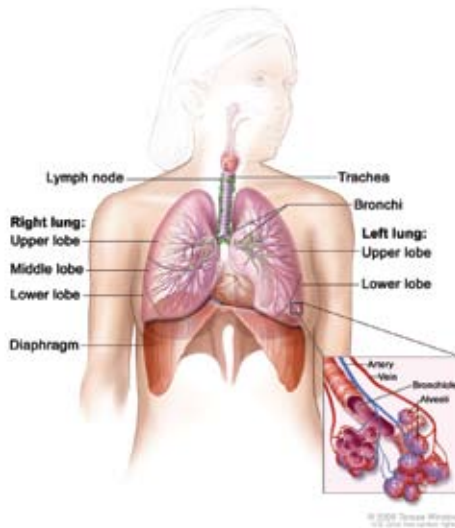
Possible Late Effects

Lower Radiation Doses

- Recurrent lung infections
- Pneumonia
- Inflammation and scarring of the lung
- Thickening and blockage of lung passageways
- Shortness of breath and fatigue
- Chest pain

Screening and Detection

- Baseline (repeat as clinically needed)
 - Chest x-ray
 - Pulmonary function tests (including DLCO and spirometry)
- Every Year
 - Patient history of respiratory function
 - Pulmonary exam



Taking Charge!

- ▶ **DO NOT SMOKE!!!**
- ▶ Avoid second-hand smoke
- ▶ Exercise regularly to help develop strong, healthy lungs
- ▶ Have a medical evaluation and be checked by a diving specialist before Scuba diving
- ▶ Avoid inhaling toxic fumes, chemicals, paint, etc.

For more information, please visit www.survivorshipguidelines.org and select "Pulmonary Health"

Potential Impact of Radiation on the Male Reproductive System

Damage to the Male Reproductive System

Damage to the male reproductive system can occur by radiation treatment to one or more of the following regions:

- ▶ Pelvis
- ▶ Testicles
- ▶ Total Body Irradiation (TBI)

The male reproductive system is composed of a variety of organs, all under the control of the pituitary gland in the brain. Of these components, one of the most important structures is the testicles. They are responsible for producing sperm, as well as the male hormone, testosterone. Sperm is required for fertility, while testosterone is needed to promote proper physical and sexual growth.

The late effects of radiation depend heavily on the boy's age at time of treatment and where and how much radiation was given.

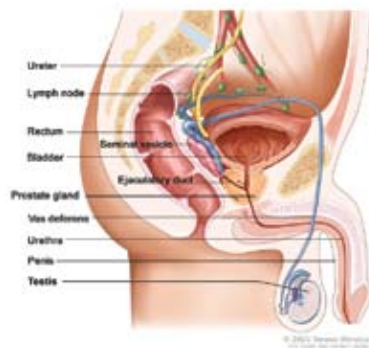
Types of Cancer Treated with Radiation that can Impact the Male Reproductive System

- Testicular cancer
- Sarcomas with primary tumors in the pelvic region (i.e. Ewing's Sarcoma, Rhabdomyosarcoma)
- Germ Cell tumors
- ALL with testicular metastasis
- AML with TBI treatment for a BMT

Possible Late Effects

Lower Radiation Doses

- Infertility (higher risk when radiation given directly to testes)
- Little or no sperm count



Radiation Doses \geq 2000 cGy

In addition to the late effects mentioned above, patients who receive higher doses of radiation may be at risk for these additional problems:

- Testosterone deficiency:
 - incomplete or delayed puberty in young boys
 - poor muscle development, weak bones, or decreased sex drive and erections in boys past puberty, unless treated with prescribed hormones
- Slow bloodflow from the scrotum into the pelvis causing swelling in the groin area

Screening and Detection

- Baseline (repeat as clinically needed)
 - Hormone blood work (testosterone/FSH/LH) starting at 11 or 12 years of age
 - Semen analysis
- Every Year
 - Patient history and physical exam relating to sexual function and growth (Tanner staging until puberty)
 - Monitoring of testicular volume by Prader orchidometer until puberty

Taking Charge!

- ▶ Talk to your doctor about getting prescribed hormones if testosterone deficiency occurs
- ▶ Consult a healthcare provider about fertility options such as freezing active sperm, surgical harvesting, and donor sperm

For more information, please visit www.survivorshipguidelines.org and select “Male Health Issues”

Potential Impact of Radiation on the Musculoskeletal System

Damage to the Musculoskeletal System

Damage to the musculoskeletal system can occur by radiation treatment to one or more of the following regions:

▶ Neck	▶ Abdomen	▶ Pelvis
▶ Chest	▶ Extremities	▶ Spine (upper, middle, lower)

The musculoskeletal system is a combination of the skeleton (bones) and their associated muscles, tendon, ligaments, and other connective tissue. Together, they provide stability, support, and allow the body to have free range of motion. The musculoskeletal system is also important in protecting the inner, vital organs.

Depending on the dosage and location, radiation treatment can damage bones and muscle and result in varying late effects.

Types of Cancer Treated with Radiation that can Impact the Musculoskeletal System

- Sarcomas with primary tumor in the abdomen, pelvic area, or extremity (i.e. Ewing's Sarcoma, Rhabdomyosarcoma)
- Neuroblastoma
- Wilm's tumor
- Germ cell tumors
- Hepatic tumor
- Osteosarcoma with lung metastasis
- AML with TBI treatment for a BMT
- ALL with central nervous disease
- Thyroid tumor
- Hodgkin lymphoma
- Non-Hodgkin's lymphoma



Possible Late Effects

Radiation Doses \geq 2000 cGy

- Skeletal Growth Complications
 - Incomplete growth of bones and muscles
 - Excess tissue buildup (fibrosis)
 - Shortened height
 - Inconsistency in length of limbs due to damage to bone growth plate during surgery (limb-length discrepancy)
 - Uneven growth
- Scoliosis – sideways rotation of the spine
- Kyphosis – rounding of the upper back, resembling a “hump”

Radiation Doses \geq 4000 cGy

In addition to the late effects mentioned above, patients who receive higher doses of radiation may be at risk for these additional problems:

- Fractures caused by radiation

Yearly Screening and Detection

- Physical exam, including:
 - Sitting height
 - Limb lengths
 - Spine exam for scoliosis and kyphosis

Taking Charge!

- ▶ Talk to your healthcare provider about the need for an orthopedic consultation or plastic surgery for reconstruction
- ▶ If at a risk for radiation induced fractures, avoid heavy lifting, straining, or weight bearing

For more information, please visit www.survivorshipguidelines.org and select “Scoliosis and Kyphosis”

Potential Impact of Radiation on the Neck/Thyroid

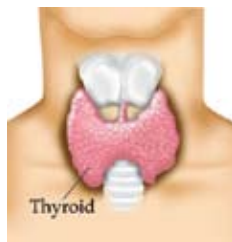
Damage to the Neck/Thyroid

Damage to the neck and thyroid glands can occur by radiation treatment to one or more of the following regions:

- | | | |
|----------------|--------|--------------------------------|
| ▶ Head/Skull | ▶ Nose | ▶ Spine (upper) |
| ▶ Mouth/Throat | ▶ Neck | ▶ Total Body Irradiation (TBI) |

The thyroid gland, located in the lower neck, is an important part of the endocrine system. The endocrine system is a group of glands and organs in the body responsible for regulating various body processes from growth and puberty to the production of bodily waste. The thyroid gland is specifically responsible for releasing hormones that control growth, metabolism, moods, and energy levels. The hormone produced by the thyroid gland, thyroxine, is under the control of TSH, another hormone produced by the pituitary gland in the brain.

Depending on the location and dose used, radiation treatment can damage the neck and thyroid resulting in possible late effects on growth and normal body function.



Types of Cancer Treated with Radiation that can Impact the Neck/Thyroid

- Hodgkin and Non-Hodgkin lymphoma
- Brain Tumors
- Sarcomas with primary tumors in the mouth, nose, neck or spine (i.e. Rhabdomyosarcoma)
- ALL with central nervous system disease
- Nasopharyngeal Carcinoma

Possible Late Effects

Radiation Doses \geq 2000 cGy

- Thyroid nodules or lumps
- Increased risk of thyroid cancer
- Hypothyroidism – thyroid gland is less active and the following symptoms may occur:
 - fatigue
 - changes in mood and emotion
 - change in voice
 - short attention span
 - weakness and body aches
 - sensitivity to cold
 - slowed growth
 - low blood pressure
 - weight gain
 - dry skin and brittle hair

Radiation Doses \geq 4000 cGy

In addition to the late effects mentioned above, patients who receive higher doses of radiation may be at risk for these additional problems:

- Artery disease
- Hyperthyroidism
 - Apprehension
 - Concentration problems
 - Abnormal heartbeat
 - Fatigue and weak muscles
 - Diarrhea
 - Weight loss
 - Swelling of the neck
 - Increased body temperature
 - Protruding eyes

Yearly Screening and Detection

- Patient history and physical exam
- Thyroid exam (more frequently during times of significant growth, e.g. puberty)
- TSH screening (more frequently during times of significant growth)
- Thyroid hormone screening (more frequently during times of significant growth)

Taking Charge!

