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Registered in Tanzania, Registration Number S.A.19229

What Is Cancer?

Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death.

Normal cells in the body

The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

How cancer starts

Cancer starts when cells in a part of the body start to grow out of control. Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell.

Cells become cancer cells because of DNA (deoxyribonucleic acid) damage. DNA is in every cell and it directs all the cell's actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, and the cell doesn't die like it should. Instead, the cell goes on making new cells that the body doesn't need. These new cells all have the same abnormal DNA as the first cell does.

People can inherit abnormal DNA, but most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in the environment. Sometimes the cause of the DNA damage may be something obvious like cigarette smoking or sun exposure. But it's rare to know exactly what caused any one person's cancer.

In most cases, the cancer cells form a tumor. Some cancers, like leukemia, rarely form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

How cancer spreads

Cancer cells often travel to other parts of the body where they begin to grow and form new tumors. This happens when the cancer cells get into the body's bloodstream or lymph vessels. Over time, the tumors replace normal tissue. The process of cancer spreading is called metastasis.

How cancers differ

No matter where cancer may spread, it's always named for the place where it started. For example, breast cancer that has spread to the liver is called metastatic breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is called metastatic prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For instance, lung cancer and skin cancer are very different diseases. They grow at different rates and respond to different treatments. This is why people with cancer need treatment that is aimed at their kind of cancer.

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Tumours that are not cancer

Not all tumours are cancer. Tumours that aren't cancer are called benign. Benign tumours can cause problems – they can grow very large and press on healthy organs and tissues. But they cannot grow into (invade) other tissues. Because they can't invade, they also can't spread to other parts of the body (metastasize). These tumours are almost never life threatening.

How common is cancer?

Half of all men and one-third of all women in the US will develop cancer during their lifetimes. Today, millions of people are living with cancer or have had cancer. The risk of developing many types of cancer can be reduced by changes in a person's lifestyle, for example, by staying away from tobacco, limiting time in the sun, being physically active and healthy eating.

There are also screening tests that can be done for some types of cancers so they can be found as early as possible – while they are small and before they have spread. In general, the earlier a cancer is found and treated, the better the chances are for living for many years.

No matter who you are, we can help. Contact us any time, day or night, for information and support. Call us at +255.753.110758 or visit www.focc.org.tz

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What is childhood leukemia?

Leukemia is a cancer that starts in early blood-forming cells. Most often, leukemia is a cancer of the white blood cells, but some leukemia's start in other blood cell types.

Any of the cells from the bone marrow can turn into a leukemia cell. Once this change takes place, the leukemia cells don't go through the normal process of maturing. Leukemia cells might reproduce quickly, and not die when they should. They survive and build up in the bone marrow, crowding out normal cells. In most cases, the leukemia cells spill into the bloodstream fairly quickly. From there it can go to other parts of the body such as the lymph nodes, spleen, liver, central nervous system (the brain and spinal cord), testicles, or other organs, where they can keep other cells in the body from functioning normally.

Some other childhood cancers, such as neuroblastoma or Wilms tumor, start in other organs and can spread to bone marrow, but these cancers are not leukemia.

Types of leukemia in children

Leukemia is often described as being either acute (fast growing) or chronic (slow growing). Almost all childhood leukemia is acute.

Acute leukemia

The main types of acute leukemia are:

- Acute lymphocytic (lymphoblastic) leukemia (ALL): About 3 out of 4 cases of childhood leukemia are ALL. This leukemia starts from the lymphoid cells in the bone marrow.
- Acute myelogenous leukemia (AML): This type of leukemia, also called *acute myeloid leukemia*, *acute myelocytic leukemia*, or *acute non-lymphocytic leukemia*), accounts for most of the remaining cases. AML starts from the myeloid cells that form white blood cells (other than lymphocytes), red blood cells, or platelets.
- **Hybrid or mixed lineage leukemia:** In these rare leukemia's, the cells have features of both ALL and AML. In children, they are generally treated like ALL and respond to treatment like ALL.

Both ALL and AML can be further divided into different subtypes.

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Chronic leukemias

Chronic leukemias are much more common in adults than in children. They tend to grow more slowly than acute leukemias, but they are also harder to cure. Chronic leukemias can also be divided into 2 types.

- Chronic myelogenous leukemia **(CML):** This leukemia rarely occurs in children. Treatment is similar to that used for adults.
- Chronic lymphocytic leukemia **(CLL):** This leukemia is extremely rare in children, so it is not discussed further in this document..

Juvenile myelomonocytic leukemia (JMML)

This rare type of leukemia is neither chronic nor acute. It begins from myeloid cells, but it usually doesn't grow as fast as AML or as slow as CML. It occurs most often in young children (under age 4). Symptoms can include pale skin, fever, cough, easy bruising or bleeding, trouble breathing (from too many white blood cells in the lungs), and an enlarged spleen and lymph nodes.

Can childhood leukemia be found early?

At this time there are no widely recommended blood tests or other screening exams for most children to look for leukemia before it starts to cause symptoms. Childhood leukemia is often found because a child has symptoms that prompt a visit to the doctor. Blood test results are abnormal, which then points to the diagnosis. The best way to find these cancers early is to pay attention to the possible signs and symptoms of this disease.

For children known to be at increased risk of leukemia (because of Li-Fraumeni syndrome or Down syndrome, for example), most doctors recommend careful, regular medical checkups and possibly other tests. The same is true for children who have had other cancers treated with chemotherapy and/or radiation therapy, and for children who have received organ transplants and are taking immune system-suppressing drugs. The risk of leukemia in these children, although higher than in the general population, is still small.

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Signs and symptoms of childhood leukemia

As leukemia cells build up in the bone marrow, they can crowd out the normal blood cell-making cells. As a result, a child may not have enough normal red blood cells, white blood cells, and blood platelets. These shortages show up on blood tests, but they can also cause symptoms. The leukemia cells may also invade other areas of the body, which can also cause symptoms.

Many of these symptoms have other causes as well, and most often they are not from leukemia. Still, it's important to let your child's doctor know about them right away so that the cause can be found and treated, if needed.

Fatigue (tiredness), pale skin: Anemia (a shortage of red blood cells) might make a child feel tired, weak, lightheaded, or short of breath. It may also cause pale skin.

Infections and fever: A child with leukemia may develop fever. This is often caused by an infection, which may not improve even with antibiotics. This is because of a lack of normal white blood cells, which would normally help fight the infection. Although children with leukemia may have very high white blood cell counts, the leukemia cells do not protect against infection the way normal white blood cells do. Fever is also sometimes caused by the leukemia cells themselves releasing certain chemicals into the body.

Easy bleeding or bruising: A child with leukemia may bruise easily, have frequent nosebleeds and bleeding gums, or bleed too much from small cuts. There may be pinhead-sized red spots on the skin caused by bleeding from tiny blood vessels. This comes from a lack of blood platelets, which normally stop bleeding by plugging holes in damaged blood vessels.

Bone or joint pain: Some children with leukemia will have bone pain or joint pain. This is from the buildup of leukemia cells near the surface of the bone or inside the joint.

Swelling of the abdomen (belly): Leukemia cells may collect in the liver and spleen, causing them to enlarge. This may be noticed as a fullness or swelling of the belly. The lower ribs usually cover these organs, but when they are enlarged the doctor can often feel them.

Loss of appetite, weight loss: If the spleen and/or liver become large enough, they may press against other organs like the stomach. This can limit the amount of food that can be eaten, leading to a loss of appetite and weight loss over time.

Swollen lymph nodes: Some leukemia spread to lymph nodes. The child, a parent, or a health professional may notice swollen nodes as lumps under the skin in certain areas of the body (such as on the sides of the neck, in underarm areas, above the collarbone, or in the groin). Lymph nodes inside the chest or abdomen may also swell, but these can only be detected by imaging tests, such as CT or MRI scans.

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Lymph nodes often enlarge when they are fighting an infection, especially in infants and children. An enlarged lymph node in a child is more often a sign of infection than leukemia, but it should be checked by a doctor and followed closely.

Coughing or trouble breathing: The T-cell type of acute lymphocytic leukemia (ALL) often affects the thymus, which is a small organ in the chest behind the breastbone (sternum) and in front of the windpipe (trachea). An enlarged thymus or lymph nodes inside the chest can press on the trachea. This can lead to coughing or trouble breathing.

Swelling of the face and arms: The superior vena cava (SVC), a large vein that carries blood from the head and arms back to the heart, passes next to the thymus. Growth of the thymus from the buildup of leukemia cells may press on the SVC, causing the blood to "back up" in the veins. This is known as *SVC syndrome*. It can cause swelling in the face, neck, arms, and upper chest (sometimes with a bluish-red skin color). It can also cause headaches, dizziness, and a change in consciousness if it affects the brain. The SVC syndrome can be life-threatening, and needs to be treated right away.

Headache, seizures, vomiting: A small number of children have leukemia that has already spread to the central nervous system (brain and spinal cord) when they are first diagnosed. Headache, trouble concentrating, weakness, seizures, vomiting, problems with balance, and blurred vision can be symptoms of spread to the central nervous system.

Rashes, gum problems: In children with acute myelogenous leukemia (AML), leukemia cells may spread to the gums, causing swelling, pain, and bleeding. If it has spread to the skin, it can cause small, darkly colored spots that look like common rashes. A collection of AML cells under the skin or in other parts of the body is called a *chloroma* or *granulocytic sarcoma*.

Extreme fatigue, weakness: One rare but very serious consequence of AML is extreme tiredness, weakness, and slurring of speech. This can occur when very high numbers of leukemia cells cause the blood to become too thick and slow the circulation through small blood vessels of the brain.

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How is childhood leukemia diagnosed?

Most of the signs and symptoms of childhood leukemia are more likely to have other causes, such as infections. Still, it's important to let your child's doctor know about such symptoms right away so that the cause can be found and treated, if needed.

Exams and tests will be done to determine the cause of the symptoms. If leukemia is found, further tests will be needed to help tell what type it is and how it should be treated.

It's important to diagnose childhood leukemia as early as possible and to determine what type of leukemia it is so that treatment can be tailored to provide the best chance of success.

Medical history and physical exam

If your child has signs and symptoms that suggest they may have leukemia, the doctor will want to get a thorough medical history to learn about the symptoms your child is having and how long they have had them. The doctor may also ask about any history of exposure to possible risk factors. A family history of cancer, especially leukemia, may also be important.

During the physical exam, the doctor will focus on any enlarged lymph nodes, areas of bleeding or bruising, or possible signs of infection. The eyes, mouth, and skin will be looked at carefully, and a nervous system exam may be done. The abdomen will be felt for signs of an enlarged spleen or liver.

Types of tests used to look for leukemia in children

If the doctor thinks your child might have leukemia, samples of cells from your child's blood and bone marrow will need to be checked to be sure of the diagnosis. Your child's doctor may refer you to a *pediatric oncologist*, a doctor who specializes in cancers (like leukemia) in children, to have some of these tests done. If leukemia is found, other tissue and cell samples may also be taken to help guide treatment.

Blood tests

The first tests done to look for leukemia are blood tests. The blood samples are usually taken from a vein in the arm, but in infants and younger children, they may be taken from other veins (such as in the feet or scalp) or from a "finger stick."

Blood counts and blood smears are the usual tests done on these samples. A complete blood count (CBC) is done to determine how many blood cells of each type are in the blood. For a blood smear, a small sample of blood is spread

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on a glass slide and looked at under a microscope. Abnormal numbers of blood cells and changes in the way these cells look may make the doctor suspect leukemia.

