



Rhabdomyosarcoma

What is cancer?

The body is made up of hundreds of millions 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.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

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 damage to DNA. DNA is in every cell and directs all its 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, but the cell doesn't die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does.

People can inherit damaged DNA, but most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. Sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

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.

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

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

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

Not all tumors are cancerous. Tumors that aren't cancer are called benign. Benign tumors 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 tumors are almost never life threatening.

What are the differences between cancers in adults and children?

The types of cancers that develop in children are different from the types that develop in adults. Although there are exceptions, childhood cancers tend to respond better to chemotherapy. Children's bodies also tend to tolerate chemotherapy better than adults' bodies do. But, because chemotherapy can have some long-term side effects, children who survive their cancer need careful attention for the rest of their lives.

Since the 1960s, most children and adolescents with cancer have been treated at specialized centers designed for them. Being treated in these centers offers them the advantage of a team of specialists who know the differences between adult and childhood cancers, as well as the unique needs of children with cancers. This team usually includes pediatric oncologists, pathologists, surgeons, radiation oncologists, pediatric oncology nurses, and nurse practitioners.

These centers also have psychologists, social workers, child life specialists, nutritionists, rehabilitation and physical therapists, and educators who can support and educate the entire family.

Most children with cancer in the United States are treated at a center that is a member of the Children's Oncology Group (COG). All of these centers are associated with a university or children's hospital. As we have learned more about treating childhood cancer, it has become even more important that treatment be given by experienced experts.

What is rhabdomyosarcoma?

Sarcomas are cancers that develop from connective tissues in the body, such as muscles, fat, membranes that line the joints, or blood vessels. There are many types of sarcomas.

Rhabdomyosarcoma is a cancer made up of cells that normally develop into skeletal muscles. The body contains 3 main types of muscles.

- Skeletal (voluntary) muscles are muscles that we control to move parts of our body.
- Cardiac muscle is the main muscle type in the heart.
- Smooth muscle is the main type of muscle in internal organs (except for the heart). For example, smooth muscles in the intestines push food along as it is digested. We do not control this movement.

About 7 weeks into the development of an embryo, rhabdomyoblasts (cells that will eventually form skeletal muscles) begin to form. These are the cells that can develop into the cancer called *rhabdomyosarcoma*. Because this is a cancer of embryonal cells, it is much more common in children, although it does occur in adults occasionally.

We think of our skeletal muscles as being mainly in our arms and legs, but these skeletal muscle cancers can start nearly anywhere in the body. Common sites include:

- Head and neck (near the eye, inside the nasal sinuses or throat, or near the spine in the neck)
- Urinary and reproductive organs (bladder, prostate gland, or any of the female organs)
- Arms and legs
- Trunk (chest and abdomen)

Rhabdomyosarcomas can even start in some parts of the body that don't normally have skeletal muscle.

Types of rhabdomyosarcoma

There are 2 main types of rhabdomyosarcomas.

Embryonal rhabdomyosarcoma

Embryonal rhabdomyosarcoma (ERMS) is the most common type of rhabdomyosarcoma. It usually affects infants and young children. The cells of ERMS look like the developing muscle cells of a 6- to 8-week-old embryo. ERMS tends to occur in the head and neck area, bladder, vagina, and in or around the prostate and testicles.

Two subtypes of ERMS, botryoid and spindle cell rhabdomyosarcomas, tend to have a better prognosis (outlook) than the more common forms.

Alveolar rhabdomyosarcoma

Alveolar rhabdomyosarcoma (ARMS) typically affects older children or teenagers and occurs more often in large muscles of the trunk, arms, and legs. ARMS cells look like the

normal muscle cells seen in a 10-week-old fetus. ARMS tends to grow faster than ERMS and usually requires more intensive treatment.

Anaplastic rhabdomyosarcoma and undifferentiated sarcoma

Anaplastic rhabdomyosarcoma (formerly called *pleomorphic rhabdomyosarcoma*) is an uncommon type that occurs in adults but is very rare in children.