- ▶ If prescribed, take thyroid medication and closely follow the schedule outlined by your healthcare provider
- ▶ Females considering pregnancy should have their thyroid hormone levels checked.

For more information, please visit www.survivorshipguidelines.org and select “Thyroid Problems”

Potential Impact of Radiation on the Neuroendocrine System

Damage to the Neuroendocrine System

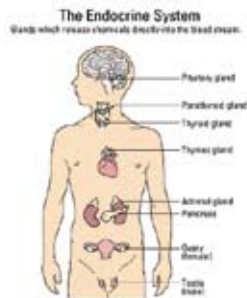
Damage to the neuroendocrine system can occur by radiation treatment to one or more of the following regions:

▶ Head/Skull	▶ Ear	▶ Total Body Irradiation (TBI)
▶ Eye/Orbit	▶ Nose	

The nervous and endocrine systems are highly interconnected, and certain radiation treatments (especially in the cranial region) can lead to damage in the endocrine system. The endocrine system is a group of glands and organs in the body responsible for regulating various body processes from growth and puberty to the production of bodily waste. The pituitary and hypothalamus glands located in the brain, control the release of hormones or “chemical messengers” that help regulate this process.

Types of Cancer Treated with Radiation that can Impact the Neuroendocrine System

- Brain Tumors
- Retinoblastoma
- Sarcomas with primary tumors in the head or facial area (i.e. Rhabdomyosarcoma)
- ALL with central nervous system disease
- Nasopharyngeal Carcinoma
- AML requiring a BMT and use of TBI



Possible Late Effects

Lower Radiation Doses

- Early puberty
- Stunted growth (growth hormone deficiency)

Radiation Doses \geq 4000 cGy

In addition to the late effects mentioned above, patients who receive higher doses of radiation may be at risk for these additional problems:

- Metabolic imbalance
- Decreased function of the ovaries or testicles
- Hormonal disorders
- Central Hypothyroidism:
 - fatigue
 - changes in mood and emotion
 - change in voice
 - short attention span
 - weakness and body aches
 - sensitivity to cold
 - slowed growth
 - low blood pressure
 - weight gain
 - dry skin and brittle hair

Screening and Detection

- Baseline (repeat as clinically needed)
 - Boys:
 - Hormone blood work (testosterone/FSH/LH) starting at 11 or 12 years of age
 - Semen analysis
 - Girls:
 - Hormone blood work (estradiol/FSH/LH) starting at 10–12 years of age
- Every 6 Months
 - Physical exam and nutritional status assessment (until growth is complete)
 - Tanner staging (until sexually mature)

■ Every Year

- 8:00am serum cortisol
- TSH and Free T4 screening (more frequently during times of growth)
- Boys:
 - Patient history regarding sexual function and growth
 - Monitoring of testicular volume by Prader orchidometer until puberty
- Girls:
 - Patient history to document sexual growth, function, menstruation, and fertility

Taking Charge!

- ▶ Ask your endocrinologist about whether or not you need synthetic growth hormone injections
- ▶ Boys:
 - Talk to your doctor about getting prescribed hormones if testosterone deficiency occurs
 - Consult a healthcare provider about fertility options such as freezing active sperm, surgical harvesting, and donor sperm
- ▶ Girls:
 - Talk to your doctor about getting prescribed hormones if estrogen deficiency occurs
 - Consult a healthcare provider about possible fertility options such as donor eggs, adoption, and child-free living
 - Females considering pregnancy should have their thyroid hormone levels checked

For more information, please visit www.survivorshipguidelines.org and select "Growth Hormone Deficiency" or "Hypopituitarism"

Potential Impact of Radiation on the Oral Cavity

Damage to the Oral Cavity

Damage to the oral cavity can occur by radiation treatment to one or more of the following regions:

- | | | |
|----------------|--------|--------------------------------|
| ▶ Head/Skull | ▶ Nose | ▶ Spine (upper) |
| ▶ Mouth/Throat | ▶ Neck | ▶ Total Body Irradiation (TBI) |

Radiation treatment to the oral cavity (the opening of the mouth) may result in side effects that can affect overall dental health.

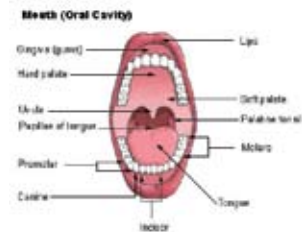
Types of Cancer Treated with Radiation that can Impact the Oral Cavity

- Brain Tumors
- Sarcomas with primary tumors in the facial area or spine (i.e. Rhabdomyosarcoma)
- ALL with central nervous system disease
- AML requiring a BMT and use of TBI
- Nasopharyngeal Carcinoma
- Thyroid tumor

Possible Late Effects

Lower Radiation Doses

- Dental abnormalities:
 - greater risk of cavities
 - change in taste
 - thinning and shortening of the of the teeth
 - greater teeth sensitivity
 - missing teeth or roots
 - limited ability to fully open mouth
 - small teeth
 - gum disease
 - early loss of teeth
 - problems with proper bite (overbite/underbite)
 - poor development of tooth enamel
 - abnormal growth of facial bones



Radiation Doses \geq 4000 cGy

In addition to the late effects mentioned, patients who receive higher doses of radiation may be at risk for these additional problems:

- Problems producing saliva
- Dry mouth
- Improper healing of the jawbone (osteoradionecrosis)

Screening and Detection

- Every 6 Months
 - Dental checkup and cleaning
- Every Year
 - Yearly patient history and oral exam

Taking Charge!

- ▶ Visit the dentist regularly every 6 months
- ▶ Have a panorex x-ray performed before any dental/orthodontic work
- ▶ Brush your teeth twice a day with fluoride toothpaste
- ▶ Floss twice a day and use alcohol-free mouthwash
- ▶ Limit foods high in sugar and carbohydrates
- ▶ Avoid tobacco products and alcohol
- ▶ Drink plenty of fluids and use artificial saliva, if needed

For more information, please visit www.survivorshipguidelines.org and select “Dental Health” or “Osteoradionecrosis”

Potential Impact of Radiation on the Spleen

Damage to the Spleen

Damage to the spleen can occur by radiation treatment to one or more of the following regions:

▶ Spleen

▶ Abdomen

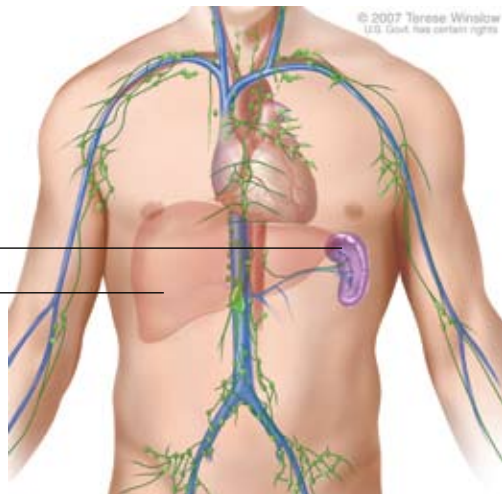
The spleen is an organ located in the abdomen that both boosts the immune system and helps in filtering bacteria from the blood. Since the spleen is responsible for producing antibodies, it is an important organ in fighting infections.

High doses of radiation may damage the spleen and lead to complications with proper immune function.

Types of Cancer Treated with Radiation that can Impact the Spleen

- Neuroblastoma
- Wilm's tumor
- Germ Cell tumors
- Hepatic tumor
- Hodgkin lymphoma

Spleen —————
Liver —————



Possible Late Effects

Radiation Doses \geq 4000 cGy

- Impaired immune function
- Increased risk of life-threatening infection, especially by encapsulated bacteria. Some common illnesses to be watchful for are:
 - Pneumonia
 - Influenza
 - Meningitis

Screening and Detection

If patient has a temperature \geq 101°F, then:

- Evaluate with blood work (blood culture and CBC) immediately
- Perform physical exam
- Administer appropriate antibiotics

Taking Charge!

- ▶ Seek medical advice to determine if daily use of antibiotics, such as penicillin, is needed
- ▶ Vaccines are an important preventative measure. The following vaccines are recommended:
 - Pneumococcal
 - Meningococcal
 - Haemophilus Influenzae Type B (HIB)
- ▶ Wearing a medical alert bracelet or carrying a wallet card describing past spleen surgery may be helpful to healthcare providers in times of emergency

For more information, please visit www.survivorshipguidelines.org and select “Splenic Precautions”

Potential Impact of Radiation on the Urinary Tract

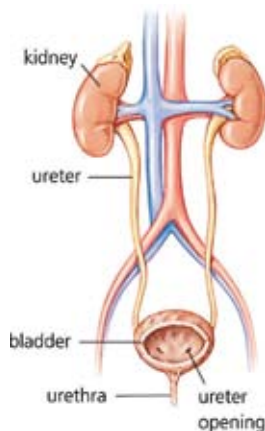
Damage to the Urinary Tract

Damage to the urinary tract can occur by radiation treatment to one or more of the following regions:

- | | |
|-----------------|--------------------------------|
| ▶ Abdomen | ▶ Pelvis |
| ▶ Spine (lower) | ▶ Total Body Irradiation (TBI) |

The kidneys and the bladder are the two main organs of the urinary tract. The kidneys are responsible for filtering out waste products from the blood and keeping it free of toxins. They also play an important role in controlling blood pressure and stimulating red blood cell production.

