CureSearch
Children's Oncology Group

Long-Term Follow-Up Guidelines
for Survivors of Childhood, Adolescent, and Young Adult Cancers

Version 1.2 – March 2004

Appendix

CureSearch Children's Oncology Group

Health Links

Healthy living after treatment for childhood cancer

APPENDIX

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Avascular Necrosis (AVN)

What is Avascular Necrosis?

Avascular necrosis (AVN) is a disorder resulting from a temporary or permanent loss of blood supply to the bone. Blood carries essential nutrients and oxygen to the bones. When the blood supply is disrupted (avascular), the bone tissues begin to break down (necrosis). This can weaken the bone and eventually result in its collapse. If this occurs near a joint, it can lead to the collapse of the joint surface, resulting in pain and inflammation (arthritis). AVN is also referred to as osteonecrosis, aseptic necrosis, and ischemic bone necrosis.

AVN can occur in any bone, but most commonly affects the ends (epiphysis) of long bones such as the thigh bone (femur), causing hip and knee problems. Other common sites include the bones of the upper arms, shoulders, and ankles. AVN can occur in a single bone, but more commonly occurs in several bones at one time (multifocal AVN).

AVN can sometimes be disabling, depending on what part of the bone is affected, how large an area is involved, and how well the bone rebuilds itself. Normal bone continuously breaks down and rebuilds itself. This process keeps the bones strong. AVN is the result of bone tissues breaking down faster than the body can repair them. If the disorder progresses, it can lead to pain and arthritis.

What causes AVN?

AVN is caused by interruption of the blood supply to the bone. If blood vessels are blocked with fat, become too thick or too small, or get too weak, they may not be able to provide the amount of blood necessary for the bone tissue to survive.

Corticosteroids (such as prednisone and dexamethasone) given during cancer treatment can affect the bone and blood vessels, resulting in AVN. Other factors that increase the risk of AVN in people who received corticosteroid therapy include treatment with high doses of radiation to weight bearing bones, treatment with orthovoltage radiation (commonly used before 1970), being older than 10 at the time of treatment, and having sickle cell disease. AVN is most likely to occur during cancer treatment, but it can sometimes happen after completion of cancer therapy.

Steroids and AVN

Corticosteroids (such as prednisone and dexamethasone) are commonly used for treatment of many cancers, such as leukemia and lymphoma. Dexamethasone is also sometimes used for treatment of nausea and vomiting associated with chemotherapy and to control brain swelling. There is no clear explanation as to how corticosteroids cause AVN, but it is believed that they may interfere with the body's ability to break down fatty substances. These substances can clog the blood vessels, causing them to narrow. This reduces the amount of blood that gets into the bone.

What are the symptoms of AVN?

People in the early stages of AVN may not have any symptoms. However, as the disorder progresses, most people will experience some joint pain. At first, the person may only experience pain when bearing weight on the affected bone or joint. As the disorder progresses, symptoms may be present even at rest. Pain may develop gradually and its intensity can range from mild to severe.

If AVN progresses and the bone and surrounding joint surfaces collapse, the pain can increase considerably and may become severe enough to limit movement in the affected joint. The period of time between the first symptoms of AVN and the loss of joint function is different for each person and ranges from several months to years.

How is AVN diagnosed?

An **x-ray** is usually the first test to be done when AVN is suspected. It can help distinguish AVN from other causes of bone pain, such as fracture. In the early stages of AVN, an x-ray may appear normal, so other tests may need to be done to establish the diagnosis. Once the diagnosis has been made, and in the later stages of AVN, x-rays are useful in monitoring the course of the condition. **MRI** is one of the most useful tools in diagnosing AVN because it can detect AVN in the earliest stages, when symptoms are not yet present. **Bone scans** are sometimes used to diagnose AVN. They are useful because one scan can show all the areas in the body affected by AVN. However, bone scans do not detect AVN at the earliest stages. A **CT scan** provides a three-dimensional image of the bone and can be useful in determining the extent of bone damage. **Surgical procedures** such as a bone biopsy can conclusively diagnose AVN, but are not commonly done.

How is AVN treated?

The goals of treatment for AVN are to improve the person’s use of the affected joint, reduce pain, stop bone damage, and ensure joint survival. Treatment can be categorized as conservative or surgical. In order to determine the most appropriate treatment, the following factors are taken into consideration:

- The person’s age
- The stage of the disorder (early or late)
- The location and the amount of bone affected (small or large)
- The status of cancer and cancer treatment

Conservative treatment

- **Medication** - to reduce pain
- **Reduced weight bearing -** to slow the damage and promote natural healing. Crutches may be recommended to limit weight or pressure on the affected joint.
- **Range of motion exercises** – to keep the joints flexible. This is also important to maintain movement and increase circulation in the joints. This can promote healing and may relieve pain. Physical therapists can teach the correct exercises.
- **Electrical stimulation** - to induce bone growth

Conservative treatments may be used alone or in combination, but they may not provide lasting improvement. Some people may require surgery to permanently repair or replace the joint.

Surgical Treatment

- **Core decompression** – is a surgery that removes the inner layer of bone. This may reduce pressure within the bone and create an open area for new blood vessels to grow. Sometimes a piece of healthy bone with good blood vessels (bone graft) is put in this area to speed up the process. This procedure works best in the early stages of AVN and should help relieve pain and promote healing.
- **Osteotomy** – is a surgery that involves taking out a piece of bone, usually a wedge, to reposition the bone so that the tissue lacking blood supply (avascular area) bears less weight than an adjacent healthy area.
- **Arthroplasty** – is also referred to as joint replacement. The affected bone is removed and replaced with an artificial joint. This treatment may be needed in the late stages of AVN and when a joint is destroyed.

Health Promoting Behaviors/Interventions

- Avoid activities that put a lot of stress on your joints. Activities that stress the joints include running, jumping, football, soccer, volleyball, basketball and similar sports. Activities that are good for joints with AVN are swimming and bicycling.
- Be consistent with recommended exercises.
- Rest joints when they hurt.
- Let your healthcare provider or physical therapist know if there are any changes in your symptoms.
- Take pain or anti-inflammatory medications as prescribed.

Resources:

- **National Institute of Arthritis and Musculoskeletal and Skin Diseases**
  National Institutes of Health, 1 AMS Circle, Bethesda, MD 20892-3675
  Phone: 301-495-4484 or 877-226-4267 (toll free), TTY: 301-565-2966
  Fax: 301-718-6366. Web: www.niams.nih.gov
- **American Academy of Orthopaedic Surgeons**
  P.O. Box 2058, Des Plaines, IL 60017
  Phone: 800-824-2663 (toll free). Web: www.aaos.org

Adapted by Katherine Myint-Hpu, PNP, from "Health Topics: Questions and Answers about Avascular Necrosis" by the National Institute of Arthritis and Musculoskeletal and Skin Diseases, January 2001, used with permission; and "Avascular Necrosis – Do You Know" by St. Jude Children's Research Hospital, used with permission.

Katherine Myint-Hpu, MSN, MPH, PNP is a pediatric nurse practitioner and coordinates the Leukemia/Lymphoma Clinic at Georgetown University Hospital, Washington, D.C.

Reviewed by Neyssa Marina MD, Joan Darling PhD, Melissa Hudson MD and Smita Bhatia MD, MPH.

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Bleomycin Alert

The lungs are very important organs that are responsible for supplying oxygen to the body and ridding it of carbon dioxide. Sometimes, treatments given for childhood cancer can cause lung damage. Because you received bleomycin during treatment for childhood cancer, it is important for you to learn about certain lung problems that can sometimes happen after treatment with bleomycin. We also suggest that you read the *"Pulmonary Health" Health Link,* which contains more information about your lungs and how to keep them healthy.

What are the problems that can happen after treatment with bleomycin?

People who received bleomycin during treatment for childhood cancer can sometimes develop lung problems many years after their treatment has been completed. These problems may include:

- Lung inflammation (interstitial pneumonitis)
- Lung scarring (pulmonary fibrosis)
- Breathing problems associated with high levels of oxygen and/or intravenous fluids (acute respiratory distress syndrome)

What is interstitial pneumonitis?

Interstitial pneumonitis is inflammation of the thin layer of tissue between the air sacs (alveoli) in the lungs. This inflammation can worsen if a person develops lung infections, such as pneumonia. Interstitial pneumonitis that occurs as a result of therapy with bleomycin sometimes develops after exposure to toxic fumes, tobacco, or high levels of oxygen given over several hours.

What is pulmonary fibrosis?

Pulmonary fibrosis is the formation of scar tissue in the small air sacs (alveoli) of the lungs. This scarring makes the lungs stiffer and affects the exchange of oxygen and carbon dioxide in the alveoli. Pulmonary fibrosis may worsen over time and can sometimes lead to early heart failure.

What is acute respiratory distress syndrome (ARDS)?

ARDS is a serious condition that occurs when alveoli in the lungs are damaged and can no longer provide oxygen to the body. People who received bleomycin in the past may be at risk for developing ARDS, usually as a result of a combination of high levels of oxygen and large amounts of intravenous fluid given during surgery. However, the risk of developing ARDS is very low. If you need a medical procedure requiring oxygen or general anesthesia, be sure to tell your surgeon, anesthesiologist, and other healthcare providers that you have received bleomycin in the past for treatment of childhood cancer.

What are factors that increase the risk of developing lung problems after treatment with bleomycin?

- High total doses of bleomycin (400 units/m^2 or more in all doses combined)
- Radiation to the chest or lungs, or total body irradiation (TBI)

- Treatment with other chemotherapy drugs that can also damage the lungs *(see related Health Link: "Pulmonary Health")*
- Exposure to high oxygen levels (such as during general anesthesia or SCUBA diving)
- Smoking

What monitoring is recommended for people who have received bleomycin for treatment of childhood cancer?

- A **yearly medical check-up** is recommended.
- A **chest x-ray and pulmonary function tests** may show lung problems that are not apparent during a check-up. For this reason, it is helpful to **have these tests done at least once** (at least 2 years after completing cancer treatment) to find out if there are any problems. Your healthcare provider can decide if further testing is needed based on these results.
- The **chest x-ray and pulmonary function tests should be repeated before any scheduled surgery that requires general anesthesia** to check for changes in the lungs that could increase the risk of breathing problems during or after anesthesia.

Are there any special precautions I should take?

If you received therapy with bleomycin, you should:

- Avoid SCUBA diving. During SCUBA diving, increased underwater pressures and high oxygen levels can damage the lungs.
- Tell your surgeon, anesthesiologist, and other healthcare providers about your medical history before any scheduled procedures that may require oxygen.
- Avoid breathing high concentrations of oxygen whenever possible, especially for long periods of time (such as over several hours). If you require oxygen, monitoring of your oxygen levels can usually be done so that you can receive the lowest oxygen concentration that is necessary.
- Get the pneumococcal (pneumonia) vaccine.
- Get yearly influenza (flu) vaccines.
- Don't smoke. If you currently smoke, talk to your healthcare provider about a program to help you quit.

Written by Margery Schaffer, RN, MSN, CPNP, pediatric nurse practitioner in the Department of Hematology/Oncology at The Children's Medical Center, Dayton, Ohio.

Reviewed by: Emmett J. Broxson, Jr. MD, Edward Walz MD, Karen Stormer, RN, CNS, CPON®, Melissa Hudson MD, Debra Friedman MD, Neyssa Marina MD, and Smita Bhatia MD, MPH.

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Keeping Your Bones Healthy After Childhood Cancer

During childhood and into young adulthood, bone formation usually occurs faster than bone loss, causing bones to grow and become heavier (more dense). As a person gets older, the process of bone removal gradually overtakes bone formation, and bones slowly lose strength as part of the normal aging process.

Osteoporosis: A Silent Disease

Osteoporosis (or osteopenia) is a disorder resulting from too little new bone formation or too much bone loss, causing bones to become weak. Most people do not have symptoms, especially in the early stages. As bones become weaker, fractures may occur after minimal trauma, such as a fall. Osteoporosis may occur in any bone, but most commonly affects the wrists and leg bones. The vertebrae of the spine often collapse, leading to loss of height, spinal curvature, and chronic pain.

How is osteoporosis diagnosed?

Although osteoporosis may be suspected based on a patient's symptoms and risk factors, the diagnosis is made by measuring bone density with special x-ray techniques called DEXA or bone density scans. These scans do not expose patients to large amounts of radiation, and generally take less than 20 minutes to perform.

People who have osteoporosis should discuss treatment options with their healthcare provider. Medications, such as bisphosphonates and calcitonin, are available specifically for the treatment of low bone density. In addition, if you have low levels of male or female hormones, or low levels of growth hormone, you may also benefit from hormone replacement therapy.

What are the risk factors for osteoporosis?

Osteoporosis is more common in people with the following characteristics:

- Female (especially after menopause)
- Family history of osteoporosis
- Caucasian or Asian race
- Small, thin frame
- Older age

The following factors may also increase the risk of osteoporosis:

- Smoking
- Diet low in calcium
- Lack of weight-bearing exercise
- Too much caffeine, alcohol, or soda
- A diet high in salt

Additional causes of osteoporosis in people who have been treated for cancer include:

- Corticosteroids (such as prednisone and dexamethasone)
- Methotrexate
- Radiation to weight-bearing bones (legs, hips, spine)
- Low levels of female or male hormones as a result of treatment, such as radiation therapy to the brain, radiation therapy to the testicles or ovaries, surgical removal of the testicles or ovaries, or high doses of alkylating chemotherapy (such as cyclophosphamide, ifosfamide, nitrogen mustard, melphalan, busulfan, BCNU, CCNU, and procarbazine)
- Growth hormone deficiency resulting from treatment, such as radiation therapy to the brain
- High levels of thyroid hormone (hyperthyroidism) resulting from treatments such as radiation therapy to the brain, neck, or chest
- High doses of thyroid hormone
- Certain anticonvulsants (phenytoin and barbiturates)
- Aluminum-containing antacids (such as Maalox® or Amphogel®)
- Gonadotropin-releasing hormone agonists such as Lupron (used for treatment of early puberty and endometriosis)
- High doses of heparin (used to prevent blood clots), especially with prolonged use
- Cholestyramine (used to control blood cholesterol)
- Chronic graft-versus-host disease requiring prolonged therapy with corticosteroids (such as prednisone) following stem cell or bone marrow transplant
- Prolonged periods of inactivity (bed rest)

Many of the medications on this list are essential treatments for certain medical conditions. If you are taking any of these medications, do not change your dosage or stop taking your medication without consulting with your healthcare provider.

What lowers the risk of osteoporosis?

Fortunately, there are many things you can do to reduce the risk of osteoporosis. Regular weight-bearing exercise (such as brisk walking, dancing, jazzercise and jogging) helps to develop and maintain healthy bones. Bicycling and swimming are excellent exercises for general fitness, but these are NOT weight-bearing exercises, and they do not help to build strong bones. **Exercises that are especially good for bone health include higher-impact weight-bearing activities, such as hopping, jogging and jumping rope. Resistance exercises, such as light weight lifting, also help to build strong bones** and are especially important for bones of the upper body, including the arms and shoulders. If you have problems with your heart, or have painful bones or joints, **be sure to discuss your individual health status and cancer treatment history with your healthcare provider before starting any new exercise program.**

A diet high in calcium also is important in preventing osteoporosis. Most doctors recommend 1000-1500 mg a day, which means a diet rich in dairy products (milk, cheese, yogurt) and leafy green vegetables. Talking with a nutritionist may help you design a healthy diet. Over- the-counter calcium supplements also may be useful.

Vitamin D is needed in order to absorb calcium. Skin makes this vitamin naturally when exposed to sunlight. Many dairy products also contain vitamin D. In general, you should not take more than 800 units of Vitamin D per day. Taking too much vitamin D may be harmful, so it's best to check with your healthcare provider before taking any vitamin D supplements.

What screening is recommended?

After reviewing your treatment history and risk factors, your healthcare provider can advise you regarding the need for bone density testing. For those at risk, a bone density scan is generally done at age 18, but this can be done at an earlier age if needed, and the timing of the test is based on evaluation of each individual patient. Follow-up scans may be needed for ongoing monitoring of bone density in some patients.

Written by Julie Blatt MD, Professor of Pediatrics, Division of Pediatric Hematology-Oncology, University of North Carolina, Chapel Hill, NC.

Reviewed by Charles Sklar MD, Melissa Hudson MD, Debra L. Friedman MD, Joan Darling PhD, and Wendy Landier CPNP.

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Breast Cancer Following Treatment for Childhood Cancer: Are You at Risk?

You have successfully been treated for cancer during childhood or adolescence and are now moving forward with your life – so the last thing you want to be reminded about is the risk of developing another cancer during adulthood. For a variety of reasons, the risk of cancer increases for everyone as they age. Depending on the specific treatment you received for childhood cancer, you may be at increased risk for developing breast cancer. It is important to understand that risk, so that you can take steps to protect your health.

What are the risk factors?

Several studies have shown that **women treated with radiation to the chest for cancer during childhood, adolescence, or young adulthood** have an increased risk of developing breast cancer as they get older, compared to women their same age in the general population. The risk of secondary breast cancer is **related to the dose of radiation**. People treated with higher doses of radiation have the highest risk. Researchers are studying this problem to better understand the risk factors and find ways to prevent secondary breast cancer.

Other **known risk factors** for developing breast cancer include:

- Early menstruation (before the age of 12)
- Late menopause (after age 55)
- Never having a baby or having a first baby after the age of 30
- Having a close relative with breast cancer
- Being overweight
- Having an inactive (sedentary) lifestyle

In addition, **possible risk factors** associated with developing breast cancer include:

- High fat diet
- Drinking too much alcohol
- Never breastfeeding
- Smoking
- Birth control pills
- Hormone replacement therapy taken for long periods of time

When is breast cancer likely to occur?

The risk of secondary breast cancer begins to increase between five and nine years following radiation therapy and continues to rise thereafter. This means that if a woman develops breast cancer following chest radiation for childhood/adolescent cancer, it usually happens at a much younger age (usually 30 to 40 years old) than in women who develop primary breast cancer (usually age 50 or older).

What can I do to protect my health?

Most women who received radiation therapy to the chest during childhood, adolescence, or young adulthood will ***NOT*** develop breast cancer. However, if you received radiation to the chest, it's important to understand that the risk ***IS*** higher for you than it is for women your age who never received radiation. So, the best way for you to protect your health is by taking steps to closely monitor your breasts. That way, if a cancer develops, it will be detected in its earliest stages, when treatment is most effective.

What monitoring is recommended?

If you were treated with chest radiation therapy during childhood, adolescence, or young adulthood, you should:

1. **Perform monthly breast self-examination**. Report any lumps or changes to your healthcare provider right away.
2. Have a **clinical breast exam** performed by your healthcare provider - at least once a year until you reach age 25 - then every 6 months thereafter.
3. Have a **yearly mammogram -** starting at age 25 **or** 8 years after you received radiation (whichever comes last).

Is there anything else I can do to minimize the risk?

The following lifestyle changes may help reduce the risk of developing breast cancer, and will also help you to stay as healthy as possible:

- Eat more fruits and vegetables (at least 5 servings a day are recommended).
- Exercise at least 30 minutes per day on most days of the week.
- If you are overweight, lose excess weight.
- Limit your intake of alcohol to no more than one drink per day.
- If you smoke, quit.
- If you have a baby, try to breastfeed for at least four months.
- If you need hormone replacement therapy or birth control pills, discuss the risks and benefits with your healthcare professional.
- Limit your exposure to potentially harmful chemicals and pesticides. Use protective equipment if you are exposed to chemicals in your workplace.

If you have questions regarding your risk of developing breast cancer, and how you can best protect your health, be sure to discuss this with your healthcare provider.

Written by Melissa Hudson MD and Wendy Landier CPNP. Portions adapted from CCSS Newsletter Winter 2001, used with permission.

Melissa Hudson, MD directs the After Completion of therapy (ACT) clinic at St. Jude Children's Research Hospital in Memphis, TN.

Wendy Landier, RN, MSN, CPNP, CPON®, is clinical director of the Survivorship Clinic in the Division of Pediatrics at City of Hope National Medical Center in Duarte, CA.

Reviewed by Smita Bhatia MD, MPH, Louis S. Constine MD, Debra Friedman MD, and Fran Wiley RN, MN.

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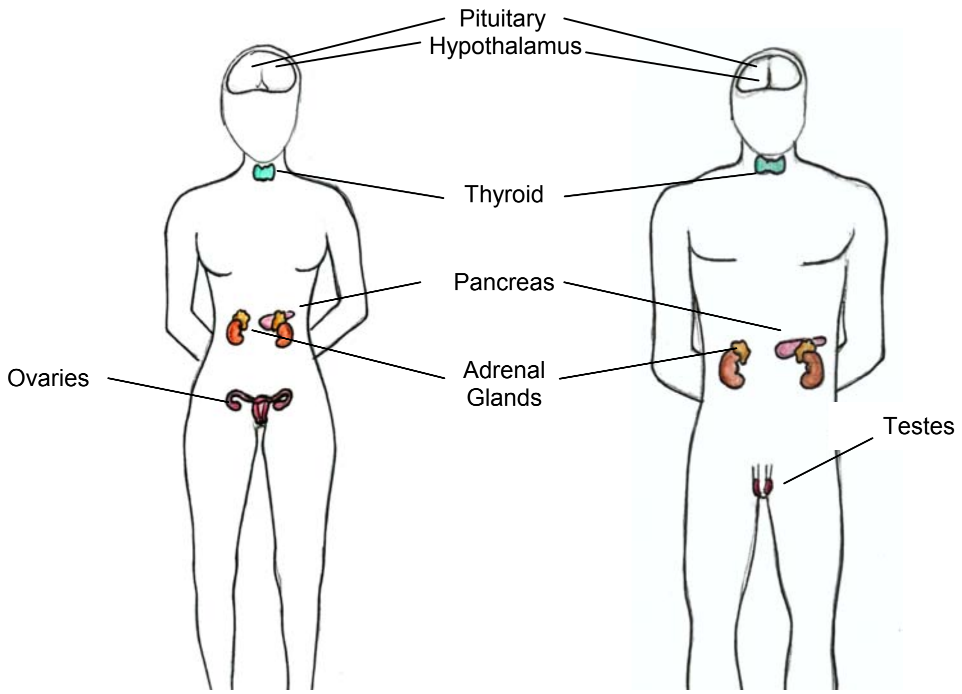
Endocrine Problems After Childhood Cancer: Central Adrenal Insufficiency

Some people who were treated for cancer during childhood may develop endocrine (hormone) problems as a result of changes in the function of a complex system of glands known as the endocrine system.

What is the endocrine system?

The endocrine system is a group of glands that regulate many body functions including growth, puberty, energy level, urine production, and stress response. Glands of the endocrine system include the pituitary, hypothalamus, thyroid, adrenals, pancreas, ovaries (in females), and testes (in males). The hypothalamus and pituitary are sometimes called the "master glands" because they control many of the other glands in the endocrine system. Unfortunately, some treatments given for childhood cancer can damage the endocrine system, resulting in a variety of problems.



What are hormones?

Hormones are chemical messengers that carry information from the endocrine glands through the bloodstream to the body's cells. The endocrine system makes many hormones (such as growth hormone, sex hormones, adrenal and thyroid hormones) that work together to maintain specific bodily functions.

What is central adrenal insufficiency?

Central adrenal insufficiency is caused by a deficiency of the pituitary hormone known as Adrenocorticotropic Hormone (ACTH). The adrenal glands (located on top of the kidneys) are stimulated by ACTH to produce a hormone known as cortisol. If the pituitary gland doesn't make enough ACTH, then cortisol will not be made by the adrenal gland. Cortisol is important for health because it helps to keep the blood sugar at a normal level and helps the body deal with physical stress, such as fevers or injuries.

What are the risk factors for central adrenal insufficiency?

- Radiation to the brain, especially in doses of 30 Gy (3000 cGy/rads) or higher, including the following fields:
    - Cranial (whole brain)
    - Craniospinal
    - Nasopharyngeal (nose and throat)
    - Oropharyngeal (mouth and throat)
    - Orbital
    - Eye
    - Ear
    - Infratemporal (midfacial area behind the cheekbones)
    - Total body irradiation (TBI)
- Surgical removal of the pituitary gland

What are the symptoms of central adrenal insufficiency?

Under normal circumstances, there may be no symptoms at all, or there may be mild symptoms, such as fatigue, weakness, poor appetite, or dizziness. However, under stressful circumstances, such as fever, infection, surgery, or injury, symptoms may become severe, and may include vomiting, diarrhea, low blood sugar, and dehydration.

What screening is recommended?

People who had **radiation in a dose of 30 Gy or higher to the central area of the brain** (hypothalamic-pituitary axis), or people who are having **symptoms** suggestive of central adrenal insufficiency, should have a **blood test** done **to check the cortisol level**. This test should be done **at least once following the completion of cancer treatment** (and is usually done at least 2 years following completion of therapy). This test is usually done **first thing in the morning**, because the cortisol level varies throughout the day and is usually highest early in the morning.

If your morning cortisol level is abnormal, your healthcare provider will probably refer you to an endocrinologist (doctor who specializes in hormone problems). The endocrinologist will do more specific tests to evaluate the problem.

How is central adrenal insufficiency treated?

Central adrenal insufficiency is treated with hydrocortisone, a medication that is given by mouth everyday on a regular schedule. In times of increased stress, such as illness or surgery, the dose of hydrocortisone is increased and can be administered by injection if necessary. If you have central adrenal insufficiency, you should wear a medical alert bracelet so that in case of accident or sudden illness, emergency medical workers will be aware of your special health needs.

Written by Debra Eshelman CPNP and Wendy Landier CPNP.

Debra Eshelman RN, MSN, CPNP, is a pediatric nurse practitioner and coordinates the After the Cancer Experience (ACE) Pediatric and Young Adult Survivor Programs at Children's Medical Center of Dallas and the University of Texas Southwestern Medical Center, Dallas, TX.

Wendy Landier RN, MSN, CPNP, CPON®, is a pediatric nurse practitioner and clinical director of the Survivorship Clinic, Division of Pediatrics, City of Hope National Medical Center, Duarte, CA.

Reviewed by Charles Sklar MD and Smita Bhatia MD, MPH.

Illustrated by Devika Bhatia.

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Dental Health Following Childhood Cancer Treatment

Treatment for cancer during childhood often increases the risk for dental problems. As a childhood cancer survivor, it is important for you to understand the reasons why dental care is especially important for maintaining your health.

What are the risk factors for dental problems after childhood cancer treatment?

- **Treatment with chemotherapy** before your permanent teeth were fully formed, especially if you were younger than 5 years old at the time of your treatment.
- **Radiation that included the mouth and/or salivary glands**, such as the following:
    - Cranial (whole brain)
    - Craniospinal
    - Nasopharyngeal (nose and throat)
    - Oropharyngeal (mouth and throat)
    - Orbital
    - Eye
    - Ear
    - Infratemporal (midfacial area behind the cheekbones)
    - Cervical (neck)
    - Cervical spine (spine in the neck area)
    - Mantle (neck and chest areas)
    - Total body irradiation (TBI)

What dental problems can occur following treatment for cancer in childhood?

- **Problems that may be a result of chemotherapy** during childhood include:
    - Increased risk for cavities
    - Shortening or thinning of the roots of the teeth
    - Absence of teeth or roots
    - Problems with development of tooth enamel resulting in white or discolored patches on the teeth, grooves and pits in the teeth, and/or easy staining of the teeth

Because teeth develop slowly, these problems are more likely to develop in people who received chemotherapy over a prolonged period (several years) during childhood.

- **Problems that may be a result of radiation** to the mouth and/or salivary glands include:
    - Increased risk for cavities
    - Shortening or thinning of the roots of the teeth
    - Absence of teeth or roots

- Faulty development of tooth enamel resulting in white or discolored patches on the teeth, grooves and pits in the teeth, and/or easy staining of the teeth
- Small teeth
- Early loss of teeth
- Baby teeth not falling out
- Problems with tooth development or delayed eruption of permanent teeth
- Increased risk of tooth sensitivity to hot and cold sensation
- Xerostomia (dry mouth due to decreased production of saliva)
- Alteration in taste
- Trismus (limited ability to fully open the mouth)
- Temporomandibular joint dysfunction (causing pain in front of the ears)
- Malocclusion (bite problem, such as overbite or underbite)
- Abnormal growth of bones of the face and neck
- Periodontal (gum) disease

What can be done for these problems?

Taking care of teeth and gums is always important, and it is even more important if you have had radiation or chemotherapy at a young age. If your gums are not healthy, they can shrink away from your teeth, causing infection in the bone supporting the roots. This bone can dissolve away slowly, causing the teeth to become loose. This condition is called periodontitis, which simply means an inflammation surrounding a tooth. Periodontitis can be prevented be proper brushing of your teeth and gums and by flossing between your teeth at least once a day. Taking good care of your teeth and gums, combined with routine visits to your dentist, can prevent the development of cavities and gum disease.