Some doctors also group undifferentiated sarcomas with the rhabdomyosarcomas. Doctors can tell that these cancers are sarcomas using lab tests, but the cells don't have any features that help classify them further.

Both of these uncommon cancers tend to grow quickly and usually require intensive treatment.

Rhabdomyosarcoma in adults

Most rhabdomyosarcomas occur in children, but they can also occur in adults. Adults are more likely to have faster-growing types of rhabdomyosarcoma, to have them in parts of the body that are harder to treat, and to have them spread to other parts of the body at the time of diagnosis. This is why, rhabdomyosarcomas in adults are often harder to treat effectively.

This document focuses on rhabdomyosarcomas in children, but most of the information here (including much of the treatment information) applies to rhabdomyosarcomas in adults as well.

What are the key statistics about rhabdomyosarcoma?

About 3% of all childhood cancers are rhabdomyosarcomas. About 350 new cases of rhabdomyosarcoma occur each year in the United States. The number of new cases has not changed much over the past few decades.

Most rhabdomyosarcomas are diagnosed in children and teenagers. About 6 out of 10 of these tumors are diagnosed in children under the age of 10. These tumors are usually embryonal rhabdomyosarcomas and occur in the head and neck area or in the genital and urinary tracts. Adolescents and adults are more likely than younger children to have alveolar rhabdomyosarcomas, which are found more often in the arms, legs, or trunk.

This disease is slightly more common in boys than in girls. There is no particular geographic location or ethnic group that has an unusually high rate of rhabdomyosarcoma.

The prognosis (outlook) for people with rhabdomyosarcoma depends on many factors, including the location, type, and size of the tumor, the results of surgery, and whether the cancer has metastasized (spread). Children aged 1 to 9 tend to have a better outlook than

infants or older children or adults. Statistics related to survival are discussed in the section, "How is rhabdomyosarcoma staged?"

What are the risk factors for rhabdomyosarcoma?

A risk factor is anything that affects the chance of having a disease such as cancer. Different cancers have different risk factors. For example, smoking is a risk factor for several types of cancer in adults.

Lifestyle-related risk factors such as diet, body weight, physical activity, and tobacco use play a major role in many adult cancers. But these factors usually take many years to influence cancer risk, and they are not thought to play much of a role in childhood cancers, including rhabdomyosarcomas.

No environmental factors (such as exposures during the mother's pregnancy or in early childhood) are known to increase the chance of getting rhabdomyosarcoma.

Age and gender

Rhabdomyosarcomas are most common in children under the age of 10, but they can also occur in teens and adults. They are slightly more common in boys than in girls.

Inherited conditions

Some people inherit a tendency to develop certain types of cancer. The DNA we inherit from our parents may have certain changes that account for this tendency to develop cancer. Some rare inherited conditions increase the risk of rhabdomyosarcoma (and usually some other tumors as well).

- Members of families with **Li-Fraumeni syndrome** are more likely to develop sarcomas, breast cancer, leukemia, and some other cancers.
- Children with **Beckwith-Wiedemann syndrome** have a high risk of developing Wilms tumor, a type of kidney cancer, but they may also develop rhabdomyosarcoma.
- **Neurofibromatosis**, also known as *von Recklinghausen disease*, usually causes multiple nerve tumors, but it also increases the risk of rhabdomyosarcoma.
- **Costello syndrome** is a very rare congenital abnormality. Children with this syndrome have high birth weights but then fail to grow well and are short. They also tend to have a large head. They are prone to develop rhabdomyosarcomas as well as other tumors.

These conditions are rare and account for only a small fraction of rhabdomyosarcoma cases. But they suggest that the key to understanding rhabdomyosarcoma will come from

studying genes and how they work in very early life to control cell growth and development.

Do we know what causes rhabdomyosarcoma?

We still do not know what causes most cases of rhabdomyosarcoma, but researchers have found some important clues in recent years.