The urinary bladder is also important for normal body function. It serves as the reservoir for urine, which is produced when the kidneys filter the blood.



Types of Cancer Treated with Radiation that can Impact the Urinary Tract

- Testicular cancer
- Sarcomas with primary tumors in the abdomen or pelvic region (i.e. Ewing's Sarcoma, Rhabdomyosarcoma)
- Germ Cell tumors
- Neuroblastoma
- Wilm's tumor
- ALL with testicular metastasis or central nervous system disease
- AML with TBI treatment for a BMT

Possible Late Effects

Lower Radiation Doses

- Kidney toxicity
- High blood pressure
- Poor kidney function

Radiation Doses \geq 3000 cGy

In addition to the late effects mentioned above, patients who receive higher doses of radiation may be at risk for these additional problems:

- Bladder inflammation, scarring, and bleeding
- Swelling of the kidneys as a result of urine backflow
- Loss of bladder control
- Bladder cancer

Screening and Detection

- Baseline (repeat as clinically needed)
 - Blood tests (BUN, Creatinine, Na, K, Cl, CO₂, Ca, Mg, PO₄)
- Every Year
 - Patient history and physical exam
 - Urinalysis

Taking Charge!

- ▶ Drink plenty of water to keep your kidneys healthy
- ▶ Immediately contact the hospital if symptoms of urinary tract infection appear
- ▶ Notify healthcare provider if using any medicines like aspirin or acetaminophen
- ▶ If you only have one healthy kidney, discuss playing contact sports with your healthcare provider first and always use a kidney guard

For more information, please visit www.survivorshipguidelines.org and select “Gastrointestinal Health,” “Liver Health,” or “Colorectal Cancer”

Tests After Radiation

Radiation Given	Recommended Follow-Up Testing
Bone	<ul style="list-style-type: none"> ▶ X-rays every 5 years ▶ Evaluation of bone growth and overlying soft tissue
Head/Nose	<ul style="list-style-type: none"> ▶ Educational assessment every year ▶ Neuropsychological testing—baseline, then every 2 to 3 years ▶ X-ray of full set of teeth (Panorex) at age 5 ▶ Monitor for early or delayed puberty ▶ Growth curve every year (every 6 months ages 10-12) ▶ Bone age (x-ray of hand) at 9 years for a baseline, then every year until puberty (based on risk factors) ▶ Blood tests: growth hormone, somatomedin C, IGFBP3, and others as indicated ▶ Complete eye examination by ophthalmologist every year that includes check for cataracts ▶ Blood tests: Free T4, TSH every year for 10 years after treatment
Flank	<ul style="list-style-type: none"> ▶ Observe for scoliosis (curvature of the spine) every year (every 6 months during puberty)
Chest	<ul style="list-style-type: none"> ▶ Blood tests: Free T4, TSH every year ▶ Chest x-ray, PFTs (breathing tests) every 3 to 5 years ▶ Breast self exam every month ▶ Breast examination by healthcare provider every year ▶ Mammogram 10 years off treatment or by age 25 (whichever comes first), then every 2 years until age 40, then every year (females only) ▶ Growth curve (sitting and standing heights) every year until fully grown ▶ Dental exam every year ▶ EKG/ECHO/chest x-ray—baseline, then every 2 to 5 years depending on risk (higher risk from higher cumulative dose, young age, female, radiation to chest)

Tests After Radiation (cont.)

Radiation Given	Recommended Follow-Up Testing
Chest (cont.)	<ul style="list-style-type: none"> ▶ Some institutions use a MUGA scan instead of an echocardiogram ▶ Holter monitor (24-hour EKG test) every 2 to 5 years depending on total dose and institution preference ▶ Exercise testing ▶ If pregnant, see an obstetrician who specializes in high-risk care ▶ Counseling about not smoking
Lung	<ul style="list-style-type: none"> ▶ Chest x-ray ▶ PFTs (breathing tests) every 3 to 5 years ▶ Breast self exam every month ▶ Breast examination by healthcare provider every year ▶ Mammogram 10 years off treatment or by age 25 (whichever comes first), then every 2 years until age 40, then every year ▶ Growth curve (sitting and standing heights) every year until fully grown ▶ EKG/ECHO/chest x-ray—baseline, then every 2 to 5 years depending on risk (higher risk from higher cumulative dose, young age, female, radiation to chest) ▶ Some institutions use a MUGA scan instead of an echocardiogram ▶ Holter monitor (24-hour EKG test) every 2 to 5 years depending on total dose and institution preference ▶ Exercise testing ▶ Counseling about not smoking
Spinal	<ul style="list-style-type: none"> ▶ Evaluation for scoliosis (curvature of the spine), kyphosis (curvature of spine in hunchback shape) ▶ Blood tests: Free T4, TSH every year for 10 years ▶ Growth curve (sitting and standing heights) every year ▶ Blood tests: LH, FSH, estrogen (females baseline at 12, then as needed)

Tests After Radiation (cont.)

Radiation Given	Recommended Follow-Up Testing
Spinal (cont.)	<ul style="list-style-type: none"> ▶ Evaluate puberty stage (Tanner) ▶ EKG/ECHO/chest x-ray—baseline, then every 2 to 5 years depending on risk (higher risk from higher cumulative dose, young age, female, radiation to chest) ▶ Holter monitor (24-hour EKG test) every 2 to 5 years depending on total dose and institution preference ▶ Exercise testing
Testicular	<ul style="list-style-type: none"> ▶ Testes exam every year by a healthcare provider ▶ Testicular self-exam every month ▶ Blood tests: LH, FSH, testosterone ▶ Puberty staging (Tanner)
Neck and Jaw	<ul style="list-style-type: none"> ▶ Dental exam every year ▶ Complete eye examination by ophthalmologist every year that includes check for cataracts
Extremity	<ul style="list-style-type: none"> ▶ Monitor for leg-length discrepancy
Orbit (Eye)	<ul style="list-style-type: none"> ▶ Complete eye examination by ophthalmologist every year ▶ X-ray of orbits every 3 to 5 years ▶ Blood tests: LH, FSH, estrogen/testosterone (baseline at 12 then as needed) ▶ Puberty staging (Tanner)
Total Body Irradiation (TBI)	<ul style="list-style-type: none"> ▶ Growth curve (sitting and standing heights) every year ▶ Bone age (x-ray of hand) as needed (except for Cytoxan-only conditioning) ▶ Growth hormone every year until maturity (except if child is receiving GH) ▶ Urinalysis (check for blood, protein, sugar)

Tests After Radiation (cont.)

Radiation Given	Recommended Follow-Up Testing
Total Body Irradiation (TBI) (cont.)	<ul style="list-style-type: none"> ▶ Puberty evaluation every year from age 8 to 18 ▶ Blood tests: LH, FSH (baseline at 12 years of age, then as needed) ▶ Menstrual history (females) every year after puberty ▶ Blood tests: Free T₄, TSH every year ▶ Complete eye examination by ophthalmologist every year that includes check for cataracts ▶ Skin checks and counseling on protecting skin from the sun
Abdomen/Pelvis	<ul style="list-style-type: none"> ▶ Blood tests: LH, FSH, estrogen/testosterone (baseline at 12 years of age, then as needed) ▶ Evaluation for scoliosis (curvature of the spine), kyphosis (curvature of spine in hunchback shape) ▶ Creatinine and BUN every year ▶ Creatinine clearance—baseline, then as needed ▶ Puberty staging (Tanner) and menstrual history ▶ Semen analysis ▶ Nutritional history ▶ Stool test for blood every year ▶ Urinalysis every year ▶ If pregnant, see an obstetrician who specializes in high-risk pregnancies
All Areas	<ul style="list-style-type: none"> ▶ Skin check of irradiated areas

Source: 'Childhood Cancer Survivors: A Practical Guide to Your Future.' Patient-Centered Guides, 2006. Adapted with permission.

SURGERY

and Related Late Effects

Surgery and Related Late Effects

THOUGH VARIOUS TREATMENTS FOR CANCER EXIST, surgery is one of the oldest ones available. It involves a surgeon physically removing the cancerous tumor and surrounding tissue, ensuring that all visible and accessible cancer cells have been eliminated. Surgery can be performed alone, or in combination with other cancer treatments such as chemotherapy and radiation.

Surgery may be used for:

- Diagnosis of the cancer (biopsy)
- To determine the stage and extent of cancer spread in some tumors
- For precise removal of tumor, while sparing healthy tissue
- In relieving complications that occur from chemotherapy and radiation

Surgery is the choice of treatment for some localized childhood cancers such as kidney tumors. In children, it is most commonly used in the treatment of bone, soft tissue, brain, kidney, adrenal, and lung cancer.