If your permanent teeth do not develop normally, you may need caps or crowns in order to improve your smile and the function of your teeth. Sometimes reconstructive surgery is needed to correct poor bone growth of the face or jaw. Radiation can sometimes make it difficult to open your mouth fully (trismus), or cause some scarring and hardening of the jaw muscles (fibrosis). Stretching exercises for the jaw may reduce fibrosis and improve your ability to open your mouth. Your dentist will be able to instruct you or refer you to occupational therapy to learn these exercises. If you have crooked or small teeth, this may be improved by bonding. If braces are needed, your dentist will do a panorex x-ray of the teeth to see if the teeth, roots and supporting bone are strong enough for braces. If you had high doses of radiation to the face or mouth and you require dental surgery, you may be at increased risk of developing a bone-healing problem (osteoradionecrosis) after the surgery. Your dentist should discuss this potential problem with a radiation oncologist prior to any dental surgery. If you had an allogeneic bone marrow or stem cell transplant (from a donor other than yourself), it is important to let your dentist know, so that the dentist can check for long-term complications indicating chronic graft versus host disease

What is xerostomia and what should I do if I have it?

Dry mouth, also called “xerostomia“ can occur after radiation to the head or neck. Other problems related to xerostomia include persistent sore throat, burning sensation in the mouth and gums, problems speaking, difficulty swallowing, hoarseness, or dry nasal passages. Dryness of the mouth is a result of decreased saliva and/or thickening of the saliva, and can lead to the development of cavities. This usually happens only with radiation doses of 40 Gy (4000 cGy/rads) or higher to the mouth and/or salivary glands.

Drinking liquids frequently and the use of artificial saliva can help relieve the symptoms of xerostomia. Sugar-free candy stimulates salvia production. Proper brushing habits are very important for people with xerostomia, as is limiting the intake of candy and other sweets. Your dentist may recommend application of a fluoride gel to your teeth at least once a day. The fluoride acts on the enamel of your teeth to make it more resistant to decay. Ask your dentist about whether you should use daily fluoride.

Should I take any special precautions when having dental work done?

Always let your dentist know if you have the following health conditions:

- **Shunt** (surgical placement of a tube to drain fluid from the brain)
- **Limb salvage procedure** (replacement of bone with a metal rod or bone graft)
- **Leaky heart valve** (this sometimes happens after radiation to the chest)

In any of these situations, bacteria that normally enter the bloodstream during dental work can result in serious infections. As a precaution against infection, if you have any of these conditions, you should take antibiotics before any dental work. The antibiotics should be prescribed by, or discussed with, your dentist. You should also let your dentist know if you have had a splenectomy (surgical removal of the spleen) or if you have had high doses of radiation (30 Gy – 3000 cGy/rads or more) to the spleen. *(Also see the following related Health Links: “Splenic Precautions,” “Limb Salvage after Bone Cancer,” and “Heart Problems Following Treatment for Childhood Cancer ”).*

What is the risk of developing oral cancer?

People who have had radiation to the head and neck during childhood may be at increased risk for oral cancers. Using tobacco in any form or using alcohol in combination with smoking greatly increases this risk. Your dentist should perform an oral cancer screening exam during each visit. If you notice any of the following, notify your dentist immediately:

- **A sore that does not heal** or that bleeds easily
- **A change in the color** of your mouth tissues
- **A lump, thickening or rough spot** in the mouth
- **Pain, tenderness or numbness** anywhere in the mouth or on the lips

Most of the time, these symptoms do not indicate any problem, but a dentist can tell if they are the sign of a serious problem.

What should I do to keep my teeth and mouth as healthy as possible?

Follow these recommendations (unless your dentist recommends otherwise):

- **See your dentist regularly at least every six months**. Make sure that your dentist knows your health history and the treatment you received. (Ask your oncologist for a summary of your treatment). Be sure that your visit includes an oral cancer screening, and be sure to notify your dentist if you notice any warning signs of oral cancer.
- **Have a panorex x-ray done before dental/orthodontic procedures** to evaluate the root development of your teeth and determine if any modifications need to be made to your dental treatment plan.
- **Brush your teeth at least twice a day.**
  - Use a fluoride-containing toothpaste to help prevent tooth decay.
  - Place your brush at a slight angle toward the gum when brushing along the gum line.
  - Use a gentle touch, since vigorous brushing could irritate your gums.
  - Clean all surfaces of the teeth.
  - Brush your tongue to remove bacteria that can cause bad breath.
- **Floss your teeth once or twice a day**
  - Floss carefully between teeth because brushing alone does not remove plaque between teeth.
  - Use a gentle touch to avoid injury to gums.
  - It is normal to have a small amount of bleeding when flossing, but if the bleeding increases or your gums are red and puffy, this may be a sign of infection and you should notify your dentist.
- **Use antibacterial, alcohol-free fluoride mouth rinses** (your dentist can recommend the best ones for you).
- **Drink liquids frequently and/or use artificial saliva** (available at most pharmacies without a prescription).
- **Apply fluoride frequently.** Your dentist may recommend a daily fluoride rinse or gel that you can use at home after brushing, in addition to the special fluoride application you may receive at your regular dental cleanings.
- **Limit sweets and carbohydrate-rich foods.**
- **Do not use tobacco products and use alcohol only in moderation** (check with your healthcare provider to see if you should drink alcohol at all, since alcohol may increase other problems following childhood cancer treatment).
- **Notify your dentist immediately if you develop any signs of infection** in your mouth or gums, such as redness, tenderness, excessive bleeding of gums, painful teeth, and/or increased areas of sensitivity.

For more information about dental health issues following childhood cancer treatment:

- **American Dental Association website** (click on “Oral Health Topics”)
  www.ada.org
- **Patient Centers website** (click on “Head and Neck”)
  http://www.patientcenters.com/survivors/news/reading.html

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Debbie Lafond is a pediatric nurse practitioner at Children’s National Medical Center in Washington, D.C.

Melissa Hudson, MD directs the After Completion of Therapy (ACT) clinic at St. Jude Children’s Research Hospital in Memphis, TN.

Reviewed by Man Wai Ng, DDS, Revonda Mosher, MS, CPNP, CPON®, Joan Darling PhD, Louis S. Constine MD, and Smita Bhatia MD, MPH.

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Educational Issues Following Treatment for Childhood Cancer

Treatment for cancer during childhood or adolescence may affect educational progress due to prolonged absences or reduced energy levels that frequently occur during treatment. In addition, some types of cancer may require therapy to control or prevent spread of the disease to the brain and/or spinal cord (central nervous system). This therapy can sometimes affect memory and learning abilities. Parents and teachers should be aware of potential educational problems that may be related to cancer treatment so that children and teens at risk can be watched closely and given extra help if the need arises.

What increases the risk of educational problems?

Factors that may place children and teens at increased risk for difficulties in school include:

- Diagnosis of cancer at a very young age
- Numerous or prolonged school absences
- A history of learning problems before being diagnosed with cancer
- Cancer treatment that results in reduced energy levels
- Cancer treatment that affects hearing or vision
- Cancer treatment that results in physical disabilities
- Cancer therapy that includes treatment to the central nervous system (see below).

Are children and teens with certain types of cancer at higher risk of developing educational difficulties?

Yes, children and teens with the types of cancer listed below are more likely to have received treatments that may affect learning and memory. Since treatment for these types of cancer varies widely, not everyone who was treated for these cancers is at increased risk.

- Brain tumors
- Tumors located in the eye or eye socket, head, or facial area
- Acute lymphoblastic leukemia (ALL)
- Non-Hodgkin's lymphoma (NHL)

What types of treatment place children and teens at higher risk for learning and memory problems?

- Methotrexate – if given in high doses intravenously (IV) or injected into the spinal fluid (intrathecal – IT)
- Cytarabine – if given in high doses intravenously (IV)
- Surgery involving the brain

- Radiation to any of the following areas:
  - Head or brain (cranial)
  - Brain and upper spine (craniospinal)
  - Eye or eye socket (orbital)
  - Ear
  - Face (including the sinuses, nose and mouth)
  - Total body (TBI)

What testing is recommended?

Any young person who has had any of the above cancer treatments, or who is having difficulties in school, should undergo a specialized evaluation by a pediatric psychologist (neuropsychological testing) at the time of entry into long-term follow-up. Even if the initial neuropsychological evaluation is normal, it is important for parents and teachers to remain watchful. Further neuropsychological evaluations may be necessary if the child or teen begins having trouble in school or develops any of the problems listed below. In addition, repeat testing is often recommended at times when academic challenges are more likely to occur, such as at entry into elementary school, middle school, high school, and during pre-college planning.

What learning problems may occur?

The brain is a very complex structure that continues to grow and develop throughout childhood and adolescence. Some problems may not become apparent until years after therapy is completed. Common problems areas include:

- Handwriting
- Spelling
- Reading
- Vocabulary
- Math
- Concentration
- Attention span
- Ability to complete tasks on time
- Memory
- Processing (ability to complete assignments that require multiple steps)
- Planning
- Organization
- Problem-solving
- Social skills

What can be done to help with learning problems?

If a problem is identified, special accommodations or services can be requested to help maximize the student's learning potential. The first step is usually to schedule a meeting with the school in order to develop a specialized educational plan. Examples of strategies that are often helpful for children and teens with educational problems related to cancer treatment include:

- Seating near the front of the classroom
- Minimizing the amount of written work required
- Use of tape-recorded textbooks and lectures
- Use of a computer keyboard instead of handwriting
- Use of a calculator for math
- Modification of test requirements (extra time, oral instead of written exams)
- Assignment of a classroom aide
- Extra help with math, spelling, reading, and organizational skills
- Access to an elevator
- Extra time for transition between classes
- Duplicate set of textbooks to keep at home

What laws protect the rights of students who have undergone treatment for cancer?

In the United States, there are three public laws that protect the rights of students with educational problems related to cancer treatment. These laws are:

The Americans with Disabilities Act (ADA)

The ADA law (PL 101-336) protects against discrimination in employment, transportation, communication, government and public accommodations for people with disabilities. It guarantees equal access to public spaces, event, and opportunities and may be particularly helpful for students seeking higher education or employment.

The Rehabilitation Act of 1973 – Section 504

This legislation provides accommodations for students with a “physical or mental impairment which substantially limits one or more major life activities,” or students who have “a record of such impairment”, or who are “perceived as having such an impairment” (The Rehabilitation Act, 1973). Qualifying conditions include chronic illnesses such as cancer, as well as many other disabilities, including hearing problems, vision problems, learning disabilities, speech disorders, and orthopedic handicaps. All childhood cancer survivors in the United States are eligible for accommodations under this law, and all educational institutions receiving federal funding (including colleges and universities) are required to comply. Accommodations may include modifications in the curriculum (such as allowing the use of a calculator and extra time for assignments or test-taking) and the environment (such as seating near the front of the classroom or allowing extra time between classes).

The Individuals with Disabilities Education Act (IDEA)

The IDEA legislation (PL 105-17) requires that public schools provide “free and appropriate education in the least restrictive environment” for disabled students between the ages of 3 and 21 years of age. In order to qualify for special education services under IDEA, the student must meet qualifications under at least one disability outlined in the law - those that most commonly apply to students treated for cancer include "specific learning disability," "traumatic brain injury," or "other health impairment." In order to access services under the IDEA legislation, parents must initiate the process by requesting that the student be evaluated for an "Individualized Education Plan" or IEP. The student will then undergo an assessment process to determine what assistance is required. A conference is then held to discuss the results of the evaluation and, if the student qualifies, to determine an individualized plan to meet the identified specialized educational needs. Services available under the IDEA legislation include tutoring, specialized classroom placements (such as a resource room), psychological services, adaptive physical education, physical, occupational and speech/language therapy, and transportation services. All services and accommodations required by the student should be specified in the IEP (the written document describing the special education program). The IEP should be reviewed and updated on an annual basis to assure that it continues to meet the student's educational needs.

Where can I get more information?

Additional information is available from the National Information Center for Children and Youth with Disabilities (phone: 1-800-695-0285; website: www.nichcy.org).

Written by Wendy Landier, RN, MSN, CPNP, CPON®, pediatric nurse practitioner and clinical director of the Survivorship Clinic, Division of Pediatrics, City of Hope National Medical Center, Duarte, CA.

Reviewed by: Debra L. Friedman MD, Melissa M. Hudson MD, Julie Blatt MD, and Joan Darling PhD.

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Emotional Issues after Childhood Cancer

The Cancer Experience

The diagnosis and treatment of childhood cancer is a stressful time for the patient and family. Patients must endure painful procedures, frequent hospitalizations and separation from their family and friends. Families worry about whether their loved one will be cured and how to prevent suffering. Often those affected may experience anger, sadness, or helplessness. Brothers and sisters may feel neglected because their family's world revolves around their sibling with cancer. Patients and families handle the stress of the cancer experience in different ways, and periods of anxiety or depression are common.

After the Cancer Experience

For survivors and their families, the end of treatment brings an entirely new set of emotions as they face the possible consequences of the cancer treatment. There are many different feelings after treatment ends. These feeling are as unique as each survivor. Persistent late effects may be constant reminders of the stressful events at diagnosis. The diagnosis of a new health problem can cause discouragement, anger, anxiety, or depression. Many survivors and their families fear recurrence of their cancer. Anniversaries of important dates, such as the diagnosis date, can bring on a variety of emotions, including happiness, relief, sadness, painful memories or a combination of these feelings. There may be feelings of grief or loss of the normalcy of childhood. "Survivor guilt" may exist if friends undergoing treatment died. Survivors, especially teenagers, may feel "invincible" and believe that since they survived cancer, they can survive anything. This can lead to the development of unhealthy or risky behaviors. Other survivors may feel especially vulnerable because of experiences they have had.

Reacting to the stresses of survivorship

For the most part, the majority of survivors and families cope well with the lifelong effects of cancer treatment. Sometimes physical problems and emotional stress may lead to anxiety and/or depression that require medical attention. Survivors may also experience periods of intense anxiety triggered by upsetting memories related to treatment, referred to as "posttraumatic stress". Posttraumatic stress symptoms may develop many years after the traumatic event and are similar to symptoms observed in people who have seen painful life-changing events, such as wars, bombings, or natural disasters. In severe cases, symptoms of depression or posttraumatic stress may negatively affect personal relationships, school or work.

Risk factors for emotional issues

Several risk factors may affect your chances of developing emotional issues after childhood cancer treatment. These risk factors include:

- Being female
- Having a family history of depression, anxiety or mental illness
- Having emotional or learning difficulties prior to the diagnosis of cancer
- Having a cancer of the central nervous system (brain and spinal tumors)
- Having cancer therapy involving the central nervous system (such as brain radiation or chemotherapy given into the spinal fluid)

When you should seek help

The table below lists common symptoms of depression and posttraumatic stress. Patients or family members with symptoms lasting two or more weeks should call their healthcare provider to discuss the need for a referral to a mental health professional. Because cancer treatments occasionally result in hormone deficiencies or other problems that can affect mood and create these symptoms, we also recommend a thorough check-up by your primary healthcare provider.

SYMPTOMS OF DEPRESSION AND POST-TRAUMATIC STRESS

Symptom	Depression	Post Traumatic Stress
Overeating, weight gain	X	
Poor appetite, weight loss	X	
Crying easily or unable to cry	X	
Chronic fatigue, poor energy	X	
Sleeping a lot	X	
Difficulty making decisions	X	
Hopelessness/thoughts of death, escape, suicide	X	
Difficulty concentrating	X	X
Not sleeping well	X	X
Increased irritability	X	X
Decreased interest in activities	X	X
Re-living painful memories of illness		X
Becoming upset, scared or angry when thinking about illness		X
Physical reactions (like rapid heart rate, nausea) when thinking about illness		X
Staying away from medical visits		X
Refusing to talk about illness		X

Treatment options

Mental health professionals (including social workers, psychologists, or psychiatrists) work in a variety of community settings. Some families prefer to start with counseling services offered by clergy at their place of worship. Another option is to ask your healthcare provider to help you find a mental health counselor. Treatments for depression and anxiety include individual or group counseling and medication. Medication usually works best in combination with some form of counseling.

Share your concerns with your healthcare professional

If concerns about complications after cancer treatment are causing feelings of anxiety or depression, discuss these feelings with your primary healthcare provider or cancer specialist to find out if they are related to your treatment. Anxiety may result from other events in your life not related to your illness. In any case, ask about what you can do to reduce the risks of health problems as your get older. It is important to remember that many people who have never been treated for a serious illness commonly suffer from anxiety and depression, and even from post-traumatic stress. Help is available to treat these problems. Talking with others about your concerns is a first step in gaining control over those aspects of your life that you are having difficulties with. Support from others can help cancer survivors and families cope with their emotions in a positive way.

Resources

There are many organizations and online networks of support available to cancer survivors. Those listed here are just a few of the many resources available:

- **Candlelighters Childhood Cancer Foundation**
  www.candlelighters.org, 800-366-CCCF
- **Association of Cancer Online Resources, Inc (ACOR)**
  www.acor.org, includes a listing of dozens of Internet support groups.
- **Oncolink**
  www.oncolink.upenn.edu/psychosocial/support/
- **American Cancer Society's Cancer Survivors Network**
  www.cancersurvivorsnetwork.org
- **Patient Centered Guides**
  www.patientcenters.com/survivors
  A comprehensive listing of support resources can be found in the book *Childhood Cancer Survivors: A Practical Guide to Your Future* (2000) by Nancy Keene, Wendy Hobbie and Kathy Ruccione, published by O'Reilly and Associates, Inc. (See chapter 2 and pages 444-457). This book provides an exceptional series of survivor excerpts about their personal cancer experiences.

Adapted by Debra Eshelman CPNP, from "Dealing with Emotions after Childhood Illness" by Melissa Hudson MD, used with permission.

Melissa Hudson, MD directs the After Completion of therapy (ACT) clinic at St. Jude Children's Research Hospital in Memphis, TN.

Debra Eshelman, RN, MSN, CPNP is a pediatric nurse practitioner and coordinates the After the Cancer Experience (ACE) Pediatric and Young Adult Survivor Programs at Children's Medical Center of Dallas and the University of Texas Southwestern Medical Center, Dallas, TX.

Reviewed by: Joe Don Cavender, MSN, RN, CPNP, Daniel Armstrong PhD, Joan Darling PhD, Catherine L. Woodman MD, and Octavio Zavala.

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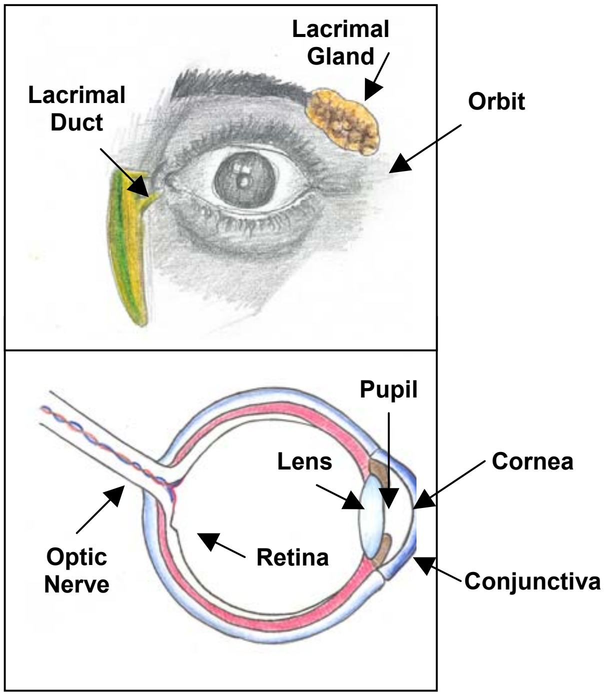
Eye Problems after Treatment for Childhood Cancer

Childhood cancer treatment sometimes requires the use of medications or radiation that can affect the eyes. Because vision can have a significant impact on daily living, it is important for survivors who received these treatments to have their eyes checked regularly.

How do the eyes work?

The eyes are remarkable organs, allowing light to be converted into impulses that are transmitted to the brain, where images are perceived. The eyes are located in the area of the skull known as the **orbit** or eye socket. A thin layer of tissue called the **conjunctiva** covers and protects the eye and eyelids. Tears are produced in the **lacrimal gland**, located in the outer corner of the eye socket, above the eyeball. Tears flow over the eye, providing lubrication, and drain into a tiny canal at the inner corner of the eye, called the **lacrimal duct**. Light enters the eye through a clear layer of tissue known as the **cornea**. The cornea bends and focuses the light, and sends it through the opening of the eye known as the **pupil**. The pupil controls how much light enters the eye. Behind the pupil is the **lens** of the eye, which focuses the light onto the **retina**, the membrane along the back wall of the eye. The nerve cells in the retina change the light into electrical impulses and send them through the **optic nerve** to the brain, where the image is perceived.



What eye problems can develop following treatment for childhood cancer?

Cataracts: Clouding of the lens of the eye. When this happens, light cannot pass through the lens easily. Common symptoms of cataracts include painless blurring of vision, sensitivity to light and glare, double vision in one eye, poor night vision, fading or yellowing of colors, and the need for frequent changes in glasses or contact lens prescriptions.

Keratoconjunctivitis sicca: Inflammation of the cornea (the clear, outer surface of the eye) and the conjunctiva (the membrane covering the eye and eyelids) due to dryness. This occurs when radiation or graft-versus-host disease reduces the amount of tears produced by the lacrimal gland. Symptoms include pain at the surface of the eye and light sensitivity.

Other eye problems:

The following eye problems are less common and are usually seen only in survivors who had radiation treatments directed at the eye or orbit:

Orbital hypoplasia: Underdevelopment of the eye and surrounding tissues, caused by radiation to the eye or to the area surrounding the eye. This can result in a small eye and orbit (orbital hypoplasia).

Lacrimal duct atrophy: Shrinking of the lacrimal duct, which drains tears from the eye. Lacrimal duct atrophy can result in problems with increased tearing.

Xerophthalmia: Scarring of the tear (lacrimal) glands following radiation to the eye or orbit. This can result in dry eyes (xerophthalmia).

Keratitis: Inflammation of the cornea (the clear, outer surface of the eye). This can cause pain at the surface of the eye and light sensitivity.

Telangiectasias: Enlargement of blood vessels in the white part of the eye. These do not usually cause any symptoms but are sometimes bothersome because of their appearance.

Retinopathy: Damage to the retina (the back surface of the eye where visual information is passed from the eye to the brain). Painless vision loss is the major symptom of retinopathy.

Optic chiasm neuropathy: Damage to the nerves that send visual information from the eye to the brain. This can result in vision loss.

Enophthalmos: Sunken eyeball within the orbit.

What cancer therapies increase the risk of developing these eye complications?

- **Certain medications increase the risk of cataracts**, but do not usually increase the risk of developing other eye complications. These include:
    - **Busulfan**
    - **Corticosteroids**, such as prednisone and dexamethasone
- **Radiation therapy** to the following areas is responsible for most treatment-related eye problems:
    - Eye
    - Orbits
    - Brain (cranial) or brain and spine (craniospinal)
    - Total body irradiation (TBI)

  Radiation doses less than 30 Gy (3000 cGy/rads) increase the risk of cataracts, but do not usually increase the risk of developing other eye complications.

  The **risk for cataracts** caused by radiation **increases with:**
    - Radiation dose of 2 Gy (200 cGy/rads) or higher during a single treatment (fraction)
    - Total radiation dose of 10 Gy (1000 cGy/rads) or higher
    - TBI given as a single dose (unfractionated TBI)
    - The passage of time (the longer off therapy the survivor is)
- **The risk for other long-term complications** affecting the eye is usually **associated with a radiation dose of 30 Gy (3000 cGy/rads) or more** to the eye or orbit.

Other factors that may increase the risk for developing certain eye problems include:

- **Chronic graft versus host dis**ease following allogeneic (from a donor other than yourself) bone marrow or stem cell transplant (increased risk for keratoconjunctivitis sicca)
- **Diabetes mellitus (**increased risk for retinopathy and optic chiasm neuropathy)
- **High blood pressure** (increased risk of optic chiasm neuropathy)
- **Frequent exposure to sunlight** (increased risk for cataracts)

What monitoring is recommended?

The chart below provides recommendations for ongoing monitoring:

Treatment	Dose	Monitoring Required	How often
Busulfan **Corticosteroids** (such as prednisone or dexamethasone)	Any	Evaluation of vision during regular medical checkup – including evaluation of vision (visual acuity) and examination for cataracts (funduscopic examination)	Yearly (If any eye problems are detected you should have an evaluation done by an ophthalmologist)
Total body irradiation (TBI)	Any	Examination by ophthalmologist	Yearly
Radiation to the brain, eye, orbit	30 Gy (3000 cGy) or higher	Examination by ophthalmologist	Yearly
	Less than 30 Gy (3000 cGy)	Examination by ophthalmologist	Every 3 years, plus yearly vision and funduscopic exams during regular medical checkups

Note: An ophthalmologist is a medical doctor (MD or DO) who specializes in eye problems – this is different from a doctor of optometry (OD), who is also a vision specialist but not a medical doctor. Examination by an ophthalmologist should include vision screening, examination for cataracts, and a full examination of the internal structures of the eye. People who develop vision problems should be followed regularly by an ophthalmologist.

If you develop any of the following symptoms, seek prompt medical evaluation. In some cases, referral to an ophthalmologist may be needed:

- Blurry vision
- Double vision
- Blind spots
- Sensitivity to light
- Poor night vision
- Persistent irritation of surface of eye or eyelids
- Excessive tearing/watering of eyes
- Pain within the eye
- Dry eyes

How are eye problems treated?

Cataracts: Not all cataracts need treatment. In many cases, an ophthalmologist may monitor the vision closely over many years, and will recommend treatment if and when it becomes necessary. The only treatment for cataracts is surgical removal of the lens and replacement with an artificial lens. Today, cataract surgery is a low-risk procedure that is performed on an outpatient basis and works well in restoring vision.

Orbital hypoplasia: Usually no treatment is needed for orbital hypoplasia. In severe cases, rebuilding of the bones around the eye may be possible.

Lacrimal duct atrophy: A surgical procedure to widen the tear drainage system can be performed if heavy tearing is a significant problem.

Xerophthalmia: Treatment of dry eye includes the frequent use of artificial tears (eye drops) or ointments to moisten the surface of the eye. In severe cases, the tear drainage system can be blocked by surgery to reduce the drainage of tears from the eye.

Keratitis and keratoconjunctivitis sicca: The frequent use of artificial tears (eye drops) or ointments to moisten the surface of the eye is recommended. Patching the affected eye during sleep may also promote healing. Keratitis caused by infection is treated with antibiotic eye drops or ointment. Rarely, surgical replacement (transplant) of the cornea is necessary.

Telangiectasias: No treatment is necessary.

Retinopathy: Retinopathy may require laser or photocoagulation (heat) treatment of the retina. Rarely, surgery to remove the eye is necessary in severe cases.

Optic chiasm neuropathy: No treatment available.

Enophthalmos: Plastic surgery can be done to build up the orbit.

What can be done if there is impaired vision?

If impaired vision is detected, it is important to follow the recommendations of your ophthalmologist regarding treatment. If vision is not correctable, services are available in most communities to assist people with visual impairments.

In addition, in the United States, services are available for people under 22 years of age through the local public school district or referral agencies (available under the Individuals with Disabilities Education Act, PL 105-17). Sometimes special accommodations, such as seating in the front of the classroom are all that is needed, but this usually requires that the parent request an Individualized Education Plan (IEP) for the child through the school district *(see related Health Link: "Educational Issues Following Treatment for Childhood Cancer")*.

The Americans with Disabilities Act (ADA, PL 101-336) guarantees people with visual impairment equal access to public events, spaces and opportunities.

How can I protect my vision?

It's important to protect your eyes whether or not you have treatment-related eye disorders. Precautions you can take include:

- Wear sunglasses with UV protection when in bright sunlight.
- When participating in sports, be sure to select protective eyewear that is appropriate for the sport. Eyewear worn for sports should be properly fitted by an eye care professional.
- Avoid toys with sharp, protruding or projectile parts.
- Never play with fireworks or sparklers of any kind to avoid accidental injury.
- Be careful when working with hazardous household chemicals.
- Wear protective eyewear when using a lawnmower, power trimmer, or edger, and when working with dangerous equipment in the workshop.
- If you do experience an eye injury, seek medical attention promptly.

Written by Teresa Sweeney RN, MSN, CPNP, pediatric nurse practitioner in the After Completion of Therapy (ACT) Clinic at St. Jude Children's Research Hospital in Memphis, TN.

Reviewed by Julie Blatt MD, Debra Friedman MD, Melissa Hudson MD and Lise Yasui.

Illustrated by Devika Bhatia.