Researchers are starting to understand how certain changes in DNA can cause normal cells to become cancerous. DNA is the chemical in each of our cells that makes up our genes – the instructions for how our cells function. It is packaged in chromosomes (long strands of DNA in each cell). We normally have 23 pairs of chromosomes in each cell (one set of chromosomes comes from each parent). We usually look like our parents because they are the source of our DNA. But DNA affects more than how we look.

Some genes are instructions for controlling when our cells grow, divide into new cells, and die. Certain genes that speed up cell division are called *oncogenes*. Others that slow down cell division, or cause cells to die at the right time, are called *tumor suppressor genes*. Cancers can be caused by DNA mutations (changes) that "turn on" oncogenes or "turn off" tumor suppressor genes.

For example, people with Li-Fraumeni syndrome have changes in the p53 tumor suppressor gene that cause it to make a defective protein. The p53 protein normally causes cells with DNA damage to either pause and repair that damage or, if repair is not possible, to self-destruct. When p53 is not working, cells with DNA damage continue to divide, causing further defects in other genes that control cell growth and development. This may lead to cancer.

Certain genes in a cell can be activated when bits of DNA are switched from one chromosome to another. This type of change, called a *translocation*, can happen when a cell is dividing into 2 new cells. This seems to be the cause of most cases of alveolar rhabdomyosarcoma (ARMS). In these cancers, a small piece of chromosome 2 (or, less frequently, chromosome 1) ends up on chromosome 13. This moves a gene called PAX3 (or PAX7 if it's chromosome 1) right next to a gene called FKHR. The PAX genes play an important role in causing cells to grow while an embryo's muscle tissue is being formed, but these genes usually shut down once they're no longer needed. The normal function of the FKHR gene is to activate other genes. Moving them together likely activates the PAX genes, which may be what leads to the tumor forming.

Research suggests that embryonal rhabdomyosarcoma (ERMS) develops in a different way. Cells of this tumor have lost a small piece of chromosome 11 that came from the mother, and it has been replaced by a second copy of that part of the chromosome from the father. This seems to cause the IGF2 gene on chromosome 11 to be overactive. The IGF2 gene codes for a protein that causes these tumor cells to grow.

Changes in several different genes are usually needed for normal cells to become cancer cells. Scientists have found other gene changes that set some rhabdomyosarcoma cells apart from normal cells, but there are likely others that have not yet been found.

Researchers now understand many of the gene changes that may lead to rhabdomyosarcoma, but it's still not clear what might cause these changes. Some gene changes may be inherited. Others may just be a random event that sometimes happens inside a cell, without having an external cause. There are no known lifestyle-related or environmental causes of rhabdomyosarcomas, so it is important to remember that there is nothing these children or their parents could have done to prevent these cancers.

Can rhabdomyosarcoma be prevented?

The risk of many adult cancers can be reduced with certain lifestyle changes (such as maintaining a healthy weight or quitting smoking), but at this time there are no known ways to prevent most cancers in children.

The only known risk factors for rhabdomyosarcoma (age, gender, and certain inherited conditions) cannot be changed. There are no known lifestyle-related or environmental causes of rhabdomyosarcomas, so at this time there is no way to protect against these cancers.

Even though we do not know how to prevent rhabdomyosarcoma, most children with this disease can be treated successfully.

Can rhabdomyosarcoma be found early?

At this time, there are no widely recommended screening tests for this cancer. (Screening is testing for cancer in people who don't have any symptoms.)

Some cases of rhabdomyosarcoma are found at an early stage. More than 1 out of 3 of these cancers is diagnosed early enough so that all visible tumor can be completely removed by a surgeon. Still, many of these turn out to already have microscopic tumor spread (spread that cannot be seen, felt, or detected by imaging tests) that is not removed by surgery.

Fortunately, many rhabdomyosarcomas start in areas where they are noticed early. For example, small tumors that start in the muscles behind the eye often cause the eye to bulge out, while tumors in the nasal cavity often cause nasal congestion, nosebleeds, or bloody mucus. When small lumps form near the surface of the body, parents often see them or feel them.