Late effects of surgery are directly related to the location and body part that surgery was performed on. In this section, we have attempted to describe some of the common surgeries children may undergo as part of their treatment. It is important to be familiar with the information most pertinent to your situation.

Types of Surgery

- ▶ Abdominal surgery
- ▶ Amputation
- ▶ Bladder
- ▶ Eye
- ▶ Kidney
- ▶ Limb Salvage Procedure and Rotationplasty
- ▶ Lung
- ▶ Neurosurgery
- ▶ Ovarian
- ▶ Pelvic
- ▶ Spleen
- ▶ Testicular
- ▶ Thyroid

Abdominal Surgery (Laparotomy)

The abdomen is the central part of the body that contains many of the organs necessary for proper gastrointestinal health and reproduction (i.e. stomach, intestines, liver, uterus etc.). Laparotomy, or opening of the abdominal cavity, is a common procedure used for both diagnosis and treatment of certain childhood cancers, such as liver, kidney, adrenal gland, and lymphoma.

Possible Late Effects

- Scar tissue and adhesions
- Complications with digestion
- Blockage of the intestines

Recommended Late Effects Screening for Abdominal Surgery

- Yearly history and physical exam to evaluate gastrointestinal health



Taking Charge!

- ▶ Eat healthy foods, especially those high in fiber, to help with proper digestion
- ▶ Avoid destructive behavior, such as smoking
- ▶ Limit the use of alcohol

For more information, please visit www.survivorshipguidelines.org and select "Gastrointestinal Health"

Amputation

Amputation is the removal of all or a part of an arm or a leg. It is used for the following:

- Treatment of certain bone and soft tissue cancers (e.g. Osteosarcoma, Ewing's Sarcoma)
- Children with very large tumors that involve the blood vessels and nerves
- Very young children with certain types of advanced cancer
- Children who do not have a good response to chemotherapy
- Children who are not candidates for limb salvage surgery
- Rarely, amputations may be needed for other complications, such as infection, that may arise during cancer treatment.

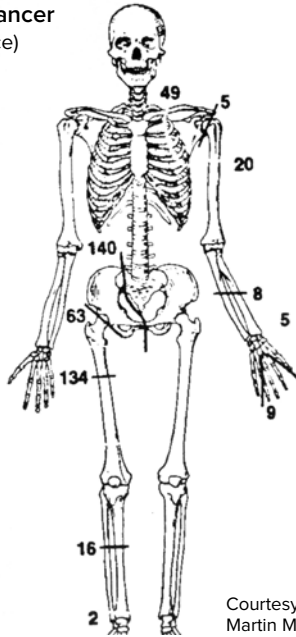
Possible Late Effects

- Chafing, bruising, or redness from an ill-fitted prosthesis
- “Phantom Limb” or the feeling that the missing limb is still there
- Pain and cramping at the site of amputation
- Overuse of other muscles and limbs, leading to back pain
- Decreased physical activity, which can lead to weight gain, obesity, and diabetes
- Sadness and feelings of depression over lost limb

Recommended Late Effects Screening for Amputation

- Yearly history and physical exam for limb function and structure (repeat more frequently if clinically necessary)
- Yearly x-ray
- Evaluation by an orthopedic surgeon every six months until bones have fully matured, after which the patient should be evaluated yearly

Amputation for Cancer
(N.I.H. Experience)
N = 466



Courtesy of
Martin Malawer, MD, FACS

Taking Charge!

- ▶ Keep the site of amputation clean and dry
- ▶ Watch for changes in skin color or rashes
- ▶ Get proper training with a physical and occupational therapist
- ▶ Eat healthy and maintain an exercise plan that involves both passive and active movement
- ▶ Carry a medical letter if you have metal implants to help with metal detectors and security checkpoints
- ▶ Speak with an oncologist or orthopedist about the future use of a prosthesis

For more information, please visit www.survivorshipguidelines.org and select "Amputation"

Bladder Surgery (Cystectomy)

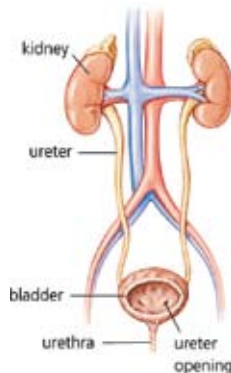
The urinary bladder is important for normal body function. It stores urine, which is produced when the kidneys filter the blood. A cystectomy is an operation to remove the urinary bladder. After the urinary bladder is removed, a new passageway is created so that urine can leave the body.

This is a rare surgery in children and is only performed for:

- Certain tumors, such as advanced rhabdomyosarcoma of the urinary bladder and prostate, Ewing's sarcoma, and other extensive sarcomas of the pelvic area
- Severe hemorrhagic inflammation of the bladder from cyclophosphamide, ifosfamide, and radiation, which does not respond to medical treatment.

Possible Late Effects

- Urinary tract infection
- Poorly functioning kidneys
- Diarrhea or kidney stones as a result of chemical imbalance
- Swelling of the kidneys as a result of urine backflow
- Vitamin deficiencies
- Increased risk of sexual dysfunction
- Possible rupture or internal leaking of the prosthetic bladder



Recommended Late Effects Screening for Bladder Surgery

- Yearly urology evaluation

Taking Charge!

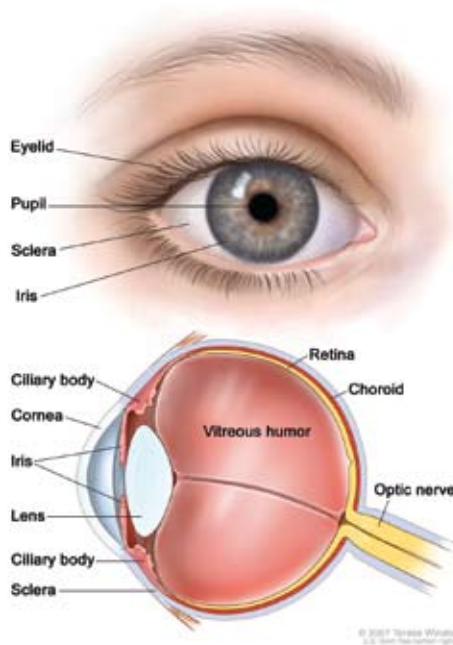
- ▶ Drink plenty of water to keep your kidneys healthy
- ▶ Become familiar with how to use a catheter and set up a regular schedule
- ▶ IMMEDIATELY notify the hospital if there are problems with self-catheterization or if vomiting or abdominal pain occurs
- ▶ Check with a healthcare provider first if using anti-inflammatory drugs such as aspirin or acetaminophen

For more information, please visit www.survivorshipguidelines.org and select “Cystectomy” or “Kidney Health”

Eye Surgery (Enucleation, Cryotherapy, Photocoagulation)

Vision is one of the most important senses, and so any surgery involving the eyes can have significant effects on daily life.

- In advanced cases of an eye cancer called retinoblastoma, one or both eyes may have to be surgically removed by a process called “**enucleation**.”
- For early stage retinoblastoma, cryotherapy or photocoagulation, combined with chemotherapy and/or radiation, are the treatments of choice
 - **Cryotherapy** – extreme cold applied by a small probe placed directly on the tumor
 - **Photocoagulation** – also called light coagulation; burns tissues with focused light from a laser directed at the tumor.



Possible Late Effects

- If only one eye is affected, poor balance and depth of field
- Incomplete growth of the eye socket
- Difficulties with proper prosthetic placement
- Repeated infections in and around the eye socket
- Self-consciousness about appearance

Recommended Late Effects Screening for Eye Surgery

- Yearly evaluation by an ophthalmologist (eye doctor) and ocularist (eye prosthesis specialist)

Taking Charge!

If only one eye is affected, it is vital to take good care of the healthy eye by:

- ▶ wearing UV protective sunglasses in bright sunlight
- ▶ wearing proper eye protection when playing certain sports or when working with dangerous equipment or chemicals
- ▶ avoiding fireworks and sharp/protruding toys and objects

For more information, please visit www.survivorshipguidelines.org and select “Eye Health”

Kidney Surgery (Nephrectomy)

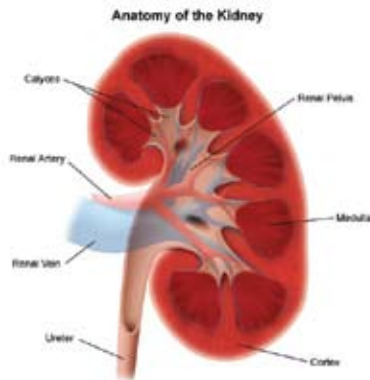
The kidneys are vital organs that are responsible for:

- Filtering out waste products from the blood and keeping it free of toxins
- Controlling blood pressure
- Stimulating red blood cell production

Treatment for some childhood cancers, such as Wilm's Tumor, sometimes requires partial or complete removal of one or both kidneys (nephrectomy). Although you can live a normal life with only one kidney, it is important that you take steps to protect your remaining kidney in order to keep it as healthy as possible.