Most children with acute leukemia – lymphocytic or myeloid – will have too many white blood cells and not enough red blood cells and/or platelets. Many of the white blood cells in the blood will be *blasts*, an early type of blood cell normally found only in the bone marrow. Even though these findings may make a doctor suspect that a child has leukemia, usually the disease cannot be diagnosed for sure without looking at a sample of bone marrow cells.

Bone marrow aspiration and biopsy

Bone marrow samples are obtained from a bone marrow aspiration and biopsy – 2 tests that are usually done at the same time. The samples are usually taken from the back of the pelvic (hip) bones, but in some cases they may be taken from the front of the pelvic bones, the breastbone (sternum [very rarely in children]), or other bones.

For a bone marrow *aspiration*, the skin over the hip bone is cleaned and numbed with local anesthetic. In most cases, the child is also given other medicines to reduce pain or even be asleep during the procedure. A thin, hollow needle is then inserted into the bone and a syringe is used to suck out (aspirate) a small amount of liquid bone marrow.

A bone marrow *biopsy* is usually done just after the aspiration. A small piece of bone and marrow is removed with a slightly larger needle that is twisted as it is pushed down into the bone. Once the biopsy is done, pressure will be applied to the site to help prevent any bleeding.

These bone marrow tests are used to diagnose leukemia and may be repeated later to tell if the leukemia is responding to treatment.

Lumbar puncture (spinal tap)

This test is used to look for leukemia cells in the cerebrospinal fluid (CSF), which is the liquid that bathes the brain and spinal cord.

For this test, the doctor first numbs an area in the lower part of the back over the spine. The doctor usually also gives the child medicine to make him or her sleep during the procedure. A small, hollow needle is then placed between the bones of the spine to withdraw some of the fluid.

This test is always done in children with leukemia, but it is important for it to be done by an expert. Doctors have found that if the spinal tap isn't performed expertly and some blood leaks into the CSF, in some cases leukemia cells may get into the fluid and grow there.

In children already diagnosed with leukemia, the first lumbar puncture is also used to give chemotherapy drugs into the CSF to try to prevent or treat the spread of leukemia to the spinal cord and brain.

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Lymph node biopsy

This type of biopsy is important in diagnosing lymphomas, but it is rarely needed for children with leukemia. During this procedure, a surgeon cuts through the skin to remove an entire lymph node (excisional biopsy). If the node is near the skin surface, this is a simple operation. But it is more involved if the node is inside the chest or abdomen. Most often the child will need general anesthesia (the child is asleep).

Lab tests used to diagnose and classify leukemia

Routine microscopic exams

As mentioned above, blood counts and smears are usually the first tests done when leukemia is a possible diagnosis. Any other samples taken (bone marrow, lymph node tissue, or CSF) are also looked at under a microscope by a pathologist (a doctor who specializes in interpreting lab tests) and may be reviewed by the patient's hematologist/oncologist (a doctor specializing in blood diseases and cancer).

The doctors will look at the size, shape, and staining patterns of the blood cells in the samples to classify them into specific types.

A key element is whether the cells look mature (like normal blood cells) or immature (lacking features of normal blood cells). The most immature cells are called *blasts*. Having too many blasts in the sample, especially in the blood, is a typical sign of leukemia.

An important feature of a bone marrow sample is its *cellularity*. Normal bone marrow contains a certain number of blood-forming cells and fat cells. Marrow with too many blood-forming cells is said to be *hyper cellular*. If too few blood-forming cells are found, the marrow is called *hypo cellular*.

Cytochemistry

In cytochemistry tests, cells from the sample are put on a microscope slide and exposed to chemical stains (dyes) that react only with some types of leukemia cells. These stains cause color changes that can be seen under a microscope. This can help the doctor determine what types of cells are present. For example, one stain causes the granules of most AML cells to appear as black spots under the microscope, but it does not cause ALL cells to change colors.

Flow cytometry and immunohistochemistry

Flow cytometry is used to test the cells from bone marrow, lymph nodes, and blood samples to determine more accurately the exact type of leukemia. It is a very important tool because it may help define the unique traits of the leukemia. It can also be used to measure the response to treatment and the existence of minimal residual disease (MRD) in some types of leukemia.

The test checks for certain substances on the surface of cells that help identify what types of cells they are. The cells in the sample are treated with special antibodies (man-made versions of immune system proteins) that stick only to these substances. The cells are then passed in front of a laser beam. If the cells now have antibodies attached to them, the laser will cause them to give off light, which is measured and analyzed by a computer.

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Flow cytometry can also be used to estimate the amount of DNA in the leukemia cells. This is important to know, especially in ALL, because cells with a high *DNA index* (1.16 or higher, which is more than 16% above normal) are often more sensitive to chemotherapy, and these leukemia have a better prognosis (outlook).

For *immunohistochemistry* tests, cells from the bone marrow or other samples are treated with special man-made antibodies. But instead of using a laser and computer for analysis, the sample is treated so that certain types of cells change color when seen under a microscope. Like flow cytometry, this test is helpful in distinguishing different types of leukemia from one another and from other diseases.

These tests are used for *immunophenotyping* – classifying leukemia cells according to the substances (antigens) on their surfaces. Different types of cells have different antigens on their surface. These antigens also change as the cells mature. Each patient's leukemia cells should all have the same antigens because they all come from the same original leukemia cell. Lab testing for antigens is a very sensitive way to diagnose and classify leukemia.

Cytogenetics

For this test, chromosomes (pieces of DNA) from leukemia cells are looked at under a microscope to detect any changes. Normal human cells contain 23 pairs of chromosomes, each of which are a certain size and stain a certain way. In some types of leukemia, chromosome changes may be seen.

For instance, sometimes 2 chromosomes swap some of their DNA, so that part of one chromosome becomes attached to part of a different chromosome. This change, called a *translocation*, can usually be seen under a microscope. Recognizing these changes can help identify certain types of acute leukemia and can help determine prognosis (outlook).

Some types of leukemia have cells with an abnormal number of chromosomes (instead of the usual 46) – they may be missing some chromosomes or have extra copies of some. This can also affect a patient's outlook. For example, chemotherapy is more likely to work in cases of ALL where the cells have more than 50 chromosomes and is less likely to be effective if the cells have fewer than 46 chromosomes. (Counting the number of chromosomes by cytogenetics provides similar information to measuring the DNA index by flow cytometry, as described above.)

Cytogenetic testing usually takes about 2 to 3 weeks because the leukemia cells must grow in lab dishes for a couple of weeks before their chromosomes are ready to be looked at under the microscope.

Not all chromosome changes can be seen under a microscope. Other lab tests can often help detect these changes.

Fluorescent in situ hybridization (FISH)

This is similar to cytogenetic testing. It uses pieces of DNA that only attach to specific parts of particular chromosomes. The DNA is linked to fluorescent dyes that can be seen with a special microscope. FISH can find most chromosome changes (such as translocations) that are visible under a microscope in standard cytogenetic tests, as well as some changes too small to be seen with usual cytogenetic testing.

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FISH can be used to look for specific changes in chromosomes. It can be used on blood or bone marrow samples. It is very accurate and can usually provide results within a couple of days.

Polymerase chain reaction (PCR)

This is a very sensitive DNA test that can also find some chromosome changes too small to be seen under a microscope, even if very few leukemia cells are present in a sample. This test can be very useful in looking for small numbers of leukemia cells (minimal residual disease, or MRD) during and after treatment that might not be detected with other tests.

Other blood tests

Children with leukemia will have tests to measure certain chemicals in the blood to check how well their body systems are working.

These tests are not used to diagnose leukemia, but in children already known to have it, they can help find damage to the liver, kidneys, or other organs caused by the spread of leukemia cells or by certain chemotherapy drugs. Tests are also often done to measure blood levels of important minerals, as well as to ensure the blood is clotting properly.

Children might also be tested for blood infections. It is important to quickly diagnose and treat infections in children with leukemia because their weakened immune systems can allow infections to spread quickly.

Imaging tests

Imaging tests use x-rays, sound waves, magnetic fields, or radioactive particles to produce pictures of the inside of the body. Leukemia does not usually form tumors, so imaging tests aren't as useful as they are for other types of cancer. But if leukemia is suspected or has been diagnosed, your child's doctor may order some of these tests to get a better idea of the extent of the disease or to look for other problems, such as infections.

Chest x-rays

A chest x-ray can help detect an enlarged thymus or lymph nodes in the chest. If the test result is abnormal, a computed tomography (CT) scan of the chest may be done to get a more detailed view.

Chest x-rays can also help look for pneumonia if your child might have a lung infection.

Computed tomography (CT) scan

The CT scan is a type of x-ray test that produces detailed, cross-sectional images of the body. Unlike a regular x-ray, CT scans can show the detail in soft tissues such as internal organs.

This test can help tell if any lymph nodes or organs in the body are enlarged. It isn't usually needed to diagnose leukemia, but it might be done if the doctor suspects the leukemia is growing in lymph nodes in the chest or in organs like the spleen or liver. It is also sometimes used to look at the brain and spinal cord, but an MRI scan may also be used for this.

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Instead of taking one picture, like a regular x-ray, a CT scanner takes many pictures as it rotates around your child. A computer then combines these pictures into detailed images of the part of the body that is being studied.

Before the scan, your child may be asked to drink a contrast solution and/or get an intravenous (IV) injection of a contrast dye that helps better outline abnormal areas in the body. He or she may need an IV line through which the contrast dye is injected.

The IV injection of contrast dye can cause a feeling of flushing or warmth in the face or elsewhere. Some people are allergic and get hives or, rarely, have more serious reactions like trouble breathing and low blood pressure. Be sure to tell the doctor if your child has any allergies or has ever had a reaction to any contrast material used for x-rays.

CT scans take longer than regular x-rays. A CT scanner has been described as a large donut, with a narrow table in the middle opening. Your child will need to lie still on the table while the scan is being done. During the test, the table slides in and out of the scanner. Some people feel a bit confined while the scan is being done. Some children might need to be sedated before the test to help make sure they stay still so the pictures come out well.

PET/CT scan: In recent years, newer devices have been developed that combine the CT scan with a positron emission tomography (PET) scan. For a PET scan, a form of radioactive sugar (known as *fluorodeoxyglucose* or FDG) is injected into the blood. (The amount of radioactivity used is very low and will pass out of the body within a day or so.) Because cancer cells in the body grow rapidly, they absorb large amounts of the radioactive sugar. A special camera can then create a picture of areas of radioactivity in the body. The picture from the PET scan is not finely detailed like those from a CT scan, but it provides helpful information about the whole body. The PET/CT scan lets the doctor compare areas of higher radioactivity on the PET scan with the more detailed appearance of that area on the CT scan.

Magnetic resonance imaging (MRI) scans

An MRI scan, like a CT scan, gives detailed images of soft tissues in the body. It is most helpful in looking at the brain and spinal cord, so it is most likely to be done if the doctor has reason to think the leukemia might have spread there (such as if the child has symptoms like headaches, seizures, or vomiting).

MRI scans use radio waves and strong magnets instead of x-rays, so there is no radiation involved. The energy from the radio waves is absorbed by the body and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into a very detailed image of parts of the body.

A contrast material called *gadolinium* is often injected into a vein before the scan to better show details. The contrast material usually does not cause allergic reactions.