Tumors starting around the testicles in young boys cause painless swelling that is often noticed early by a parent. Many rhabdomyosarcomas start in the bladder or other parts of the genitourinary tract and may cause trouble emptying the bladder or lead to blood in the urine or in diapers. In girls with rhabdomyosarcoma of the vagina, the tumor may cause bleeding or a mucus-like discharge from the vagina. There are many other causes of

bleeding, of course, and most of them are not very serious, but it is important to have this checked by a doctor.

It may be harder to recognize tumors in the arms, legs, and trunks of older children because they may often have pain or bumps from sports or play injuries. Have your child's doctor evaluate any pain, swelling, or lumps that grow quickly or don't go away after a few weeks.

Families known to carry inherited conditions that raise the risk of this cancer (listed in "What are the risk factors for rhabdomyosarcoma?") or that have several family members with cancer (particularly childhood cancers) should talk with their doctors about the possible need for more frequent checkups. It is not common for this type of cancer to run in families, but close attention to possible early signs of cancer may help find it early, when treatment is most likely to be successful.

How is rhabdomyosarcoma diagnosed?

Certain signs and symptoms might suggest that a person may have rhabdomyosarcoma, but tests are typically needed to confirm the diagnosis.

Signs and symptoms of rhabdomyosarcoma

The symptoms of rhabdomyosarcoma depend largely on where the tumor is:

- When the tumor is in the trunk, limbs, or groin, the first sign is usually a mass or swelling that often doesn't cause any pain or other problems.
- Tumors around the eye can cause the eye to bulge or the child to appear to be cross-eyed.
- When it is in the ear or nasal sinuses, rhabdomyosarcoma can mimic an earache or a sinus infection.
- Tumors in the bladder and vagina may bleed or grow big enough to make it difficult or painful to urinate or have bowel movements.
- Tumors in the abdomen or pelvis can cause vomiting, abdominal pain, or constipation.
- Rhabdomyosarcoma rarely develops in the bile ducts, but when it does it can cause yellowing of the eyes or skin.

One or more of these symptoms usually leads parents to bring a child to the doctor. Less often, the child may have symptoms related to more advanced rhabdomyosarcoma, such as enlarged lymph nodes, bone pain, chronic cough, weakness, or weight loss.

Keep in mind that many of these signs and symptoms are more likely to be caused by something other than rhabdomyosarcoma. Still, if your child has any of these symptoms, check with your doctor so that the cause can be evaluated and treated, if needed.

Medical history and physical exam

If your child has any signs or symptoms that may suggest rhabdomyosarcoma, the doctor will want to get a complete medical history to learn about any symptoms the child is having and how long they have been present. The doctor will also examine your child to look for possible signs of rhabdomyosarcoma or other health problems. For example, the doctor may be able to see or feel an abnormal mass in the body.

If symptoms or the results of the physical exam suggest rhabdomyosarcoma might be present, other tests probably will be done. These might include imaging tests, biopsies, and/or lab tests.

Imaging tests

Imaging tests use x-rays, 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 find out whether a suspicious area might be cancerous
- To determine the extent of a tumor or learn how far a cancer may have spread
- To help determine if treatment has been successful

Most patients who have or may have cancer will get one or more of these tests.

Plain x-rays

These are sometimes used to look for tumors, but their use is limited mainly to looking at bones. They are sometimes done to look for cancer that might have spread to the lungs, although they wouldn't be needed if a chest CT scan is being done.

Computed tomography (CT or CAT) scan

The CT scan is an x-ray test that produces detailed cross-sectional images of parts of your child's body. 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. Unlike a regular x-ray, a CT scan creates detailed images of the soft tissues in the body.

This test can provide fairly detailed information about a tumor, including how large it is and whether or not it has invaded nearby structures. It can also be used to look at nearby lymph nodes, as well as the lungs or other areas of the body where the cancer may have spread.

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 is injected. 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. During the test, the table slides in and out of the scanner, a ring-shaped machine that completely surrounds the table. Your child will need to lie still on a table while this is being done. Younger children may be given medicine to help keep them calm or even asleep during the test.