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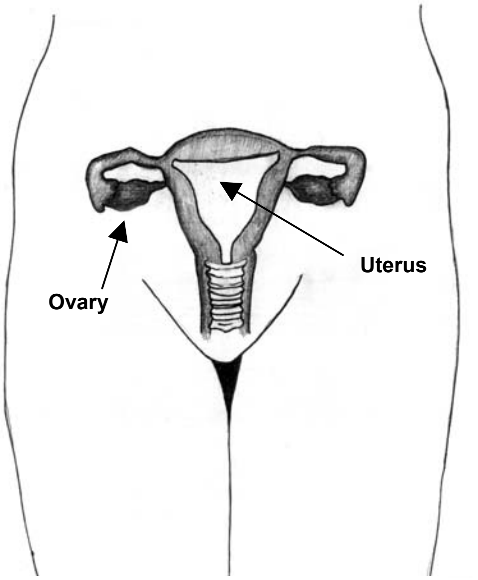
Female Health Issues after Treatment for Childhood Cancer

The effects of childhood cancer therapy on female reproductive function depend on many factors, including the person's age at the time of cancer therapy, the specific type and location of the cancer, and the treatment that was given. It is important to understand how the ovaries and female reproductive organs function and how they may be affected by therapy given to treat cancer during childhood.

The female reproductive organs

At birth, a girl's ovaries contain all the eggs they will ever have. When it is time for a girl to begin pubertal development, the pituitary gland in the brain signals the ovaries by releasing two hormones (FSH and LH). The ovaries secrete the female hormones, estrogen and progesterone, necessary for reproductive function. During each menstrual cycle, at least one egg usually matures and is released from the ovaries. If the egg is not fertilized, menstruation begins. The cycle then repeats itself about every 28 days. With each menstrual cycle, the supply of eggs decreases. When most of the eggs are depleted from a woman's ovaries, menopause begins. During menopause, the menstrual cycles stop, the ovaries stop making hormones, and the woman is no longer able to become pregnant.



How does cancer therapy affect the ovaries?

Certain chemotherapy drugs, radiation therapy, and surgery can sometimes damage the ovaries, reducing the reserve supply of eggs. When the ovaries are not able to produce eggs or hormones, this is called **ovarian failure**.

What are the causes of ovarian failure?

Chemotherapy of the "alkylator" type (such as cyclophosphamide, nitrogen mustard and busulfan) is most likely to affect ovarian function. The total dose of alkylators used during cancer treatment is important in determining the likelihood of ovarian damage. With higher total doses, the likelihood of damage to the ovaries increases. If treatment for childhood cancer included a combination of both radiation and alkylating chemotherapy, the risk of ovarian failure may also be increased.

Radiation therapy can affect ovarian function in two ways**:**

Primary (direct) failure of the ovaries can be caused by radiation that is aimed directly at or near the ovaries. The age of the person at the time of radiation and the total radiation dose can affect whether or not ovarian failure occurs. Generally, younger girls tend to have less damage to the ovaries than people who received equal doses but who were teenagers or young adults at the time of radiation. However, doses of 10-20 Gy (1000 – 2000 cGy/rads) or higher usually cause the ovaries to stop functioning in most females of any age.

Secondary (indirect) failure of the ovaries can occur as a result of radiation therapy to the brain. The pituitary gland, located in the center of the brain, regulates the production of two hormones (FSH and LH) needed for proper ovarian function. Radiation to the brain, especially at doses of 30 Gy (3000 cGy/rads) or higher can damage the pituitary gland, leading to low levels of these hormones.

Surgery. If both ovaries were removed during cancer therapy, this always results in ovarian failure. This type of ovarian failure is sometimes called "surgical menopause".

What types of cancer therapy increase the risk of ovarian failure?

Females who received the following therapy may be at risk for ovarian failure:

- **Radiation therapy** to any of the following areas:
  - Abdomen (including para-aortic)
  - Pelvis (including iliac/inguinal)
  - Spine
  - "Inverted Y" or total lymphoid radiation
  - TBI (total body irradiation)
  - Cranial radiation at doses of 30 Gy (3000 cGy/rads) or higher
- **Chemotherapy** - the class of drugs called "alkylators" can cause ovarian failure when given in high doses. Examples of these drugs are:
  - Cyclophosphamide (Cytoxan®)
  - Ifosfamide
  - Nitrogen mustard
  - Procarbazine
  - Melphalan
  - Busulfan
  - Chlorambucil
  - Lomustine (CCNU)
  - Carmustine (BCNU)
  - Thiotepa
  - Dacarbazine (DTIC®)
  - Temozolamide
  - Carboplatin
  - Cisplatin
- **Surgery:**
  - Removal of both ovaries

What are the effects of childhood cancer therapy on the female reproductive system?

1. Failure to enter puberty. Pre-pubertal girls who received cancer therapy that resulted in ovarian failure will need hormonal therapy (hormones prescribed by a doctor) in order to progress through puberty. It is important for young girls who had cancer treatment that can affect ovarian function to have their hormone levels checked before the expected onset of puberty. If a problem is detected, they should be referred to an endocrinologist (hormone doctor) for further evaluation and management.

2. Temporary cessation of menstrual cycles. Many females who were already menstruating will stop having monthly periods during their cancer therapy. In most cases, menstrual cycles will resume sometime after cancer treatment ends, although the timing of this is unpredictable. In some cases, it may take up to several years to restart menstruation. Since eggs are released before the menstrual cycles, pregnancy can occur before the menstrual periods resume. ***If pregnancy is undesired, birth control (contraception) should be used, even if the menstrual cycles have not resumed.***

3. Permanent cessation of menstrual cycles (premature menopause). Menopause (the permanent cessation of menstrual cycles) generally occurs in women between the ages of 45 and 55. Females who were already menstruating prior to their cancer therapy sometimes develop ovarian failure as a result of their cancer treatment and never resume menstrual cycles. Others may resume menstrual cycles, but then stop menstruating much earlier than would normally be expected. If a woman who received alkylating chemotherapy agents or abdominal radiation during her cancer treatment is currently having menstrual periods, she may still be at risk for entering menopause at an early age. ***If a woman at risk for premature menopause desires to have children, it is best not to delay childbearing beyond the early thirties, because the period of fertility may be shortened after having cancer therapy.***

4. Lack of female hormones. Females with ovarian failure do not make enough estrogen. Estrogen isn't just needed for reproduction – it's also a very important hormone that is necessary for maintaining strong healthy bones, a healthy heart, and overall well-being. Young women with ovarian failure should see an endocrinologist (hormone specialist) for hormone replacement therapy, which will be necessary until they reach middle age.

5. Infertility. Infertility is the inability to achieve a pregnancy after at least one year of unprotected intercourse. In women, infertility occurs when the ovaries cannot produce eggs (ovarian failure), or when the reproductive organs are unable to sustain a pregnancy. Infertility may be the result of surgery, radiation therapy, chemotherapy, or any combination of these. *There may also be other reasons for infertility that are unrelated to cancer therapy.*

If a woman has regular monthly menstrual periods and normal hormone levels (FSH, LH and estradiol), she is likely to be fertile and able to have a baby. If a woman does NOT have monthly menstrual periods, or if she has monthly menstrual periods ONLY with the use of supplemental hormones, or if she had to take hormones in order to enter or progress through puberty, she is likely to be infertile.

Women who had surgical removal of both ovaries will be infertile. Women who had surgical removal of the uterus (hysterectomy) will also be unable to bear a child.

Women who are infertile should discuss their options with a fertility specialist and their oncologist. The use of donor eggs (surrogacy) may be an alternative for some women. Additional options may include adoption of a biologically unrelated child or child-free living.

6. Pregnancy risks. Certain therapies used during treatment for childhood cancer can sometimes increase the risk of problems that a woman may experience during pregnancy, labor, and childbirth. The following women may be at increased risk:

- Women who had radiation to the abdomen (including para-aortic areas), pelvis (including iliac/inguinal areas), or total body (TBI) may have an increased risk of miscarriage, premature delivery, or problems during labor.
- Women who received anthracycline chemotherapy (such as doxorubicin or daunorubicin), and women who received radiation to the left side of the abdomen or to the chest may be at risk for heart problems that can worsen with pregnancy and labor (see related Health Link: "*Heart Problems Following Treatment for Childhood Cancer"*).
- A small percentage of women who had a diagnosis of Wilms tumor may have an increased risk of problems with the uterus during pregnancy.

Women with these risk factors should be followed closely by an obstetrician who is qualified to care for women with high-risk pregnancies.

Fortunately, in most cases, there is no increased risk of cancer or birth defects in children born to childhood cancer survivors. In rare cases, if the type of cancer in childhood was a genetic (inherited) type, then there may be a risk of passing that type of cancer on to a child. You should check with your oncologist if you are not sure whether the type of cancer you had was genetic.

What monitoring is recommended?

Females who have had any of the cancer treatments that may affect ovarian function should have a yearly check-up that includes careful evaluation of menstrual history, hormonal status, and progression through puberty. Blood may be tested for hormone levels (FSH, LH, and estradiol). If any problems are detected, a referral to an endocrinologist (hormone specialist) and/or other specialists may be recommended. For women with ovarian failure, a bone density test (special type of x-ray) to check for thinning of the bones (osteoporosis) may also be recommended.

Written by Marcia Leonard, RN PNP, Coordinator, Long Term Follow Up Clinic, Department of Pediatric Hematology-Oncology, University of Michigan Medical Center, Ann Arbor, MI.

Reviewed by: Charles Sklar MD, Julie Blatt MD, Daniel Green MD, Melissa Hudson MD, Smita Bhatia MD, MPH, and Peggy Kulm RN, MA.

Illustrated by Devika Bhatia.

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Finding Appropriate Healthcare After Treatment for Childhood Cancer

As a childhood cancer survivor, it is important for you to have regular medical checkups, particularly since some of the treatments that you received may increase your risk for health problems as you get older. Sometimes it is challenging to find and pay for the medical care that you need. There are several things you can do to make sure you are getting the best possible care for your needs. Here are some suggestions.

If possible, find a long-term follow-up clinic. Many childhood cancer programs have long-term follow-up clinics. If you are still followed in a childhood cancer center, or if there is a childhood cancer center near where you live, call them and find out if they have a long-term follow-up program. Long-term follow-up clinics are usually designed to optimize healthcare for survivors by screening for late effects and educating survivors about ways to lower their health-related risks. They are generally an excellent place to get a comprehensive health evaluation, usually on a yearly basis. But long-term follow-up programs are not usually designed to meet the everyday healthcare needs of survivors, and most programs require that you also have a primary healthcare provider to take care of your ongoing medical needs. In addition, some long-term follow-up programs are only able to follow survivors until they reach adulthood, which may mean that they can see survivors only until they reach age 18 or 21. Therefore, even if you are attending a long-term follow-up clinic, it is also important to find a primary healthcare provider who is interested in taking care of your ongoing medical needs.

Choose a primary healthcare provider in your community. The best primary healthcare providers for adults are usually family practitioners or internists. The chance of finding a primary healthcare provider who has experience taking care of childhood cancer survivors is low, due to the rarity of serious illnesses like cancer in children. However, it is important to look for a healthcare provider who is thorough, well-trained, and a good listener. Ask friends and family members to help you identify healthcare providers with these qualities who are practicing in your area. Make an appointment for a general check-up and discuss your past medical history and health risks during this visit. It is best to do this at a time when you are well, and not when you are being seen because of an illness.

Tell your healthcare provider about the Childhood Cancer Survivor Long-Term Follow-Up Guidelines, available on the Children's Oncology Group website at www.survivorshipguidelines.org. This comprehensive set of healthcare screening and management guidelines is designed for use by healthcare professionals who are providing ongoing medical follow-up for childhood cancer survivors.

Organize a medical team to provide your local care. Get advice from your childhood cancer doctor and your primary healthcare provider about who should be on your medical team. Your team should always include a primary healthcare provider and a dentist. Depending on your situation, you may also need to include other professionals that are important for your continued health, such as a physical therapist or psychologist. Your primary healthcare provider can help you select these individuals and provide referrals for their services.

Share your medical records with all the members of your medical team. Ask the hospital or clinic to send copies of your treatment records to all your new healthcare providers. If possible, ask the doctor who treated your childhood cancer to provide you with a summary of your diagnosis and treatment, future health risks, and recommended screening. Keep a copy of the summary and important sections of your pediatric medical records in a personal medical file. Be sure that every new healthcare provider you see is aware of your medical history and any special health risks you may have because of your cancer treatment. If you need help in obtaining your medical records, *call the hospital, clinic, or medical center where you received your treatment.*

Be a partner in the healthcare that you receive. To find out if you are getting adequate care, ask yourself the following questions:

- Do I know my cancer diagnosis and specific treatment I received?
- Do I know about the health problems that can occur after this treatment?
- Have I shared this information with my healthcare providers?
- Does my healthcare provider check periodically for health problems specifically related to my childhood cancer?
- Does my healthcare provider advise me about things I should or should not do to keep healthy after my treatment for childhood cancer?

Explore all resources for paying for healthcare. Healthcare is expensive and people who have had a serious illness often face many hurdles when trying to obtain adequate insurance coverage. However, you may still be able to get insurance, even with your health history. Milestones of five, seven, and ten years from the end of treatment seem to be important to insurers. Ask your healthcare provider to write a letter to the insurance company documenting your long-term remission.

If you aren't insured, you should seek assistance from social service organizations or social workers to identify possible programs to help you obtain low cost insurance. There may be State or Federal public assistance programs that you may qualify for. If you need medical care and currently do not have insurance, you can talk to your healthcare provider about arranging a payment plan for primary care services. You may be able to have lab work done for a reduced rate at your county or city health department. If you need an evaluation by a specialist or an expensive test, ask your healthcare provider if you can be referred to a medical specialist or facility that offers discounted rates or payment plans for individuals who are uninsured.

As a survivor of childhood cancer, you have already overcome many obstacles. The process of obtaining and paying for healthcare can sometimes seem discouraging, but it is worth the effort!!

Survivorship Healthcare Coverage Checklist

Define your current healthcare needs. Ask yourself:

- Do I mainly need a healthcare provider for general check-ups?
- Do I have chronic health problems that require frequent medical visits?
- Do I have problems that need periodic monitoring by specialists?
- Am I on expensive prescription medications?
- Do I require prosthetic or rehab services?

Explore all resources for healthcare coverage:

- Private insurance coverage through a parent's or spouse's policy
- Health insurance coverage offered by your college or employer
- State or federal public assistance programs
- Discounted or free healthcare through health department clinics or church-based programs
- Low cost or free prescription programs provided by some pharmaceutical companies for people with low incomes

If you are insured, get the facts about your policy.

- What services are covered?
- Does your plan offer a discounted prescription program?
- Are referrals to specialists controlled through a primary care physician?
- Are limitations set on pre-existing medical conditions?
- Is coverage in effect only while the patient is a full-time student?
- Does coverage expire at certain age?

Ask for help in understanding current resources and locating new ones.

- Ask family members, friends, hospital or clinic insurance managers and insurance representatives to explain unclear details about insurance benefits.
- Call a clinic or hospital social worker to ask for help in finding state or community healthcare resources.
- Check out services offered by national nonprofit organizations (example, Lions Club for ocular prostheses).
- Be proactive in obtaining and maintaining health insurance coverage.
- Contact your state insurance office to get a list of insurance providers in your state.
- Call your county department of human services to find out if you qualify for healthcare through state or federal programs for people with low income or disability.
- Begin applications.
- Avoid lapses in coverage. Plan for transitions in health insurance coverage that occur with college graduation or job changes.

Be aware of the laws that help you keep insurance benefits:

- **COBRA** (Consolidated Omnibus Budge Reconciliation Act) requires employers or larger businesses to make insurance available for a limited time to employees (and their dependents) who are fired or laid off.
- **HIPAA** (Health Insurance Portability and Accountability Act of 1996) allows people with pre-existing conditions to keep comprehensive insurance coverage when they are changing insurance plans or jobs. Certain conditions apply that may limit the help available to you under HIPAA. Contact your social worker, insurance provider, or state insurance department with questions.

Be persistent when meeting obstacles. Try not to get overwhelmed.

- Follow through with applications.
- Appeal denials with letters of support from your healthcare provider.
- Begin new applications.
- Contact groups such as Candlelighters and the National Coalition of Cancer Survivors for more information about healthcare resources.
- Don't give up!

Recommended Resources:

The National Coalition of Cancer Survivors is a patient-led advocacy organization for cancer survivors. Their booklet, "A Cancer Survivor's Almanac," lists hundreds of organizations and agencies that offer help regarding specific cancer-related issues, including finding affordable healthcare. The booklet is available on their website, http://www.canceradvocacy.org. Their phone number is (877) 622-7937.

HIPAA. Information about the Health Insurance Portability and Accountability Act of 1996, which helps people with pre-existing health conditions get and keep health insurance, is available on the website of the U.S. Department of Health and Human Services at: http://cms.hhs.gov/hipaa/hipaa1/content/cons.asp

State Insurance Commissioners. Contact information for insurance commissioners of each state is also listed on the HIPAA site at: http://cms.hhs.gov/hipaa/hipaa1/content/contacts.asp#ContactCMS

Candlelighters Childhood Cancer Foundation® (CCCF) is a non-profit organization whose mission is to educate, support, serve, and advocate for families of children with cancer and childhood cancer survivors. 800-366-CCCF (800-366-2223) http://www.candlelighters.org/

Cancer Care, a nonprofit organization dedicated to providing emotional support, information, and practical help to people with cancer and their loved ones. 1-800-813-HOPE (4637). http://www.cancercare.org/

Written by Melissa Hudson, MD, Sally Wiard, MSW, LCSW, and Allison Hester, RN, MSN, CPNP. Adapted from the CCSS Newsletter, Spring 2003, used with permission.

Melissa Hudson, MD directs the After Completion of therapy (ACT) clinic at St. Jude Children's Research Hospital in Memphis, TN.

Sally Wiard, MSW, LCSW is a social worker in the After Completion of therapy (ACT) clinic at St. Jude Children's Research Hospital in Memphis, TN.

Allison Hester, RN, MSN, CPNP is a pediatric nurse practitioner in the After Completion of therapy (ACT) clinic at St. Jude Children's Research Hospital in Memphis, TN.

Reviewed by Leslie L. Robison PhD, Kevin Oeffinger MD, Peggy Kulm RN, MA, and Octavio Zavala.

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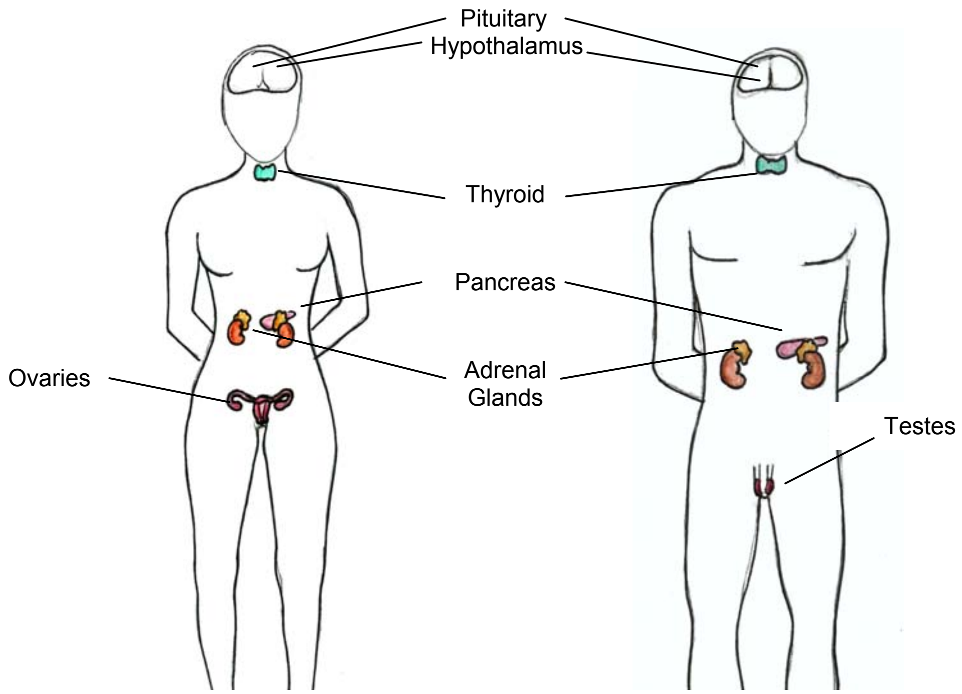
Endocrine Problems after Childhood Cancer:
Growth Hormone (GH) Deficiency

Some people who were treated for cancer during childhood may develop endocrine (hormone) problems as a result of changes in the function of a complex system of glands known as the endocrine system.

What is the endocrine system?

The endocrine system is a group of glands that regulate many body functions including growth, puberty, energy level, urine production, and stress response. Glands of the endocrine system include the pituitary, hypothalamus, thyroid, adrenals, pancreas, ovaries (in females), and testes (in males). The hypothalamus and pituitary are sometimes called the "master glands" because they control many of the other glands in the endocrine system. Unfortunately, some treatments given for childhood cancer can damage the endocrine system, resulting in a variety of problems.



What are hormones?

Hormones are chemical messengers that carry information from the endocrine glands through the bloodstream to the body's cells. The endocrine system makes many hormones (such as growth hormone, sex hormones, adrenal and thyroid hormones) that work together to maintain specific bodily functions.

What is growth hormone deficiency?

Growth hormone (GH) is made by the pituitary gland. In order for children to grow to their full height potential, they need adequate amounts of GH. GH works with thyroid hormone, exercise, proper nutrition, and rest to help children and teenagers grow. GH also helps maintain normal blood sugar levels and is necessary for the normal development of teeth. In addition to helping with bone growth, GH affects how well the heart and blood vessels work, how the body uses fat, makes muscle, and strengthens bones, and generally influences overall health throughout life. In healthy people, GH production continues into adulthood. Adults need small amounts of GH to maintain proper amounts of fat, muscle and bone. GH may also play a role in stimulating and controlling areas of the brain that regulate mood and emotion.

Cancer treatments, such as radiation or surgical procedures to structures in the head or brain, may cause malfunction of the glands that control growth. As a result, the pituitary gland may not make enough GH, resulting in growth hormone deficiency. GH deficiency can also occur in people who have never had cancer treatment.

Signs and symptoms of growth hormone deficiency

A noticeable slowing of growth (height) is one of the most obvious signs of GH deficiency in children. A GH deficient child usually grows less than 2 inches per year. Children with GH deficiency are smaller and tend to look younger than peers, but they usually have normal body proportions.

Adults who have GH deficiency may have a variety of different physical symptoms, such as thinning of the bones, decreased muscle strength, increased body fat, or high blood cholesterol levels. Adults may also have emotional symptoms such as feeling tired, anxious, irritable, pessimistic, unmotivated, or having a decreased interest in sex.

Risk factors for growth hormone deficiency

Risk factors related to treatment for cancer during childhood include:

- Cancer treatment before reaching adult height, especially if you were very young age at the time of cancer treatment
- Radiation to the head or brain, especially in doses of 18 Gy (1800 cGy/rads) or higher, including the following fields:
    - Cranial (whole brain), especially if given before bone marrow or stem cell transplant
    - Craniospinal
    - Nasopharyngeal (nose and throat)
    - Oropharyngeal (mouth and throat)
    - Eye and Orbit
    - Ear
    - Infratemporal (midfacial area behind the cheekbones)
    - Total body irradiation (TBI), especially at a dose of 10 Gy (1000 cGy/rads) or higher in a single fraction or 12 Gy (1200 cGy/rads) or higher in fractionated (split) doses
- Surgery to the brain, especially the central region of the brain where the pituitary gland is located (suprasellar region)

Recommended screening after cancer treatment

All childhood cancer survivors should have a **yearly physical examination** including measurement of height and weight, and assessment of pubertal status, nutritional status, and overall well-being. **For patients with the risk factors listed above, this screening should be done every 6 months until growth is completed.** If there are **signs of poor growth,** an x-ray of the wrist (**bone age x-ray**) should be done. Evaluation for other potential causes of growth problems, such as low thyroid function, should also be explored.

If GH deficiency is suspected, your healthcare provider will probably refer you to an endocrinologist (doctor who specializes in hormone problems). The endocrinologist will do more specific tests to evaluate the problem.

How is growth hormone deficiency treated?

If GH deficiency is detected, your endocrinologist will suggest treatment options for you. Usually this involves supplementing or replacing the GH that your pituitary gland is not making on its own. Synthetic GH is given by injection. GH is usually given for several years, until the person reaches acceptable adult height or maximum potential. Your endocrinologist can provide you with a realistic expectation about your growth potential. Treatment options for GH deficiency that persists into adulthood should be discussed on an individual basis with your endocrinologist.

Written by Debra Eshelman, RN, MSN, CPNP, pediatric nurse practitioner and coordinator for the After the Cancer Experience (ACE) Pediatric and Young Adult Survivor Programs at Children's Medical Center of Dallas and the University of Texas Southwestern Medical Center, Dallas, TX.

Reviewers: Lillian R. Meacham MD, Priscilla Rieves, MS, RN, CPNP, Charles Sklar MD, Julie Blatt MD, Melissa Hudson MD, and Winnie Kittiko RN, MS.

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Health Promotion through Diet and Physical Activity

Good nutrition and physical exercise offer many benefits to childhood cancer survivors. These include:

- Healing tissues and organs damaged by cancer and its treatment
- Building strength and endurance
- Reducing the risk of certain types of adult cancers and other diseases
- Decreasing stress and providing a feeling of well-being

Impact of Childhood Cancer on Nutrition and Physical Activity

The effects of childhood cancer on nutrition and physical activity will be different for each individual survivor. Nutrition can be affected in a number of ways. Some people may have aversions to certain foods due to tastes, smells, or sights associated with their prior therapy. Others may have developed intolerance to certain foods, such as milk products. People who have had radiation to the face or neck may have a lack of saliva that can cause foods to taste pasty and dry. Dental problems can cause problems with chewing food. People who have had radiation to the abdomen or who have chronic graft-versus-host disease after stem cell transplant may have trouble absorbing certain foods. Any of these problems can result in poor nutrition and trouble maintaining a healthy weight.

Other survivors may have problems with gaining too much weight. Treatments for childhood cancer that can result in problems with excess weight gain include radiation to the brain, head, or total body. This is more likely to occur if the radiation was given in high doses, or if the person also received treatment with corticosteroids (prednisone or dexamethasone). Associated health problems that may result from radiation and contribute to weight gain include low levels of growth hormone or thyroid hormone.

There are many factors that can influence a survivor's ability to perform physical exercise. Individuals who have had an amputation, bone graft or joint replacement surgery, high dosages of radiation to a bone, or joint damage as a result of treatment may have restrictions or limitations in their activities. Heart or lung damage from cancer treatment may also limit the ability to be physically active. Nerve damage from cancer therapy can sometimes impair sensation and coordination. Individuals who have survived brain tumors often have problems with balance and coordination as a result of their tumor, surgery, or therapy. *(See related Health Links: Limb Salvage after Bone Cancer, Avascular Necrosis, Peripheral Neuropathy, Pulmonary Health, and Heart Problems Following Treatment for Childhood Cancer).*

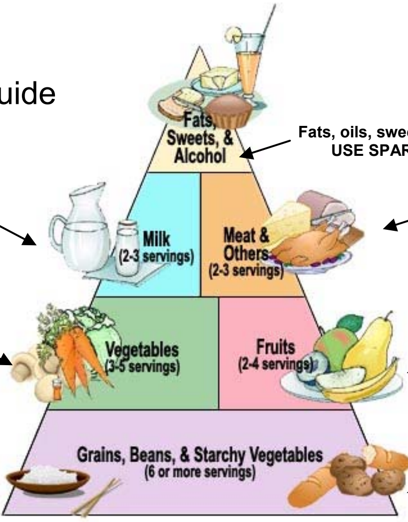
Childhood cancer and its treatment should not be used as an excuse for not eating a healthy diet or staying physically active. However, many survivors, like many people who have never experienced cancer, make lifestyle choices (such as what they eat and how they exercise) that are not always in their best interest. Now is a good time to begin making healthy choices about diet and exercise. These choices can have a positive effect on your health for many years to come.

Developing a Healthy Nutrition Plan

Suggestions for a healthy diet include:

- Choose a variety of foods from all the food groups. Use the Food Guide Pyramid to help choose foods for a well-balanced meal plan.
- Eat at least 5 servings a day of fruits and vegetables, including citrus fruits and dark-green and deep-yellow vegetables.
- When drinking juice, choose 100% fruit or vegetable juice.
- Eat plenty of high-fiber foods, such as whole grain breads, rice, pasta and cereals. Avoid foods high in sugars or refined carbohydrates.
- Buy a new fruit, vegetable, low-fat food, or wholegrain product each time you shop for groceries.
- Decrease the amount of fat in your meals by baking or boiling foods.
- Limit intake of red meat and substitute fish, poultry or beans. When you eat meat, select leaner and smaller portions.
- Limit fried and high-fat foods, such as French fries, snack chips, cheeseburgers, and pizza
- Choose low-fat milk and dairy products.
- Avoid salt-cured, smoked, charbroiled and pickled foods.