MRI scans take longer than CT scans – often up to an hour. Your child may have to lie inside a narrow tube, which is confining and can be distressing, so sedation is sometimes needed. Newer, more open MRI machines may be another option, although they still require that your child be able to lie still. All MRI machines make loud buzzing and clicking noises that your child may find disturbing. Some places provide headphones or earplugs to help block this out.

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Ultrasound

Ultrasound uses sound waves and their echoes to produce a picture of internal organs or masses.

This test can be used to look at lymph nodes near the surface of the body or to look for enlarged organs inside the abdomen such as the kidneys, liver, and spleen. (It can't be used to look at organs or lymph nodes in the chest because the ribs block the sound waves.)

For this test, a small, microphone-like instrument called a *transducer* is placed on the skin (which is first lubricated with gel). It gives off sound waves and picks up the echoes as they bounce off the organs. The echoes are converted by a computer into an image that is displayed on a computer screen.

This is a fairly easy test to have, and it uses no radiation. Your child simply lies on a table, and a technician moves the transducer over the part of the body being looked at.

Bone scan

This test is not done often for childhood leukemia, but it may be useful if your child has bone pain that might be from either an infection or cancer in the bones. If your child has already been diagnosed with leukemia or if a PET scan (described above) has already been done, there is usually no need for a bone scan.

For this test, the doctor or nurse injects a small amount of a slightly radioactive chemical into the bloodstream. (The amount of radioactivity used is very low and will pass out of the body within a day or so.) The substance settles in areas of damaged bone throughout the skeleton over the course of a couple of hours. Your child then lies on a table for about 30 minutes while a special camera detects the radioactivity and creates a picture of the skeleton. Younger children may be given medicine to help keep them calm or even asleep during the test.

Areas of bone changes appear as hot spots on the skeleton because they attract the radioactivity, but the image isn't very detailed. If an area lights up on the scan, other imaging tests such as x-rays or CT or MRI scans may be done to get a more detailed look at the area. If leukemia is a possibility, a biopsy of the area may be needed to confirm this.

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What is retinoblastoma?

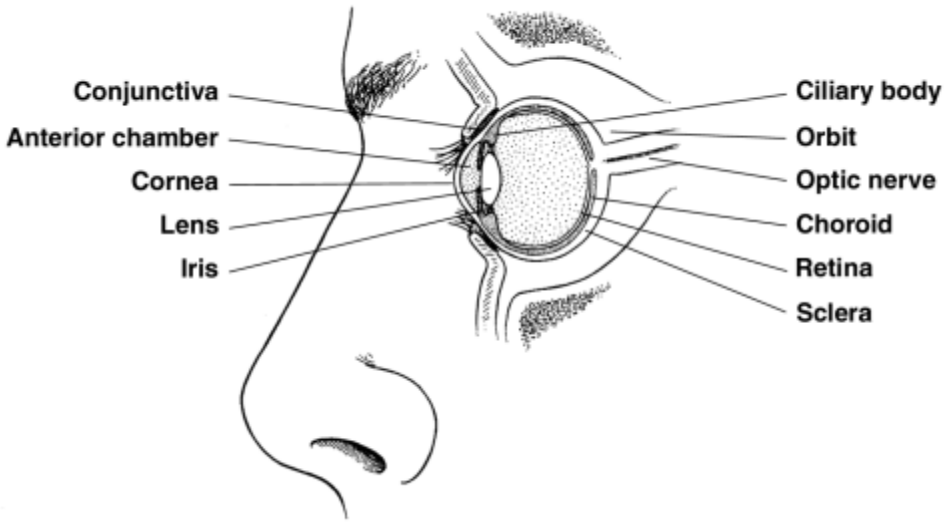
Most cancers are named for the part of the body where the cancer starts. Retinoblastoma is a cancer that starts in the retina, the very back part of the eye. It is the most common type of eye cancer in children. Rarely, children can have other kinds of eye cancer, such as medulloepithelioma, which is described briefly below. But the information in this document focuses on retinoblastoma and no other kinds of eye cancer.

To understand retinoblastoma, it helps to know something about the parts of the eye and how they work.

About the eye

The main part of the eye is the eyeball (also known as the globe), which is filled with a jelly-like material called *vitreous*. The front of the eyeball has a lens with an iris (the colored part of the eye that acts like a camera shutter), which allows light to enter the eye and focuses it on the retina.

The retina is the inner layer of cells in the back of the eye. It is made up of specialized nerve cells that are sensitive to light. These light-sensing cells are connected to the brain by the optic nerve, which runs out the back of the eyeball. The pattern of light (image) that reaches the retina is sent through the optic nerve to an area of the brain called the *visual cortex*, allowing us to see.



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How does retinoblastoma develop?

The eyes develop very early as babies grow in the womb. During the early stages of development, the eyes have cells called *retinoblasts* that divide into new cells and fill the retina. At a certain point, the cells stop dividing and develop into mature retinal cells.

Rarely, something goes wrong with this process. Instead of maturing into special cells that detect light, some retinoblasts continue to divide and grow out of control, forming a cancer known as *retinoblastoma*.

The chain of events that leads to retinoblastoma is complex, but it almost always starts with a change (mutation) in a gene called the *retinoblastoma (RB1 or Rb) gene*. The normal *RB1* gene helps keep cells from growing out of control, but the change in the gene stops it from working like it should. Depending on when and where the change in the *RB1* gene occurs, 2 different types of retinoblastoma can result.

Congenital (hereditary) retinoblastoma

In about 1 out of 3 retinoblastomas, the abnormality in the *RB1* gene is congenital (present at birth) and is in all the cells of the body, including all of the cells of both retinas. This is known as a *germ line mutation*.

In most of these children, there is no family history of this cancer. Only about 25% of the children born with this gene change inherit it from a parent. In about 75% of children the gene change first occurs during early development in the womb. The reasons for this are not clear.

Children born with a mutation in the *RB1* gene usually develop retinoblastoma in both eyes (known as *bilateral retinoblastoma*), and there are often several tumors within the eye (known as *multifocal retinoblastoma*).

Because all of the cells in the body have the changed *RB1* gene, these children also have a higher risk of developing cancers elsewhere in the body.

- A small number of children with this form of retinoblastoma will develop another tumor in the brain, usually in the pineal gland at the base of the brain (a pineoblastoma). This is also known as *trilateral retinoblastoma*.
- For survivors of hereditary retinoblastoma, the risk of developing other cancers later in life is also higher than average.

Sporadic (non-hereditary) retinoblastoma

In about 2 out of 3 cases of retinoblastoma, the abnormality in the *RB1* gene develops on its own in only one cell in one eye. It is not known what causes this change. A child who has sporadic (non-hereditary) retinoblastoma develops only one tumor in one eye. This type of retinoblastoma is often found at a later age than the hereditary form.

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How does retinoblastoma grow and spread?

If retinoblastoma tumors are not treated, they can grow and fill much of the eyeball. Cells might break away from the main tumor on the retina and float through the vitreous to reach other parts of the eye, where they can form more tumors. If these tumors block the channels that let fluid circulate within the eye, the pressure inside the eye can rise. This can cause glaucoma, which can lead to pain and loss of vision in the affected eye.

Most retinoblastomas are found and treated before they have spread outside the eyeball. But retinoblastoma cells can occasionally spread to other parts of the body. The cells sometimes grow along the optic nerve and reach the brain. Retinoblastoma cells can also grow through the covering layers of the eyeball and into the eye socket, eyelids, and nearby tissues. Once tissues outside the eyeball are affected, the cancer may then spread to lymph nodes (small bean-shaped collections of immune system cells) and to other organs such as the liver, bones, and bone marrow (the soft, inner part of many bones).

Intraocular medulloepithelioma

Medulloepithelioma is another type of tumor that can start in the eye. It is not a type of retinoblastoma, but it is mentioned here because it also usually occurs in young children. These tumors are very rare.

Medulloepitheliomas start in the ciliary body, which is near the front of the eye (see image above). Most of these tumors are malignant (cancerous), but they rarely spread outside the eye. They usually cause eye pain and loss of vision.

The diagnosis is made when a doctor finds a tumor mass in the eye by using an ophthalmoscope (an instrument that helps doctors to look inside the eye). Like retinoblastoma, the diagnosis is usually made based on where the tumor is inside the eye and how it looks. A biopsy (removing cells from the tumor to be looked at under a microscope) to confirm the diagnosis is almost never done because it might harm the eye or risk spreading the cancer outside of the eye. Treatment for medulloepithelioma is almost always surgery to remove the eye.

Can retinoblastoma be found early?

Retinoblastoma is a rare cancer, and there are no widely recommended screening tests to look for retinoblastoma in children without symptoms. Still, many retinoblastomas are found early by parents, relatives, or a child's doctor.

During children's regular physical exams, doctors routinely check their eyes. Some of the things doctors look for include changes in how the eyes look (inside or outside), changes in how the eyes move, and changes in the child's vision. Any of these might be a sign of retinoblastoma, although they are more often caused by something else.

Sometimes, a parent or relative may notice that a young child's eye doesn't look normal, prompting a visit to the doctor. It is important for parents to be aware of the possible signs and symptoms of retinoblastoma, and to report

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anything unusual to the doctor as soon as possible. Most often the cause is something other than retinoblastoma, but it is important to have it checked so that the cause can be found and treated right away, if needed.

For children in families known to carry an abnormal *RB1* gene, or in families with a history of retinoblastoma who have not had genetic testing for the *RB1* gene, doctors recommend regular eye exams during the first years of life to detect any tumors at an early stage. These children often have an eye exam a few days after birth, again at about 6 weeks of age, then every few months until at least age 5. This gene defect can be found by a special blood test, so most doctors now advise that children with parents or siblings with a history of retinoblastoma have this genetic test done during the first few weeks after birth. The results of the test then help define how often eye exams should be done.

Most cases of hereditary retinoblastoma develop and are diagnosed in infants only a few months old. Usually, if tumors develop in both eyes, it happens at the same time. But in some children, tumors develop in one eye first, then a few months (or even years) later in the other eye. So even if retinoblastoma is diagnosed in only one eye, these children will still need regular exams of the other eye for several years after treatment.

If a child has retinoblastoma that is thought to be hereditary, many doctors also recommend magnetic resonance imaging (MRI) scans of the brain at regular intervals for up to 5 years to check for a trilateral retinoblastoma (a brain tumor such as a pineoblastoma).

Signs and symptoms of retinoblastoma

Retinoblastomas are often found when a parent or doctor notices a child's eye looks unusual.

White pupillary reflex

This is the most common early sign of retinoblastoma. Normally when you shine a light in the eye, the pupil (the dark spot in the center of the eye) looks red because of the blood in vessels in the back of the eye. In an eye with retinoblastoma, the pupil often appears white or pink instead, which is known as a *white pupillary reflex* (or *leukocoria*).

This white glare of the eye may be noticed by a parent after a flash photograph is taken, especially if the pupils are different colors. It also might be noted by the child's doctor during a routine eye exam.

Lazy eye

Sometimes the eyes do not appear to look in the same direction, a condition often called *lazy eye*. (Doctors call this *strabismus*.) There are many possible causes of this in children. Most of the time lazy eye is caused by a mild weakness of the muscles that control the eyes, but retinoblastoma is also one of the rare causes.