Spiral CT (also known as helical CT) is now available in many medical centers. This type of CT scan uses a faster machine. The scanner part of the machine rotates around the body continuously, allowing doctors to collect the images much more quickly than with a standard CT. This lowers the chance of blurred images occurring as a result of body movement. It also lowers the dose of radiation received during the test. The slices it images are thinner, which yields more detailed pictures.

Magnetic resonance imaging (MRI) scan

Like CT scans, MRI scans give detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets instead of x-rays. 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 a very detailed image of parts of the body. A contrast material called gadolinium may be injected into a vein before the scan to better show details. The contrast material usually does not cause allergic reactions.

This test may be used instead of a CT scan to look at the tumor and the tissues around it. MRI scans can help determine the exact extent of a tumor, as they provide a detailed view of the muscle, fat, and connective tissue around the tumor. This is important when planning surgery or radiation therapy. MRI is also very useful if your child's doctor is concerned about possible spread to the spinal cord or brain.

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 can 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 may be disturbing. Sometimes, younger children are given medicine to help keep them calm or even asleep during the test.

Bone scan

A bone scan can help show if a cancer has spread to the bones, and is often part of the workup for children with rhabdomyosarcoma. This test is useful because it provides a picture of the entire skeleton at once.

For this test, a small amount of low-level radioactive material is injected into a vein (IV). The substance settles in areas of damaged bone throughout the entire 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 active bone changes attract the radioactivity and show up as "hot spots" on the scan. These areas may suggest cancer is present, but other bone diseases can also cause the same pattern. For an accurate diagnosis, other imaging tests such as plain x-rays or MRI scans, or even a bone biopsy might be needed.

Positron emission tomography (PET) scan

For a PET scan, a radioactive substance (usually a type of sugar related to glucose, known as FDG) is injected into the blood. The amount of radioactivity used is very low. Because cancer cells in the body are growing quickly, they absorb large amounts of the radioactive sugar. A special camera can then create a picture of areas of radioactivity in the body.

PET scans are not used routinely to diagnose rhabdomyosarcoma, but they can sometimes be very helpful in finding out if suspicious areas on other imaging tests (such as bone scans or CT scans) are tumors. PET scans can also be repeated during treatment to monitor the cancer over time. The picture from a PET scan is not finely detailed like a CT or MRI scan, but it provides helpful information about the whole body.

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

Biopsy methods

The results of imaging tests may strongly suggest that cancer is present, but a biopsy (removing some of the tumor for viewing under a microscope and other lab testing) is the only way to be certain. Usually several different kinds of lab tests are done on the sample to sort out what kind of tumor it is.

Biopsies can be done in several ways. The approach that is used will depend on where the mass is located, the age of the child, and the expertise and experience of the doctor doing the biopsy.

Surgical biopsy

The most common approach is to surgically remove a small piece of tumor while the child is under general anesthesia (asleep) and have it looked at by a pathologist (a doctor who specializes in diagnosing diseases from the results of lab tests). In some cases, nearby lymph nodes may also be removed and tested to see if the tumor has spread.

Needle biopsies

If for some reason a surgical biopsy cannot be done, a less invasive biopsy using a needle may be used. There are 2 kinds of needle biopsies, each of which has pros and cons.

Core needle biopsy: Core needle biopsies use a large, hollow needle that can be inserted into a tumor to withdraw a piece of tissue (core sample). If the tumor is near the surface of the body, the doctor can guide the needle into the tumor by touch. But if the tumor is deep within the body, imaging tests such as ultrasound or CT scans may be needed to guide the needle into place. The core sample that is removed is then used in lab tests to help make the diagnosis.

The main advantage of a core needle biopsy is that it does not require surgery, so there is no large incision, perhaps no general anesthesia (but some children may still need it), and less expense. On the other hand, the specimen is smaller, and the biopsy may miss the cancer if the needle is not aimed correctly. If the specimen is not a good sample of the tumor, another biopsy will be needed.