The Food Guide Pyramid



Fats, oils, sweets, alcohol
USE SPARINGLY

Milk, yogurt, cheese
2-3 SERVINGS

Meat, poultry, fish, eggs, nuts
2-3 SERVINGS

Vegetables
3-5 SERVINGS

Fruits
2-4 SERVINGS

Bread, cereal, rice, pasta, beans, starchy vegetables
6 OR MORE SERVINGS

If you need to lose weight, it is advisable to consult with your health care team and a nutritionist to develop a nutrition plan. Herbal or dietary supplements should be discussed to determine if they are truly healthy. There are several questions you should ask yourself to make sure your nutrition plan will be effective.

- Do you have a realistic, achievable weight goal?
- Does your plan include foods that you will enjoy eating for the rest of your life, not just a few weeks or months?
- Does your plan include a variety of foods?
- Are foods on your plan easily available at your supermarket?
- Does your plan fit into your lifestyle, daily schedule and budget?
- Does your plan include lifestyle changes that will help you maintain your weight loss?

Developing a Healthy Physical Exercise Plan

Check with your healthcare team before starting a physical exercise plan or engaging in new sports and recreational activities. It is important to be aware of activities that you can participate in actively and those you should avoid.

When selecting an exercise plan, ask yourself these questions:

- Do you have reasonable goals based on your present strength and endurance?
- Is the activity safe for you to perform?
- Does the plan fit into your lifestyle and schedule?
- Does the activity require special equipment or protective gear and will your budget cover the expense?
- Do you need to make modifications in the sport or activity based on a special need?
- Do you enjoy doing the sport or activity?

Here are a few helpful suggestions when implementing your exercise plan:

- Start out slow. Don't attempt activities that are too strenuous or put you at risk for muscle strain.
- Begin your exercise plan with a warm-up program and end with a cool-down activity, such as stretching and slow easy movements.
- Use correct posture when exercising.
- Exercise until you are tired, but not in pain.
- Identify the muscles you want to strengthen and choose exercises that work on those muscles
- Balance exercises between different parts of your body.
- To avoid injury, use the right equipment and shoes.
- Avoid running, jogging, or aerobic dancing on hard surfaces such as asphalt or concrete.
- Increase your workout by no more than 10 percent per week.

The National Cancer Institute recommends at least moderate intensity exercise at least 30 minutes per day on most days of the week. If you don't have the time for a 30-minute session all at once, you can break it up into three different sessions of 10 minutes each. The American Cancer Society recommends that children and adolescents engage in at least 60 minutes per day of moderate to vigorous physical activity at least 5 days per week. Here are some practical suggestions to try to incorporate physical activity in your daily schedule.

- Park a good distance from your place of work and walk the extra distance each day.
- Set aside 30 minutes a day to take a brisk walk.
- Take the stairs instead of the elevator.
- If you have a sit-down job, get up and stretch your muscles every hour and take a walk during your lunch or break.
- Ride a bike to work or for running errands.

- Plant a garden, wash your car yourself, mow the lawn, paint furniture, clean out the garage and catch up on all those chores you have been meaning to do – instead of watching TV or playing on the computer.
- Watch TV or read the newspaper while on a stationary bike or treadmill.
- Plan active family outings, instead of attending a movie.
- Exercise with a friend you enjoy spending time with.
- Join a sports team.

Physical Activity for Survivors with Special Needs

Survivors who have special needs can participate in most activities, but the assistance of a physical or occupational therapist may be necessary to help adapt the activity for success. A social worker may be able to assist with obtaining medical reimbursement or provide suggestions for obtaining funding for special equipment. Specialized programs for individuals with special needs, organizations and other resources are often available through your healthcare center or in your local community.

Adapted by Sharon Frierdich CPNP from "Staying Physically Healthy, Play Safely, Play Well," St. Jude Children's Research Hospital, used with permission.

Sharon Frierdich, RN, MS, CPNP is a pediatric nurse practitioner, Pediatric Hematology/Oncology, University of Wisconsin Children's Hospital, Madison, WI.

Reviewed by Kevin Oeffinger MD, Missy Layfield and Octavio Zavala.

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Hearing Problems after Treatment for Childhood Cancer

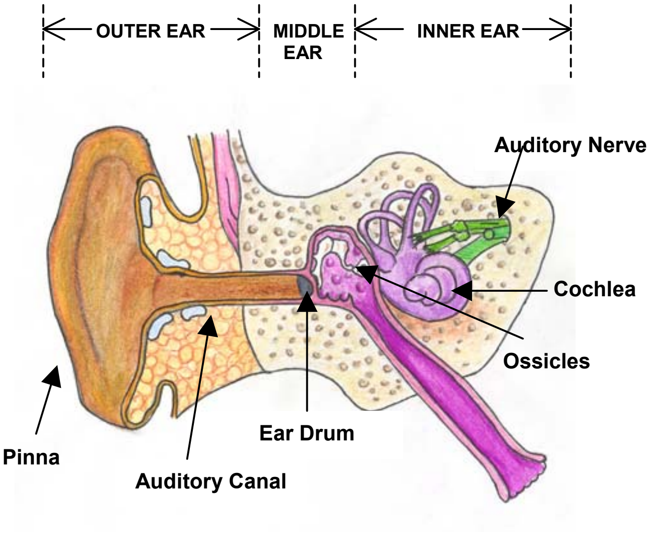
Some chemotherapy drugs, other medications, or radiation needed for treatment of childhood cancer can damage hearing. Hearing loss interferes with daily living. If you received these treatments, it is important to have your hearing checked and to obtain treatment if hearing loss is found.

How do the ears work?

It's easier to understand hearing loss if you understand how the ears work. The ear is made up of three main parts, known as the outer, middle, and inner ear.

Outer ear

Sound waves travel through the air and first enter the body through the outer ear. The part of the ear that can be seen outside the body is called the pinna. The pinna collects and funnels sound into the auditory (ear) canal. The auditory canal is like a tunnel. It makes the sound louder and directs it toward the middle ear.



Middle Ear

The eardrum separates the outer ear from the middle ear, a chamber that is normally filled with air. Inside the middle ear are three tiny bones (ossicles) that form a chain connecting the eardrum to the opening of the inner ear. Sound waves cause the eardrum to vibrate. These vibrations cause the three tiny bones in the middle ear to move, transmitting the sound to the inner ear.

Inner Ear

The inner ear is known as the cochlea, and it is filled with fluid. The cochlea contains thousands of tiny nerve endings, known as sensory hair cells. Sounds travels in waves through the fluid of the inner ear. The sensory hair cells change the sound waves into nerve impulses that are sent to the brain by way of the auditory nerve (also known as the eighth cranial nerve). In the cochlea, the sensory hair cells are arranged in order of pitch, from low-pitched sounds (such as a man's voice) to very high-pitched sounds (such as a bird's chirping). Each hair cell is sensitive to a specific range of pitches.

What are the types of hearing loss?

Hearing loss that occurs in the outer or middle ear is called a ***conductive hearing loss***. This means that the hearing loss is due to a problem in transmission of sound from the air to the inner ear. An example of this would be changes in hearing because of fluid collection in the middle ear. Sometimes this happens when people have ear infections. The fluid "muffles" the sound when it is traveling through the middle ear.

Hearing loss that results from damage to the inner ear or auditory nerve is called ***sensorineural hearing loss***. An example of this would be damage to the sensory hair cells in the inner ear from chemotherapy. Even though sound waves still move through the inner ear fluid, they can no longer be changed into nerve impulses, so the sound does not reach the brain. Sensory hair cells that process high-pitched sounds are usually damaged first, followed by damage to the sensory hair cells that process lower-pitched sounds.

Hearing loss with both conductive and sensorineural components is called **mixed hearing loss**.

What types of cancer therapy increase the risk of hearing loss?

The following cancer treatments can potentially cause hearing loss:

- Chemotherapy from the “platinum” group, such as cisplatin and carboplatin
- Antibiotics from the “aminoglycoside” group, such as gentamicin or tobramycin
- Diuretics from the “loop” classification, such as furosemide (Lasix) or ethacrynic acid (Edecrin)
- Radiation to the head, especially when the beam is directed at the brainstem or ear
- Surgery involving the brain, ear or auditory (eighth cranial) nerve

Which survivors are most likely to have hearing loss?

Survivors at highest risk for hearing loss are those who:

- Had other risk factors for hearing loss before the diagnosis of cancer (such as prior treatment with aminoglycoside antibiotics, low birth weight, or meningitis)
- Were younger than 4 years of age at the time that they received treatments that can cause damage to the ear
- Received cisplatin in a total (cumulative) dose of 360 mg/m^2 or higher. (Information about the dose of carboplatin that places survivors at highest risk for hearing loss is not definitive; however, carboplatin doses of about 2000 mg/m^2 have been associated with significant hearing loss).
- Received radiation to the ear, brain, nose, sinuses, throat, or midfacial area behind the cheekbones, especially at doses of 30 Gy (3000 cGy/rads) or higher
- Had a tumor, surgery, or severe infection that involved the brain, ear or auditory nerve, or required placement of a VP shunt
- Received more than one type of treatment that can cause hearing loss (such as the combination of brain radiation and cisplatin chemotherapy, or treatment with both cisplatin and carboplatin chemotherapy)
- Had poor kidney function at the time that they received chemotherapy or other medications that can damage hearing

What are the effects of childhood cancer treatment on hearing?

Radiation to the ear or brain can cause inflammation or ear wax buildup in the outer ear, problems with fluid buildup in the middle ear, or stiffness of the eardrum or middle ear bones. Any of these problems can result in conductive hearing loss. Radiation can also damage the sensory hair cells in the inner ear, causing sensorineural hearing loss. Damage from radiation may affect one or both ears, depending on the area of radiation treatment. Conductive hearing loss may improve over time, but sensorineural hearing loss is usually permanent.

Platinum chemotherapy and aminoglycoside antibiotics damage sensory hair cells in the inner ear, causing sensorineural hearing loss. Most often, the effect is similar in both ears and is permanent.

Damage from loop diuretics is caused by changes in the balance of fluids and salts within the inner ear, resulting in tissue swelling and problems with transmission of nerve signals. Fortunately, this type of hearing loss is usually temporary, but sometimes it can be permanent, especially when the diuretic is given in combination with platinum chemotherapy or aminoglycoside antibiotics.

What are the symptoms of hearing loss?

Symptoms of hearing loss may include:

- Ringing or tinkling sounds in the ear
- Difficulty hearing in the presence of background noises
- Not paying attention to sounds (such as voices, environmental noises)
- Some people may have no symptoms at all

What monitoring is recommended?

Testing should be done by an experienced audiologist (a professional trained in hearing disorders).

- Hearing is usually tested by doing an **audiogram**. An audiogram is done in a soundproof room. The person being tested wears earphones and listens for sounds of different pitches and different degrees of loudness. Even very young children can usually have an audiogram done by an experienced pediatric audiologist using a game format.

- People who are not able to have an audiogram (such as those who are unable to understand the test instructions) can have their hearing tested using **Brainstem Auditory Evoked Response (BAER)**. The person having this test is usually given medicine so that they go to sleep. Then the brainwaves are recorded while sounds are delivered to the sleeping person through earphones.

How often should hearing be tested?

The chart below provides recommendations for monitoring:

Treatment	Dose	How often hearing should be tested
Cisplatin Carboplatin	Any	• **Once, at entry into long-term follow-up** (at least 2 years after completion of cancer therapy). • **If problems are detected, repeat yearly** until stable. • **If there is evidence of progressive hearing loss, test more frequently** as needed, until stable.
Radiation field: • Ear • Brain (cranial) • Infratemporal (area behind the cheekbones) • Nasopharyngeal (nose, sinuses and/or throat)	30 Gy (3000 cGy) or higher	• **Yearly for 5 years** after completion of cancer treatment (and if younger than age 10, continue yearly testing until reaching age 10). Then: - If no hearing problem is detected, test every 5 years. - If a hearing problem is present, test at least yearly or as recommended by a hearing specialist.
	Less than 30 Gy (3000 cGy)	• **Once, at entry into long-term follow-up** (at least 2 years after completion of cancer therapy). • **Repeat as needed**, if problems are detected.
Aminoglycoside antibiotics or loop diuretics	Any	• If there is any suspicion of a hearing problem, **test at least once** following completion of therapy.

What can be done if hearing loss is detected?

If hearing loss is detected, it is important to have an evaluation by an audiologist or otologist (doctor who specializes in hearing disorders). Hearing loss can have a significant impact on a person's ability to communicate and carry out daily activities. Younger children are at significant risk for school, learning, and social difficulties and problems with language development. It is therefore very important for a person with hearing loss to find the services and assistance that will best help to maximize their potential to communicate effectively. There are many options available, and these can be used in various combinations, depending on the hearing problem.

Hearing aids make sounds louder. Several types are available, depending on the age and size of the person and the extent of hearing loss. Most children under 12 years of age wear a behind-the-ear model to allow for adjustments as the child grows. These are available in a variety of colors – allowing for personalization and assisting with the child's acceptance of the hearing aid. Teenagers and adults may benefit from a smaller, in-the-ear or in-the-canal model. It is very important that the hearing aid batteries are fresh and that the hearing aid is turned to the "on" position when in use.

Auditory trainers (also known as "FM trainers") are devices that are particularly useful in the school setting. The person who is speaking (usually the teacher) wears a microphone that transmits sound over FM radio waves. The person with hearing loss wears a receiver that picks up the sound. This device can be worn alone or attached to the hearing aid and allows the person with hearing loss to hear the speaker clearly, even in a noisy environment.

Other assistive devices are also available for people with hearing loss. These include and telephone amplifiers and teletypewriters (TTYs – sometimes also referred to as Telephone Devices for the Deaf or TDDs). Specialized appliances designed for people with hearing loss include alarm clocks that vibrate and smoke detectors with flashing lights. Closed captioning for television is widely available. The Internet is also a helpful communication tool for people with hearing loss, providing options such as e-mail, on-line discussions, and access to information via websites. Newer pagers offer text messaging, instant messaging, Internet access, and photo transmission.

Telecommunication relay services are available in video and voice/text formats. The video relay service is internet-based and allows a person using signed language to communicate via a video interpreter, who translates the signed language into voice or text. The voice/text relay service allows a person using a teletypewriter to communicate through an operator, who then relays the message to the hearing person in spoken form.

Cochlear implants may be an option for people with profound hearing loss who are unable to benefit from hearing aids. These electronic devices are surgically placed behind the ear and electrodes are threaded into the inner ear. A microphone and speech processor are then used to transmit sound to the electrodes, stimulating the auditory nerve and allowing sound perception by the brain. After the cochlear implant is installed, auditory training is given for a period of time to teach the individual to recognize and interpret sounds.

Alternate or supplementary communication methods, including speechreading, signed language and cued speech, are available for people with significant hearing loss. Spoken language may also be an option, but usually requires an intensive educational approach with speech therapy. In the United States, healthcare organizations that receive federal funding are required to provide sign language interpreters when requested by a patient.

Community and educational resources in the United States include services through local public school districts or referral agencies (available under the IDEA legislation, PL 105-17), such as intensive speech therapy and auditory trainers for classroom use. Sometimes special accommodations, such as seating in the front of the classroom are all that is needed, but this usually requires that the parent request an Individualized Education Plan (IEP) for the child through the school district *(see related Health Link: "Educational Issues Following Treatment for Childhood Cancer")*. Many hospitals have a teacher or school liaison that can assist with arranging for the IEP and other specialized services they may be needed. The Americans with Disabilities Act (ADA, PL 101-336) guarantees people with hearing loss equal access to public events, spaces and opportunities, including text telephones and telephone amplifiers in public places, and assistive listening devices in theaters. Some theaters also offer special showings of newly released movies with captioning.

What can I do to protect my hearing?

If you have experienced hearing loss, or have received therapy that has the potential to damage your hearing, you should discuss this with your healthcare provider. Be sure to obtain prompt evaluation and treatment for ear infections, swimmer's ear, and earwax impaction. Whenever possible, ask your healthcare provider to consider alternatives to medications that have the potential to cause further hearing loss, including aminoglycoside antibiotics, loop diuretics, salicylates (such as aspirin) and chelating agents (such as deferoxamine).

You should also take care to protect your ears from loud noises. In fact, loud noises can cause significant damage to your ears. Examples of items and activities that can be hazardous to your hearing include:

Appliances	Occupations	Recreation
Hair dryers	Firefighters	Hunting
Vacuum cleaners	Construction workers, farmers	Boating or water skiing
Lawn mowers	Airport workers	Motorcycling or four-wheeling
Yard trimmers or leaf blowers	Cab, truck, and bus drivers	Stereo headphones

If you cannot avoid exposure to noise, you should:

- Wear hearing protectors such as ear plugs or ear muffs
- Limit periods of exposure to noise (for example, if you are at a loud concert, go to a quieter area for a while to give your ears a break)

Be aware of the noise in your environment and take control of it when you can.

Written by Wendy Landier, RN, MSN, CPNP, CPON,® pediatric nurse practitioner and clinical director of the Survivorship Clinic, Division of Pediatrics, City of Hope National Medical Center, Duarte, CA.

Portions adapted from "Noise and Hearing Loss; Do You Know. . .An Educational Series for Patients and Their Families," St. Jude Children's Research Hospital, Memphis, TN (used with permission).

Reviewed by Kathleen Ruccione RN, MPH, FAAN, CPON,® Debra Friedman MD, Smita Bhatia MD, MPH, Louis S. Constine MD, and Melissa Hudson MD.

Illustrated by Devika Bhatia.

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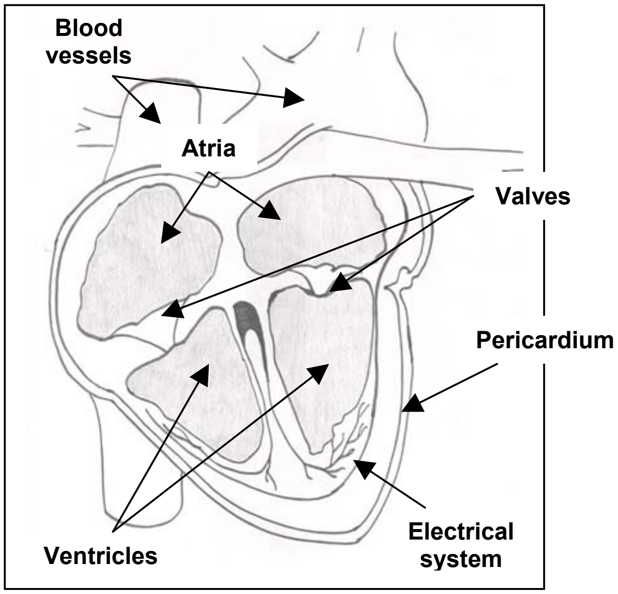
Heart Problems Following Treatment for Childhood Cancer

Most childhood cancer survivors do not develop heart problems; however, certain types of cancer treatment given during childhood can sometimes result in problems with the heart. Since heart problems may occur many years after cancer treatment, it is important for childhood cancer survivors to be aware of any treatments they may have received that can affect the heart. That way, they can take steps to keep their heart healthy, including regular medical check-ups and tests to monitor heart function. And if a problem develops, it can be detected and treated early.

How does the heart work?

The heart is a muscular organ that is at the center of the body's circulatory system. The heart is responsible for pumping blood with oxygen and nutrients to body tissues. There are four chambers (two atria and two ventricles) within the heart that work together to pump blood. Valves direct the flow of blood through the heart chambers and into the blood vessels. The rhythm of heart contraction and rate of the heartbeat are coordinated by nerves that send electrical impulses to different parts of the heart. A thin membrane (pericardium) surrounds and protects the heart and anchors it within the chest.



What types of cancer treatments can cause heart problems?

The heart can be affected by certain types of chemotherapy and by radiation therapy.

Anthracycline chemotherapy

The anthracyclines are a type of chemotherapy used to treat many childhood cancers. This type of chemotherapy can sometimes affect the heart. Commonly used anthracyclines include:

- Doxorubicin (Adriamycin®)
- Daunorubicin (daunomycin, Cerubidine®)
- Idarubicin (Idamycin®)
- Mitoxantrone (Novantrone®)
- Epirubicin

Radiation therapy

Heart problems may also result from radiation therapy to the heart or surrounding tissues. This includes radiation to the following areas:

- Chest or thorax (including “mantle” and “mediastinal” treatment fields)
- Lungs
- Spine (chest or “thoracic” portion)
- Whole or upper abdomen
- Left kidney region (left flank or left upper abdomen)
- Total body (TBI)

What heart problems can occur after treatment for childhood cancer?

There are several types of heart problems that may result from cancer treatments:

- The muscle cells of the heart may be damaged so that the heart doesn’t contract and relax normally (**cardiomyopathy**).

- The electrical pathways that conduct impulses to control heart rhythm may be scarred or damaged, resulting in abnormally fast, slow, or irregular heart beats (**arrhythmias**).

- The valves and blood vessels of the heart may be damaged, resulting in stiff or leaky valves (**valvular stenosis or insufficiency**).

- The protective covering of the heart may become inflamed (**pericarditis**) or scarred (**pericardial fibrosis**).

- The blood vessels of the heart may become scarred or blocked (**coronary artery disease**), preventing delivery of oxygen and nutrients to the heart and other tissues.

In severe cases, these problems may result in the death of heart tissue (heart attack or myocardial infarction) or an inability of the heart to pump blood properly (congestive heart failure).

Which types of cancer treatment are associated with which heart problems?

- **Anthracyclines** may cause problems with heart muscle function (cardiomyopathy) and abnormal heart rhythms (arrhythmias).

- **Radiation therapy** may result in scarring and stiffening of heart tissues, causing abnormal heart rhythm (arrhythmia) and problems with the heart muscle (cardiomyopathy), heart valves (valvular stenosis or insufficiency), blood vessels (coronary artery disease), and membrane surrounding the heart (pericarditis or pericardial fibrosis).

Are there other risk factors for heart problems?

Some other medical conditions may also increase the risk of heart problems from chemotherapy or radiation therapy. These include obesity, high blood pressure, high cholesterol or triglyceride levels in the blood, and diabetes. You may have a higher risk of having heart problems if these conditions run in your family. Heart disease is also more common in women who have gone through menopause, so female survivors who go through an early menopause may be at higher risk. Many health behaviors can add to the risk of heart disease including smoking, having an inactive (sedentary) lifestyle, and eating a diet high in fat.

Who is at risk for developing heart problems?

The risk of developing a heart problem after childhood cancer treatment is related to several factors:

- The age of the patient at the time of cancer therapy
- The total dose of anthracycline chemotherapy
- The total dose of chest radiation
- The amount of the heart tissue included in the radiation treatment field
- Treatment with other medications that affect heart function
- The presence of other conditions that affect heart function

Most childhood cancer survivors who were treated with anthracyclines or chest radiation have no heart damage at all. Some survivors have very mild changes in heart size or function that have not gotten worse over time. Only a small number of survivors have developed severe heart problems leading to heart failure or dangerous heart rhythms. Overall, the risk of developing heart problems after childhood cancer therapy is highest in survivors treated with higher doses of anthracyclines or chest radiation, especially those who received both treatments at a young age.

Since we do not understand why some survivors develop heart problems after treatment for childhood cancer and others do not (even when they have gotten the same treatment), it is important for each childhood cancer survivor treated with anthracyclines or chest radiation to continue to have regular medical check-ups so that if a problem with the heart develops, it can be detected and treated early.

The highest risk factors for anthracyclines and radiation are listed below separately, although there is overlap:

What factors are associated with increased risk for heart problems after anthracycline chemotherapy?

- Receiving a total anthracycline dose of 300 mg/m^2 (milligrams per square meter of body surface area) or more when younger than 18 years of age
- Receiving a total anthracycline dose of 550 mg/m^2 or more when 18 years or older

- Being female
- Being of African descent
- Being younger at the time of treatment. (Anyone treated before the age of 5 years, and especially those treated as infants, are at increased risk.)
- Receiving high doses of cyclophosphamide (Cytoxan®) before a bone marrow or stem cell transplant
- Receiving treatment with Amsacrine, another chemotherapy drug that may affect the heart
- Receiving treatment with radiation to the heart or surrounding tissues

What factors are associated with increased risk for heart problems after treatment with radiation?

- Receiving radiation at doses of 20 Gy (2000 cGy/rads) or more to the following areas (fields):
    - Chest/thorax
    - Mantle (from the chin to the upper abdomen)
    - Mediastinal (central part of the chest)
    - Lung
    - Whole or upper abdomen
    - Left kidney region (left upper abdomen or left flank)
- Receiving radiation to the spine at doses of 30 Gy (3000 cGy/rads) or higher
- Receiving total body irradiation (TBI)
- Receiving high doses of cyclophosphamide (Cytoxan®) before a bone marrow or stem cell transplant
- Receiving anthracycline chemotherapy
- Receiving treatment with Amsacrine, another chemotherapy drug that may affect the heart
- Receiving treatment many years ago. (Modern radiation techniques using lower total doses and better heart shielding are less likely to cause damage.)

What are the symptoms of heart problems?

- Shortness of breath
- Dizziness
- Lightheadedness, near fainting or fainting
- Severe fatigue preventing exercise or normal play
- Chest pain that feels like a heavy pressure or fullness and travels to the arm, chin or face.

- Sweating, nausea or shortness of breath with chest pain
- Sharp piercing pain in the center or the left side of the chest (often worsens with taking a deep breath)
- Very swollen feet or ankles (so swollen that if a finger is pressed firmly on the area for a few seconds it leaves an indentation)
- Cough and wheezing that doesn't go away
- Periods of heart racing or throbbing
- Periods of irregular heartbeat (feeling of the heart skipping beats)

What other conditions or activities can make these heart problems worsen?

A heart affected by anthracyclines and chest radiation may not be able to handle the stress of certain conditions that dramatically increase the heart rate, blood pressure, or volume of blood in the circulatory system. These changes may occur during **pregnancy** or during illnesses with **high fevers.** If your cancer treatment included medicines that can affect heart function, be sure that your doctor is aware, so that steps can be taken to reduce the stress on your heart.

Some drugs may cause stress on the circulatory system, including **cocaine, diet pills, ephedra, mahuang, and performance enhancing drugs**. These types of drugs have been associated with worsening of heart function and even death in childhood cancer survivors who received anthracycline chemotherapy.

Exercise is usually good for the heart, but some types of exercise are particularly stressful to the heart. These include intensive isometric activities, such as **heavy weight lifting and wrestling.** When a person is squatting to lift a very heavy weight, the heart must work harder because the blood pressure in the circulatory system increases as a person strains. Using lower amounts of weights to perform an exercise no more than 15 to 20 times in a row with ease (limited high repetition weight lifting) is much less stressful to the heart and is more likely to be safe.

Aerobic exercise (brisk walking, running) is also generally safe and actually healthy for the heart. To be safe, survivors treated with anthracyclines or chest radiation therapy should check with their healthcare provider before beginning any exercise program. Those who choose to engage in strenuous or varsity team sports should discuss appropriate guidelines and a plan for ongoing monitoring with their cardiologist.

What monitoring is required for potential heart problems?

Anyone treated with anthracycline chemotherapy or chest radiation for childhood cancer should have a yearly check-up that should include specific evaluation of any symptoms relating to the heart. In addition, an electrocardiogram (ECG, EKG) should be done at the time the survivor enters long-term follow-up (usually about 5 years from diagnosis or 2 years from completion of therapy). An echocardiogram or MUGA scan is also recommended at the first long-term follow-up visit, then according to the following schedule (or as recommended by your healthcare provider):

Schedule for Echocardiogram or MUGA Scans

Age at treatment*	Chest radiation	Total anthracycline dose**	Recommended frequency of ECHO or MUGA
< 1 year	Yes	Any	Every year
	No	<200 mg/m^2	Every 2 years
		≥200 mg/m^2	Every year
1 to 4 years old	Yes	Any	Every year
	No	<100 mg/m^2	Every 5 years
		≥100 to <300 mg/m^2	Every 2 years
		≥300 mg/m^2	Every year
≥5 years old	Yes	<300 mg/m^2	Every 2 years
		≥300 mg/m^2	Every year
	No	<200 mg/m^2	Every 5 years
		≥200 to <300 mg/m^2	Every 2 years
		≥300 mg/m^2	Every year

* age at first treatment with anthracycline or chest radiation (whichever was given first)

** based on total doses of doxorubicin/daunorubicin or the equivalent doses of other anthracyclines

Survivors who received **radiation at a dose of 40 Gy (4000 cGy) or higher** to the heart or surrounding tissues **or radiation at a dose of 30 Gy (3000 cGy) or higher plus anthracycline chemotherapy** should have an **evaluation by a cardiologist for stress testing** 5 to 10 years following radiation, then as recommended by the cardiologist.