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Other possible signs and symptoms

Less common signs and symptoms of retinoblastoma include:

- Vision problems
- Eye pain
- Redness of the white part of the eye
- Bleeding in the front part of the eye
- Bulging of the eye
- A pupil that does not get smaller when exposed to bright light
- A different color in each iris (the colored part of the eye)

Many of these signs and symptoms are more likely to be caused by something other than retinoblastoma. Still, if your child has any of these, check with your child's doctor so that the cause can be found and treated, if needed.

How is retinoblastoma diagnosed?

Retinoblastomas are usually found when a child is brought to a doctor because he or she has certain signs or symptoms.

Most types of cancer can be found by physical exam and imaging tests, but treatment is usually not begun until the diagnosis is confirmed by a biopsy. During a biopsy, the doctor removes a sample from the tumor and sends it to a lab to be looked at under a microscope.

But biopsies are not usually done to diagnose retinoblastoma for 2 reasons. First, taking a biopsy specimen from a tumor in the eye cannot be done easily without harming the eye and risking spreading cancer cells outside the eye. Second, retinoblastoma can be diagnosed accurately by doctors who have experience with this disease, and it is unlikely to be confused with other eye problems in children.

Medical history and physical exam

If your child has signs or symptoms of retinoblastoma, the doctor will examine your child's eyes and get a complete medical history. The doctor will ask about the child's symptoms and may ask about any family history of retinoblastoma or other cancers. This information is important when deciding if more tests and exams are needed. Your family history is also useful for determining whether other relatives could possibly pass this gene on to their children or develop this cancer themselves (if they are young children) and might benefit from genetic counseling.

If a retinoblastoma is suspected, the doctor will refer you to an ophthalmologist (a doctor who specializes in eye diseases), who will examine the eye closely to be more certain about the diagnosis. The ophthalmologist will use

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special lights and magnifying lenses to look inside the eye. Usually, the child needs to be under general anesthesia (asleep) during the exam so that the doctor can take a careful and detailed look.

If a diagnosis of retinoblastoma seems likely based on the eye exam, imaging tests will be done to help confirm it and to find out how far it may have spread within the eye and possibly to other parts of the body. Usually an ophthalmologist who specializes in treating cancers of the eye (called an *ocular oncologist*) will make the final determination. This doctor should also be part of the team of doctors treating the cancer.

Imaging tests

Imaging tests use x-rays, sound waves, magnetic fields, or radioactive substances to create pictures of the inside of the body. Imaging tests may be done for a number of reasons, including:

- To help tell if a tumor in the eye is likely to be a retinoblastoma
- To determine how large the tumor is and how far it has spread
- To help determine if treatment has been effective

Children with retinoblastoma may have one or more of these tests.

Ultrasound

Ultrasound uses sound waves to create images of tissues inside the body, such as the inner parts of the eye. For this test, a small ultrasound probe is placed up against the eyelid or eyeball. The probe gives off sound waves and detects the echoes that bounce off the tissues inside and around the eye. The echoes are converted by a computer into an image on a computer screen.

Ultrasound is one of the most common imaging tests for confirming the diagnosis of retinoblastoma. It is painless and does not expose the child to radiation, but the child may need to be sedated (made sleepy) so that the doctor can get a good look at the eye. This test can be very useful when tumors in the eye are so large they prevent doctors from seeing inside the whole eye because ultrasound can “see through” tissues.

Optical coherence tomography (OCT) is a similar type of test that uses light waves instead of sound waves to create very detailed images of the back of the eye.

Magnetic resonance imaging (MRI) scans

MRI scans are often used for retinoblastomas because they provide very detailed images of the eye and surrounding structures without using radiation. This test is especially good at looking at the brain and spinal cord. Most children with retinoblastoma will have at least one MRI scan. For children with bilateral retinoblastomas (tumors in both eyes), many doctors continue to do MRI scans of the brain for several years after treatment to look for tumors of the pineal gland (sometimes called *trilateral retinoblastoma*).

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Unlike CT scans (described next), MRI scans use radio waves and strong magnets to create images instead of x-rays. A contrast material called *gadolinium* may be injected into a vein before the scan to see details better.

MRI scans may take up to an hour. Your child may have to lie inside a narrow tube, which is confining and can be upsetting. Newer, more open MRI machines can help with this, but the test still requires staying still for long periods of time. The machines also make buzzing and clicking noises that may be disturbing. Young children may be given medicine to help keep them calm or even asleep during the test.

Computed tomography (CT) scan

The CT scan is an x-ray test that produces detailed cross-sectional images of parts of the body. CT scans can help determine the size of a retinoblastoma tumor and how much it has spread within the eye and to nearby areas. Normally, either a CT or an MRI scan is needed to do this, but usually not both.

Because CT scans give off radiation, which might raise a child's risk for other cancers in the future, most doctors prefer to use MRI. However, a CT scan can show deposits of calcium in the tumor much better than an MRI, which can be very helpful when the diagnosis of retinoblastoma is not clear.

Instead of taking one picture, like a regular x-ray, a CT scanner takes many pictures as it rotates around your child while he or she lies on a table. A computer then combines these pictures into images of slices of the part of the body being studied.

Before the scan, your child may receive an IV (intravenous) injection of a contrast dye that helps better outline structures in the body. The dye may cause some flushing (a feeling of warmth, especially in the face). Some people are allergic and get hives. Rarely, more serious reactions like trouble breathing or low blood pressure can occur. Be sure to tell the doctor if your child has any allergies or has ever had a reaction to any contrast material used for x-rays.

CT scans take longer than regular x-rays, but not as long as MRI scans. A CT scanner has been described as a large donut, with a narrow table in the middle opening. Your child will need to lie still on the table while the scan is being done. During the test, the table slides in and out of the scanner. Your child may need to be sedated before the test to stay still and help make sure the pictures come out well.

Bone scan

A bone scan can help show if the retinoblastoma has spread to the skull or other bones. Most children with retinoblastoma do not need to have a bone scan. It is normally used only when there is a strong reason to think retinoblastoma may have spread beyond the eye.

For this test, a small amount of low-level radioactive material is injected into a vein (intravenously, or IV). (The amount of radioactivity used is very low and will pass out of the body within a day or so.) The material settles in areas of damaged bone throughout the skeleton over the course of a couple of hours. Your child then lies on a table for about 30 minutes while a special camera detects the radioactivity and creates a picture of the skeleton. Younger children may be given medicine to help keep them calm or even asleep during the test.

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This test shows the entire skeleton at once. Areas of active bone changes appear as “hot spots” on the skeleton – that is, they attract the radioactivity. These areas may suggest the presence of cancer, but other bone diseases can also cause the same pattern. To help tell these apart, other tests such as plain x-rays or MRI scans of the bone might be needed.

Other tests

Some other types of tests are not commonly needed for retinoblastomas, but they may be helpful in some situations.

Biopsy

For most cancers, a biopsy (removing a tissue sample from the tumor and looking at it under a microscope) is needed to make a diagnosis. Trying to biopsy a tumor at the back of the eye can often damage the eye and may spread tumor cells, so this is almost never done to diagnose retinoblastoma. Instead, doctors make the diagnosis based on eye exams and on imaging tests such as those listed above. This is why it is very important that the diagnosis of retinoblastoma is made by experts.

Lumbar puncture (spinal tap)

Retinoblastomas may grow along the optic nerve, which connects the eye to the brain. If the cancer has spread to the surface of the brain, this test can often find cancer cells in samples of cerebrospinal fluid (the fluid that surrounds the brain and spinal cord). Most children with retinoblastoma do not need to have a lumbar puncture. It is normally used only when there is a reason to think retinoblastoma may have spread into the brain.

For this test, the doctor first numbs an area in the lower part of the back over the spine. The child is typically given anesthesia so they will sleep and not move during the procedure. This can help ensure the spinal tap is done cleanly. A small, hollow needle is then placed between the bones of the spine to withdraw a small amount of the fluid. The fluid is then looked at under a microscope to check for cancer cells.

Bone marrow aspiration and biopsy

These 2 tests may be done to see if the cancer has spread to the bone marrow, the soft, inner part of certain bones. These tests are usually not needed unless the retinoblastoma has spread to tissues next to the eye and doctors suspect that the cancer may have also spread through the bloodstream to the bone marrow.

The tests are typically done at the same time. The samples are usually taken from the back of the pelvic (hip) bone, but in some cases they may be taken from other bones.

In *bone marrow aspiration*, the skin over the hip and the surface of the bone may be numbed with a local anesthetic. This test can be painful, so the child will probably be given other medicines to reduce pain or even be asleep during the procedure. A thin, hollow needle is then inserted into the bone, and a syringe is used to suck out (aspirate) a small amount of liquid bone marrow.

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A *bone marrow biopsy* is usually done just after the aspiration. A small piece of bone and marrow is removed with a slightly larger needle that is pushed down into the bone. Once the biopsy is done, pressure is applied to the site to help stop any bleeding. The samples are then looked at under a microscope to see if tumor cells are present.

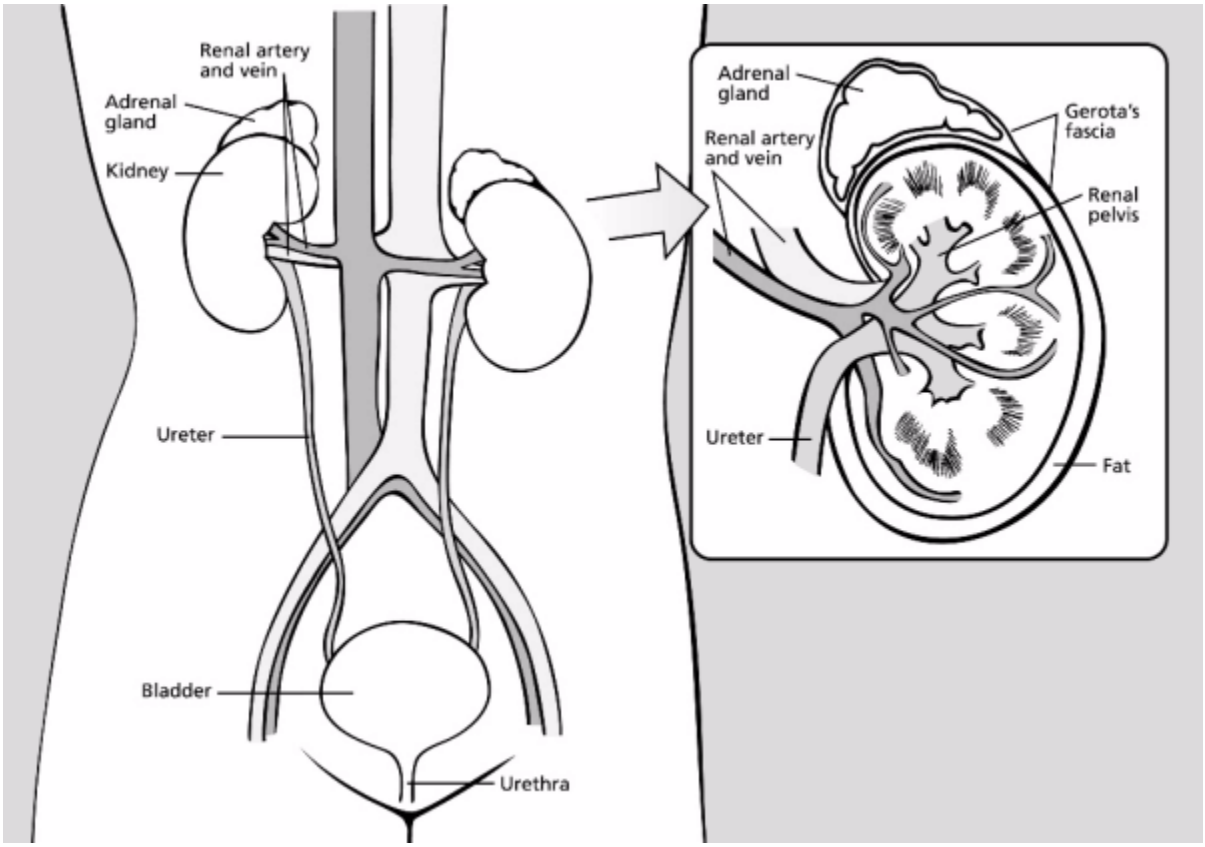
What is Wilms tumor?