Possible Late Effects:

- Kidney toxicity
- Excessive protein levels in urine
- Poor kidney function
- Fluid buildup around the testicles (males)



© Children's Hospital Boston

Recommended Late Effects Screening for Kidney Surgery

- Yearly urine analysis
- Yearly physical exam and blood pressure evaluation
- Kidney function tests (BUN, creatinine) must be checked at the beginning of follow up care and repeated as needed
- Yearly examination of testes for fluid build-up

Taking Charge!

- ▶ Drink plenty of water to keep your kidneys healthy
- ▶ Immediately contact the hospital if symptoms of urinary tract infection appear
- ▶ Notify healthcare provider if using any medicines like aspirin or acetaminophen
- ▶ Discuss playing contact sports with your healthcare provider first and always use a kidney guard
- ▶ Use other good safety practices, such as wearing a seatbelt

For more information, please visit www.survivorshipguidelines.org and select “Kidney Health”

Limb-Salvage Surgery and Rotationplasty

Limb-salvage surgery means removal of the entire diseased bone without damaging the surrounding nerves and blood vessels. The diseased bone is usually removed and replaced by a reconstructed, functional alternative, such as a metal implant or bone graft, from either the patient (autograft), a donor (allograft), or a metal/graft combination. Limb-salvage surgery is most frequently used for cancers of the soft tissue or bone.

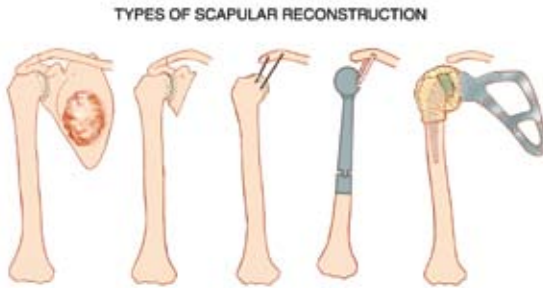
Rotationplasty is a procedure, usually used in younger children with bone tumors, such as osteosarcoma, that involve the knee joint. In this procedure, the affected thigh bone adjoining the knee is removed along with the knee joint, but the connection of the lower leg to the upper thigh is maintained. The lower portion of the leg is then rotated 180° and attached to the thigh bone. The ankle becomes the replacement for the removed knee, and an artificial limb is fitted over the foot and ankle. The benefit of rotationplasty is that it allows greater functional use of the limb in children who require removal of the knee.

Possible Late Effects

- Improper healing of donated bone (nonunion) in patients with bone grafts, which can later lead to increased risk of fractures
- Inconsistency in length of limbs due to damage to bone growth plate during surgery (limb-length discrepancy)
- Stiffening of muscles, tendons, and ligaments around the joint (contracture)
- Loosening or wearing out of the prosthetic
- Decreased physical activity, which can lead to weight gain, obesity, and diabetes
- Possible need for additional surgeries to adjust for growth

Specific Late Effects Screening for Limb Sparing Procedures

- Yearly history and physical exam for limb function and structure (repeat more frequently if clinically necessary)
- Yearly x-ray
- Evaluation by an orthopedic surgeon every six months until bones have fully matured, after which the patient should be evaluated yearly



Courtesy of Martin Malawer, MD, FACS

Taking Charge!

- ▶ Watch for pain, swelling, and infection at the site of surgery and report any fevers to a healthcare provider
- ▶ Use antibiotics before any kind of dental work or invasive medical treatment due to a higher risk of infection
- ▶ Get proper training by physical and occupational therapists
- ▶ Eat healthy and maintain an exercise plan that involves both passive and active movement
- ▶ Carry a medical letter if you have metal implants to help in situations with metal detectors or security checkpoints

For more information, please visit www.survivorshipguidelines.org and select "Limb Sparing Procedures"

Lung Surgery

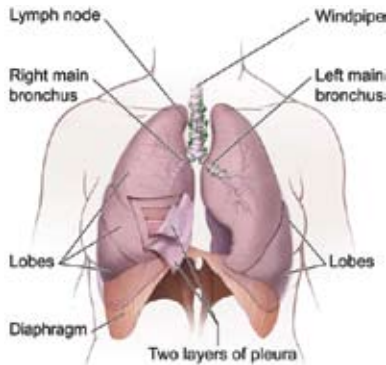
The lungs are one of the most important organs in the human body and are essential for breathing. Respiration is achieved by regulation of gas exchange within the body via the lungs; ensuring that oxygen is transported into the bloodstream, while carbon dioxide is exhaled out into the atmosphere.

Lung surgery may involve:

- **Lobectomy** – removal of a lobe
- **Wedge Resection** – removal of a small area of a lobe
- **Metastatectomy** – removal of tumor deposits in the lung tissue
- **Thoracotomy** – removal of tumor from the lung by opening the chest cavity

Childhood cancers that need removal of a portion or lobe of the lung include:

- Osteosarcoma
- Ewing's sarcoma
- Other solid tumors that have spread to the lung
- Fungal infection in the lung not responding to medical treatment



Possible Late Effects:

- Recurrent lung infections
- Pneumonia
- Inflammation of the lung
- Shortness of breath and fatigue

Recommended Late Effects Screening for Lung Surgery

- Yearly patient history and physical exam including lung exam
- Chest x-ray at initial long-term follow-up, and then as clinically needed
- Pulmonary function tests are needed at initial long-term follow-up, and then only as needed for abnormality or worsening lung function
- Yearly flu (influenza) vaccine
- Pneumonia (pneumococcal) vaccine

Taking Charge!

- ▶ **DO NOT SMOKE!!!**
- ▶ Avoid second-hand smoke
- ▶ Exercise regularly to help develop strong, healthy lungs
- ▶ Have a medical evaluation and be checked by a diving specialist before scuba diving
- ▶ Avoid inhaling toxic fumes, chemicals, paint, etc.

For more information, please visit www.survivorshipguidelines.org and select "Pulmonary Health"

Neurosurgery (Brain and Spinal Cord)

Brain surgery can sometimes result in side effects that affect a patient's daily life. If the surgery involves a vital function area, the patient's educational abilities, behavior, and physical movement may be affected. The treatment for most brain tumors is surgery.

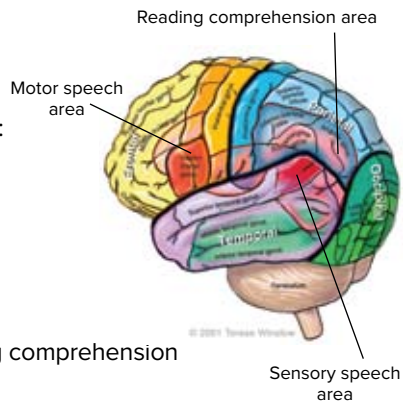
Spinal cord surgery is performed for the treatment of spinal tumors or cancer that has spread to the spine from a different site. Emergency spinal cord surgery is needed when there is risk of impending paralysis from a tumor pressing on the spinal cord. Resulting damage to the nerves may result in inability to pass urine or stool properly or affect sexual function.

A shunt, a device used to drain fluid from the brain, may be needed in both brain and spinal cord surgeries.

Brain Surgery

Possible Late Effects:

- Educational difficulties, such as:
 - shortened attention span
 - slower processing speed
 - affected memory
 - problems in organizing and planning
 - difficulties in math and reading comprehension
- Movement changes, such as:
 - paralysis
 - improper motor function
 - poor coordination of muscle movements (Ataxia)
 - eye complications
- Changes in behavior
- Seizures
- Fluid buildup in the brain
- Shunt malfunction



Recommended Late Effects Screening for Neurosurgery (Brain)

- Yearly history and physical exam to evaluate educational and neuropsychological progress
- Yearly evaluation by a physical/rehabilitation therapist
- Yearly evaluation by a neurologist until three years post-surgery, except for patients having seizures—patients with seizures should be evaluated every six months
- For patients with shunts:
 - Yearly evaluation by neurosurgeon
 - Abdominal x-ray after pubertal growth spurt

Taking Charge!

- ▶ Be proactive in school by:
 - sitting in the front of the classroom
 - modifying testing requirements, such as getting extra time or oral exams
 - getting extra help and tutoring
 - having a teacher's aide assigned
 - making a personalized educational plan with your teachers suited to your needs
- ▶ Familiarize yourself with the laws in place to protect your rights to fair education and employment
- ▶ Eat healthy and maintain an exercise plan

For more information, please visit www.survivorshipguidelines.org and select "Educational Issues"

Spinal Cord Surgery

Possible Late Effects:

- Bladder dysfunction
- Loss of bladder control (urinary incontinence)
- Bowel dysfunction
- Loss of control over the bowels (fecal incontinence)
- Boys
 - sexual dysfunction
 - erection problems
- Girls
 - sexual dysfunction



Recommended Late Effects Screening for Neurosurgery (Spinal Cord)

- Yearly history and physical exam to evaluate gastrointestinal history and sexual function
- Rectal exam as clinically needed
- For patients with shunts:
 - Yearly evaluation by neurosurgeon
 - Abdominal x-ray after pubertal growth spurt

Taking Charge!