Survivors who received **radiation** to the heart or surrounding tissues should also have a **blood test to check for other cardiac risk factors** (lipid profile and fasting glucose) every 3 to 5 years.

Additional evaluation by a cardiologist is recommended **for female survivors who are pregnant or planning pregnancy** and received any of the following therapy:

- Anthracycline chemotherapy at a dose of 300 mg/m^2 or more
- Radiation at a dose of 30 Gy (3000 cGy) or higher to the heart or surrounding tissues
- Radiation at any dose to the heart or surrounding tissues, if the patient also received anthracycline chemotherapy
- Total body irradiation (TBI) plus high doses of cyclophosphamide (Cytoxan®) prior to bone marrow or stem cell transplant
- Total body irradiation (TBI) plus anthracycline chemotherapy

Heart monitoring may be necessary due to the extra strain on the heart during the later stages of pregnancy and during labor and delivery. Suggested monitoring includes an echocardiogram before and periodically during pregnancy, especially during the third trimester, and cardiac monitoring during labor and delivery.

How are these heart tests done?

An **electrocardiogram** (ECG, EKG) is a test used to evaluate heart rate and rhythm. Electrodes (small sticky patches) are placed on the chest, arms, and legs. Wires are attached to the electrodes and the electrical impulses of the heart are then recorded.

An **echocardiogram** (heart ultrasound) is used to test the muscle function of the heart and how well the heart pumps. The person lies on a table and has conductive jelly applied to the chest. Then a transducer (device that emits the ultrasound waves) is placed on the chest to obtain different views of the heart. Slight pressure is applied on the transducer and can sometimes cause discomfort. The test results are displayed on videotape and photographed for the doctor to study later. Many measurements are done during this test to help find out if the heart muscle is pumping blood well. The ultrasound tests also looks at the valves of the heart to see that they open and close normally. Electrodes are usually placed on the chest to monitor the heart's electrical impulses during the test.

A **MUGA** (multiple-gated acquisition) scan is another way of testing the motion of the heart and how well it pumps blood to the body. During this test, a small amount of radioactive isotope is injected into a vein. The person then lies on a table and a special camera moves above the table to obtain pictures of the heart in motion. Electrodes are also placed on the chest to monitor the heart's electrical impulses during the test.

A **cardiac stress test** measures heart function during periods when the heart is working hard. During this test, the heart and blood pressure are usually monitored while the person walks on a treadmill.

What happens if a problem with the heart is detected?

Your healthcare provider will advise you about the follow-up care you need. Sometimes, a referral to a cardiologist (heart specialist) is needed for additional evaluation and/or treatment with medications

What can be done to prevent heart problems?

With increasing age, the risk of certain types of heart disease (such as heart attacks and hardening of the arteries) also increases. Factors that may increase the risk of heart problems include smoking, being overweight, eating a high fat diet, and not exercising. Medical conditions that increase the risk include diabetes, high blood pressure, and high blood cholesterol. You can reduce your risk of heart problems by:

- Not smoking (or quitting if you currently smoke).
- Staying at a healthy body weight.
- Limiting the fat in your diet to no more than 30% of calories.
- Exercising moderately for at least 30 minutes on most days of the week.

If you have diabetes, high blood pressure, or high blood cholesterol, keep these under good control with diet or medication as recommended by your healthcare provider. Be sure to promptly report any symptoms of heart problems to your healthcare provider.

Written by Debra L. Friedman MD, Melissa M. Hudson MD and Wendy Landier, CPNP.

Debra L. Friedman MD directs the ACCESS Cancer Survivorship Program at Children's Hospital and Regional Medical Center in Seattle WA

Melissa M. Hudson MD directs the After Completion of therapy (ACT) clinic at St. Jude Children's Research Hospital in Memphis, TN.

Wendy Landier RN, MSN, CPNP, CPON®, is a pediatric nurse practitioner and clinical director of the Survivorship Clinic at City of Hope National Medical Center in Duarte, CA

Reviewed by: Roberta G. Williams MD, Julie Blatt MD and Joan Darling PhD.

Illustrated by: Devika Bhatia

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Hepatitis after Childhood Cancer

Treatment for childhood cancer often requires transfusion of blood and blood products. Unfortunately, some of these life-saving blood products may also have contained viruses that can infect the liver. Infection of the liver is called "hepatitis". There are two main types of hepatitis (hepatitis B and hepatitis C) that can be transmitted through blood products. Before the blood supply was routinely screened for these infections, people who received blood products may have been infected with these viruses. In the United States, routine screening of blood donors for hepatitis B began in 1971. The most accurate screening test for hepatitis C became available in 1992. Survivors who received blood products before these dates may have been infected by these viruses. (Note: the dates that other countries began screening donors for hepatitis may be different.)

Hepatitis B and C can also be spread through other types of blood contact (such as needle sharing among drug users, tattoos, body piercing, hemodialysis and organ transplantation). These infections can also occur as a result of sexual contact with an infected person, or from an infected mother to a newborn baby at birth, although this method of infection occurs much more commonly with hepatitis B than with hepatitis C.

What is the liver?

The liver is a triangular-shaped organ tucked under the ribcage on the right side of the body. In an average adult, the liver is about the size of a football and weighs about three pounds. It is responsible for filtering out toxins from the blood, aiding with digestion and metabolism, and producing many important substances including blood-clotting proteins.

What are the signs and symptoms of hepatitis?

Most people do not experience symptoms of hepatitis B or C when first (acutely) infected. Some people have symptoms similar to the flu, such as fatigue, loss of appetite, nausea, vomiting, or low-grade fever. Some people may experience symptoms more directly related to the liver, such as jaundice (yellowish eyes and skin), dark urine, severe itching, or pale (clay-colored) stools. In rare cases, people may become very ill (fulminant hepatitis) and develop liver failure.

Hepatitis may completely resolve and cause no further health problems. Unfortunately, many people who become infected with hepatitis B or C during childhood become "chronically" infected. People with chronic hepatitis infections may have no symptoms and feel well, but they are at risk for scarring (cirrhosis) of the liver and other complications. In rare cases, liver cancer can develop. People with chronic hepatitis infections are also at risk for spreading the infection to others.

What are common findings in people with hepatitis?

Most people with chronic hepatitis have no signs or symptoms. Chronic infection over a long time may cause progressive liver damage. Signs of liver damage include enlargement of the liver and spleen, swelling or collection of fluid in the abdomen, yellow color of the eyes and skin (jaundice), and low blood clotting factors.

What tests are done to check for hepatitis?

A **blood test** can be done to check for viral hepatitis:

- People with **chronic hepatitis B infection** will test positive for hepatitis B surface antigen (HbsAg) and usually also test positive for hepatitis B core antibody (HbcAb or anti-HBc).
- People with **chronic hepatitis C infection** usually test positive for the hepatitis C antibody (HCAb). If the test for hepatitis C antibody is positive, or if the person has impaired immunity (immunosuppression), the hepatitis C "PCR" test may also be done to check the level of hepatitis C virus in the blood.

Who is at risk for hepatitis B and C?

Anyone who received the following blood or serum products are at risk for hepatitis B (if transfused before 1972) and hepatitis C (if transfused before 1993):

- Packed red blood cells
- Whole blood
- White blood cells (granulocytes)
- Platelets
- Fresh frozen plasma
- Cryoprecipitate
- Immunoglobulin preparations (IVIG, VZIG)
- Bone marrow or stem cells from an allogeneic donor (someone other than yourself)

Other risk factors include:

- Blood clotting factors (such as Factor VIII or Factor IX) made before 1987
- Solid organ transplants (such as kidney, liver, or heart) before 1993
- Long-term kidney dialysis (lasting for at least several months)
- Shooting or snorting drugs
- Body piercing, tattoos
- Sharing razors, nail clippers, or toothbrushes with people who have hepatitis
- Occupational exposure to blood and body fluids
- High-risk sexual behavior, multiple sexual partners, unprotected sexual intercourse

What follow up is needed for those at risk?

- Anyone who is at risk for hepatitis B or C should have blood tests done to see if they are infected.
- If your blood tests show evidence of chronic hepatitis infection you should:
  - Have blood tests (ALT, AST, bilirubin, AFP, prothrombin time) at least yearly to monitor the status of the liver.
  - Receive ongoing evaluation (and in many cases treatment) by a liver specialist.

What can I do to keep my liver healthy?

- If you do not have immunity to hepatitis A and B, get immunized against these common infections in order to protect your liver (there is currently no vaccine to protect against hepatitis C). You can find out if you have immunity to hepatitis A and B by having a blood test (Hepatitis A IgG antibody and Hepatitis B surface antibody).
- If you drink alcohol, do so in moderation.
- Drink plenty of water.
- Eat a well-balanced, high-fiber diet. Cut down on fatty, salty, smoked and cured foods.
- Do not take more than the recommended doses of medications.
- Avoid taking unnecessary medications.
- Do not mix drugs and alcohol.
- Do not use illegal street drugs.
- Be careful about using herbs and natural supplements, especially when combined with medications.
- If you are sexually active, use barrier protection (such as latex condoms) during intimate sexual contact to prevent infection by viruses that can harm the liver.
- Avoid exposure to chemicals (solvents, aerosol cleaners, insecticides, paint thinners, and other toxins) that can be harmful to the liver. If you must use these substances, wear a mask and gloves and work in a well-ventilated area.

If you have chronic hepatitis, you should also:

- See a liver specialist for evaluation and possible treatment.
- Tell your healthcare providers about all over-the-counter medications and supplements that you are taking.
- Avoid alcohol.
- Avoid over-the-counter pain or fever-reducing medications containing acetaminophen (such as Tylenol or “aspirin-free” products).
- Female patients who are pregnant should discuss their hepatitis status with their healthcare providers (including their obstetrician and the infant’s pediatrician).

How can the spread of infection be prevented?

Hepatitis B and C are not spread by casual contact, such as hugging or shaking hands. However, **if you have hepatitis B or C**, in order to prevent spreading the infection to others you should:

- Avoid direct contact of your blood and body fluids with others.
- Clean any spilled blood or body fluids with bleach.
- Cover cuts or other open sores.
- Avoid sharing sharp personal objects, such as razors, toothbrushes, nail clippers, ear or body rings, or any object that may come in contact with blood.
- Be sure that new sterile needles are used for body piercing, injections, or acupuncture. Never share needles.

- Make sure all close household members and sexual partners are screened for hepatitis B. If they do not have immunity, they should be given the hepatitis B vaccine.
- If you are sexually active, use barrier precautions (such as latex condoms) during intimate sexual contact.
- Talk with your healthcare provider about whether your sexual partner should be tested for hepatitis C.

Written by Wendy Landier, RN, MSN, CPNP, CPON®, pediatric nurse practitioner and clinical director of the Survivorship Clinic, Division of Pediatrics, City of Hope National Medical Center, Duarte, CA.

Reviewed by: Melissa Hudson MD and Smita Bhatia MD, MPH.

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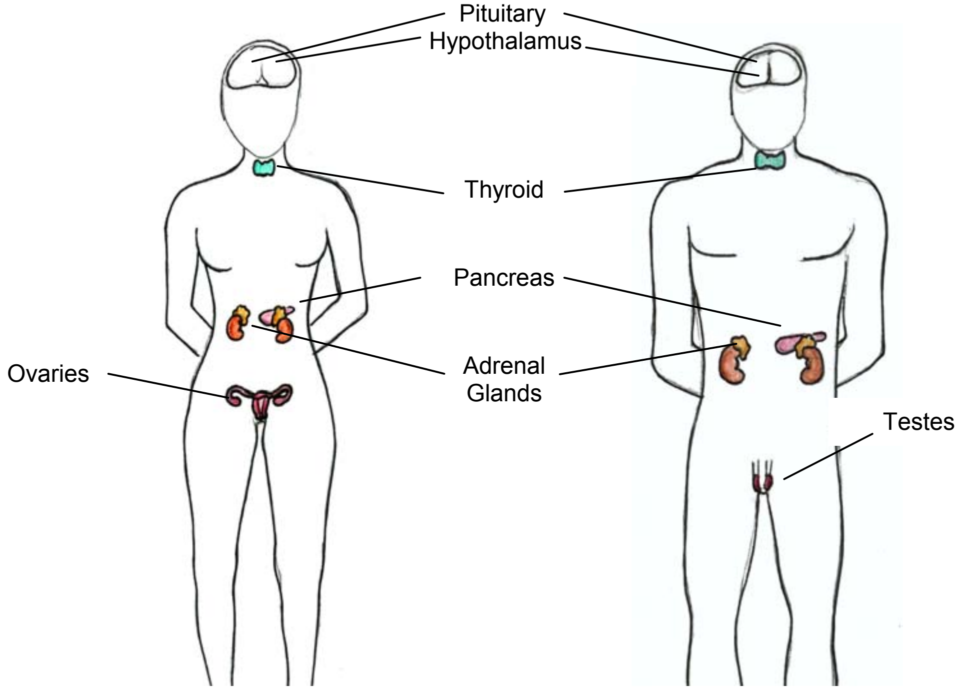
Endocrine Problems after Childhood Cancer:
Hyperprolactinemia

Some people who were treated for cancer during childhood may develop endocrine (hormone) problems as a result of changes in the function of a complex system of glands known as the endocrine system.

What is the endocrine system?

The endocrine system is a group of glands that regulate many body functions including growth, puberty, energy level, urine production, and stress response. Glands of the endocrine system include the pituitary, hypothalamus, thyroid, adrenals, pancreas, ovaries (in females), and testes (in males). The hypothalamus and pituitary are sometimes called the “master glands” because they control many of the other glands in the endocrine system. Unfortunately, some treatments given for childhood cancer can damage the endocrine system, resulting in a variety of problems.



What are hormones?

Hormones are chemical messengers that carry information from the endocrine glands through the bloodstream to the body’s cells. The endocrine system makes many hormones (such as growth hormone, sex hormones, adrenal and thyroid hormones) that work together to maintain specific bodily functions.

What is hyperprolactinemia?

Hyperprolactinemia is a condition that occurs when there is too much of the hormone known as prolactin in the body. Prolactin is a hormone secreted by the pituitary gland.

Its main function is to enhance breast development in females during pregnancy and to induce lactation (milk production) after childbirth. Too much prolactin can affect the reproductive system, resulting in problems with functioning of the ovaries (in females) or testicles (in males). In females, high levels of prolactin can cause galactorrhea (breast milk production by a person who is not breastfeeding) and irregular or absent menstrual periods. In males, high levels of prolactin can cause galactorrhea and decreased testosterone levels that may result in a diminished sex drive (libido). In preteens and teens, excess prolactin may interfere with normal pubertal development.

Risk factors for hyperprolactinemia

The risk of developing hyperprolactinemia after treatment for childhood cancer is quite low. Risk factors for its development include radiation to the pituitary gland in doses of 50 Gy (5000 cGy/rads) or higher, the development of a second tumor (usually non-cancerous) in the pituitary region, pregnancy, and certain medications and drugs (such as marijuana and alcohol). Rarely, thyroid failure (a condition in which the thyroid gland fails to secrete enough thyroid hormone) can cause hyperprolactinemia. Correcting the thyroid problem may correct the high prolactin level.

Recommended screening

All childhood cancer survivors should have a yearly comprehensive health check-up. If hyperprolactinemia is suspected, a prolactin blood test will be done. If a problem is detected, your healthcare provider may order additional tests (such as a CT scan or MRI of the brain) and refer you to an endocrinologist (a doctor who specializes in the treatment of hormone problems) for further evaluation and treatment.

How is hyperprolactinemia treated?

Endocrinologists may use medications to suppress prolactin production. If a tumor is detected, surgery or radiation are sometimes needed. The length and type of treatment varies for each patient and should be discussed with your doctor.

Written by Debra Eshelman, RN, MSN, CPNP, pediatric nurse practitioner and coordinator of the After the Cancer Experience (ACE) Pediatric and Young Adult Survivor Programs at Children's Medical Center of Dallas and the University of Texas Southwestern Medical Center, Dallas, TX.

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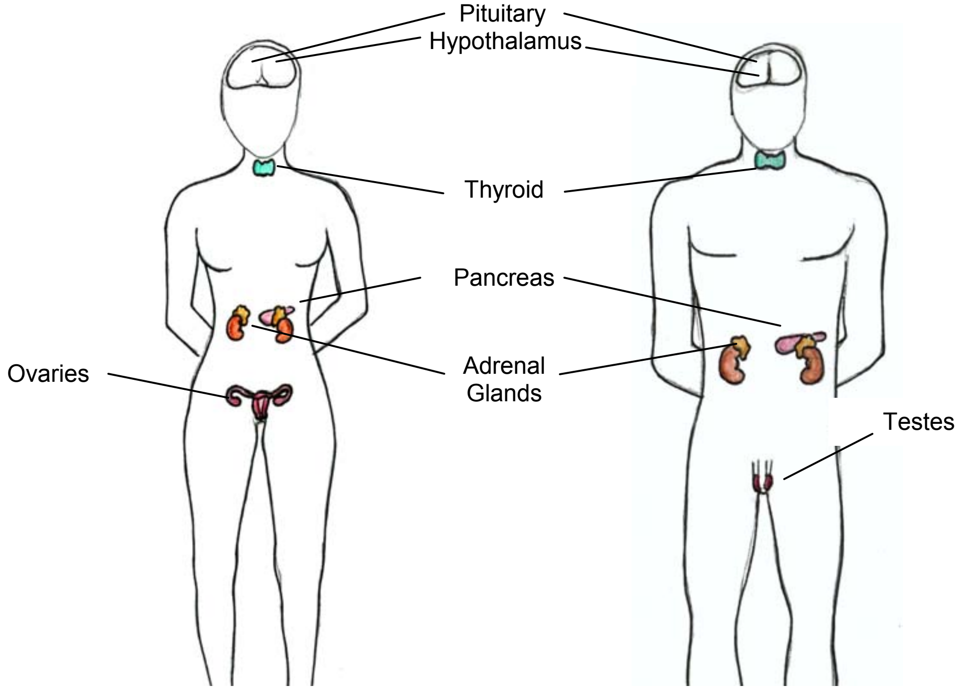
Endocrine Problems After Childhood Cancer:
Hypopituitarism

Some people who were treated for cancer during childhood may develop endocrine (hormone) problems as a result of changes in the function of a complex system of glands known as the endocrine system.

What is the endocrine system?

The endocrine system is a group of glands that regulate many body functions including growth, puberty, energy level, urine production, and stress response. Glands of the endocrine system include the pituitary, hypothalamus, thyroid, adrenals, pancreas, ovaries (in females), and testes (in males). The hypothalamus and pituitary are sometimes called the “master glands” because they control many of the other glands in the endocrine system. Unfortunately, some treatments given for childhood cancer can damage the endocrine system, resulting in a variety of problems.



What are hormones?

Hormones are chemical messengers that carry information from the endocrine glands through the bloodstream to the body’s cells. The endocrine system makes many hormones (such as growth hormone, sex hormones, adrenal and thyroid hormones) that work together to maintain specific bodily functions.

What is hypopituitarism?

Hypopituitarism is the decrease or lack of one or more of the pituitary hormones. The lack of three or more of the pituitary hormones is referred to as panhypopituitarism.

Pituitary hormones include:

- **Growth hormone (GH)** – stimulates the growth of bone and other body tissues, and also affects how the body uses fat, makes muscle, strengthens bones, and generally influences overall health throughout life
- **Adrenocorticotropic hormone (ACTH)** – stimulates the adrenal gland to produce cortisol
- **Thyroid stimulating hormone (TSH)** – stimulates the thyroid gland to produce thyroid hormones
- **Reproductive hormones (gonadotropins),** including **luteinizing hormone (LH) and follicle stimulating hormone (FSH)** – stimulate the testes and ovaries to make sex hormones
- **Antidiuretic hormone (ADH)** – helps to control the balance of water in the body by controlling urine output
- **Prolactin** – controls milk production in women who are breastfeeding

What causes hypopituitarism?

Risk factors related to childhood cancer treatment include:

- Radiation to the brain, especially in doses of 30 Gy (3000 cGy/rads) or higher, including the following fields:
    - Cranial (whole brain)
    - Craniospinal
    - Nasopharyngeal (nose and throat)
    - Oropharyngeal (mouth and throat)
    - Orbital
    - Eye
    - Ear
    - Infratemporal (midfacial area behind the cheekbones)
    - Total body irradiation (TBI)
- Surgical removal of the pituitary gland

Other risk factors for pituitary problems include infections, severe head trauma, or the lack of development of the pituitary from birth.

What are the symptoms of hypopituitarism?

The symptoms depend on the specific hormones that are lacking. One or more of the following hormones may be affected:

Adrenocorticotropic hormone (ACTH) deficiency:
The adrenal glands (located on top of the kidneys) are stimulated by ACTH to produce cortisol. If the pituitary gland doesn't make enough ACTH, then cortisol will not be made. Cortisol helps keep the body's blood sugar at a normal level and helps the body deal with physical stress, such as fever or injury. For more information about ACTH deficiency, *see the related Health Link: Central Adrenal Insufficiency.*

Growth hormone (GH) deficiency:
Growth hormone affects the growth of body tissues and bone as well as fat, muscle, and sugar metabolism. For more information about growth hormone problems, *see the related Health Link: Growth Hormone Deficiency.*

Gonadotropin (FSH, LH) deficiency:
LH and FSH control the production of male and female hormones. In males LH and FSH stimulate the testicles to make testosterone, and in females LH and FSH stimulate the ovaries to make estrogen and progesterone, resulting in development of sexual characteristics during puberty. If the body doesn't have enough LH and FSH during puberty, there can be problems with pubertal development. For more information about male and female hormonal issues, *see the related Health Links: Male Health Issues after Childhood Cancer Treatment* and *Female Health Issues after Childhood Cancer Treatment.*

Thyroid Stimulating Hormone (TSH) deficiency:
TSH stimulates the thyroid gland to release thyroxin, which is important for brain development, growth, and metabolic balance. People with too little thyroxin may develop the following symptoms: tiredness, sleeping too much, weight gain, slow growth, poor appetite, cold intolerance, dry skin, constipation or coarse, dry thin hair. For more information about thyroid problems*, see the related Health Link: Thyroid Problems after Childhood Cancer.*

What screening is recommended?

All cancer survivors should have a yearly physical examination including measurement of height and weight, assessment of their progression through puberty, and assessment of overall well-being. If a hormone problem, such as hypopituitarism is suspected, further tests may be done and a referral may be made to an endocrinologist (doctor who specialized in hormone problems).

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Introduction to Long-Term Follow-Up After Treatment for Childhood, Adolescent, or Young Adult Cancer

Congratulations! You have "graduated" to long-term follow-up. ***You can now think of yourself as a cancer survivor, not as a cancer patient!*** In long-term follow-up, the goal is to help you stay as healthy as possible—to stay well and to do well in school or at work.

Even though you are a cancer survivor, it is still important that you continue to have regular medical care. In some cases, your care may continue at the same hospital or clinic where you received your treatment, but you may be seen by different doctors and nurses in a special Long-Term Follow-Up Program. In other cases, you may receive care from a healthcare provider working in partnership with your treatment center, or from a provider who is closer to your home. No matter where you receive your care, it is important that you learn what you need to know about your treatment and the follow-up care that you need so that you can stay in the very best health possible.

Your cancer treatment summary

When you graduate to long-term follow-up, it is important that you get a record of the cancer treatment that you received. This record, known as a ***Cancer Treatment Summary***, should contain the following information:

- Name of the disease that you had, the date when you were diagnosed, and the site/stage of the disease
- Date(s) and description(s) of any relapses
- Name, address, and phone number of hospital(s) or clinic(s) where you received your care
- Name, address, and phone numbers of your cancer doctor (oncologist) and other health team members responsible for your care
- Names of all the chemotherapy medicines that you received and how they were given (such as by mouth or into the vein)
- Specific information about certain chemotherapy drugs as follows:
    - Total doses of the following types of chemotherapy:
        - Alkylators
        - Anthracyclines
        - Bleomycin
    - Designation of "high dose" (1000 mg/m^2 or more in any single dose) versus "standard dose" for cytarabine and methotrexate
    - Total doses of other chemotherapy agents should be included if available
- Name and dates of any surgeries that you had and the name of the surgeon(s)
- Radiation therapy summary, including type, dates, site(s), total dose, dose per treatment (fraction), and fractions of any radiation that you received
- Name, address and phone number of the doctor supervising your radiation treatments
- Dates and types of any bone marrow or stem cell transplant(s) and the name, address and phone number of the doctor supervising your transplant(s)

- Type of conditioning (chemotherapy and/or radiation) received for bone marrow or stem cell transplant
- Any treatment or preventive measures used for graft-versus-host disease (a potential complication of bone marrow or stem cell transplant)
- Names and dates of any significant complication(s), and treatments received for complication(s)

Keep a copy of your cancer treatment summary in a safe place, and give a copy to each of your healthcare providers.

Your follow-up schedule

Most cancer survivors need long-term follow-up visits about once a year. During these visits, it is important to talk about your progress and check for problems that can happen after treatment for cancer. Talk with your healthcare provider about your individual situation and determine a schedule for the follow-up care that will meet your needs.

Between visits

Once you “graduate” to long-term follow-up care, you will usually need to identify a local healthcare provider that you can visit or call if you are injured or sick. Make an appointment for a check-up with this healthcare provider so that they can get to know you before an illness arises. If a problem comes up that may be related to your cancer treatment, your local healthcare provider can discuss this with your long-term follow-up team.

Late effects after treatment for childhood, adolescent, or young adult cancer

Problems that happen after treatment for cancer are known as “late effects.” Fortunately, most long-term survivors don’t have serious late effects, but it is important to catch any problems early. You may have already learned about some of the possible late effects that can happen after treatment for cancer. Some of the more common ones are reviewed here.

Growth

Treatment for cancer during childhood, especially radiation to the brain or spine, can sometimes slow or stunt growth. Yearly measurements help to predict whether you will reach a normal height. If you are “at risk” for being short as an adult, your healthcare provider may also recommend other specialized tests and treatments.

Heart

A small percentage of survivors treated with chest radiation or certain chemotherapy drugs known as “anthracyclines” (such as doxorubicin or daunomycin) have problems with the heart. This is most likely to happen in people who received higher doses of these medicines, and in those who received their treatment before their heart finished growing. Your healthcare provider may recommended tests to check your heart function, and may arrange for a cardiologist (heart specialist) to see you if the tests show any sign of these problems.

Fertility

Radiation to the abdomen or pelvis and certain anticancer drugs can affect sexual development and reproduction. Some survivors may be at risk for delayed puberty, infertility (inability to have children), or early menopause. Check-ups and certain blood tests can help determine if you have any of these problems. These issues are important, and if you have any concerns, you should be sure to discuss them with your healthcare provider. If there is a problem, arrangements may be made for you to see a specialist.

Thyroid

Head or neck radiation can sometimes cause the thyroid gland to stop working properly. This gland helps regulate growth, weight, and the balance of body chemicals. Blood tests can be done to check thyroid hormone levels. Low thyroid levels are easily treated with oral medication.

Second Cancers

Some chemotherapy drugs and radiation can increase the risk of a second (different) cancer. Some survivors may have genetic changes that put them at risk for second cancers. Tobacco, excessive sun exposure, and other chemicals and behaviors can also increase this risk. Talk with your healthcare provider about ways to lower your risk and to detect common cancers at an early stage.

School and Work

Problems with schoolwork or jobs can occur as a result of some types of cancer treatment. Psychologists can work with your local school system to make sure that any special needs are met. Also, financial assistance for education and job training may be available through government programs. Social workers can help to explain these programs.

Moving toward the future

Thinking about developing late effects after surviving cancer can be anxiety provoking. But it is quite possible that you will NOT develop any serious complications. And if you do, it is best to catch them early, so that you can begin treatment right away. So don’t let anxiety get in the way of taking the very best care of your health.

Being treated for cancer at a young age is always a difficult experience. Having survived that experience, you have learned many things. Most likely, you are a stronger person than you were before you were diagnosed with cancer. As you move forward into your future, use those strengths to your advantage. Make healthy choices. Keep your follow-up appointments. And always remember that YOU are the most important member of your healthcare team!

Written by Wendy Landier, RN, MSN, CPNP, CPON®, pediatric nurse practitioner and clinical director of the Survivorship Clinic in the Division of Pediatrics, City of Hope National Medical Center, Duarte, California.

Portions adapted from "Introduction to the After Completion of Therapy Clinic," St. Jude Children's Hospital, Memphis, TN, used with permission.

Reviewed by Melissa Hudson MD and Smita Bhatia MD, MPH.

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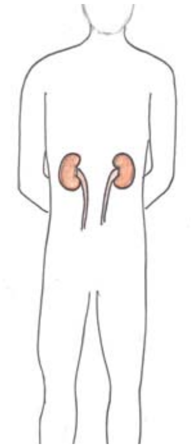
Kidney Health after Childhood Cancer

The kidneys are vital organs responsible for filtering out waste products from the blood, controlling blood pressure, and stimulating red blood cell production. Treatment for childhood cancer can sometimes damage the kidneys. It is important to understand how the kidneys function so that you can keep your kidneys as healthy as possible.