Wilms tumor (also called *Wilms' tumor* or *nephroblastoma*) is a type of cancer that starts in the kidneys. It is the most common type of kidney cancer in children. It is named after Max Wilms, a German doctor who wrote one of the first medical articles about the disease in 1899.

About the kidneys

To understand Wilms tumor, it helps to know about the kidneys and what they do.

The kidneys are 2 bean-shaped organs that are attached to the back wall of the abdomen (see picture). Each kidney is about the size of a fist. One kidney is just to the left and the other just to the right of the backbone. The lower rib cage protects the kidneys.



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The kidneys' main job is to filter the blood and rid the body of excess water, salt, and waste products. The filtered products and extra water are changed into urine. Urine leaves the kidneys through long, slender tubes called *ureters* that connect to the bladder. Urine flows down the ureters into the bladder, and is stored there until the person urinates.

The kidneys also have other jobs:

- They help control blood pressure by making a hormone called *renin*.
- They help make sure the body has enough red blood cells. They do this by making a hormone called *erythropoietin*, which tells the bone marrow to make more red blood cells.

Our kidneys are important, but we actually need less than one complete kidney to do all of its basic functions. Tens of thousands of people in the world are living normal, healthy lives with just one kidney.

Wilms tumors

Wilms tumors are the most common cancers in children that start in the kidneys. Most Wilms tumors are *unilateral*, which means they affect only one kidney. Most often there is only one tumor, but 5% to 10% of children with Wilms tumors have more than one tumor in the same kidney. About 5% of children with Wilms tumors have *bilateral* disease (cancer in both kidneys).

Wilms tumors often become quite large before they are noticed. The average newly found Wilms tumor is many times larger than the kidney in which it started. Most tumors are found before they have spread (metastasized) to other organs.

Even though a doctor might think a child has a cancer such as Wilms tumor based on a physical exam or imaging tests, they cannot be certain until a sample of the tumor is looked at under a microscope.

Types of Wilms tumor

Wilms tumors are grouped into 2 major types based on how they look under a microscope (their histology):

Favorable histology: Although the cancer cells in these tumors don't look quite normal, there is no anaplasia (see next paragraph). More than 9 of 10 Wilms tumors have a favorable histology. The chance of cure for children with these tumors is very good.

Unfavorable histology (anaplastic Wilms tumor): In these tumors, the look of the cancer cells varies widely, and the cells' nuclei (the central parts that contain the DNA) tend to be very large and distorted. This is called *anaplasia*. The more anaplasia a tumor has, the harder it is to cure.

Other types of kidney cancers in children

About 9 of 10 kidney cancers in children are Wilms tumors, but in rare cases children may develop other types of kidney tumors.

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Mesoblastic nephroma

These tumors usually appear in the first few months of life. Patients are usually cured with surgery, but sometimes chemotherapy is given as well. These tumors sometimes come back soon after treatment, so children who have had these tumors need to be watched closely for the first year afterward.

Clear cell sarcoma of kidney (CCSK)

These tumors are much more likely to spread to other parts of the body than Wilms tumors, and they are harder to cure. Because these tumors are rare, treatment is often given as part of a clinical trial. It is usually similar to the intensive treatment used for Wilms tumors with unfavorable histology.

Malignant rhabdoid tumor of the kidney

These tumors occur most often in infants and toddlers. They tend to spread to other parts of the body quickly, and most have already spread by the time they are found, which makes them hard to cure. Because these tumors are rare, treatment is often given as part of a clinical trial, and usually includes chemotherapy with several different drugs.

Renal cell carcinoma

This is the most common type of kidney cancer in adults, but it also accounts for a small number of kidney tumors in children. It's rare in young children, but it's actually more common than Wilms tumor in older teens.

Surgery to remove the kidney is the main treatment for these cancers if it can be done. The outlook for these cancers depends largely on the extent (stage) of the cancer at the time it's found, whether it can be completely removed with surgery, and its subtype (based on how the cancer cells look under a microscope). If the cancer is too advanced to be removed by surgery, other types of treatment may be needed.

Can Wilms tumor be found early?

Wilms tumors are usually found when they start to cause symptoms such as swelling in the abdomen (belly), but by this point they have often grown quite large. They can be found earlier in some children with tests such as an ultrasound of the abdomen. But because Wilms tumors are so rare, it's not practical to do an ultrasound exam as a screening test (a test to look for disease in people with no signs or symptoms) in all children who are not at increased risk. There are no blood tests or other tests that are useful in screening otherwise healthy children for Wilms tumors.

On the other hand, screening for Wilms tumor is very important for children who have syndromes or birth defects known to be linked to this disease. For these children, most doctors recommend physical exams by a specialist and ultrasound exams on a regular basis (for example, about every 3 or 4 months at least until the age of 8) to find any kidney tumors when they are still small and have not yet spread to other organs.

Wilms tumor can also run in families, although this is rare. Talk to your doctor if you have any relatives who have had a Wilms tumor. If you do, the children in your family may need to have regular ultrasound exams. If a man or woman is known to have a *WT1* gene mutation, testing can be done to see if they have passed the mutation on to their children. (This can be done even before birth.)

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Signs and symptoms of Wilms tumor

Wilms tumors can be hard to find early because they can often grow quite large without causing any symptoms. Children may look healthy and play normally.

Swelling or a hard mass in the abdomen (belly): This is often the first sign of a Wilms tumor. Parents may notice this while bathing or dressing the child. It feels firm and is often large enough to be felt on both sides of the belly. It's usually not painful, but it might cause belly pain in some cases.

Other possible symptoms: Some children with Wilms tumor may also have:

- Fever
- Nausea
- Loss of appetite
- Shortness of breath
- Constipation
- Blood in the urine

Wilms tumors can also sometimes cause high blood pressure. This does not usually cause symptoms on its own, but in rare cases it can get high enough to cause problems such as bleeding inside the eye or even a change in consciousness.

Many of the signs and symptoms above are more likely to be caused by something other than a kidney tumor. Still, if your child has any of these symptoms, check with your child's doctor so that the cause can be found and treated, if needed.

How are Wilms tumors diagnosed?

Wilms tumors are usually found when a child is brought to a doctor because of symptoms he or she is having. The doctor might suspect a child has a Wilms tumor based on a physical exam or other tests, but the diagnosis can only be made for certain once a sample of the tumor is removed and looked at under a microscope.

Medical history and physical exam

If your child has signs or symptoms that suggest he or she may have a kidney tumor, the doctor will want to get a complete medical history to learn more about the symptoms and how long they have been there. The doctor may also ask if there's a family history of cancer or birth defects, especially in the genitals or urinary system.

The doctor will examine your child to look for possible signs of a kidney tumor or other health problems. The main focus will likely be on the abdomen and on any increase in blood pressure, which is another possible sign of a kidney tumor. Blood and urine samples might also be collected at this time for testing (see "Lab tests" below).

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Imaging tests

If the doctor thinks your child might have a kidney tumor, he or she will probably order one or more of the imaging tests below. These tests use sound waves, x-rays, magnetic fields, or radioactive substances to create pictures of the inside of the body. Imaging tests are done for a number of reasons, including:

- To help find out if there is a tumor in the kidney(s), and if so, if it is likely to be a Wilms tumor
- To learn how far the tumor may have spread, both within the kidney and to other parts of the body
- To help guide surgery or radiation therapy
- To look at the area after treatment to help determine if it has worked

Ultrasound (sonogram)

This is often the first imaging test done if the doctor suspects your child has a Wilms tumor because it's easy to have, it does not use radiation, and it gives the doctor a good view of the kidneys and the other organs in the abdomen.

Ultrasound uses sound waves to create images of internal organs. For this test, your child lies on a table while a small wand called a *transducer* is placed on the skin (which is first lubricated with a gel) over the belly. It gives off sound waves and picks up the echoes as they bounce off the kidney. The echoes are converted by a computer into a black and white image on a screen.

The echo patterns made by most kidney tumors look different from those of normal kidney tissue. Different echo patterns also can help doctors tell some types of cancerous and non-cancerous kidney tumors apart from one another.

Ultrasound is also very useful when looking for tumor thrombus (tumor growing into the main veins coming out of the kidney). This helps in planning for surgery, if it is needed.

The test is not usually painful, but it might cause some discomfort if the transducer is pressed down hard on the abdomen.

Computed tomography (CT, CAT) scan

The CT scan is an x-ray test that produces detailed cross-sectional images of parts of your child's body, including organs such as the kidneys. This is one of the most useful tests to look for a mass inside the kidney. It's also helpful in checking whether a cancer has grown into nearby veins or has spread to organs and tissues beyond the kidney, such as the lungs.

Instead of taking one picture, like a regular x-ray, a CT scanner takes many pictures as it rotates around your child while he or she lies on a table. A computer then combines these pictures into images showing slices of the part of the body being studied.

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Before the scan, your child may be asked to drink a contrast solution and/or get an intravenous (IV) injection of a contrast dye that better outlines abnormal areas in the body. Your child may need an IV line for the dye. The contrast may cause some flushing (a feeling of warmth, especially in the face). Some people are allergic and get hives. Rarely, more serious reactions like trouble breathing or low blood pressure can occur. Be sure to tell the doctor if your child has any allergies or has ever had a reaction to any contrast material used for x-rays.

CT scans take longer than regular x-rays. A CT scanner has been described as a large donut, with a narrow table in the middle opening. Your child will need to lie still on the table while the scans are being done. During the test, the table slides in and out of the scanner. Younger children may be given medicine to help keep them calm or even asleep during the test to help make sure the pictures come out well.

Magnetic resonance imaging (MRI) scans

An MRI scan might be done if the doctor needs to see very detailed images of the kidney or nearby areas. For example, it might be done if there's a chance that a kidney tumor might have reached a major vein (the inferior vena cava) in the abdomen. An MRI scan might also be used to look for possible spread of cancer to the brain or spinal cord if doctors are concerned the cancer may have spread there.

Like CT scans, MRI scans provide detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets to create the images instead of x-rays and don't expose your child to radiation.

A contrast material called *gadolinium* may be injected into a vein before the scan to better see details. It usually does not cause allergic reactions, but it can cause other problems in children with kidney disease, so doctors are careful when they use it.

MRI scans take longer than CT scans – often up to an hour. Your child may have to lie inside a narrow tube, which is confining and can be distressing. Newer, more open MRI machines may help with this, but the test still requires staying still for long periods of time. The MRI machine also makes loud buzzing and clicking noises that your child may find disturbing. Younger children may be given medicine to help keep them calm or even asleep during the test.

Chest x-ray

Chest x-rays may be done to look for any spread of Wilms tumor to the lungs, as well as to have a baseline view of the lungs to compare with other x-rays that might be done in the future. If a CT scan of the chest is done, this test is not needed.