- ▶ Set up a regular schedule if taking medications for bladder control
- ▶ Familiarize yourself with proper catheterization technique, if required

For more information, please visit www.survivorshipguidelines.org and select "Neurogenic Bladder" or "Male Health Issues"

Ovarian Surgery (Oophorectomy)

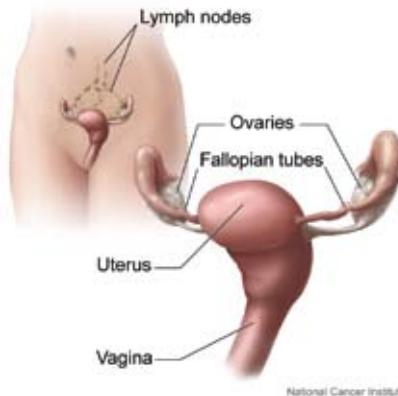
The ovaries are a vital component of the female reproductive system. They are responsible for creating the female hormone, estrogen, which is needed to promote proper physical and sexual growth. Ovaries also contain a girl's limited supply of eggs which are required for fertility.

Late effects of surgery depend heavily on the girl's age at time of treatment and whether one ovary (unilateral oophorectomy) was removed or both (bilateral oophorectomy).

This surgical procedure is performed for certain germ cell tumors.

Possible Late Effects:

- Estrogen deficiency (permanent if both ovaries removed), which can lead to:
 - incomplete or delayed puberty in young girls
 - poor muscle development, weak bones, or heart complications, unless treated with prescribed hormones
- Ovarian failure resulting in stopped egg and hormone production (permanent if both ovaries removed)
- Infertility (permanent if both ovaries are removed)
- Temporary pause of menstruation or premature menopause (permanent if both ovaries removed)



Recommended Late Effects Screening for Ovarian Surgery

- Yearly history and physical exam to document sexual growth (Tanner staging until puberty), function, menstruation, and fertility
- Hormone blood work (estradiol/FSH/LH) starting at 10–12 years of age, and then yearly until puberty is complete
- Girls with both ovaries removed or ovarian failure are at a higher risk for osteoporosis and need to have a bone density test performed as recommended
- Girls with both ovaries removed should meet with a gynecologist or endocrinologist at age 11 to begin hormone replacement therapy

Taking Charge!

- ▶ Talk to your doctor about getting prescribed hormones if estrogen deficiency occurs
- ▶ Consult a healthcare provider about possible fertility options such as donor eggs, adoption, and child-free living
- ▶ Discuss with a gynecologist the possibility of early menopause if only one ovary was removed and consider earlier childbearing, if desired. If children are not desired, continue to use birth control even if menstruation has stopped.
- ▶ Speak with an oncologist about the possible rare genetic risk of passing down your cancer

For more information, please visit www.survivorshipguidelines.org and select “Female Health Issues”

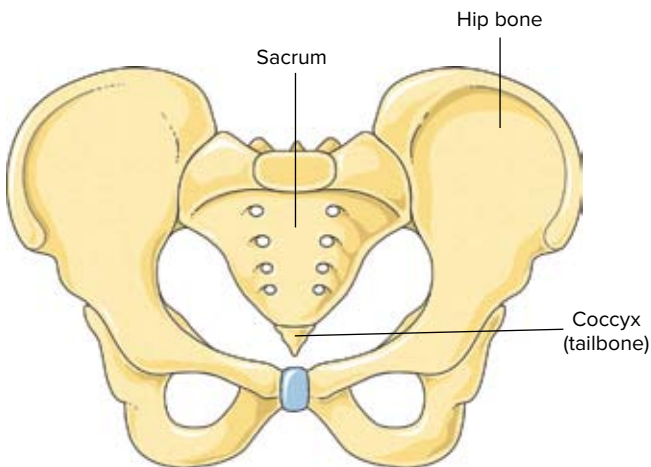
Pelvic Surgery

The pelvis is the bony support structure for the lower part of the body and is located at the lower end of the spine. Pelvic surgery involves the structures that lie within the pelvis, such as the rectum, urinary tract, and reproductive organs.

Soft tissue sarcomas, rectal cancer, or cervical cancer sometimes require pelvic surgery.

Possible Late Effects:

- Loss of bladder control (urinary incontinence)
- Blockage of the urinary tract (urinary tract obstruction)
- Loss of control over the bowels (fecal incontinence)
- Boys:
 - sexual dysfunction
 - complications with erection and ejaculation
 - swelling of the scrotum (hydrocele)
 - slow bloodflow from the scrotum into the pelvis causing swelling in the groin area
- Girls:
 - sexual dysfunction



Recommended Late Effects Screening for Pelvic Surgery

- Yearly history to analyze urinary function, bowel movements, and bathroom habits
- Rectal exam should be performed as clinically indicated
- Boys:
 - Yearly testicular exam to look for swelling
 - Yearly history regarding sexual function and proper ejaculation
- Girls:
 - Yearly history regarding sexual function

Taking Charge!

- ▶ It is important to drink plenty of water to keep your kidneys healthy
- ▶ Eat proper amounts of fiber to help with digestion and use laxatives as needed
- ▶ Be observant of symptoms of urinary tract infection and immediately contact the hospital if symptoms appear
- ▶ Use the bathroom regularly and create and follow a schedule to maintain healthy bathroom use

For more information, please visit www.survivorshipguidelines.org and select "Male Health Issues"

Spleen Surgery (Splenectomy)

The spleen is an organ located in the abdomen that boosts the immune system and helps in filtering bacteria from the blood. Since the spleen is responsible for producing antibodies, it is an important organ in fighting infections.

Splenectomy, or removal of the spleen, used to be an important part of treatment for lymphomas many years ago. It is rarely performed these days.

Possible Late Effects:

- Impaired immune function
- Increased risk of life-threatening infection, especially by encapsulated bacteria. Some common illnesses to be watchful for are:
 - Pneumonia
 - Influenza
 - Meningitis

Recommended Late Effects Screening for Spleen Surgery

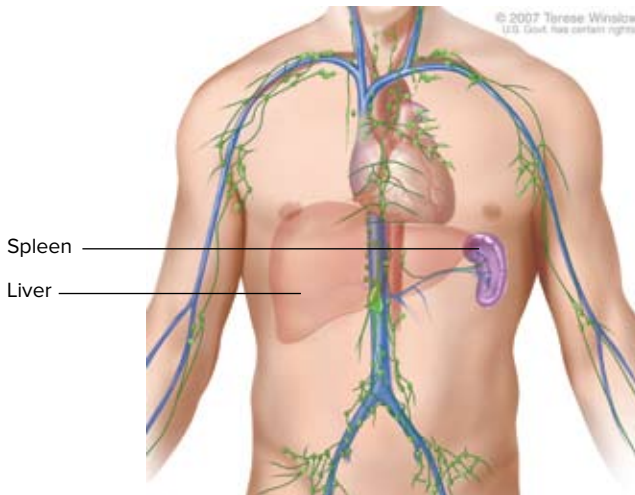
If patient has a temperature $\geq 101^{\circ}\text{F}$, then:

- Evaluate with blood work (blood culture and CBC) immediately
- Perform a physical exam
- Administer appropriate antibiotics

Taking Charge!

- ▶ Seek medical advice to determine if daily use of antibiotics, such as penicillin, is needed
- ▶ Vaccines are an important preventative measure. The following vaccines are recommended:
 - Pneumococcal
 - Meningococcal
 - Haemophilus Influenzae Type B (HIB)
- ▶ Wearing a medical alert bracelet or carrying a wallet card describing past spleen surgery may be helpful to healthcare providers in times of emergency

For more information, please visit www.survivorshipguidelines.org and select "Splenic Precautions"



Testicular Surgery (Orchiectomy)

The testicles are a vital component of the male reproductive system, as they are responsible for producing the male hormone, testosterone, as well as sperm. Sperm is required for fertility, while the testosterone hormone is needed to promote proper physical and sexual growth.

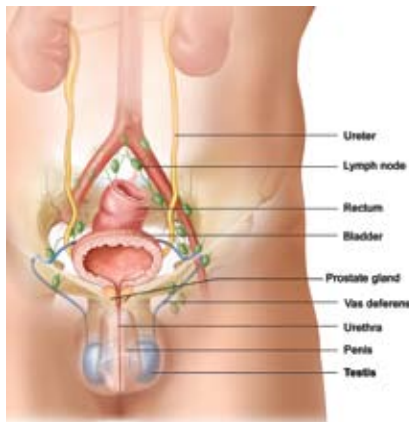
The late effects of surgery depend heavily on the boy's age at time of treatment and whether one testicle (unilateral orchiectomy) was removed or both (bilateral orchiectomy).

An orchiectomy is usually performed for cancers involving the testes.