How do the kidneys work?



The kidneys are two bean-shaped organs, each approximately the size of an adult fist, located below the ribcage near the middle of the back. The kidneys filter about 200 quarts of blood each day, removing harmful waste products and excess water, and returning important elements (such as calcium, sodium and potassium) to the blood. Filtering occurs in tiny units inside the kidneys, known as nephrons. Each kidney has approximately one million nephrons. After the blood is filtered by the nephrons, the excess water and waste products become urine. The urine flows from the kidneys to the bladder through tubes called ureters. The bladder then stores the urine until it is full, at which time the waste is emptied from the body through the urethra.

How is kidney function measured?

Kidney function is measured in percentages. Two normal kidneys account for 100% of kidney function. A single kidney provides about 50% of kidney function. One can lead a normal life with one kidney as long as the single kidney remains healthy. When kidney function drops to less than 50% of normal, the risk of health problems increases. Serious health problems are more frequent when kidney function drops to below 20%. Dialysis or transplant is necessary if kidney function falls to 15% or below.

What treatments for childhood cancer can cause kidney problems?

Certain treatments used for childhood cancer can sometimes cause kidney problems that can begin years after completion of therapy. There may also be other risk factors present that can increase the chance of kidney problems. If you have any of the following risk factors, you should take extra care to keep your kidneys healthy:

Radiation involving the kidneys, including:

- Kidney (renal) radiation
- Whole abdominal radiation
- Para-aortic radiation
- Spinal radiation at doses of 15Gy (1500 cGy/rads) or higher
- Total Body Irradiation (TBI)

Certain medications that can cause kidney damage, including:

- Cisplatin (especially if total of all doses was 200 mg/m^2 or higher)
- Carboplatin
- Methotrexate

- Ifosfamide (especially if total of all doses was 60 grams/m^2 or higher). Treatment with Ifosfamide at a young age (under the age of 5 years) increases the likelihood of kidney problems.
- Certain antibiotics used to treat bacterial and fungal infections, such as tobramycin, gentamicin, and amphotericin
- Certain medications used to treat graft-versus-host disease, such as cyclosporine and FK-506 (tacrolimus)

Other risk factors that may increase the chance of kidney problems include:

- **Nephrectomy** (surgical removal of a kidney) – *see the related Health Link "Single Kidney Health"*
- **Medical conditions that may affect the kidney**, such as high blood pressure, diabetes, or a tumor involving the kidney
- **History of urinary tract problems**, such as frequent urinary tract infections, back-flow of urine into the kidney (reflux), or other urinary tract abnormalities
- **Cystectomy** (removal of the bladder) – this increases the risk of chronic urinary tract infections and other kidney problems

What are the signs and symptoms of a kidney problem?

- Swelling, especially of the feet and ankles (edema)
- Low red blood count (anemia)
- High blood pressure (hypertension)
- People who have signs of serious kidney problems, such as edema, low red blood count, and hypertension, may also have other symptoms, including fatigue, nausea and vomiting, drowsiness, itchy skin, or headaches.

What follow up is recommended?

If you had treatment with ***ifosfamide****,* ***cisplatin****, or* ***carboplatin****, you should:*

- **Have a medical check-up at least yearly.** This should include a **blood pressure check, blood tests for kidney function (BUN, creatinine), and a urinalysis**.
- **Have a blood test for electrolytes** (blood salts and minerals) **at your first long-term follow-up visit** (at least 2 years after completing cancer treatment), **then every 5 years** (and more often if problems are detected). People with low levels of blood salts and minerals may need to take supplements (prescribed by a healthcare provider). This can be important for long-term health. For example, persistently low levels of blood magnesium can lead to heart problems.
- **Have a baseline check of kidney function** at least once (at least 2 years after completing cancer treatment). This should be either a timed urine test (creatinine clearance) or a GFR scan (special x-ray that measures kidney function using a small amount of radioactive material injected through a vein). If any problems are detected, this test should be repeated periodically to monitor your kidney function. Your healthcare provider may also refer you to a nephrologist (kidney specialist) for additional evaluation.

If you had treatment with ***radiation involving the kidneys*** *or* ***cystectomy****, you should:*

- **Have a medical check-up at least yearly.** This should include a **blood pressure check, blood tests for kidney function (BUN, creatinine), and a urinalysis**.
- **If you have high blood pressure or abnormal BUN, creatinine, or urinalysis**, you should have a **blood test for electrolytes** (blood salts and minerals) **and a creatinine clearance test or GFR scan.** The creatinine clearance test is a timed urine collection. The GFR scan is a special x-ray that measures kidney function using a small amount of radioactive material injected through a vein. If any problems are detected, these tests should be repeated periodically to monitor your kidney function. Your healthcare provider may also refer you to a nephrologist (kidney specialist) for additional evaluation.
- If you have had a **cystectomy** (bladder removal), you should also have a **urine culture** and an **evaluation by a urologist** (urinary tract specialist) **at least once a year.**

If you had treatment with ***methotrexate*** *(and did not receive any of the other treatments listed above), you should:*

- **Have a medical check-up, including blood pressure check, at least yearly.**
- **Have blood tests for kidney function (BUN, creatinine) and a urinalysis at your first long-term follow-up visit** (at least 2 years after completing cancer treatment).
- **If you have high blood pressure or abnormal BUN, creatinine, or urinalysis**, you should have a **blood test for electrolytes** (blood salts and minerals) **and a creatinine clearance test or GFR scan.** The creatinine clearance test is a timed urine collection. The GFR scan is a special x-ray that measures kidney function using a small amount of radioactive material injected through a vein. If any problems are detected, these tests should be repeated periodically to monitor your kidney function. Your healthcare provider may also refer you to a nephrologist (kidney specialist) for additional evaluation.

What can I do to keep my kidneys healthy?

- **Drink plenty of water**, especially when playing sports, while out in the sun, and during hot weather.
- **Call your healthcare provider immediately if you have symptoms of a urinary tract infection** (burning when you urinate, urinating more frequently than usual, and/or feeling an urgent sensation to urinate).
- **Use non-steroidal anti-inflammatory drugs with caution.** These include pain or fever medicines (over-the-counter and by prescription) that contain aspirin, ibuprofen, acetaminophen or naproxen. These medications have been known to cause kidney damage (analgesic nephropathy), especially when taken in excessive doses or when two or more of these medications are combined with caffeine or codeine and taken over long periods of time. If you require long-term medications for management of pain, be sure to discuss the alternatives with your healthcare provider, and to choose medications that are not harmful to your kidneys.
- **Have a health checkup at least once a year** including the tests recommended above based on the cancer treatment you received.

Summary of Recommendations for Follow-Up

Treatment received	Recommended Follow-Up	How Often
• Ifosfamide • Cisplatin • Carboplatin	Medical check-up including blood pressure check	Yearly
	Blood tests to check kidney function (BUN & creatinine)	Yearly
	Urinalysis	Yearly
	Blood test for electrolytes (blood salts and minerals)	First long-term follow-up visit,* then every 5 years
	Kidney function test (creatinine clearance or GFR)	First long-term follow-up visit,* repeated periodically if problems are detected
• Radiation involving the kidneys • Cystectomy	Medical check-up including blood pressure check	Yearly
	Blood tests to check kidney function (BUN & creatinine)	Yearly
	Urinalysis	Yearly
	Blood test for electrolytes (blood salts and minerals) and kidney function test (creatinine clearance or GFR)	If high blood pressure, protein in the urine, or abnormal BUN or creatinine. Repeat periodically if problems detected.
• Cystectomy (also refer to above recommendations)	Urine culture	Yearly
	Check-up by urologist	Yearly
• Methotrexate	Medical check-up including blood pressure check	Yearly
	Blood tests to check kidney function (BUN & creatinine)	First long-term follow-up visit*
	Urinalysis	First long-term follow-up visit*
	Blood test for electrolytes (blood salts and minerals) and kidney function test (creatinine clearance or GFR)	If high blood pressure, protein in the urine, or abnormal BUN or creatinine. Repeat periodically if problems detected.

* First long-term follow-up visit should be at least 2 years after completing cancer therapy

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Written by Anne Mauck, RN, MSN, CPNP, pediatric nurse practitioner in the Division of Pediatric Hematology Oncology, Virginia Commonwealth University Health System, Richmond, Virginia.

Reviewed by Dr E. Clifton Russell, Dr. Nancy L. Dunn, Dr. Gita Massey, Dr. Vimal Chadha, Elizabeth Hall CPNP, Kevin Oeffinger, MD, Wendy Landier CPNP, Daniel Green, MD, Melissa Hudson MD, Smita Bhatia, MD, MPH, and Catherine L. Woodman MD.

Illustrated by Devika Bhatia.

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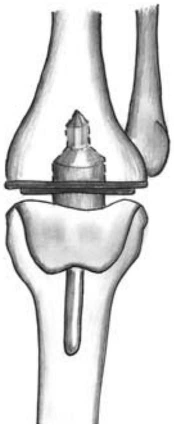
Limb Salvage After Bone Cancer



What is "limb salvage"?

Limb salvage is a surgical procedure that replaces a diseased bone and reconstructs a functional limb by using a metal implant, a bone graft from another person (allograft), or a combination bone graft and metal implant (allo-prosthetic composite).

What are the goals of this procedure?

The goals are the complete resection of the tumor with minimal complications while maintaining acceptable function, durability, and appearance of the limb.

What are the potential late effects after a limb salvage procedure?

- **Nonunion** - For people who had reconstruction with a bone graft, nonunion (non-healing) of the bones is a possible late complication. In the allograft procedure, the portion of bone removed due to tumor is replaced with donated bone. Nonunion occurs when one or both ends of the replaced bone do not heal, making fracture more likely, especially if the area is stressed. Surgery for additional bone grafting may be necessary.
- **Limb-length discrepancy** - Bones are constantly growing throughout childhood and adolescence until adult height is reached. Each bone has a growth plate (area where growth activity occurs). Often, bone cancers are located near the growth plate, requiring removal of this area during the limb salvage procedure. Since the reconstructed section of bone cannot grow, a limb-length discrepancy may occur. Surgeries or other procedures may be necessary to accommodate growth.
- **Prosthetic loosening** - Sometimes the implanted joint can loosen or wear out, especially in people who are active. These complications may require further surgery to tighten or replace part or all of the implant. **If you notice any loosening of the implant notify your healthcare provider.**
- **Contractures** - After a limb salvage procedure, muscles, tendons and ligaments sometimes stiffen or shrink, forming contractures (permanent tightening of the joint). This is more likely to occur in people who are not physically active. Periodic follow-up with a physical and/or occupational therapist is helpful in order to prevent the formation of contractures.

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What is the recommended follow-up care after a limb salvage procedure?

- **Follow-up visits** are usually done by the **orthopedic surgeon** (bone specialist) **every 6 months until the person is full-grown, then every year.** The follow-up intervals may lengthen as time progresses.
- **X-rays** are usually done at least **yearly**.
- **Life-long follow-up** by an orthopedic surgeon is **recommended**.

What can you do to promote health after limb salvage surgery?

- **Physical and occupational therapy** play an important role in successful rehabilitation after limb salvage surgery. Both **passive and active range-of-motion exercises** are important in maintaining optimal limb function.
- If there is **pain, swelling, redness** or any **other signs of infection** at the surgical site, or if you develop **fever**, **contact your healthcare provider promptly.**
- Due to a **life-long risk of infection, antibiotics** should be taken **prior to all dental procedures (including teeth cleaning),** and for **other invasive medical procedures** such as those involving the respiratory, gastrointestinal, or urinary tracts. Infection can result if bacteria enter the blood stream during these procedures and become attached to the internal metal components (screws, plates, rods, joints).
- Some metal implants may pose a **problem when going through security screening**, such as at the airport. It is good idea to **carry a medical letter** indicating that you have had bone cancer and a metal implant.

Written by Asako Komiya, RN, MSN, PNP, Pediatric Nurse Practitioner, Division of Pediatrics, City of Hope National Medical Center, Duarte, CA.

Reviewed by J. Dominic Femino MD, Neyssa Marina MD, Winnie Kittiko RN, MS, and Catherine L. Woodman MD.

Illustrated by Devika Bhatia.

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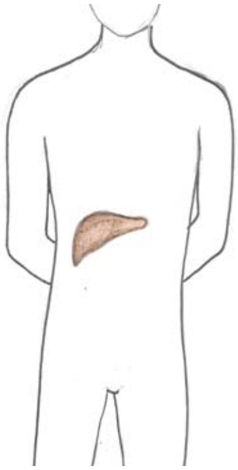
Liver Health after Childhood Cancer

Treatment for childhood cancer can sometimes damage the liver. It is important to know about how the liver functions so that you can keep your liver as healthy as possible.

What is the liver?

The liver is a triangular-shaped organ tucked under the ribcage on the right side of the body. In an average adult, the liver is about the size of a football and weighs about three pounds. The liver is responsible for filtering out toxins from the blood, aiding with digestion and metabolism, and producing many important substances, including blood-clotting proteins.



What are the signs and symptoms of liver damage?

Many people with liver damage have no symptoms at all. Some people may develop jaundice (yellowish eyes and skin), dark urine, pale (clay-colored) stools, severe itching, easy bruising or bleeding, chronic fatigue, nausea, loss of appetite, or other symptoms. The liver sometimes enlarges (hepatomegaly), and as liver damage increases, the liver may become hard (fibrosis) and scarred (cirrhosis). Eventually, there can be accumulation of fluid in the abdomen (ascites), swelling of the spleen (splenomegaly), or bleeding into the esophagus or stomach. Very rarely, liver cancer may develop.

Who is at risk?

People who had radiation to the following areas may be at risk for liver problems:

- Total Body Irradiation (TBI)
- Radiation to the whole abdomen
- Radiation to the liver, especially at doses of 20 Gy (2000 cGy/rads) or higher

The following chemotherapy drugs also have the potential to cause liver damage, although the most likely time for this to happen is during treatment or shortly after treatment ends. It is very uncommon for these medicines to cause liver problems years after treatment:

- Methotrexate
- Mercaptopurine
- Dactinomycin

Other risk factors include:

- Medical conditions that involve the liver, such as a liver tumor or surgical removal of a large portion of the liver
- Pre-existing liver problems
- Excessive alcohol use
- Chronic liver infection (hepatitis)
  - see related Health Link: "Hepatitis after Childhood Cancer"

- History of multiple transfusions
  - *see related Health Link: "Hepatitis after Childhood Cancer"*
- Chronic graft-versus-host disease (as a result of bone marrow or stem cell transplant)

What tests are done to monitor the liver?

There are three main types of blood tests used to monitor the liver.

- **Liver enzyme tests** monitor levels of specialized proteins that are normally present inside liver cells. If liver cells are damaged, these proteins can leak out, causing high blood levels of liver enzymes. The most common liver enzyme tests are:
  - Alanine aminotransferase (ALT), sometimes also called SGPT
  - Aspartate aminotransferase (AST), sometimes also called SGOT
- **Liver function tests** are indicators of how well the liver is working. Common liver function tests include:
  - Bilirubin (a waste product formed during the breakdown of red blood cells)
  - Albumin (a major blood protein that is produced by the liver)
  - Prothrombin Time (PT), a measure of blood clotting
- **Tests for liver infection,** including specific tests for viral hepatitis A, B, and C.

What follow up is needed for those at risk?

A blood test to evaluate the liver (including ALT, AST, and bilirubin) should be done **when the survivor enters into long-term follow-up** (usually about 5 years from diagnosis or 2 years following completion of therapy). **The liver should also be checked for enlargement by a healthcare professional during yearly physical examinations.** If problems are identified, additional tests and a referral to a liver specialist may be recommended. People at risk for hepatitis may need further testing (*see related Health Link, "Hepatitis after Childhood Cancer").*

What can I do to keep my liver healthy?

- If you do not have immunity to hepatitis A and B, get immunized against these common infections in order to protect your liver (there is currently no vaccine to protect against hepatitis C). You can find out if you have immunity to hepatitis A and B by having a blood test (Hepatitis A IgG antibody and Hepatitis B surface antibody).
- If you drink alcohol, do so in moderation.
- Drink plenty of water.
- Eat a well-balanced, high-fiber diet. Cut down on fatty, salty, smoked and cured foods.
- Do not take more than the recommended doses of medications.
- Avoid taking unnecessary medications.
- Do not mix drugs and alcohol.
- Do not use illegal street drugs.

- Check with your healthcare provider before starting any new over-the-counter medications or herbs and supplements to be sure that they do not have harmful effects on the liver.
- If you are sexually active, use barrier protection (such as latex condoms) during intimate sexual contact to prevent infection by viruses that can damage the liver.
- Avoid exposure to chemicals (solvents, aerosol cleaners, insecticides, paint thinners, and other toxins) that can be harmful to the liver. If you must use these substances, wear a mask and gloves and work in a well-ventilated area.

Written by Wendy Landier, RN, MSN, CPNP, CPON®, pediatric nurse practitioner and clinical director of the Survivorship Clinic, Division of Pediatrics, City of Hope National Medical Center, Duarte, CA.

Reviewed by: Melissa Hudson MD and Smita Bhatia MD, MPH.

Illustrated by Devika Bhatia.

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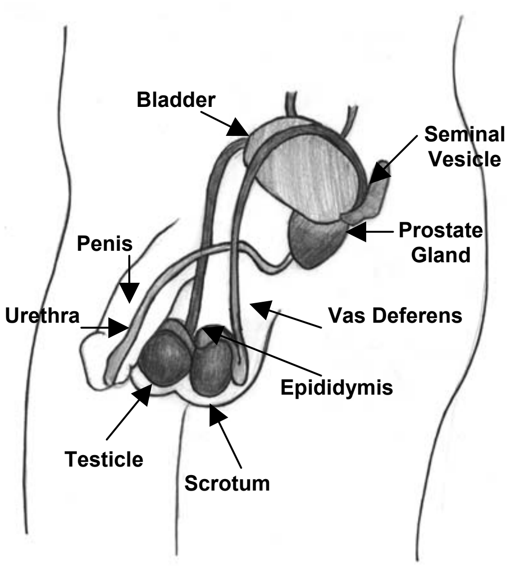
Male Health Issues after Treatment for Childhood Cancer

The effects of childhood cancer therapy on male reproductive function depend on many factors, including the person's age at the time of cancer therapy, the specific type and location of the cancer, and the treatment that was given. It is important to understand how the male reproductive organs function and how they may be affected by therapy given to treat cancer during childhood.

The male reproductive organs



The male reproductive system is made up of the scrotum, testicles, vas deferens, epididymis, seminal vesicles, prostate gland, penis, and urethra, and is controlled by the pituitary gland in the brain. The testicles are located in the scrotum (the loose pouch of skin that hangs behind the penis). The testicles are made up of Leydig cells (cells that produce the male hormone - testosterone) and germ cells (cells that produce sperm). When a boy enters puberty, the pituitary gland releases two hormones (FSH and LH) that signal the testicles to begin producing sperm and testosterone. As puberty progresses, testosterone causes deepening of the voice, enlargement of the penis and testicles, growth of facial and body hair, and muscular development of the body. Sperm produced by the testicles mature in the epididymis (a coiled tube that sits on top of each testicle) and then travel into the vas deferens (sperm storage area). The seminal vesicles and prostate gland produce fluids that mix with the sperm to create semen. When a man ejaculates, sperm are pumped out through the vas deferens, mixed with fluids from the prostate and seminal vesicles, and exit the body through the urethra (tube that carries fluids out of the penis).

How does cancer therapy affect the male reproductive system?

The most common effect of cancer therapy on the male reproductive system is **infertility** (the inability to initiate a pregnancy). Infertility can occur as a result of certain types of **chemotherapy**, **radiation** to the brain or testicles, or **surgery** involving the male reproductive system.

Another possible effect of cancer therapy on the male reproductive system is **testosterone deficiency,** also known as "hypogonadism" or "Leydig cell failure." This is the inability to produce enough of the male hormone, testosterone, and can result from damage to the Leydig cells or pituitary gland **caused by radiation to the testicles or brain**. If this occurs in a young boy, he will not be able to go into puberty without the help of hormones prescribed by a doctor. Males who develop testosterone deficiency after puberty will need hormonal therapy in order to maintain their muscular development, bone and muscle strength, proper distribution of body fat, sperm production, sex drive, and potency.

What are the causes of male reproductive problems after childhood cancer treatment?

Chemotherapy of the "alkylator" type (such as cyclophosphamide, nitrogen mustard and procarbazine) **may cause infertility**. The total dose of alkylators used during cancer therapy is important in determining the likelihood of damage to sperm-producing cells. The higher the total dose, the more potential for developing infertility. If alkylating chemotherapy was used in combination with radiation, the risk of infertility may be increased.

Radiation therapy can affect testicular function in two ways**:**

- **Radiation aimed directly at or near the testicles**. The sperm-forming cells (germ cells) are very sensitive to the effects of radiation therapy. Most males who receive radiation to the testicles at doses of 6 Gy (600 cGy/rads) or higher will be infertile. Even radiation doses of 3 Gy (300 cGy/rads) or lower may cause a drop in the number and quality of sperm produced. This reduction in sperm production may be temporary, but infertility can sometimes occur even at very low radiation doses. Testosterone production often continues even if the sperm-forming cells are no longer functioning, because the cells that produce testosterone (Leydig cells) are not as sensitive to radiation. However, testicular radiation in doses of 20 Gy (2000 cGy/rads) or higher often causes the Leydig cells to stop functioning, resulting in testosterone deficiency.
- **Radiation to the pituitary gland in the brain**. Brain radiation can result in damage to the pituitary gland, leading to low levels of the hormones (FSH and LH) needed to signal the testicles to make sperm and testosterone. Males with low levels of these hormones will need to take testosterone for the rest of their lives. However, it is sometimes possible for these men to attain fertility with the use of specialized hormone treatments. Men who have infertility as a result of brain radiation and wish to achieve fertility should see a fertility specialist.

Surgery that involves removal of *both* testicles will result in infertility and testosterone deficiency. Surgery such as retroperitoneal lymph node dissection (RPLD) may cause damage to the nerves in the pelvic area and may prevent the ejaculation of sperm. Removal of the prostate or bladder may result in difficulties achieving an erection and/or ejaculation. In these situations, sperm production may be unaffected and fertility may still be possible by using specialized techniques, such as sperm harvesting and artificial insemination. If fertility is desired, consultation with a fertility specialist is recommended.

What types of cancer therapy increase the risk of problems with the male reproductive system?

- **Chemotherapy** - the class of drugs called "alkylators" can cause **infertility** when given in high doses. Examples of these drugs are:
  - Cyclophosphamide (Cytoxan)
  - Ifosfamide
  - Nitrogen mustard
  - Procarbazine
  - Melphalan
  - Busulfan
  - Chlorambucil
  - Lomustine (CCNU)

  - Carmustine (BCNU)
  - Thiotepa
  - Dacarbazine (DTIC)
  - Temozolamide
  - Carboplatin
  - Cisplatin

- **Radiation therapy** to any of the following areas may cause **infertility**.
  - Testicles
  - Pelvis
  - “Inverted Y” or total nodal radiation
  - Inguinal/femoral areas
  - TBI (total body irradiation)
  - Spinal - if dose was 24 Gy (2400 cGy/rads) or higher
  - Cranial (brain) - if dose was 30 Gy (3000 cGy/rads) or higher

  In addition to causing infertility, **high doses of** radiation to the testicles (usually 20 Gy or higher) **or brain** (usually 30 Gy or higher) **may also cause testosterone deficiency**.

- **Surgeries** that may cause **infertility** or disrupt normal sexual functioning include:
  - Removal of both testicles (this surgery will always result in infertility)
  - Retroperitoneal lymph node dissection (RPLD)
  - Cystectomy (removal of the bladder)
  - Prostatectomy (removal of the prostate)

  In addition, **removal of both testicles** will also result in **testosterone deficiency**.

What monitoring is recommended?

Males who have had any cancer treatments placing them at risk for problems with the reproductive system should have a yearly check-up that includes careful evaluation of their hormone and puberty status. Blood may be tested for hormone levels (FSH, LH, and testosterone). If any problems are detected, a referral to an endocrinologist (hormone specialist), urologist (specialist in the male reproductive organs) and/or fertility specialist may be recommended.

What can be done for testosterone deficiency?

Males with low testosterone levels should receive testosterone replacement therapy. Testosterone is available in several forms, including gels, skin patches, and injections. Your endocrinologist will determine which form of therapy is best for you.

How will I know if I am infertile?

Infertility is not related to sexual function. In some men with infertility, there may be a decrease in the size or firmness of the testicles, but in others, there are no physical indications of infertility.

Males who had surgical removal of both testicles will not be able to make sperm, and infertility will be permanent. In other males, the only sure way to check for sperm production is to have a semen analysis performed. This test checks the appearance, movement and concentration of sperm in the semen. A semen analysis that shows **azoospermia** (no sperm in the semen sample) on more than one sample is a likely indicator of infertility.

In men who have azoospermia as a result of radiation, return of sperm production is unlikely. However, in men who have azoospermia as a result of chemotherapy, the effect on male fertility is highly variable. Recovery of sperm production may occur months or years after the completion of chemotherapy in some men. For others, the damage may be permanent. It may be impossible to determine if sperm production will resume at some time in the future, especially if chemotherapy ended only a few years prior to the semen analysis. For this reason, **always assume that you can make someone pregnant unless you are absolutely sure that you cannot!!**

When should I get a semen analysis?

Any sexually mature male who is concerned about fertility should have a semen analysis performed. Most hospitals or clinics that have an adult urology or obstetric/gynecology department will have the facilities to perform a semen analysis. Not all insurance companies cover the cost of this analysis, so you should check with your insurance company to be sure, or check with the hospital or clinic regarding the costs of this procedure. If the results are within normal limits, there is no need to do anything further.

What if the sperm count is very low?

If the results show no sperm (azoospermia) or very low sperm counts, the test should be repeated several times. Sperm recovery following chemotherapy may take as long as 10 years, so if you have had chemotherapy that may cause low sperm counts, it may be important to check periodically over several years. Also, men's sperm counts vary considerably from day to day, so sub-normal test results may improve if additional samples are checked after waiting for a month or two. Sperm production and quality may continue to improve as more time passes from the chemotherapy treatment.

Men who have low sperm counts cannot rely on this to prevent pregnancy. Pregnancy can occur with low sperm counts. **Some method of birth control must be used if pregnancy is not desired.** If pregnancy is desired, men with low sperm counts may benefit from various assisted reproductive techniques such as artificial insemination or in-vitro fertilization (IVF).

What are my options if I have no sperm in the sample?

If semen analysis shows no sperm, and fertility is desired, a consultation with a doctor who specializes in male infertility should be obtained. Medical advancements dealing with male infertility are being made. Recently, surgeons have been able to locate areas of active sperm production in the testes of men who were thought to be azoospermic. Surgical harvesting of the sperm has allowed conception with techniques devised for men with absent or very low sperm counts. *Occasionally, azoospermia may be unrelated to chemotherapy altogether, and treatment for another disorder may be indicated.*

Options for using banked sperm depend on the amount and quality of material saved. Men who banked sperm prior to cancer treatment will need to work with a doctor specializing in reproductive medicine, so that the cryopreserved (frozen) sperm can be used in an optimal manner.

Another option for males who produce no sperm may be donor insemination. This results in pregnancy with a child that is biologically related only to the mother. Additional options include adoption of a biologically unrelated child or child-free living.

What if only one testicle was surgically removed?

Although fertility and testosterone production are not usually affected if only one testicle was surgically removed, you should take precautions to protect the remaining testicle from injury by always wearing an athletic supporter with a protective cup when participating in any activities that may potentially cause injury to the groin area (such as contact sports, baseball, etc.). If your remaining testicle was treated with radiation, or if you received chemotherapy that can affect testicular function, the effects of these treatments are the same as discussed above.

What are the risks if pregnancy occurs after childhood cancer treatment?

Fortunately, in most cases, there is no increased risk of cancer or birth defects in children born to childhood cancer survivors. In rare cases, if the type of cancer in childhood was a genetic (inherited) type, then there may be a risk of passing that type of cancer on to a child. You should check with your oncologist if you are not sure whether the type of cancer you had was genetic.

Written by Marcia Leonard, RN PNP, Coordinator, Long Term Follow Up Clinic, Department of Pediatric Hematology-Oncology, University of Michigan Medical Center, Ann Arbor, MI.

Reviewed by: Charles Sklar MD, Julie Blatt MD, Daniel Green MD, Smita Bhatia MD, MPH, and Missy Layfield.

Illustrated by Devika Bhatia.

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Peripheral Neuropathy

What is peripheral neuropathy?