Bone scan

Bone scans can help show if cancer has spread to bones. Doctors don't usually order this test unless they think your child has a type of Wilms tumor that is likely to spread.

For this test, a small amount of low-level radioactive material is injected into a vein (intravenously, or IV). (The amount of radioactivity used is very low and will pass out of the body within a day or so.) The substance settles in areas of damaged bone throughout the skeleton over the course of a couple of hours. Your child then lies on a table for about

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30 minutes while a special camera detects the radioactivity and creates a picture of the skeleton. Younger children may be given medicine to help keep them calm or even asleep during the test.

Areas of active bone changes will appear as hot spots on the skeleton – that is, they attract the radioactivity. These areas may suggest the presence of cancer, but other bone diseases can also cause the same pattern. To help tell these apart, other tests such as plain x-rays or MRI scans of the bone might be needed.

Lab tests

Lab tests might be done to check urine and blood samples if your child's doctor suspects a kidney problem. They may also be done after a diagnosis of Wilms tumor has been made.

A urine sample may be tested (urinalysis) to look for blood and other substances in the urine to see if there are problems with the kidneys. The urine may also be tested for substances called *catecholamines*. This is done to make sure your child doesn't have another kind of tumor called neuroblastoma. (Neuroblastomas often start in the adrenal gland, which lies just above the kidney.)

Blood tests are not used to find Wilms tumors, but they can sometimes show if a child has kidney problems. They can also be done to check a child's general health (especially before surgery) and to look for side effects during treatment such as chemotherapy. These may include tests to count the number of white blood cells, red blood cells, and blood platelets, and tests to measure certain chemicals and salts in the blood that give clues about how well the kidneys and liver are working.

Kidney biopsy/surgery

Most of the time, imaging tests can give doctors enough information to decide if a child probably has a Wilms tumor, and therefore if surgery should be done. But the actual diagnosis of Wilms tumor is made when a sample of the tumor is removed and looked at under a microscope. The cells in Wilms tumors have a distinct appearance when looked at this way. Doctors also look at the sample to determine the histology of the Wilms tumor (favorable or unfavorable),

In most cases, the sample is removed during surgery to treat the tumor. Sometimes if the doctors are less certain about the diagnosis or if they are not sure the tumor can be removed completely, a sample of the tumor may be taken during a biopsy as a separate procedure done before surgery. The biopsy may be done either as a type of surgery or using a long, hollow needle that's inserted through the skin and into the tumor.

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What is non-Hodgkin lymphoma in children?

Lymphoma is a type of cancer that starts in cells called *lymphocytes*, which are part of the body's immune system. There are 2 kinds of lymphomas:

- Hodgkin disease (also known as Hodgkin lymphoma), which is named after Dr. Thomas Hodgkin, who first described it
- Non-Hodgkin lymphoma (NHL)

These types of lymphomas behave, spread, and respond to treatment differently, so it is important to tell them apart.

Both types of lymphoma are more common in adults, but they can also occur in children and teens. Among this younger age group, NHL tends to occur in younger children, while Hodgkin disease is more likely to affect older children and teens.

Hodgkin disease is very similar in adults and children, and treatment is the same for both.

The lymph system and lymphoid tissue

To understand NHL, it helps to know about the body's lymph system.

The lymph system (also known as the *lymphatic system*) is part of the body's immune system, which helps fight infections and some other diseases. It also helps fluids move around within the body. The lymph system is made up mainly of:

- **Lymphoid tissue:** includes the lymph nodes and related organs (see below) that are part of the body's immune and blood-forming systems
- **Lymph:** a clear fluid that travels through the lymph system, carrying waste products and excess fluid from tissues, as well as lymphocytes and other immune system cells
- **Lymphatic vessels:** small tubes, similar to blood vessels, through which lymph travels to different parts of the lymph system

Lymphocytes

Lymphoid tissue is made up mainly of cells called *lymphocytes*, a type of white blood cell. The 2 main types of lymphocytes are *B lymphocytes* (B cells) and *T lymphocytes* (T cells). Normal B cells and T cells do different jobs.

B lymphocytes: B cells normally help protect the body against germs (bacteria or viruses) by making proteins called antibodies. The antibodies attach to the germs, marking them for destruction by other parts of the immune system.

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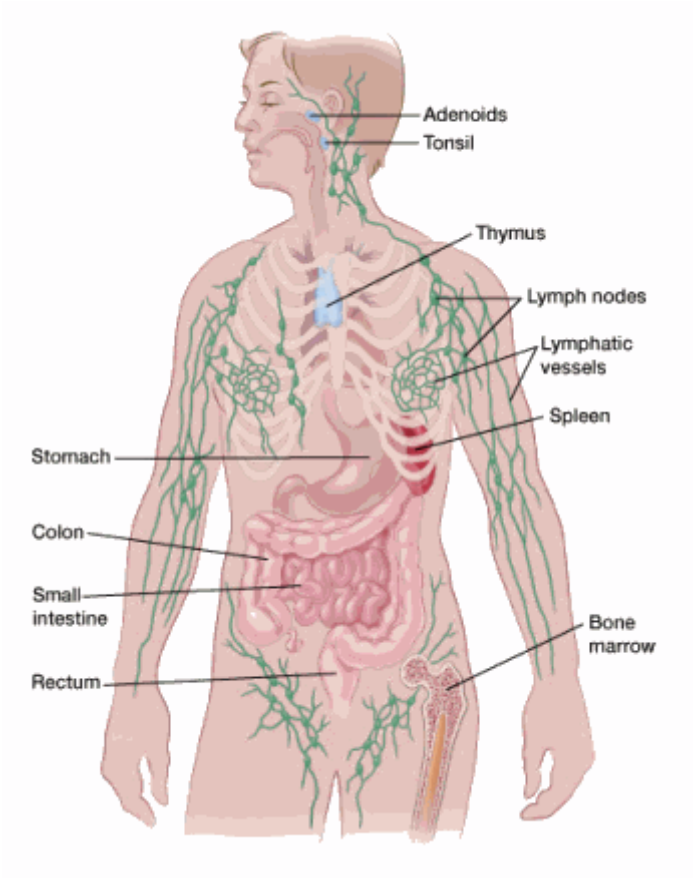
T lymphocytes: There are several types of T cells, each with a special job. Some T cells directly destroy cells infected with viruses, fungi, or certain kinds of bacteria. Other types of T cells play a role in either boosting or slowing the activity of other immune system cells.

Both types of lymphocytes can develop into lymphoma cells, but B-cell lymphomas are much more common in the United States than T-cell lymphomas. Different types of lymphoma can develop from both B and T lymphocytes, based on how mature the cells are when they become cancerous and other factors.

Treatment for lymphoma depends on which type it is, so determining the exact type of lymphoma is important.

Organs that have lymphoid tissue

Because lymphoid tissue is in many parts of the body, lymphomas can start almost anywhere.



The major sites of lymphoid tissue are:

Lymph nodes: Lymph nodes are bean-sized collections of lymphocytes and other immune cells throughout the body. They can sometimes be felt under the skin in the neck, under the arms, and in the groin. Lymph nodes are connected to each other by a system of lymphatic vessels.

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Lymph nodes get bigger when they fight infection. Lymph nodes that grow because of infection are called *reactive nodes* or *hyperplastic nodes* and are often painful when they are touched. An enlarged lymph node in a child is not usually a sign of a serious problem. Lymph nodes in the neck are often enlarged in children with sore throats or colds. But a large lymph node is also the most common sign of lymphoma. Lymph node enlargement is discussed more in "Signs and symptoms of non-Hodgkin lymphoma in children."

Spleen: The spleen is an organ under the lower part of the rib cage on the left side of the body. The spleen makes lymphocytes and other immune system cells to help fight infection. It also stores healthy blood cells and filters out damaged blood cells, bacteria, and cell waste.

Thymus: The thymus is a small organ behind the upper part of the breast bone and in front of the heart. Before birth, the thymus plays a vital role in development of T lymphocytes. The thymus shrinks and becomes less important as people get older, but it continues to play a role in immune system function.

Adenoids and tonsils: These are collections of lymphoid tissue in the back of the throat. They help make antibodies against germs that are breathed in or swallowed. They are easy to see when they become enlarged during an infection, which occurs often in children, or if a lymphoma develops.

Digestive tract: Lymphoid tissue is also in the stomach and intestines, as well as many other organs.

Bone marrow: The bone marrow (the soft inner part of certain bones) makes red blood cells, blood platelets, and white blood cells. Red blood cells carry oxygen from the lungs to the rest of the body. Platelets help control bleeding by plugging up small holes in blood vessels. White blood cells fight infections. The main types of white blood cells are granulocytes and lymphocytes. Bone marrow lymphocytes are mainly B cells. Lymphomas sometimes start from bone marrow lymphocytes.

Types of non-Hodgkin lymphoma in children

Lymphomas are most often classified by how the cancer cells look under the microscope. Key features include the size and shape of the cells and how they are arranged (their pattern of growth).

- Size is described as large or small.
- Shape is described as cleaved (showing folds or indentations) or non-cleaved.
- The growth pattern may be either diffuse (cancer cells are scattered) or follicular (cells are arranged in clusters).

Not every lymphoma is described using all 3 features (size, shape, and growth pattern). Special lab tests are often needed to accurately classify lymphomas.

The most common types of non-Hodgkin lymphoma (NHL) in children are different from those in adults. Nearly all NHLs in children belong to 1 of 3 main types:

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- Lymphoblastic lymphoma
- Burkitt lymphoma (small non-cleaved cell lymphoma)
- Large cell lymphoma

All 3 types are high grade (meaning they grow quickly) and diffuse, but it is important to distinguish among them because they are treated differently.

There are many other types of NHL. These are much more common in adults and are rare in children, so they are not discussed further in this document.

Lymphoblastic lymphoma

Lymphoblastic lymphoma accounts for about 25% to 30% of NHL in children. It is most common in teens, and boys are affected about twice as often as girls.

The cancer cells of this lymphoma are very young lymphocytes called *lymphoblasts*. They are the same cells as those seen in acute lymphoblastic leukemia (ALL) in children. In fact, if more than 25% of the bone marrow is made up of lymphoblasts, the disease is classified and treated as ALL instead of lymphoma.

Most cases of lymphoblastic lymphoma develop from T cells and are called *precursor T-lymphoblastic lymphomas*. These lymphomas often start in the thymus, forming a mass in the area behind the breast bone and in front of the trachea (windpipe). This can cause problems breathing, which may be the first symptom of lymphoblastic lymphoma.

Less often, this cancer develops in the tonsils, lymph nodes of the neck, or other lymph nodes. It can spread very quickly to the bone marrow, other lymph nodes, the surface of the brain, and/or the membranes that surround the lungs and heart.

A small fraction of lymphoblastic lymphomas develop from B cells (called *precursor B-lymphoblastic lymphomas*). These lymphomas more often begin in lymph nodes outside the chest, particularly in the neck. They can also involve the skin and bones.

Lymphoblastic lymphoma can grow very quickly and can often interfere with breathing, so it needs to be diagnosed and treated quickly.

Burkitt lymphoma

Burkitt lymphoma, also known as *small non-cleaved cell lymphoma*, accounts for about 40% of childhood NHL in the Tanzania. It is most often seen in boys, usually when they are around 5 to 10 years old.