Possible Late Effects:

- Infertility* (permanent if both testicles removed)
- Testosterone deficiency* (permanent if both testicles removed), which can lead to:
 - incomplete or delayed puberty in young boys
 - poor muscle development, weak bones, or decreased sex drive and erections in boys past puberty, unless treated with prescribed hormones

*Infertility and testosterone deficiency are usually not affected in patients with one testicle removed, unless also treated with radiation and chemotherapy



Recommended Late Effects Screening for Testicular Surgery

- Yearly history to analyze sexual growth and function
- Yearly physical exam to monitor Tanner Staging until puberty
- Yearly monitoring of testicular volume by Prader orchidometer until puberty
- Hormone blood work (testosterone/FSH/LH) is needed starting at 11 or 12 years of age, and then yearly until puberty is complete (if both testicles removed)
- Hormone blood work should be performed as clinically suggested in patients with only one testicle removed
- Sperm analysis (optional)

Taking Charge!

- ▶ Talk to your doctor about getting prescribed hormones if testosterone deficiency occurs
- ▶ Consult a healthcare provider about fertility options such as freezing active sperm, surgical harvesting, and donor sperm
- ▶ Consider getting a testicular prosthesis
- ▶ Protect remaining testicle (if only one was removed) with protective athletic supporter and cup when taking part in certain sports and activities

For more information, please visit www.survivorshipguidelines.org and select “Male Health Issues”

Thyroid Surgery (Thyroidectomy)

The thyroid gland, located in the lower neck, is an important part of the endocrine system. The endocrine system is a group of glands and organs in the body responsible for regulating various body processes, from growth and puberty to the production of bodily waste.

The thyroid gland is specifically responsible for releasing hormones that control growth and mental development, as well as the body's metabolism and energy levels. The hormone produced by the thyroid gland, thyroxine, is under the control of TSH, another hormone produced by the pituitary gland in the brain.

Thyroidectomy is removal of the thyroid gland. It is done for thyroid cancer and may be partial or complete.

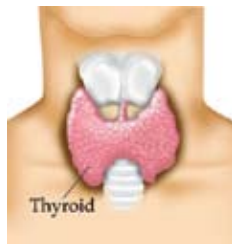
Possible Late Effects:

Primary Hypothyroidism—when part or all of the thyroid is surgically removed, the thyroid hormones needed for maintaining metabolism and energy levels greatly decrease, resulting in effects such as:

- overworking of the pituitary and high secretion of TSH to counter missing thyroid hormones
- fatigue
- changes in mood and emotion
- change in voice
- short attention span
- weakness and body aches
- sensitivity to cold
- slowed growth
- low blood pressure
- weight gain
- dry skin and brittle hair
- risk of hypoparathyroidism (low calcium levels)

Recommended Late Effects Screening for Thyroid Surgery

- Yearly patient history and physical exam, including thyroid exam (more frequently during times of significant growth)
- Yearly TSH and thyroid hormone screening (more frequently during times of significant growth)



Taking Charge!

- ▶ Take the prescribed thyroid pills and closely follow the schedule outlined by your healthcare provider
- ▶ Females considering pregnancy should have their thyroid hormone levels checked.

For more information, please visit www.survivorshipguidelines.org and select "Thyroid Problems"

Recommended Follow-up after Surgery

If Treatment Included	Recommended Follow-Up Testing
Abdominal Surgery	<ul style="list-style-type: none"> ▲ Serum electrolytes and magnesium every year
Adrenal Gland Removal	<ul style="list-style-type: none"> ▲ Symptoms of adrenal insufficiency
Amputation	<ul style="list-style-type: none"> ▲ Examination with attention to range of motion and muscle contractures ▲ Prosthesis check every year, more often during growth spurts ▲ Antibiotics prior to dental work if an allograft
Cryotherapy and Photocoagulation	<ul style="list-style-type: none"> ▲ Complete eye examination every year
Cystectomy	<ul style="list-style-type: none"> ▲ Annual urology evaluation
Enucleation (removal of the eye)	<ul style="list-style-type: none"> ▲ Socket examination each year
Laparotomy	<ul style="list-style-type: none"> ▲ Gastrointestinal and nutrition status evaluation
Limb Salvage	<ul style="list-style-type: none"> ▲ Bone x-ray every 3 years, or as recommended by an orthopedic surgeon, or if symptoms arise ▲ Counseling on exercise restrictions
Lung Surgery	<ul style="list-style-type: none"> ▲ Annual patient history and physical exam including lung exam ▲ Chest x-ray at initial long-term follow-up, and then as clinically needed ▲ Pulmonary function tests are needed at initial long-term follow-up, and then only as needed for abnormality or worsening lung function ▲ Annual flu vaccine ▲ Pneumonia vaccine

Recommended Follow-up after Surgery (cont.)

If Treatment Included	Recommended Follow-Up Testing
Nephrectomy (removal of kidney)	<ul style="list-style-type: none"> ▲ Urinalysis (check for blood, protein, sugar) ▲ Blood tests: BUN, Cr, Ca, Mg, PO₄—baseline and every year for 5 years ▲ Creatinine clearance—baseline and at 5 years ▲ Counseling about kidney protection
Neurosurgery (Brain)	<ul style="list-style-type: none"> ▲ Annual history and physical exam to evaluate educational and neuropsychological progress ▲ Annual evaluation by a physical/rehabilitation therapist ▲ Annual evaluation by a neurologist until three years post-surgery, except for patients having seizures patients with seizures should be evaluated every six months ▲ Patients with shunts should have an annual neurosurgeon evaluation and an abdominal x-ray after pubertal growth spurt
Neurosurgery (Spinal Cord)	<ul style="list-style-type: none"> ▲ Annual history and physical exam to evaluate gastrointestinal history and sexual function ▲ Rectal exam as clinically needed ▲ Patients with shunts should have an annual neurosurgeon evaluation and an abdominal x-ray after pubertal growth spurt
Oophorectomy	<ul style="list-style-type: none"> ▲ Annual history and physical exam to document sexual growth (Tanner staging until puberty), function, menstruation, and fertility ▲ Hormone blood work (estradiol/FSH/LH) starting at 10 -12 years of age, and then yearly until puberty is complete ▲ Girls with both ovaries removed need to have a bone density test performed as recommended ▲ Girls with both ovaries removed should meet with a gynecologist or endocrinologist at age 11 to begin hormone replacement therapy

Recommended Follow-up after Surgery (cont.)

If Treatment Included	Recommended Follow-Up Testing
Orchiectomy	<ul style="list-style-type: none"> ▶ Annual history to analyze sexual growth and function ▶ Annual physical exam to monitor Tanner Staging until puberty ▶ Annual monitoring of testicular volume by Prader orchidometer until puberty ▶ Hormone blood work (testosterone/FSH/LH) is needed starting at 11 or 12 years of age, and then yearly
Pelvic Surgery	<ul style="list-style-type: none"> ▶ Annual history to analyze urinary function, bowel movements, and bathroom habits ▶ Rectal exam should be performed as clinically indicated ▶ Annual patient history regarding sexual function ▶ Annual testicular exam for boys
Splenectomy	<ul style="list-style-type: none"> ▶ Penicillin daily (erythromycin if allergic to penicillin) ▶ Antibiotics prior to dental work ▶ Pneumovax (recommendations on frequency vary) ▶ Annual influenza vaccine ▶ Fever above 100.4°F requires evaluation for infection by a doctor
Thyroidectomy	<ul style="list-style-type: none"> ▶ Annual patient history and physical exam, including thyroid exam (more frequently during times of significant growth) ▶ Annual TSH and thyroid hormone screening (more frequently during times of significant growth)

Source: 'Childhood Cancer Survivors: A Practical Guide to Your Future.' Patient-Centered Guides, 2006. Adapted with permission.

BONE MARROW/STEM CELL TRANSPLANTATION

and Related Late Effects

Bone Marrow/Stem Cell Transplantation and Related Late Effects

BONE MARROW/STEM CELL TRANSPLANTATION (BMT/SCT) is a special procedure for patients with cancer or other diseases which affect the bone marrow. It involves taking cells that are normally found in the bone marrow (stem cells); filtering those cells; and giving them back to either the patient they were taken from or to another person. The goal of BMT/SCT is to transfuse healthy bone marrow cells into a person after their own unhealthy bone marrow has been eliminated.

Bone marrow/stem cell transplantation can be used to treat:

- Different types of cancers e.g. leukemia, lymphoma
- Inherited blood diseases
- Inherited metabolic diseases
- Inherited immune deficiencies

What is Bone Marrow?

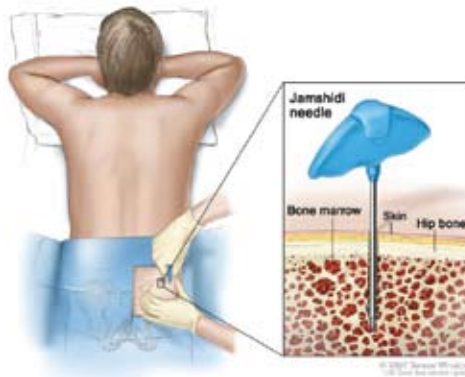
Bone marrow is the soft, fatty tissue inside the bones where blood cells (red blood cells, platelets, and white blood cells) are produced. Marrow can be either red or yellow. At birth, we all have red marrow, which produces the blood cells. Red marrow is gradually converted to yellow marrow with age. Red marrow is usually found in the flat bones such as the ribs, breastbone, vertebrae, hip bone, skull, and upper ends of the femur and humerus. For a BMT, marrow is usually taken from the hip bone. This is called 'bone marrow collection' or 'harvesting'.