Peripheral neuropathy, or damage to the peripheral nerves (nerves outside the brain or spinal cord), is a potential side effect of chemotherapy drugs and may cause the hands or feet to hurt, tingle, and feel numb or weak. Though the discomfort is felt in a muscle or joint, the real damage is to the nerves that control the muscles. Nerves are made up of special cells that carry messages to and from the brain and spinal cord. Damage to the nerve is often caused by a breakdown of the myelin sheath, the coating around nerve fibers that acts as an electrical insulator. There may also be direct damage to the nerve cells from pressure or trauma (for example from a tumor or surgery). Symptoms usually start during treatment and persist, and are not late in onset. Symptoms often improve once treatment has stopped, but for some survivors symptoms may persist for months or years.

Symptoms of peripheral neuropathy:

- Burning, tingling, or prickling sensation usually in the hands or feet.
- Numbness or sensitivity to pain or temperature
- Extreme sensitivity to touch
- Sharp shooting pain
- Poor balance or coordination
- Loss of reflexes
- Muscle weakness
- Noticeable changes in the way you walk

Muscle weakness may begin around the arch of the foot and in the palm of the hand. It may be difficult to grip things or to perform certain tasks or activities such as writing, buttoning clothes, or tying shoes. The muscles that pull the foot up may weaken and the reflexes may be lost, causing the front part of the foot to fall flat to the floor. This may result in poor balance or coordination, especially when tired. There may be a tendency to drag the feet or lift them high to prevent the feet from dragging.

Who is at risk?

People who have received any of the following chemotherapy drugs may be at risk:

- Vincristine
- Vinblastine
- Cisplatin
- Carboplatin

People at highest risk for peripheral neuropathy are those who have received higher doses of these drugs or combinations of these drugs. Other risk factors include surgery, severe weight loss, and diabetes or a pre-existing nerve disease. Prolonged pressure on nerves from artificial limbs, wheelchairs, or crutches can also contribute to nerve damage.

Recommended screening

Anyone who has received cancer treatment during childhood should have a yearly comprehensive medical check-up. If peripheral neuropathy is suspected, a thorough neurological examination should be included in this check-up. If a significant problem is detected, a referral to a neurologist (doctor who specializes in problems of the nervous system) may be needed for further testing. People with peripheral neuropathy may also benefit from physical and/or occupational therapy.

Treatment

Rehabilitation services

Since there is no treatment that can cure or reverse nerve damage, treatment is directed toward symptom management. Physical therapy is often helpful in providing exercises to improve strength, balance, and coordination. Occupational therapy can provide help to improve hand/eye coordination and other skills needed for daily life.

Orthotic devices

Support for feet or ankles can be improved with orthotic devices. Arch supports or splints help prevent the arch from flattening and help improve walking. Splints called ankle-foot-orthoses (AFOs) may be recommended to prevent the ankle from moving too much from side to side and to support the foot when walking.

Pain management

Your healthcare provider may prescribe medication to control the pain, tingling, and burning sensation. The type of medication depends on the frequency and severity of pain. It is also important to know that some medications will have side effects of their own. Elastic stockings, warm packs or exercise may also help with the discomfort. These measures will not replace medication but may decrease the need for them. They may also assist in improving mobility and independence.

Additional recommendations:

- **Avoid shoes that are too tight or too loose** - Just as shoes that are too tight can cause throbbing, rubbing, and cramping, shoes that are too loose can worsen pain and may not provide enough support for already wobbly feet. Well-fitting sneakers or shoes that provide support but are also flexible are best.
- **Be sensitive to temperature** - Many people report that neuropathy feels worse in hot weather or when feet are heavily covered which may prevent adequate air circulation.
- **Keep feet uncovered in bed -** Bed sheets resting on toes can cause discomfort due to friction between the sheet and toes.
- **Massage** - Massaging your hands or feet, or having someone else massage them can be extremely soothing and relaxing and can increase circulation and boost endorphins (chemicals produced in the body that help control pain).
- **Cool soaks** - Cool water soaks to painful hands or feet can sometimes dull pain enough to fall asleep or until pain medication has time to work.

For additional information, contact:

Neuropathy Association, 60 East 42nd Street, Suite 942, New York, NY 10165-0999
Website: www.neuropathy.org E-mail: info@neuropathy.org Phone: 212 692-0662

Written by Susan Shannon, RN, MSN, CPNP, CPON®, pediatric nurse practitioner and coordinator of the "STAR" Late Effects program at Miller Children's Hospital in Long Beach, CA.

Reviewed by Thanh Le, MD, Joetta Deswarte-Wallace RN, MSN, Neyssa Marina MD, and Debra Friedman MD.

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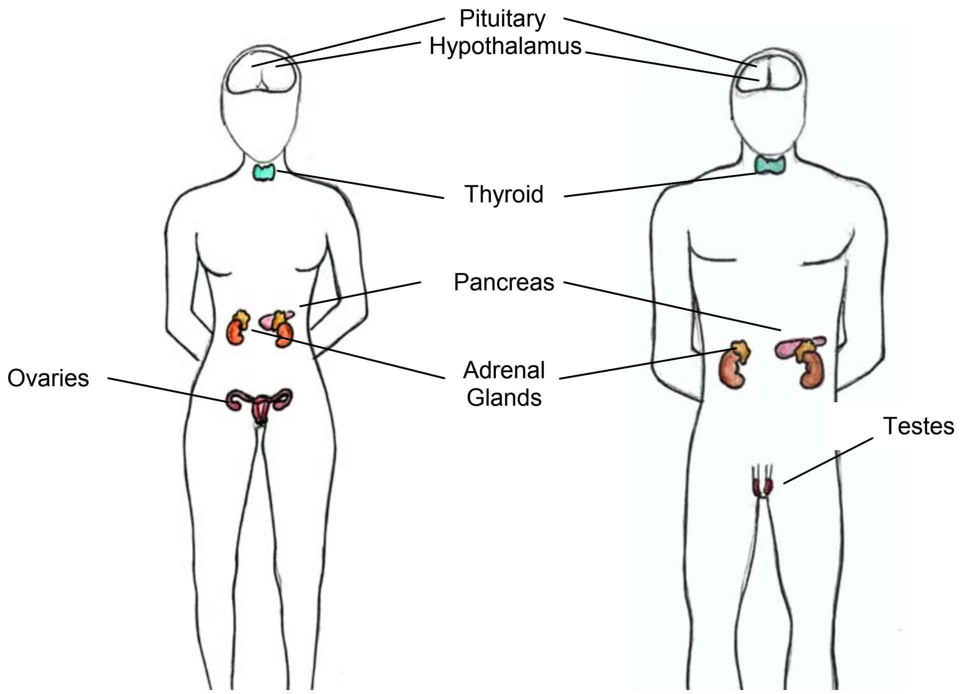
Endocrine Problems after Childhood Cancer:
Precocious Puberty

Some people who were treated for cancer during childhood may develop endocrine (hormone) problems as a result of changes in the function of a complex system of glands known as the endocrine system.

What is the endocrine system?

The endocrine system is a group of glands that regulate many body functions including growth, puberty, energy level, urine production, and stress response. Glands of the endocrine system include the pituitary, hypothalamus, thyroid, adrenals, pancreas, ovaries (in females), and testes (in males). The hypothalamus and pituitary are sometimes called the "master glands" because they control many of the other glands in the endocrine system. Unfortunately, some treatments given for childhood cancer can damage the endocrine system, resulting in a variety of problems.



What are hormones?

Hormones are chemical messengers that carry information from the endocrine glands through the bloodstream to the body's cells. The endocrine system makes many hormones (such as growth hormone, sex hormones, adrenal and thyroid hormones) that work together to maintain specific bodily functions.

What are the normal ages when puberty occurs?

Puberty occurs at different ages in different children. In fact, there is a wide range of ages at which puberty first begins. The timing of puberty is influenced by a person's genetic background, and the onset of puberty at a young age may run in families. Girls usually begin to develop breasts and then pubic hair at around 10 or 11 years of age, but the range of normal is between 8 and 13 years old. Menstrual periods usually start around 12 to 13 years of age, but may occur earlier or later and still be normal. Boys usually develop enlarging testicles and then pubic hair between 11 and 12 years of age, but the range of normal is between 9 and 14 years old.

What is precocious puberty?

Precocious puberty means having signs of puberty (such as pubic hair or breast growth) at an age younger than the normal range. Early puberty causes the development of sexual traits earlier than expected, and leads to rapid bone growth that can result in short stature. Most doctors agree that a girl has precocious puberty if she develops sexual traits earlier than age 8, and a boy has precocious puberty if he develops sexual traits prior to age 9.

What are the risk factors for developing precocious puberty?

Risk factors related to childhood cancer treatment include:

- Radiation to the head or brain, especially in doses of 18 Gy (1800 cGy/rads) or higher, including the following fields:
    - Cranial (whole brain)
    - Craniospinal
    - Nasopharyngeal (nose and throat)
    - Oropharyngeal (mouth and throat)
    - Orbital
    - Eye
    - Ear
    - Infratemporal (midfacial area behind the cheekbones)
- Total body irradiation (TBI)
- Female gender
- Younger age at treatment

Early puberty is also more common in overweight children. Excess weight may or may not be related to cancer treatment.

Why does precocious puberty happen?

The hypothalamus and pituitary glands may signal the ovaries (in girls) or testicles (in boys) to make female or male hormones at an earlier time. In other cases, signs of puberty occur early because of abnormalities in the ovaries, testicles or adrenal glands. Tests are done to learn if the cause of precocious puberty is in the brain or in another part of the body.

What screening is recommended?

All childhood cancer survivors should have a physical examination at least once a year, including measurement of height and weight, and evaluation of pubertal progress.

If the survivor has any of the risk factors described above, or if there are signs of accelerated growth or early puberty, the following tests are recommended:

- A blood test for FSH (follicle stimulating hormone), LH (luteinizing hormone) and sex hormone (estradiol or testosterone) level
- Bone age x-ray (an x-ray that measures the developmental age or maturation of bone)

How is precocious puberty treated?

If a problem is detected, a referral may be made to an endocrinologist (doctor who specializes in hormone problems). Medications may be used to temporarily stop puberty and to decrease the rate of bone maturation. It is also important to evaluate and manage the psychological effects of beginning puberty too early. Although children with precocious puberty may have a mature physical appearance, their thoughts, emotions and behaviors are still that of their actual (chronological) age.

Written by Debra Eshelman, RN, MSN, CPNP, pediatric nurse practitioner and coordinator of the After the Cancer Experience (ACE) Pediatric and Young Adult Survivor Programs at Children's Medical Center of Dallas and the University of Texas Southwestern Medical Center, Dallas, TX.

Reviewed by Lillian R. Meacham MD, Priscilla Rieves, MS, RN, CPNP, Charles Sklar MD, Julie Blatt MD, and Peggy Kulm RN, MA.

Illustrated by Devika Bhatia.

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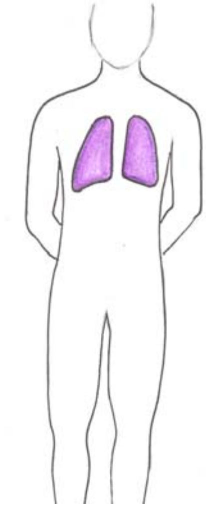
Pulmonary Health

The lungs are very important organs that are responsible for supplying oxygen to the body and ridding it of carbon dioxide. Sometimes, treatments given for childhood cancer can cause lung damage. If you received any treatments that have the potential to cause lung problems, it is important to learn about the lungs, and what you can do to keep them as healthy as possible.

How the lungs function

The lungs transfer oxygen from the air to the blood, where it is circulated to the vital organs in the body. The lungs also get rid of carbon dioxide, a waste product made by the body's cells. In order for oxygen to reach the blood, it must move through tiny air sacs (alveoli) in the lungs and into tiny blood vessels (capillaries) that surround each air sac. When the air sacs become damaged or scarred, there is less area for oxygen to enter the bloodstream, and less oxygen reaches the blood. The person may then need to breathe faster in order to get enough oxygen. This can make the person feel short of breath. Other lung problems can be caused by inflammation (swelling) of the air passages in the lungs or increased mucous production as a result of irritation or infection. Symptoms can include cough, wheezing, chest pain, and shortness of breath.



Am I at risk for lung problems?

If you received any of the following treatments during your cancer therapy, you may be at risk for developing lung problems:

- Bleomycin *(See the "Bleomycin Alert" Health Link for more information)*
- Carmustine (also known as BCNU)
- Lomustine (also known as CCNU)
- Busulfan
- Radiation to the chest (including mantle, mediastinal, or whole lung fields)
- Radiation to the abdomen (including whole abdomen or any upper abdominal field)
- Radiation to the spine in doses of 30 Gy (3000 cGy/rads) or higher
- Total body irradiation (TBI)
- Surgery to the chest or lung (this does NOT include surgery for placement of a central line, such as a Hickman, Broviac, Port-a-Cath or Mediport)
- Bone marrow transplant or stem cell transplant from a donor other than yourself (allogeneic transplant), if you then developed chronic graft versus host disease (chronic GVHD)

Certain chemotherapy drugs known as anthracyclines, such as daunorubicin (Daunomycin®), doxorubicin (Adriamycin®), and idarubicin (Idamycin®) can damage the heart and may contribute to lung problems, especially if given in combination with bleomycin, BCNU, CCNU, and radiation treatment.

Other factors that may increase your risk are:

- Younger age at the time of cancer treatment
- A history of lung infections, asthma or other lung problems
- Tobacco use or exposure to second hand smoke

What problems can develop?

Problems can include scarring of the lungs (pulmonary fibrosis), repeated lung infections (such as chronic bronchitis or recurrent pneumonia), and rupture of the tiny air sacs in the lungs or thickening and blockage of air passages within the lungs (restrictive/obstructive lung disease).

What are the symptoms of lung damage?

Symptoms may include shortness of breath, frequent coughing and/or wheezing, chest pain, and frequent lung infections, such as bronchitis or pneumonia. Becoming easily fatigued or short of breath during mild exercise (exercise intolerance) is sometimes an early symptom of lung damage.

What monitoring is recommended?

- A **yearly medical check-up** is recommended.
- A **chest x-ray and pulmonary function tests (including DLCO and spirometry)** may show lung problems that are not apparent during a check-up. For this reason, it is helpful to **have these tests done at least once** (at least two years after completing cancer treatment) to find out if there are any problems. Your healthcare provider can decide if further testing is needed based on these results.
- In some cases, your healthcare provider may recommend repeating the chest x-ray and pulmonary function tests **if you are scheduled for surgery that requires general anesthesia** to check for changes in the lungs that could increase the risk of breathing problems during or after anesthesia.

Are there any special precautions I should take?

If you have had any of the treatments listed above you should:

- Get the pneumococcal (pneumonia) vaccine.
- Get yearly influenza (flu) vaccines.
- Avoid SCUBA diving, unless you have undergone a thorough medical evaluation and received clearance from a diving medicine specialist.

What can I do to prevent lung problems?

- If you don't smoke, dip, or chew tobacco, DON'T START.
- If you smoke or use tobacco, **quitting is the <u>most</u> important thing** you can do to maintain and improve your overall health.
- Avoid second-hand smoke.

- Get regular physical exercise.
- Avoid breathing toxic fumes from chemicals, solvents, and paints.
- Follow all safety precautions in your workplace, such as the use of protective ventilators in some work environments. Report any unsafe working conditions to the Occupational Safety and Health Administration (OSHA).

Where can a smoker find help in order to quit?

Your most important resources for quitting smoking are your family, friends and your healthcare provider. Listed below are some additional sources of education and support:

Telephone Resources:

If you don't have access to the Internet, you can call the following organizations to request educational materials (usually free) about how to quit smoking:

American Cancer Society 1-800-ACS-2345

American Heart Association 1-800-AHA-USA1

American Lung Association 1-800-LUNG-USA

On-Line Resources:

If you have access to the Internet, you may find the following websites helpful:

www.surgeongeneral.gov/tobacco/
Very specific tips for getting ready to quit and how to handle the first week. Also has information on myths that can keep you from quitting.

www.cdc.gov/tobacco/
The Center for Disease Control's Tobacco Information and Prevention Source (TIPS) includes guides for quitting the tobacco habit.

www.lungsusa.org/ffs
The American Lung Association's free on-line "Freedom From Smoking" program.

Where can I find more information about how to keep my lungs healthy?

More information about the lungs, and how to keep them healthy, is available at:

www.nhlbi.nih.gov/health/public/lung/
The National Heart, Lung and Blood Institute's web site containing general information for patients and families.

www.nlhep.org/
The National Lung Health Education Program has information for patients about how to keep lungs healthy.

Written by Charlene Maxen RN, CNP, CPON®, and Sarah Friebert MD. Charlene Maxen is a Pediatric Subspecialty Manager and Dr. Sarah Friebert is the Director of the Pediatric Palliative Care Program in the Division of Hematology/Oncology at Childrens Hospital Medical Center of Akron in Akron, Ohio.

Reviewed by: Melissa Hudson MD, Debra Friedman MD, John R. Mussman, Neyssa Marina MD, and Kevin Oeffinger MD.

Illustrated by Devika Bhatia.

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Raynaud's Phenomenon

What is Raynaud's Phenomenon?

Raynaud's is a condition that may cause some areas of your body to feel numb and cool in response to cold temperatures or stress. The condition is a disorder that causes occasional narrowing of blood vessels, limiting blood flow for brief periods of time. This is called a vasospasm. During periods of vasospasm, the skin is deprived of oxygen, and may become pale and then turn a bluish color. As the blood vessels relax and blood flow resumes, the skin may become red. The hands and feet are most commonly affected, but Raynaud's may also involve the nose, lips, cheeks, and earlobes.

Symptoms

- Changes in skin color (often from white to blue to red)
- Changes in skin temperature (affected areas feel cooler)
- Numbness or prickly feeling in the fingers (not thumb) and toes (usually without pain)
- Occasional episodes of pain (described as throbbing) and swelling

What happens during an attack?

For most people, cold temperature or stress triggers an attack. Typically, when the body is exposed to cold, the hands and feet lose heat rapidly. In order to conserve heat, the body reduces blood flow near the skin surface and moves it deeper in the body. For people with Raynaud's, this normal response is exaggerated by sudden spasms of the small blood vessels that supply blood to the fingers and toes. This greatly reduces the blood supply to the hands and feet, causing changes in the skin color and temperature. The first sign is often pallor (or whiteness), in response to the spasm. The skin may then appear blue (cyanotic) and feel numb or cold, because of a lack of oxygen-rich blood. Finally, the skin may turn red and become swollen, as the small blood vessels relax and dilate, and blood flow returns. Commonly, throbbing and tingling may occur in the fingers and toes as the attack ends. Raynaud's attacks can last from seconds to hours.

Who is at risk?

Childhood cancer survivors who received treatment with vinblastine or vincristine sometimes develop Raynaud's.

Prevention

Raynaud's is usually a chronic condition that you may need to manage for life. Some people may see improvement slowly over several years. Prevention of attacks is key:

- **Dress warmly when outdoors.**
- **Take precautions indoors.** Wear socks. Avoid drafts such as when opening the refrigerator or freezer. Wear mittens when handling cold items. Use the air conditioner sparingly. Use insulated drinking glasses.
- **Avoid putting unprotected hands in cold water.**
- **Do not use tobacco.** Nicotine constricts blood vessels and causes the skin temperature to drop, which may lead to an attack.

- **Exercise.** Regular exercise can enhance circulation and help control stress.
- **Control stress.** Since stress is often a trigger for Raynaud's attacks, managing stress may help make the attacks shorter and less frequent.

Treatment

Treatment is directed at reducing the number and severity of attacks in order to prevent tissue damage. People with Raynaud's should follow all of the above recommendations for preventing attacks. In addition, if attacks are triggered by exposure to cold, placing the affected body part in warm water may help to stop symptoms. Other treatment methods include medications and biofeedback.

Medications

Medications that help to dilate blood vessels and promote circulation are sometimes prescribed for management of severe symptoms.

Certain prescription medications can sometimes make symptoms worse. These include birth control pills and some heart and blood pressure medicines. If you are taking any of these medications and are having symptoms of Raynaud's, consult with your healthcare provider regarding possible alternatives.

Certain over-the-counter cold or diet pills can make symptoms worse and should be avoided. These include drugs that contain **pseudoephedrine** (such as Actifed, Chlor-Trimeton, and Sudafed).

Biofeedback

Using your mind to control stress and body temperature may help to decrease the severity and frequency of attacks. This may include guided imagery and/or deep breathing exercises. A psychologist may be helpful in designing a biofeedback program that meets your needs.

Written by Susan Shannon, RN, MSN, CPNP, CPON®, pediatric nurse practitioner and coordinator of the "STAR" Late Effects program at Miller Children's Hospital in Long Beach, CA.

Reviewers: Thanh Le MD, Joetta Deswarte-Wallace RN, MSN, Neyssa Marina MD, Debra Friedman MD, Melissa Hudson MD, Rebecca D. Pentz PhD, and John R. Mussman.

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Reducing the Risk of Second Cancers

Learning about the risk of developing a second cancer can be frustrating and anxiety provoking. After your battle with childhood cancer, the last thing you want to be reminded about is the risk of developing a second cancer during adulthood. For a variety of reasons, the risk of cancer increases for everyone as they age. Several studies have shown that as childhood cancer survivors become older, they have a slightly higher risk of developing (a second) cancer compared to people their same age in the general population. Things that can contribute to this risk are the person's age during therapy, their specific treatment, and their genetic and family history.

Who is at risk for second cancer?

- **People who received certain chemotherapy drugs.** Some treatments for childhood cancer increase the risk of second cancers. Rarely, people can develop acute myeloid leukemia after treatment. Secondary leukemia usually occurs, if at all, within the first 10 years following treatment of the original cancer. The risk of developing a secondary leukemia is increased for people who were treated with high doses of alkylating agents (such as cyclophosphamide or nitrogen mustard), epipodophyllotoxins (such as etoposide or teniposide), and anthracycline chemotherapy drugs (such as doxorubicin or daunorubicin).
- **People who received radiation therapy, especially at a young age.** Radiation therapy given for childhood cancer increases the risk of developing a secondary solid tumor as a person ages. The most common sites include the skin, breast, central nervous system (the brain and spine), thyroid gland, and bones. In contrast to secondary leukemias, secondary solid tumors most commonly appear 10 or more years after treatment. The risk of developing a secondary solid tumor is increased when radiation is delivered at high doses and over large fields to children at a young age. Newer equipment and techniques allow radiation oncologists to treat just the areas involved by cancer and shield normal tissues.
- **People who have a history of cancer in their family.** Some cancer patients have inherited gene changes (mutations) that increase the chances of getting a second cancer. But overall, these inherited changes are relatively uncommon and account for less than 10 percent of patients with cancer. Doctors suspect the presence of a cancer gene when a family history shows multiple cancers among young people in every generation, or when cancer occurs in both sides of paired organs (such as the eyes, breasts, kidneys, etc.) If you have any questions or think that cancer may "run in your family" you should talk to your healthcare provider. A review of your family medical history will tell whether genetic counseling or testing is needed.

What if you are in a high-risk group?

You can find out if you are at high risk for developing a second cancer by going over your cancer treatment and family history with your healthcare provider or a cancer specialist. In some cases, early or more frequent screening may be recommended to increase the likelihood that second cancers are detected early, when they are most effectively treated. Be sure to get all screening tests that are recommended for you.

What monitoring is recommended?

By practicing health maintenance behaviors, you can improve your awareness of changes in your body and increase the likelihood that problems will be detected at earlier stages. All childhood cancer survivors should have a yearly comprehensive health check-up. You should also have any cancer screening evaluations appropriate for you based on your age, sex, and treatment history. Knowing the details of your previous medical history, including exposures to chemotherapy, radiation, and surgery, is vital to your future health. This information should be available to you or your healthcare provider from the hospital or clinic where you received your cancer therapy. Developing a relationship with a primary care provider who knows your cancer treatment history, risks of late complications, and recommended screening evaluations will improve the chances of catching problems at earlier, more treatable stages.

What symptoms should I be alert for?

Be sure to report any new or persistent symptoms to your healthcare provider promptly. Types of symptoms that you should report include:

- Easy bruising or bleeding
- Paleness of the skin
- Excessive fatigue
- Bone pain
- Changes in moles
- Sores that do not heal
- Lumps
- Difficulty swallowing
- Changes in bowel habits
- Persistent abdominal pain
- Blood in the stools
- Blood in the urine
- Painful urination or defecation
- Persistent cough or hoarseness
- Shortness of breath
- Bloody sputum
- Discolored areas or sores in the mouth that do not heal
- Persistent headaches
- Vision changes
- Persistent early morning vomiting.

What can I do to lower the risk of getting a second cancer?

Avoid cancer-promoting habits. Survivors should not smoke or chew tobacco and should avoid exposure to secondhand smoke when at all possible. Because skin cancers are one of the most common second cancers after childhood cancer, especially for those treated with radiation therapy, you should take extra care to protect your skin from sun exposure. This includes regularly using sunscreen with sun protection factor (SPF) of 15 or more, wearing protective clothing, avoiding outdoor activities from 10 am to 2 pm when the sun's rays are most intense, and not tanning.

Drink alcohol only in moderation. Heavy drinkers, especially those who use tobacco, have a high risk of cancer of the mouth, throat, and esophagus. The risk of breast cancer may be increased in women who drink alcohol. Limiting the use of alcohol can reduce these cancer risks and decrease the chances of other alcohol-related problems, such as liver disease.

Eat right. A high intake of dietary fat has been linked to the risk of several common adult cancers. People who eat high-fat diets have a greater risk of getting colon cancer; this may also be true for breast and prostate cancers. High-fat diets are also associated with obesity, heart disease, and other health problems. To reduce all of these risks, daily fat intake should be limited to 30% or less of your total calories.

Dietary fiber is found in whole grains, several types of vegetables, and certain fruits. Fiber reduces the time it takes for wastes to pass through the intestinal tract. High-fiber foods also tend to be low in fat.

Eating cruciferous vegetables also helps reduce cancer risk. Cruciferous vegetables include cabbage, brussel sprouts, broccoli, and cauliflower. Eating these vegetables is thought to protect against cancer by blocking the effects of cancer-causing chemicals in other foods. Cruciferous vegetables are also high in fiber and low in fat. These foods should be included frequently in the diet.

Some chemicals used to preserve foods are cancer-promoting (carcinogenic) in large quantities. Diets high in salt-cured and pickled foods and lunchmeats that contain preservatives like nitrites can increase the risk of cancer in the stomach and esophagus. Some of these foods, especially lunchmeats, are also high in fat. Foods of this kind should be eaten rarely and in small portions.

Diets rich in vitamins C and A have been shown to reduce cancer risk in animal studies. People whose diets are rich in vitamin C appear less likely to get cancer, especially cancer of the stomach and esophagus. The best way to get these nutrients is to eat lots of fresh fruits and vegetables. Citrus fruits, melons, cruciferous vegetables, and greens are high in vitamin C. Good sources of vitamin A are dark green and deep yellow vegetables and certain fruits. If your diet is low in vitamins, a vitamin supplement may help, but avoid extra high doses, since these can cause serious side effects.

Start today by taking time to review your health habits, and practice healthy behaviors that will help keep your risk of second cancers to a minimum.

Written by Melissa Hudson MD and Allison Hester, RN, MSN, CPNP. Portions adapted from CCSS Newsletter, Fall 1999 and Winter 2001, used with permission.

Melissa Hudson, MD directs the After Completion of therapy (ACT) clinic at St. Jude Children's Research Hospital in Memphis, TN.

Allison Hester, RN, MSN, CPNP is a pediatric nurse practitioner in the After Completion of therapy (ACT) clinic at St. Jude Children's Research Hospital in Memphis, TN.

Reviewed by Smita Bhatia MD, MPH, Debra Friedman MD, and Fran Wiley RN, MN.

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Scoliosis and Kyphosis After Treatment for Childhood Cancer

The spine, or "backbone" is actually a group of bones stacked in a straight line down the middle of the back, held together with muscles and ligaments. Treatment for childhood cancer can sometimes result in abnormal curvatures of the spine, known as scoliosis and kyphosis.

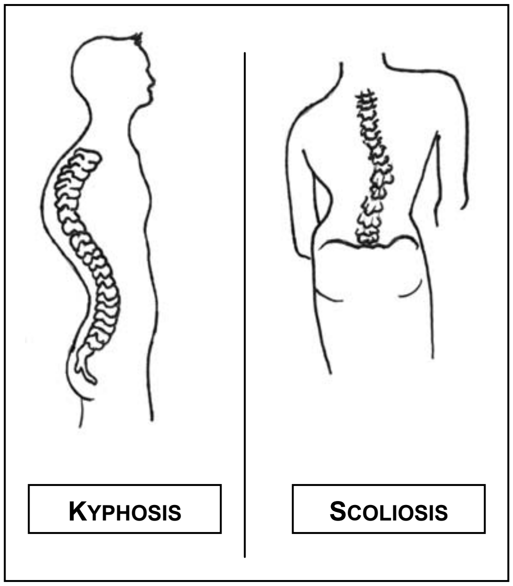
What is scoliosis?