A subtype of Burkitt lymphoma, sometimes called *Burkitt-like lymphoma* or *non-Burkitt lymphoma*, shares some features with diffuse large B-cell lymphoma (described below) when seen under the microscope, but it is still treated like Burkitt lymphoma.

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Burkitt lymphoma is named after the doctor who first described it in African children. In certain parts of Africa, Burkitt lymphoma accounts for nearly all childhood NHL and over half of all childhood cancers. In African children this lymphoma usually develops in the jaw or other facial bones.

Burkitt lymphomas in other parts of the world, including Tanzania, almost always start in the abdomen (belly). Typically, a child will develop a large tumor in his or her abdomen that can sometimes block the bowels (intestines). This can cause belly pain, nausea, and vomiting. Burkitt lymphoma can also sometimes start in the neck or tonsils, or rarely in other parts of the body.

This lymphoma develops from B lymphocytes, and it is one of the fastest growing cancers known. It can spread to other organs, including the surface of the brain or inside the brain. Because of this, it must be diagnosed and treated quickly.

Large cell lymphomas

These lymphomas start in more mature forms of T cells or B cells and can grow almost anywhere in the body. They are not as likely to spread to the bone marrow or brain, nor do they grow as quickly as other childhood lymphomas. These lymphomas tend to occur more often in older children and teens. There are 2 main subtypes of large cell lymphoma.

Anaplastic large cell lymphoma (ALCL): This lymphoma represents about 10% of all NHL in children. It usually develops from mature T cells. It may start in lymph nodes in the neck or other areas, and may be found in the skin, lungs, bone, digestive tract, or other organs.

Diffuse large B-cell lymphoma: This lymphoma accounts for about 15% of childhood lymphomas. It starts in B cells, as the name implies. These lymphomas often grow as large masses in the mediastinum (the space between the lungs), in which case they are referred to as *primary mediastinal B-cell lymphomas*. But they are also sometimes found in other areas such as lymphoid tissue in the neck or abdomen, or in the bones.

Treatment is basically the same for both types of large cell lymphoma, although the cure rate tends to be slightly higher for the diffuse large B-cell type.

Can non-Hodgkin lymphoma in children be found early?

Non-Hodgkin lymphoma (NHL) in children is uncommon, and there are no widely recommended screening tests for this cancer. (Screening is testing for cancer in people without any symptoms.) Still, in some cases NHL can be found early.

The best way to find this cancer early is to be aware of the possible signs and symptoms of this disease and to take your child to the doctor if something concerns you.

Careful, regular medical checkups are important for children, especially those with known risk factors for NHL, such as those who have certain inherited immune deficiencies, who have had cancer treatment or an organ transplant, or who

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have an HIV infection. These children do not usually develop NHL, but it is important for parents and doctors to know the possible symptoms and signs of lymphoma.

Signs and symptoms of non-Hodgkin lymphoma in children

Childhood non-Hodgkin lymphoma (NHL) can cause many different signs and symptoms, depending on where it is in the body. In some cases it might not cause any symptoms until it grows quite large. Common symptoms include:

- Enlarged lymph nodes (seen or felt as lumps under the skin)
- Swollen abdomen (belly)
- Feeling full after only a small amount of food
- Shortness of breath or cough
- Fever
- Weight loss
- Night sweats
- Fatigue (extreme tiredness)

Enlarged lymph nodes

Non-Hodgkin lymphoma may grow in lymph nodes under the skin (on the sides of the neck, in the underarm area, above the collar bone, or in the groin area). The enlarged nodes are often seen or felt as lumps under the skin. They are often noticed by the child, parent, or a health care professional. Enlarged lymph nodes in children are more often caused by infections than by NHL.

Lymphoma in the abdomen (belly)

If the lymphoma grows inside the abdomen, it can make it swollen and painful. There may also be a buildup of fluid that causes even more swelling.

Lymphoma can sometimes enlarge the spleen and make it press on the stomach. This can make a child feel full after eating only a small amount of food.

When lymphoma causes swelling near the intestines, bowel movements may be blocked, this may lead to abdominal pain, nausea, or vomiting.

The lymphoma may also block urine from leaving the kidneys. This can lead to kidney problems, which can cause low urine output, tiredness, loss of appetite, nausea, or swelling in the hands or feet.

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Lymphoma in the chest

When lymphoma starts in the thymus or lymph nodes in the chest, it can press on the nearby trachea (windpipe). This can lead to coughing, shortness of breath, and trouble breathing.

The superior vena cava (SVC) is a large vein that carries blood from the head and arms back to the heart. It passes next to the thymus and lymph nodes inside the chest. Lymphomas in this area may push on the SVC, which can make the blood back up in the veins. This is can lead to swelling in the face, neck, arms, and upper chest (sometimes with a bluish-red skin color). It can also cause trouble breathing, as well as headaches, dizziness, and a change in consciousness if it affects the brain. This condition, known as *SVC syndrome*, can be life-threatening, and needs to be treated right away.

Lymphoma in the brain and spinal cord

Some types of lymphoma can spread to the area around the brain and spinal cord. This can cause problems such as headache, vision changes, facial numbness, and trouble speaking.

Lymphoma in the skin

Some lymphomas can affect the skin itself. They can cause itchy, red or purple lumps or nodules under the skin.

General symptoms

Along with causing symptoms and signs in the part of the body where it starts, NHL can also cause general symptoms such as:

- Fever and chills
- Sweating (particularly at night)
- Unexplained weight loss

When talking about lymphoma, doctors sometimes call these *B symptoms*. B symptoms are often found in more rapidly growing lymphomas.

Other symptoms can be caused by low blood cell counts. Blood counts can become low if lymphoma spreads to the bone marrow and crowds out the normal, healthy cells that make new blood cells. This can lead to problems like:

- Severe or frequent infections (from low white blood cell counts)
- Easy bruising or bleeding (from low blood platelet counts)
- Fatigue and pale skin (from low red blood cell counts [anemia])

Many of the signs and symptoms above are more likely to be caused by something other than a lymphoma, such as an infection. Still, if your child has any of these symptoms, check with the doctor so that the cause can be found and treated, if needed.

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How is non-Hodgkin lymphoma diagnosed in children?

Non-Hodgkin lymphoma (NHL) is usually found when a child is brought to a doctor because of signs or symptoms he or she is having. The doctor might suspect a child could have a lymphoma based on the signs and symptoms, but tests are needed to confirm the diagnosis. The exams and tests below are used to diagnose the disease, to find out what type of lymphoma it is, and to learn how advanced it is.

Medical history and physical exam

If any signs and symptoms suggest a child might have lymphoma, the doctor will want to get a thorough medical history to learn more about the symptoms and how long they have been present. The doctor might also ask if there is any history of possible risk factors, such as immune system problems.

During the physical exam, the doctor will probably focus on any enlarged lymph nodes or other areas of concern. For example, the abdomen may be felt for signs of an enlarged spleen or liver. Enlarged lymph nodes in children are usually caused by infections, so the doctor will look for an infection in the part of the body near any swollen lymph nodes.

Because infections are the most common cause of enlarged lymph nodes, this is often what doctors think of first, so the diagnosis of NHL in a child can sometimes be delayed. There is usually little cause for concern in children with swollen lymph nodes unless they are very large (more than 1 inch across). Even in these instances, the child is usually watched closely for a time or given a course of antibiotics first to see if the nodes will shrink. If not, more tests are done, usually a biopsy removing a swollen node (or a large portion of it) (see next section). But if the lymph nodes seem to be growing quickly or the child's health seems to be getting worse, a biopsy may be needed right away.

Biopsy

A doctor can't make a diagnosis of NHL in a child based only on symptoms or a physical exam. Most of the symptoms NHL can cause are more often caused by non-cancerous problems, like infections. They may also be caused by other kinds of cancers. If a child does have NHL, it's important to tell which type it is, because each type is treated slightly differently.

For these reasons, an accurate diagnosis is needed, and the only way to do this is to remove some or all of an abnormal lymph node (or tumor) for viewing under a microscope and other lab tests. This is called a *biopsy*.

Types of biopsies used to diagnose non-Hodgkin lymphoma

There are several types of biopsies. Doctors choose which one to use based on the situation. The goal is to get a sample large enough to make an accurate diagnosis as quickly as possible, with as few side effects as possible.

Excisional or incisional biopsy: These are the most common types of biopsy done if lymphoma is suspected. An exception might be for large tumors in chest, for which a needle biopsy (described below) might be used instead.

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In these procedures, a surgeon cuts through the skin to remove either an entire lymph node (excisional biopsy) or a small part of a large tumor (incisional biopsy).

If the node is near the skin surface, this is an operation that might be done with both local anesthesia (numbing medicine used only at the biopsy site) and sedation or with general anesthesia (where the child is in a deep sleep). If the node is inside the chest or abdomen, then general anesthesia is usually needed.

This method almost always provides enough of a sample to diagnose the exact type of NHL.

Fine needle aspiration (FNA) or core needle biopsy: In an FNA biopsy, the doctor uses a very thin, hollow needle attached to a syringe to withdraw (aspirate) a small amount of tissue from an enlarged lymph node or a tumor mass. For a core needle biopsy, the doctor uses a larger needle to remove a slightly larger piece of tissue.

If an enlarged lymph node is near the surface, the doctor can aim the needle while feeling the node. If the enlarged node or tumor is deep in the body (such as in the chest or abdomen), the doctor can guide the needle while watching it on a CT scan or ultrasound (see discussion of imaging tests later in this section).

The main advantage of a needle biopsy is that it does not require surgery. This can be especially important for tumors in the chest, because general anesthesia (where the child is in a deep sleep) can sometimes be dangerous for these children. It is also useful when the lymphoma is in other sites outside of the lymph nodes, such as the bones.

In children, needle biopsies can often be done using local anesthesia to numb the area, along with sedation to make the child sleepy. General anesthesia is needed less often.

The main drawback of needle biopsies (especially FNA) is that in some cases the needle might not remove enough of a sample to make a definite diagnosis. Most doctors don't use needle biopsies if they strongly suspect lymphoma (unless other types of biopsies can't be done for some reason). But if the doctor suspects that lymph node swelling is caused by an infection (even after antibiotics), a needle biopsy may be the first type of biopsy done. If a biopsy is needed, doctors typically prefer to do a core biopsy instead of FNA. An excisional biopsy might still be needed to diagnose and classify lymphoma, even after a needle biopsy has been done.

Once lymphoma has been diagnosed, needle biopsies are sometimes used to check areas in other parts of the body that might be lymphoma spreading or coming back after treatment.

Other types of biopsies

These other types of biopsies are not normally used to diagnose lymphoma, but they might be done to help determine the extent of spread if a lymphoma has already been diagnosed.

Bone marrow aspiration and biopsy: These tests help determine if a lymphoma has reached the bone marrow. The 2 tests are usually done at the same time. The biopsy samples are usually taken from the back of the pelvic (hip) bones, although in some cases they may be taken from the front of the hip bones or from other bones.

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For a bone marrow *aspiration*, the skin over the hip and the surface of the bone is numbed with local anesthetic. In most cases, children will be given other medicines to make them drowsy or brief general anesthesia so they are asleep during the biopsy. A thin, hollow needle is then inserted into the bone and a syringe is used to suck out a small amount of liquid bone marrow.

A bone marrow *biopsy* is usually done just after the aspiration. A small piece of bone and marrow is removed with a slightly larger needle that is put into the bone. Once the biopsy is done, pressure will be applied to the site to help stop any bleeding.