How does a Bone Marrow/Stem Cell Transplant Work?

Concept

The concept of BMT/SCT is to use high-dose chemotherapy with or without radiation therapy to kill the rapidly dividing cancer cells. After the diseased cells are destroyed, the previously collected donor stem cells are transplanted to replace those cells that were destroyed.

The new cells travel into the patient's bloodstream and into the bone marrow and begin making new blood cells.



Procedure for Bone Marrow Collection

Procedure

The transplant procedure is simple and involves infusing the donor marrow through an intravenous catheter, just like a blood transfusion. The new marrow cells travel through the blood vessels and fill the empty spaces in the long bones.

Engraftment occurs when the new marrow begins producing healthy blood cells, which typically occurs two to six weeks after transplantation.

Types of Transplants

Autologous

Stem cells are collected from the blood or bone marrow of the patient prior to high-dose therapy and are stored until time of transplant. The patient is then treated with high-dose chemotherapy and total body irradiation to destroy the cancer cells, and the stem cells are then returned back into the patient.

Allogeneic

This type of transplant requires two people: the donor and the recipient (the patient). Donated bone marrow must match the patient's tissue type. Allogeneic transplant donors may be related (usually a brother or a sister), or unrelated with a very close tissue match (found through the national marrow donor program). Donors are matched through special blood tests called HLA tissue typing.

Syngeneic

The donor is the patient's identical twin. Many late effects are avoided because the marrow is an identical tissue match.

Peripheral Blood Stem Cell Transplant

In this type of transplant, the patient's or a donor's stem cells (young cells) are harvested in a procedure called apheresis. Blood is removed through an intravenous catheter in the arm and is circulated through a machine which takes out the stem cells. The remaining blood is returned to the patient and the stem cells are frozen until needed.

Umbilical Cord Blood Transplant

Umbilical cord blood, a rich source of stem cells, is collected from the umbilical cord and placenta after a baby is born. The cord blood is obtained either during the birth of a sibling of the patient, or from preserved unrelated donor cord blood. The cord blood is tested, frozen, and stored at a cord blood bank for future use.

Possible Late Effects

As improvements have continued in BMT/SCT technology, a larger numbers of childhood cancer survivors remain free of the disease for which they were transplanted.

However, there are complications that can cause long term problems. Certain groups of children, adolescents, and young adults are more at risk for side effects than others.

The risk of developing late effects depends on:

- Total dosage of individual chemotherapy drugs
- Combinations of particular chemotherapy drugs
- Location and type of radiation therapy
- Age at diagnosis
- Type of tumor

Effects from Chemotherapy

Prior to transplant, high dose chemotherapy is given to destroy cancer cells. This part of the treatment is called ‘conditioning’. The drugs given vary from protocol to protocol, and depend on the disease and patient history. Chemotherapy is usually given over a course of two to six days.

Chemotherapy agents most commonly used are:

- Cyclophosphamide (Cytosan)
- Busulfan (Myleran)
- VP16 (Etoposide)
- Ara-C (Cytarabine)

To learn about specific screening guidelines for chemotherapy drugs, please see the section ‘Chemotherapy and Related Late Effects.’

Effects from Total Body Irradiation (TBI)

Total body irradiation given prior to a BMT/SCT can cause multiple problems. They are as follows:

- Neurocognitive effects (Learning disabilities)
- Dental problems
- Growth delay or decreased growth
- Low thyroid function
- Cataracts
- Lung problems
- Kidney problems
- Delayed puberty development
- Liver problems
- Second malignancy
- Fertility problems or infertility

To learn about specific screening guidelines for organs affected by radiation, please see the section 'Radiation Therapy and Related Late Effects.'

Effects from TBI and Cyclophosphamide

- Survivors who received TBI may experience delayed puberty. They are also at risk for infertility, which may not become evident until they try to become pregnant or father a child
- If they received TBI and cyclophosphamide together, infertility is very likely to occur
- Survivors, who received cyclophosphamide alone with no radiation, may remain fertile depending on factors such as age at treatment and dose of drug received
- All survivors who received TBI should be followed closely by an endocrinologist who can prescribe hormones to assist in normal puberty development

Graft Versus Host Disease

A complication known as graft-versus-host disease (GVHD) sometimes develops with allogeneic transplants.

GVHD occurs when white blood cells from the donor (the graft) identify cells in the patient's body (the host) as foreign, and attack them. The severity of GVHD is increased for those patients who received unrelated or mismatched donors.

GVHD can be acute and/or chronic, and patients can develop neither, one, or both.

- Acute GVHD usually occurs at the time of engraftment or shortly after
- Chronic GVHD can occur anytime during or after the third month post-transplant, and may last for months or years

The most commonly damaged organs by both acute and chronic GVHD are the:

- skin (rash, discoloration, tightening of the skin, hair loss)
- liver (jaundice, abnormal liver function tests)
- intestines (diarrhea, cramping, weight loss)

Other organs also at risk for damage by chronic GVHD are:

- eyes (dry, light sensitive)
- mouth and esophagus (dry mouth, tooth decay, difficulty swallowing)
- lungs (shortness of breath, wheezing, coughing)
- joints (decreased mobility)

Survivors with chronic GVHD can develop one, a few, or many of these problems.

If GVHD develops, it can be serious. To prevent this complication, the patient may receive medications that suppress the immune system. These drugs include:

- cyclosporine
- steroids (prednisone or dexamethasone)
- methotrexate
- tacrolimus (FK506)

Additionally, the donated stem cells can be treated to remove the white blood cells that cause GVHD in a process called “T-cell depletion.”

Clinical trials are being conducted to find better ways to prevent and treat GVHD.

SUGGESTED EVALUATION

for Selected Late Effects

A Guide for Your Primary Health Care Provider

Suggested Evaluation for Selected Late Effects

Late Effect	Screening Test	Recommendations if Screening is Abnormal
Short Stature	Growth curve Sitting height Parental heights	Bone age, growth hormone tests Thyroid function tests Endocrinologist consultations
Obesity or Weight Loss	Growth curve Diet history	Thyroid function tests Nutritionist, endocrinologist consultation
Scoliosis	Physical examination	Spine radiography; evaluate again during adolescent growth spurt Orthopedist consultation
Bone Asymmetries (hypoplasia, atrophy)	Bone lengths, circumference	Orthopedist consultation; bone radiography; plastic surgeon consultation
Avascular Necrosis or Osteoporosis	History of pain, fractures Bone radiography	Bone scan Serum estradiol level ; Ca, P Orthopedist consultation; physical therapist consultation
Soft Tissue Hypoplasia, Contractures, Edema	Physical examination	Plastic surgeon consultation
Dental Abnormalities	Physical examination	Dentist, oral surgeon consultation
Learning Disabilities	Communication with school, family; psychological testing	CT or MRI scan of head; special education classes
Leukoencephalopathy	CT or MRI (See also Learning Disabilities)	Cerebrospinal fluid basic myelin protein; neurologist consultation
Neuropathy	Physical examination	Neurologist consultation
Hearing Loss	Audiogram	Otolaryngologist consultation; audiologist consultation

Infertility	History (primary versus secondary dysfunction) Gonadal function testing Thyroid function testing	Endocrinologist consultation Obstetrician or gynecologist consultation Endocrinologist consultation
Thyroid Dysfunction	Thyroid function testing	Endocrinologist consultation
Cardiomyopathy or Pericarditis	Electrocardiogram; echocardiogram; radionuclide angiography	Cardiologist consultation
Vasooclusive Disease	Angiography; Doppler pulses	Vascular surgeon
Pneumonitis or Pulmonary Fibrosis	Chest radiography Pulmonary function test	Lung biopsy Pulmonologist consultation
Chronic Enteritis	Growth curves Nutritional assessment	Serum folate, carotene Small-bowel studies; barium enema; gastroenterologist consultation
Hepatitis or Cirrhosis	Liver function tests	Liver biopsy, hepatitis screen; liver scan; gastroenterologist consultation
Nephritis, Rickets (Tubular Defects)	Urinalysis; BUN, creatinine, serum electrolytes, CO ₂ , Ca, P, alkaline phosphatase, wrist radiographs	24-h creatinine clearance or glomerular filtration rate; intravenous urogram or sonogram; nephrologist consultation
Hemorrhagic Cystitis	Urinalysis	Cytoscopy; urologist consultation
Thrombotic Thrombocytopenic Purpura	CBC/platelets, BUN, creatinine; peripheral blood smear	
Sepsis	Compliance with prophylactic antibiotics	
Second Malignancy	Studies on an individual basis	

Source: "Childhood Cancer Survivorship: Improving Care and Quality of Life." Institute of Medicine. Adapted with permission.