Scoliosis is a sideways rotation of the spine. Instead of appearing as a straight line when viewed from the back, the spine appears curved, like the letter "S" or the letter "C". Signs of scoliosis may include:

- Uneven shoulder blades
- Uneven hips
- Uneven waist
- "Leaning" of the back to one side
- Head not centered above pelvis
- One leg longer than the other

What is kyphosis?

Kyphosis is an abnormal rounding of the upper part of the back. When viewed from the side, it may appear as if the person is slouching or has a "hump" on the back.



What causes scoliosis?

Scoliosis occurs in many young people, especially teenagers, and is most often "idiopathic," meaning that the cause is not known. However, people who have received radiation, to the chest, abdomen or spine, especially when combined with surgery, are at increased risk for uneven development of the muscles, bones and soft tissues of the back, resulting in scoliosis.

What are the risk factors for scoliosis after treatment for childhood cancer?

People at risk include those who had:

- Radiation to the trunk (including any area from the shoulders down to the pelvis), especially if:
  - The dose was 20 Gy (2000 cGy/rads) or higher.
  - The radiation treatment area was to one half of the chest or abdomen.
  - There was also surgery to the chest, abdomen, or spine.
- Orthovoltage type radiation (commonly used before 1970)
- A tumor in or near the spine
- A diagnosis of neurofibromatosis

Health Link

Healthy living after treatment for childhood cancer

What causes kyphosis?

Kyphosis sometimes develops from stretching of the spinal ligaments, causing the natural curve of the spine to increase. Kyphosis can also be caused by uneven development of the back muscles and ligaments as a result of radiation.

What are the risk factors for kyphosis after treatment for childhood cancer?

People at risk include those who had:

- Radiation to the chest or thorax (including mantle, mediastinal, whole lung, whole abdomen, or any upper abdominal field), especially in doses of 20 Gy (2000 cGy/rads) or higher
- Total body irradiation (TBI)
- Spinal radiation at a dose of 30 Gy (3000 cGy/rads) or higher
- Orthovoltage type radiation (commonly used before 1970)
- A tumor in or near the spine
- A diagnosis of neurofibromatosis

How is the diagnosis made?

Signs of scoliosis or kyphosis may be detected on physical examination. X-rays of the spine confirm the diagnosis. Scoliosis is diagnosed when there is at least a 10-degree lateral (side-to-side) curve on the x-ray. Kyphosis is diagnosed when there is at least a 50-degree curve on the x-ray.

What treatment is needed?

Treatment for kyphosis and scoliosis is usually done in stages. The first stage is usually "observation." During this stage, the curve is closely monitored, especially during periods of rapid growth, such as during puberty. If the curve does not get worse, observation may be all that is necessary.

If the curve progresses, the next step is usually bracing (a plastic body brace worn under the clothing). The goal of bracing is to halt progression or help correct the abnormal spinal curvature.

The final treatment step is surgery. This is done in cases of serious curves that are not manageable with observation or bracing alone.

What monitoring is required?

If scoliosis or kyphosis is suspected, a x-ray of the spine should be obtained. If the curve is more than 10 degree for scoliosis or more than 50 degrees for kyphosis, a referral is usually made to an orthopedic (bone) specialist.

Written by Wendy Landier, RN, MSN, CPNP, CPON®, pediatric nurse practitioner and clinical director of the Survivorship Clinic at City of Hope National Medical Center in Duarte, CA.

Reviewed by Melissa Hudson MD, Debra Friedman MD, Smita Bhatia MD, MPH, and Louis S. Constine, MD.

Illustrated by Devika Bhatia.

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Keeping Your Single Kidney Healthy

The kidneys are vital organs responsible for filtering out waste products from the blood, controlling blood pressure, and stimulating red blood cell production. Treatment for childhood cancer sometimes requires removal of one kidney (nephrectomy). Although you can live a healthy 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.

What follow up is recommended?

- **Have a medical check-up at least yearly.** This should include a **blood pressure check, blood tests for kidney function (BUN, creatinine), and a urinalysis**.
- **If you have high blood pressure, or abnormal BUN, creatinine, or urinalysis**, you should have a **blood test for electrolytes** (blood salts and minerals) **and a creatinine clearance test or GFR scan.** The creatinine clearance test is a timed urine collection. The GFR scan is a special x-ray that measures kidney function using a small amount of radioactive material injected through a vein. **If any problems are detected, these tests should be repeated periodically** to monitor your kidney function.
- If you have **high blood pressure**, **protein in the urine**, or **other signs** of worsening kidney problems, you should have an **evaluation by a nephrologist** (kidney specialist).

What can I do to keep my kidney healthy?

- **Drink plenty of water**, especially when playing sports, while out in the sun, and during hot weather.
- **Call your healthcare provider immediately if you have symptoms of a urinary tract infection** (burning when you urinate, urinating more frequently than usual, and/or feeling an urgent sensation to urinate).
- **Check with your healthcare provider or pharmacist before taking any new medicines** (prescription, over-the-counter, or herbal). Be sure that your healthcare provider or pharmacist is aware that you have a single kidney.
- **Use non-steroidal anti-inflammatory drugs with caution.** These include pain or fever medicines (over-the-counter and by prescription) that contain aspirin, ibuprofen, acetaminophen or naproxen. These medications have been known to cause kidney damage (analgesic nephropathy), especially when taken in excessive doses or when two or more of these medications are combined with caffeine or codeine and taken over long periods of time. If you require long-term medications for management of pain, be sure to discuss the alternatives with your healthcare provider, and to choose medications that are not harmful to your kidney.
- **Have a health checkup at least once a year** that includes a blood pressure measurement, a urine test for protein, and blood tests measuring kidney function.

- Some healthcare providers recommend that people with only one kidney should avoid contact sports or use a kidney guard if participating in contact sports. **We urge you to discuss your kidney status with your healthcare provider before making decisions about participation in sports and recreational activities.**
- **The most common cause of kidney injury is due to accidents, most often involving automobiles, bicycles (especially handlebar injuries), and falls**. Because of this, it is important to use seatbelts properly when riding in a vehicle (lap belts should be worn across the hips, not around the waist), and to use common sense when bicycling (avoid racing and stunt riding), in order to prevent kidney injury whenever possible. If you are involved in an accident and a kidney injury is suspected, seek immediate medical evaluation.

Are there any other risk factors for kidney problems?

Certain treatments for childhood cancer can sometimes cause kidney problems. These include **radiation to the kidney**, **chemotherapy** that can affect the kidney (cisplatin, carboplatin, methotrexate and/or ifosfamide), or **other medications** that can affect the kidney (certain antibiotics or medications used for treatment of graft-versus-host disease). In addition, **other risk factors** that may increase the chance of kidney problems include **medical conditions**, such as high blood pressure or diabetes, **urinary tract problems** such as frequent urinary infections or back-flow of urine into the kidney (reflux), or bladder removal (cystectomy). ***If you have any of these risk factors, please read the related Health Link, "Kidney Health."***

Written by Wendy Landier, RN, MSN, CPNP, CPON®, pediatric nurse practitioner and clinical director of the Survivorship Clinic, Division of Pediatrics, City of Hope National Medical Center, Duarte, California.

Reviewed by Smita Bhatia MD, MPH, Daniel Green MD, Rebecca L. Pentz PhD, Melissa Hudson MD, Kevin Oeffinger MD, and Michael L. Ritchey MD.

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Skin Health After Childhood Cancer

Very few people realize that the skin is the largest organ in the body. The skin is the body's first line of defense against outside invaders. It also keeps the body temperature normal and stores water, fat and vitamin D. Such an important organ requires care and monitoring. Treatment for childhood cancer sometimes causes damage to the skin.

Who is at risk?

- **Survivors who received radiation** to any part of the body, including total body irradiation (TBI). People at highest risk include those who received:
  - Radiation before reaching puberty
  - Radiation dose of 2 Gy (200 cGy/rads) or more during a single radiation treatment (fraction)
  - Orthovoltage-type radiation (commonly used before 1970)
- **Survivors who have chronic graft versus host disease** following allogeneic (from a donor other than yourself) bone marrow or stem cell transplant

What problems can occur?

The following are possible long-term skin effects that may be seen after cancer therapy.

Telangiectasias

These small blood vessels on the surface of the skin are commonly referred to as "spider veins," and in the cancer survivor they can occur in the field of radiation. Telangiectasias are caused by changes to the lining of blood vessels resulting from radiation. These do not typically cause any health problems and require no specific care.

Fibrosis

Another effect of radiation to the skin is called fibrosis. This is caused by scarring of the lining of blood vessels, resulting in a "woody" skin texture (fibrosis). The skin may not be as flexible in the fibrotic area and may be more easily injured. Care of fibrotic skin should include routine moisturizing and avoidance of trauma. Because the blood supply is not as good in fibrotic skin, healing may be slow after cuts and scrapes, so avoiding these when at all possible is important.

Scleroderma

People who have had a bone marrow or stem cell transplant from an allogeneic donor (someone other than themselves), and who have chronic graft versus host disease (GVHD), sometimes develop scleroderma. In this condition, the donor white blood cells do not recognize the patient's skin cells as their own, and begin to attack them. This causes the skin to become stiff and inflexible. This may happen anywhere on the body, but if it happens to the skin around joints, it can make the joints less mobile. The therapy for scleroderma is treatment of the underlying GVHD. It is also important to avoid injury to this skin, since healing time will be prolonged.

Vitiligo

Vitiligo is loss of pigment on patches of the skin. This can occur after allogeneic bone marrow or stem cell transplant and may be due to graft versus host disease (GVHD) or other autoimmune reactions seen after transplant. In this situation, the white blood cells do not recognize certain normal skin cells (melanocytes) and so they attack and destroy them. Melanoctyes are the cells in the body that control skin color. Without melanocytes, the skin has a milky white appearance. Vitiligo usually occurs only in patches. The therapy for vitiligo is treatment of the underlying GVHD or autoimmune process. Even if this therapy is successful, the color may not return to the skin because the damage to the melanocytes may be permanent. While all skin should be protected from sun, skin that has lost its pigment is very vulnerable, and sunscreen should always be applied to these areas before going outdoors.

Hyperpigmentation

Hyperpigmentation is a darkening of the skin that may occur after radiation or some types of chemotherapy. The chemotherapy agents most commonly associated with hyperpigmenation include bleomycin, busulfan, cyclophosphamide, dactinomycin, 5-flourouracil, hydroxyurea and methotrexate. The dark discoloration can occur on the skin or nails. There is no specific treatment for hyperpigmentation associated with cancer therapy, but it usually continues to fade over time without any treatment.

Skin Cancers

People who have received radiation are at risk for developing skin cancers, usually in the radiation field. Other risk factors include light skin color, chronic sun exposure, severe sunburn, atypical moles or a large number of moles on the body, and a family history of skin cancer. The good news about skin cancer is that if it is diagnosed early, it is usually very treatable. There are three major forms of skin cancer.

Basal Cell Carcinoma (BCC) is the most frequent form of skin cancer. BCC usually appears as a rough, raised, area of skin. As the BCC progresses, it may become an ulcer or sore that does not heal. BCC can occur anywhere on the skin, but is seen most frequently in areas of sun and/or radiation exposure. Protecting your skin from the sun is the most important thing you can do to avoid developing BCC. Treatment for BCC is surgical removal of the affected skin. BCC can spread to surrounding tissues but does not usually spread throughout the body and is not usually life threatening.

Squamous cell carcinoma (SCC) is another form of skin cancer that can develop from exposure to sun or radiation. Its appearance is similar to BCC, usually an ulcerated sore that does not heal. SCC can be more aggressive than BCC and can spread more readily to surrounding tissues and even to other parts of the body. With early surgical treatment SCC is usually curable, so it is important to report any suspicious sores to your healthcare provider right away.

Melanoma is a much more serious form of skin cancer. Unlike BCC, left untreated it can spread to other organs and can be lethal. Melanoma often arises from moles. The key to successful treatment of melanoma is early diagnosis. Moles should be monitored for the changes. Monitoring of moles can be remembered using the "ABCD" warning signs:

A is for Asymmetry (one half of the mole looks different than the other half)

B is for Border (moles that have an irregular, scalloped or poorly defined border)

C is for Color (variations in color from one area of the mole to another, such as different shades of tan and brown or black, or colors such as white, red or blue within a mole)

D is for Diameter (moles larger than 6 millimeters – about the diameter of a pencil eraser – should be evaluated).

If you notice any of the "ABCD" changes, have your healthcare provider check the mole. Moles that have any of these changes usually need to be removed.

What monitoring is needed?

If you have any of the following risk factors, you should c**heck your skin monthly for changes**, and have a thorough **skin examination** by a healthcare provider **at least once a year**:

- You received radiation to any area, including total body irradiation (TBI)
- You have ever had skin cancer or melanoma, or you have a family history of skin cancer or melanoma
- You have "dysplastic" (atypical) moles
- You had a severe sunburn at a young age

What can I do to keep my skin healthy?

The most important thing to remember in caring for your skin is to protect it from the sun. Here are some things you can do:

- Wear protective clothing or sunscreen at all times when your skin is exposed to the sun, even on cloudy or hazy days. The American Cancer Society recommends a sunscreen with an SPF (sun protection factor) of 15 or higher.
- Sand, snow, concrete, water and high altitudes all increase the risk of sun damage – take extra caution to protect your skin in these environments.
- Do not attempt to tan your skin - avoid tanning booths.
- Avoid outdoor activities from 10am to 2pm when the sun's rays are most intense (11am to 3pm during daylight savings time). Plan outdoor activities in the early morning or late afternoon hours.
- Reapply sunscreen frequently or use a water resistant sunscreen when swimming or perspiring heavily. This will not only help to protect you from developing skin problems, but will also help you to maintain a youthful appearance.

If you have any questions or concerns about your skin, contact your healthcare provider. Take good care of your skin and it will take care of you!

Written by Kathy Ruble, RN, CPNP, AOCN®, Coordinator, Long Term Follow-up Program, Johns Hopkins University, Baltimore, MD.

Reviewed by Julie Blatt MD, Louis S. Constine MD, Rebecca D. Pentz PhD, and Debra Friedman MD.

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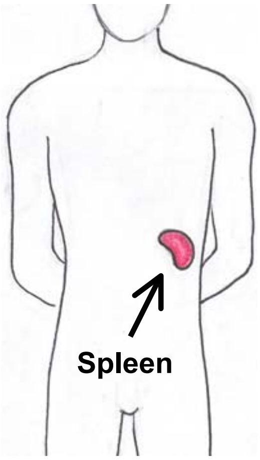
Precautions for People Without a Functioning Spleen

What is the spleen?

The spleen is an organ located in the upper left side of the abdomen, tucked under the rib cage, behind the stomach. It is normally about the size of a person's fist. The spleen produces antibodies and filters bacteria from the blood. This helps the body to fight infections.



What are the risks of a non-functioning spleen?

Because your spleen was removed or you received a high dose of radiation to the spleen (30 Gy - 3000 cGy/rads or higher) during your cancer treatment, you are more likely than other people to develop serious infections. These infections can be fatal if not treated immediately. The types of infections most likely to occur in people without a functioning spleen are those caused by encapsulated bacteria (germs with an outer coating that protect them from the body's immune system). Some common types of encapsulated bacteria include *Streptococcus pneumoniae, Haemophilus influenzae, and Neisseria meningitidis*.

What are the signs of infection?

Fever is a sign of infection. Often, fever is caused by a virus (like the flu) and not by dangerous bacteria. However, there is no way to know if bacteria are the cause of a fever unless a blood culture is done (by taking a blood sample and testing it for the presence of bacteria). Unfortunately, it takes anywhere from a few hours to a few days for the blood culture results to become available. **Therefore, whenever you have a fever you must be treated with antibiotics as if you had a serious infection**, at least until the blood culture results are known.

Other symptoms of infection include unusual tiredness, muscle aches, chills, headache, vomiting, diarrhea, and abdominal pain. These symptoms can be warning signs of infection even if you do not have a fever. Check with your healthcare provider if you develop these symptoms. Take your temperature regularly any time that you develop symptoms of illness.

What should I do if I get a fever?

If your temperature is **101°F (38.3°C) or higher you should:**

- **Seek <u>immediate</u> medical attention (even if you are taking antibiotics).**
- **Tell your healthcare provider that you do not have a functioning spleen.**
- **Report any symptoms** that you are experiencing (such as those listed above).
- **Have a blood sample taken** for blood count and culture.
- **Receive a strong antibiotic** (by injection into a vein or muscle), at least until the blood culture results are available.

Is there anything I can do to prevent infections?

Vaccines: Vaccines may reduce your chances of a serious infection. **We recommend that you receive the Pneumococcal, Meningococcal, and HIB** (*Haemophilus influenzae* type B) **vaccines.** Check with your healthcare provider to see whether you have had all of these vaccines and whether you need booster doses (additional doses given after the original vaccine). Everyone should have at least one booster of Pneumococcal vaccine, given 3 to 5 years after the first shot. Some healthcare providers recommend additional boosters. **Many healthcare providers also recommend yearly influenza (flu) vaccine,** in order to reduce the risk of bacterial infections that can sometimes occur as a complication of the flu. It's also important to know that **even if you have received vaccines, you are still at risk for infection**, because **vaccination is not 100% protective.**

Antibiotics: Some healthcare providers may recommend that you take daily preventive (prophylactic) antibiotic pills, such as penicillin, with the hope of preventing serious bacterial infections. Others may give you a prescription to have on hand and instruct you to start taking antibiotics at the first sign of illness. Still others may recommend a prescription for antibiotics only if you are traveling to an area where it will be difficult to obtain medical care. **In any case, whether or not you are taking antibiotics, it is essential that you seek immediate medical attention any time that you develop fever, chills, or other symptoms of serious illness.** Delaying a medical visit for even a few hours can be very dangerous for you, because if you do have a bacterial infection, it can worsen rapidly.

Other precautions:

Because you do not have a functioning spleen, you are also at increased risk for problems with the following infections:

Malaria: If you travel to countries where malaria is common, take special precautions to avoid getting malaria. Ask your healthcare provider for anti-malarial medications before you travel to infested areas. During travel, use insect repellants and other protective measures, such as netting and protective clothing.

Dog Bites: Dog bites can result in serious bacterial infections. If you receive a dog bite that breaks the skin, you should seek immediate medical attention for treatment with antibiotics.

Ticks: People without a functioning spleen are at increased risk for an infection caused by *Babesia*, a germ transmitted by deer ticks. These ticks are most commonly found in the northeastern United States and in some European countries. (Note: this is **not** the type of germ that causes lyme disease). You should wear protective clothing and use insect repellants when going outdoors in tick-infested areas. If you receive a tick bite while in an area infested with *Babesia*, you should remove the tick and talk to your healthcare provider about what to do.

How will my healthcare providers know about my non-functioning spleen?

Be sure to tell all of your doctors, dentists, and other healthcare providers that you do not have a functioning spleen. You should also **wear a medical alert emblem** (bracelet or necklace) so that in case you are unable to communicate in a medical emergency, you will be readily identified as not having a functioning spleen.

We also recommend that you carry a wallet card, such as the one below, with guidelines for healthcare professionals regarding the management of fever in people without a functioning spleen.

Written by Teresa Sweeney, RN, MSN, CPNP, Pediatric Nurse Practitioner in the After Completion of Therapy (ACT) Clinic at St. Jude Children's Research Hospital in Memphis, Tennessee.

Reviewed by Smita Bhatia, MD, MPH, Julie Blatt, MD, Melissa Hudson MD, Kevin Oeffinger, MD, Lise Yasui, Wendy Landier, CPNP, and the COG Late Effects Committee.

Illustrated by Devika Bhatia.

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Wallet Card for Patients Without a Functioning Spleen

MEDICAL ALERT:

Asplenic Patient

Name: ______________________________
Primary Physician: ____________________
Physician Phone: ______________________

(See other side for suggested management)

Medical Alert: Asplenic Patient

This patient is asplenic and at risk for potentially fatal, overwhelming infections. Immediate medical attention is required for fever of ≥101°F (38.3°C) or other signs of serious illness. Suggested management includes:

1) Physical exam, CBC and blood culture.
2) Administration of a long-acting, broad-spectrum parenteral antibiotic (e.g., ceftriaxone) accompanied by close clinical monitoring while awaiting blood culture results.
3) Hospitalization and broadening of antimicrobial coverage (e.g., addition of vancomycin) may be necessary under certain circumstances, such as the presence of marked leukocytosis, neutropenia, or significant change from baseline CBC; toxic clinical appearance; fever ≥104°F; meningitis, pneumonia, or other serious focus of infection; signs of septic shock; or previous history of serious infection.

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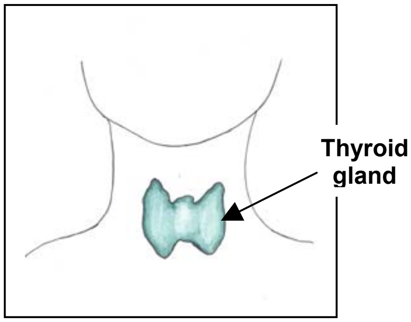
Thyroid Problems After Childhood Cancer

Some treatments given for childhood cancer may affect the thyroid gland. These effects are usually very easy to treat. Regular check-ups may help find thyroid problems early so that the proper treatment can be started.

What is the thyroid gland?



The thyroid gland is located in the lower part of the neck in front of the windpipe. The gland makes two hormones, thyroxine (T4) and triiodothyronine (T3), that play an important role in growth and mental development, and help to regulate the body's metabolism. The thyroid gland is controlled by the pituitary, a gland in the brain which makes thyroid stimulating hormone (TSH). TSH is released from the pituitary in response to the levels of T4 and T3 in the blood. If the levels are low, the pituitary makes more TSH to signal the thyroid to increase the production of thyroid hormones. If T4 and T3 are high, the pituitary makes less TSH to signal the thyroid gland to slow down production.

The possible late effects

Damage to the thyroid gland after childhood cancer is usually the result of radiation to the brain or neck. This damage may not show up for years after treatment. Several different types of thyroid problems may develop including an underactive thyroid (hypothyroidism), overactive thyroid (hyperthyroidism), and growths on the thyroid that may be benign (nodules) or malignant (cancer).

Hypothyroidism occurs when the thyroid gland is not active enough. This is the most common thyroid problem seen in childhood cancer survivors. When the thyroid gland is underactive, thyroid hormone levels are low and the body's metabolism slows down. There are three different types of hypothyroidism seen in childhood cancer survivors:

- **Primary hypothyroidism** is caused by direct damage to the thyroid gland. Blood tests in people with primary hypothyroidism show a high TSH because the pituitary gland is responding to the lower than normal levels of T3 and T4 produced by the damaged thyroid gland.
- **Central hypothyroidism** is caused by damage to the pituitary gland in the brain. Blood tests in people with central hypothyroidism show low TSH, T3 and T4 levels because the pituitary gland does not produce enough TSH to signal the thyroid gland to keep the proper levels of T3 and T4 in the blood.
- **Compensated hypothyroidism** occurs when the pituitary gland has to overwork the thyroid gland to keep the level of thyroid hormones normal in the blood. This may be a temporary problem after radiation, or it may be a sign that the thyroid gland is beginning to fail. Blood tests in people with compensated hypothyroidism show higher than normal TSH levels and normal T3 and T4 levels. Some survivors with compensated hypothyroidism may be treated with thyroid hormone in order to decrease the workload on the thyroid gland.

Signs and symptoms of **hypothyroidism** may include:

- Feeling tired and listless
- Hoarse voice
- Problems concentrating
- Feeling sad/depressed
- Mood changes
- Constipation
- Weakness
- Feeling cold all of the time
- Puffiness around the eyes
- Slowing of normal growth
- Delayed onset of puberty
- Puffiness of the face and hands
- Weight gain
- Dry skin
- Brittle hair
- Muscle and joint aches
- Slowing of the heart rate
- Low blood pressure
- High cholesterol level
- Poor exercise tolerance

Hyperthyroidism occurs when the thyroid gland is too active. In this condition thyroid hormone levels are high and the body's metabolism speeds up.

Signs and symptoms of **hyperthyroidism** may include:

- Jitteriness
- Anxiety
- Problems concentrating
- Feeling tired
- Muscle weakness
- Tremors
- Fast or irregular heartbeat
- Increased sweating
- Feeling hot all of the time
- Diarrhea
- Weight loss
- Irregular menstrual periods
- Bulging or protruding eyes
- Neck tenderness and swelling
- Poor exercise tolerance

Thyroid nodules and **thyroid cancer** are growths that may occur many years after radiation to the thyroid gland. Both usually begin as slow-growing, painless lumps in the neck. Most thyroid growths do not usually cause any symptoms.

Who is at risk for thyroid problems?

People who received radiation that may have affected the thyroid gland directly are at risk for primary hypothyroidism, compensated hypothyroidism, hyperthyroidism, thyroid nodules, and/or thyroid cancer. The following radiation fields have the potential to affect the thyroid gland directly:

- Neck (cervical or mantle)
- Head/brain (cranial)
- Head/brain/spine (craniospinal)
- Spine
- Nose, mouth, and/or throat (nasopharyngeal, oropharyngeal)
- Chest (mediastinal, whole lung)
- Total body irradiation (TBI)

People who received radiation that may have affected the pituitary gland in the brain are at risk for central hypothyroidism. The following radiation fields have the potential to affect the pituitary gland:

- Head/brain (cranial)
- Head/brain/spine (craniospinal)
- Eye/orbit
- Ear/infratemporal region (midfacial area behind the cheekbones)
- Nose, mouth, and/or throat (nasopharyngeal, oropharyngeal)
- Total body irradiation (TBI)

Other factors that have been shown to increase the risk of thyroid problems after childhood cancer include being:

- Female
- Treated with higher radiation doses
- Treated at a young age

Thyroid problems may occur soon after radiation, but generally do not occur until several years later. If treated promptly, thyroid problems are easily managed.

What follow up is needed for those at risk?

Since thyroid problems may occur many years after cancer treatment, a yearly check-up is recommended for survivors who are at risk of developing thyroid problems. This check-up should include evaluation of growth in children and teens, palpation (feeling) of the thyroid gland, and a blood test to measure the levels of TSH and T4. During periods of rapid growth, healthcare providers may recommend more frequent monitoring of thyroid levels.

Female survivors at risk for thyroid problems who are planning to become pregnant should have their thyroid levels checked before attempting pregnancy. It is important to do this before becoming pregnant, because mothers with thyroid disease have a higher chance of having babies with developmental problems. It is also important to monitor thyroid levels periodically during pregnancy.

How are thyroid problems treated?

If problems with thyroid levels are identified, you may be referred to an endocrinologist (hormone specialist) for continuing treatment. If a lump is detected on the thyroid, you may be referred to a surgeon or other specialist for evaluation and management.

All types of **hypothyroidism** are treated with daily thyroid pills. Treatment is usually for life. In some cases of compensated hypothyroidism, treatment may be stopped if the thyroid gland begins to work normally.

Hyperthyroidism may be treated in several ways. Sometimes medication is given on a temporary basis to prevent thyroid hormone production. Thyroid ablation (destroying the hormone-producing cells in the gland by drinking a radioactive liquid iodine called I-131) may be done. Surgery to remove the thyroid gland is another treatment. Your healthcare provider will determine which treatment option is the best choice for you. Treatment for hyperthyroidism may result in hypothyroidism, which is then treated with a daily thyroid pill.

Thyroid nodules. Thyroid growths that are felt on physical exam need additional testing. This is generally done with an ultrasound (picture made using sound waves) and biopsy (sampling the thyroid tissue to check for cancer cells). Surgery may be done to remove enlarging nodules because of the concern about thyroid cancer.

Thyroid cancer. Treatment for thyroid cancer involves surgery to remove the cancer and as much additional normal thyroid tissue as the surgeon feels is necessary. After surgery, additional treatment with radioactive iodine (I-131) may be needed to destroy any remaining thyroid tissue. After treatment for thyroid cancer, most individuals will need to take daily thyroid pills.

Written by Melissa Hudson MD and Wendy Landier CPNP.

Melissa Hudson, MD directs the After Completion of therapy (ACT) clinic at St. Jude Children's Research Hospital in Memphis, TN.

Wendy Landier, RN, MSN, CPNP, CPON®, is a pediatric nurse practitioner and clinical director of the Survivorship Clinic at City of Hope National Medical Center in Duarte, CA

Reviewed by Charles Sklar MD, Debra L. Friedman MD, Julie Blatt MD, and Joan Darling PhD.

Illustrated by Devika Bhatia.

Note: Throughout this *Health Links* series, the term "childhood cancer" is used to designate pediatric cancers that may occur during childhood, adolescence, or young adulthood. *Health Links* are designed to provide health information for survivors of pediatric cancer, regardless of whether the cancer occurred during childhood, adolescence, or young adulthood.

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