Lumbar puncture (spinal tap): This test is used to look for lymphoma cells in the cerebrospinal fluid (CSF), which is the liquid that bathes the brain and spinal cord.

For this test, the doctor first numbs an area in the lower part of the back near the spine. The doctor usually also gives the child medicine to make him or her sleep during the procedure. A small, hollow needle is then placed between the bones of the spine to withdraw some of the fluid.

In children already diagnosed with lymphoma, a lumbar puncture can also be used to put chemotherapy drugs into the CSF to try to prevent or treat the spread of lymphoma to the spinal cord and brain.

Pleural or peritoneal fluid sampling: If lymphoma spreads to the thin membranes that line the inside of the chest and abdomen it can cause fluid to build up. Pleural fluid (inside the chest) or peritoneal fluid (inside the abdomen) can be removed using a hollow needle put through the skin into the chest or abdomen.

Before the procedure, the doctor uses a local anesthetic to numb the skin and may give the child other medicines so they are drowsy or asleep during the procedure. The fluid is then drawn out and looked at under the microscope to check for lymphoma cells.

When this procedure is used to remove fluid from the chest, it's called a *thoracentesis*. When it is used to collect fluid from inside the abdomen, it's known as a *paracentesis*.

Lab tests on biopsy samples to diagnose and classify lymphoma

All biopsy samples and fluids are looked at under a microscope by a pathologist (a doctor with special training in using lab tests to identify cancer cells). The doctor looks at the size and shape of the cells and how they are arranged. This may reveal not only if a child has lymphoma, but also what type of lymphoma it is. Because diagnosing lymphoma can be tricky, it helps if the pathologist specializes in diseases of the blood.

Pathologists can sometimes tell which kind of lymphoma a child has by looking at the cells, but usually other types of lab tests are needed to confirm the diagnosis.

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Immunohistochemistry

In this test, a part of the biopsy sample is treated with special antibodies (man-made versions of immune system proteins) that attach only to specific molecules on the cell surface. These antibodies cause color changes, which can be seen under a microscope. This test can help distinguish different types of NHL from one another and from other diseases.

Flow cytometry

Like immunohistochemistry, this test looks for certain substances on the outer surface of cells that help identify what types of cells they are. But this test can look at many more cells than immunohistochemistry can.

For this test, a sample of cells is treated with special antibodies that stick to the cells only if these substances are on their surfaces. The cells are then passed in front of a laser beam. If the cells now have antibodies attached to them, the laser will cause them to give off light, which can be measured and analyzed by a computer. Groups of cells can be separated and counted by these methods.

This is the most commonly used test for *immunophenotyping* – classifying lymphoma cells according to the substances (antigens) on their surfaces. Different types of lymphocytes have different antigens on their surface. These antigens may also change as each cell matures.

Flow cytometry can help determine whether lymph node swelling is due to lymphoma, some other cancer, or a non-cancerous disease. It has also become very useful in helping doctors determine the exact type of lymphoma so that they can select the best treatment.

Cytogenetics

Doctors use this technique to evaluate the chromosomes (long strands of DNA) in the lymphoma cells. They look at the cells under a microscope to see if the chromosomes have any translocations (where part of one chromosome has broken off and is now attached to another chromosome), as happens in certain types of lymphoma. Some lymphoma cells may also have too many chromosomes, too few chromosomes, or other chromosome changes. These changes can be used to help identify the type of lymphoma.

Cytogenetic testing usually takes about 2 to 3 weeks because the lymphoma cells must grow in lab dishes for a couple of weeks before their chromosomes are ready to be viewed under the microscope.

Molecular genetic tests

These tests look more closely at lymphoma cell DNA. They can detect most changes that can be seen under a microscope on cytogenetic tests, as well as others that can't be seen.

Fluorescent in situ hybridization (FISH): FISH is similar to cytogenetic testing. It uses pieces of DNA that only attach to specific parts of chromosomes. The DNA is linked to fluorescent dyes that can be seen with a special microscope. FISH can find most chromosome changes (such as translocations) that can be seen under a microscope on standard cytogenetic tests, as well as some changes too small to be seen with usual cytogenetic testing.

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FISH can be used to look for specific changes in chromosomes. It can be used on regular blood or bone marrow samples. It is very accurate and can usually provide results within a couple of days, which is why this test is now used in many medical centers.

Polymerase chain reaction (PCR): This is a very sensitive DNA test that can also find some chromosome changes too small to be seen under a microscope, even if there are very few lymphoma cells in a sample.

Blood tests

Blood tests measure the amounts of certain types of cells and chemicals in the blood. They are not used to diagnose lymphoma, but they might be one of the first types of tests done in children with symptoms to help the doctor determine what is going on.

If a child has been diagnosed with lymphoma, these tests can also sometimes help determine how advanced the lymphoma is.

The complete blood count (CBC) is a test that measures the levels of different cells in the blood, such as the red blood cells, the white blood cells, and the platelets. In children already known to have lymphoma, low blood cell counts might mean that the lymphoma is growing in the bone marrow and damaging new blood cell production.

Blood levels of a chemical called *LDH* will often be abnormally high in patients with fast-growing lymphomas.

Blood chemistry tests can help detect liver or kidney problems caused by the spread of lymphoma cells or certain chemotherapy drugs. Blood tests can also help determine if treatment is needed to correct low or high blood levels of certain minerals. Tests may also be done to make sure the blood is clotting properly.

For some types of lymphoma, the doctor might also want to order other blood tests to see if the child has been infected with certain viruses, such as the Epstein-Barr virus (EBV), hepatitis B virus (HBV), or human immunodeficiency virus (HIV). Infections with some of these viruses can affect your child's treatment.

Imaging tests to diagnose and stage non-Hodgkin lymphoma

Imaging tests use x-rays, sound waves, magnetic fields, or radioactive substances to create pictures of the inside of the body. In a child with known or suspected lymphoma, these tests might be done to look more closely at an abnormal area that might be lymphoma, to learn how far the lymphoma may have spread, or to find out if treatment has been effective. Children with NHL usually get some (but not all) of the following imaging tests.

Chest x-ray

A chest x-ray may be done to look for enlarged lymph nodes inside the chest.

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Computed tomography (CT or CAT) scan

The CT scan is an x-ray test that produces detailed, cross-sectional images of the body. Unlike a regular x-ray, CT scans can show the detail in soft tissues (such as internal organs). They can help tell if any lymph nodes or organs in the body are enlarged. CT scans can be used to look for enlarged lymph nodes or other masses in the chest, abdomen, pelvis, head, and neck.

Instead of taking one picture, like a standard x-ray does, a CT scanner takes many pictures as it rotates around the child. A computer then combines these pictures into images of slices of the part of the body being studied.

Before the scan, your child may be asked to drink a contrast solution and/or get an intravenous (IV) injection of a contrast dye that helps better outline abnormal areas in the body. Your child may need an IV line through which the contrast dye will be injected. The injection can cause some flushing (redness and warm feeling). Some people are allergic and get hives or, rarely, more serious reactions like trouble breathing and low blood pressure. Be sure to tell the doctor if your child has any allergies or has ever had a reaction to any contrast material used for x-rays.

CT scans take longer than regular x-rays. A CT scanner has been described as a large donut, with a narrow table in the middle opening. Your child will need to lie still on the table while the scan is being done. During the test, the table slides in and out of the scanner. Some younger children may be given medicine to help keep them calm or even asleep during the test to help make sure the pictures come out well.

CT-guided needle biopsy: CT scans can also be used to guide a biopsy needle precisely into a suspected tumor or enlarged lymph node. For this procedure, the child remains asleep on the CT scanning table, while a radiologist advances a biopsy needle through the skin and toward the mass. CT scans are repeated until the needle is within the mass. A biopsy sample is then removed and looked at under a microscope.

Ultrasound (sonogram)

Ultrasound uses sound waves and their echoes to produce a picture of internal organs or masses.

Ultrasound can be used to look at lymph nodes near the surface of the body or to look inside the abdomen (belly) for enlarged lymph nodes or organs such as the liver, spleen, and kidneys. (It can't be used to look inside the chest because the ribs block the sound waves.) It is also sometimes used to help guide a biopsy needle into an enlarged lymph node.

For this test, a small wand called a *transducer* is moved around on the skin (which is first lubricated with gel). The transducer gives off sound waves and picks up the echoes as they bounce off the organs. The echoes are converted by a computer into a black and white image on a computer screen.

This is usually an easy test to have, and it uses no radiation. Your child simply lies on a table, and a technician moves the transducer over the part of the body being looked at. The test is not usually painful, but it might be uncomfortable if the transducer is pressed down hard on the abdomen.

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Magnetic resonance imaging (MRI) scans

An MRI scan, like a CT scan, gives detailed images of soft tissues in the body. This test is not used as often as CT scans for lymphoma, but MRI is very useful for looking at the brain and spinal cord if a child has symptoms that might be caused by problems in the nervous system.

MRI scans use radio waves and strong magnets instead of x-rays, so there is no radiation. The energy from the radio waves is absorbed and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into very detailed images of parts of the body.

A contrast material called *gadolinium* is often injected into a vein before the scan to better see details. The contrast material usually does not cause allergic reactions.

MRI scans take longer than CT scans, often up to an hour. Your child may have to lie inside a narrow tube, which can be distressing, so sedation is sometimes needed. Newer, more open MRI machines may be another option, although your child will still have to lie still. The MRI machine makes loud buzzing and clicking noises that your child may find disturbing. Some places provide headphones or earplugs to help block this noise out.

Positron emission tomography (PET) scan

For a PET scan, a form of radioactive sugar (known as *fluorodeoxyglucose* or *FDG*) is injected into the blood. (The amount of radioactivity used is very low and will pass out of the body within a day or so.) Because lymphoma cells grow quickly, they absorb large amounts of the sugar. After about an hour, your child will be moved onto a table in the PET scanner. He or she will lie on the table for about 30 minutes while a special camera creates a picture of areas of radioactivity in the body. The picture is not finely detailed like a CT or MRI scan, but it provides helpful information about the whole body.

PET scans can be used for many reasons in a child with lymphoma:

- They can help tell if an enlarged lymph node contains lymphoma or is benign.
- They can help spot small areas in the body that might be lymphoma, even if the area looks normal on a CT scan.
- They can help tell if a lymphoma is responding to treatment. Some doctors will repeat the PET scan after 1 or 2 courses of chemotherapy. If the chemotherapy is working, the lymph nodes will no longer take up as much of the radioactive sugar.
- They can be used after treatment in helping decide whether an enlarged lymph node still contains lymphoma or is merely scar tissue.

Some newer machines can do both a PET and CT scan at the same time (PET/CT scan). This lets the doctor compare areas of higher radioactivity on the PET scan with the more detailed appearance of that area on the CT scan.

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Bone scan

This test is not usually needed unless a child is having bone pain or has lab test results that suggest the lymphoma might have reached the bones.

For a bone scan, a radioactive substance called *technetium* is injected into the blood. (The amount of radioactivity used is very low and will pass out of the body within a day or so.)

The substance travels to damaged areas of the bone over a couple of hours. Your child then lies on a table for about 30 minutes while a special camera detects the radioactivity and creates a picture of the skeleton. Younger children may be given medicine to help keep them calm or even asleep during the test.

A bone scan can detect bone damage from lymphoma. But a bone scan may also pick up non-cancerous problems, so other tests might be needed to be sure.

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