Fine needle aspiration (FNA) biopsy: This technique uses a very small hollow needle attached to a syringe to withdraw (aspirate) a small tumor sample. An FNA biopsy is ideally suited to tumors near the surface of the body that can be reached easily.

The downside of FNA is that the sample is very, very small. The pathologist must be experienced with this technique and be able to decide which tests will be most helpful on a very small sample. In cancer centers that have the experience, equipment, and knowledge to extract the most information from very small amounts of tissue, FNA can be a valuable – though certainly not foolproof – diagnostic approach, but it is not usually the preferred biopsy technique.

Bone marrow aspiration and biopsy

These tests aren't used to diagnose rhabdomyosarcoma, but they may be done after the diagnosis to find out if the tumor has spread to the bone marrow. The 2 tests are usually done at the same time. The samples are usually taken from the back of both of the pelvic (hip) bones, but in some patients they may be taken from the sternum (breastbone) or other bones.

These tests may be done during the surgery to treat the main tumor (while the child is still under anesthesia), or they may be done as a separate procedure.

If the bone marrow *aspiration* is being done as a separate procedure, the child lies on a table (on his or her side or belly). After cleaning the skin over the hip, the doctor numbs the area and the surface of the bone with local anesthetic, which may cause a brief stinging or burning sensation. Even with the local anesthetic, most patients still have some brief pain when the marrow is removed. 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 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. The biopsy may also cause some brief pain. Once the biopsy is done, pressure will be applied to the site to help stop any bleeding.

Lumbar puncture (spinal tap)

Lumbar puncture is not a common test for rhabdomyosarcoma, but it may be done for tumors in the head near the covering of the brain (the meninges). This test is used to look for cancer 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 may also recommend that the child be given something to make him or her sleep so the spinal tap can be done without difficulty or causing harm. A small, hollow needle is then placed between the bones of the spine to withdraw some of the fluid.

Lab tests on the biopsy samples

A pathologist will look at the biopsy samples under a microscope to try to determine if cancer cells are present. If the pathologist diagnoses cancer, the next step is to figure out if the cancer is a rhabdomyosarcoma. In rare cases, the pathologist can see that the cancer cells have small muscle striations (myofibrils), which confirm that the cancer is a rhabdomyosarcoma. But in most cases, other lab tests are needed to confirm the diagnosis.

Pathologists may use special stains on the samples to identify the type of tumor. The stains contain special proteins (antibodies) that specifically attach to substances in rhabdomyosarcoma cells but not other cancers. The stains produce a distinct color that can be seen under a microscope. This lets the pathologist know that the tumor is a rhabdomyosarcoma.

Sometimes the tumor will also be tested for genetic abnormalities. Genetic tests look for chromosome translocations and other DNA changes such as those discussed in the section "Do we know what causes rhabdomyosarcoma?"

If a diagnosis of rhabdomyosarcoma is made, the pathologist will also use these tests to help determine which kind of rhabdomyosarcoma your child has. This is important because it affects how the child is treated. For example, alveolar rhabdomyosarcoma, which tends to be more aggressive, requires more intensive treatment than embryonal rhabdomyosarcoma.

How is rhabdomyosarcoma staged?

Once the type of tumor has been identified, doctors need to assess, as accurately as possible, how much of it there is and where it has spread. The answers to "how much" and "where" are expressed in a kind of shorthand known as staging.

The outlook (prognosis) for people with cancer depends, to a large extent, on the cancer's stage. The stage of a cancer is one of the most important factors in choosing treatment.

Your child's doctors will use the results of the imaging tests and biopsies (described in "How is rhabdomyosarcoma diagnosed?") and the direct examination of the organs

during surgery to try to determine how far the cancer has spread. If there is any doubt about the extent of the cancer, more biopsies may be done on tissues at the edge of the tumor, nearby lymph nodes, and any suspicious lumps in other parts of the body.

Staging for rhabdomyosarcoma is fairly complex. Doctors first determine 3 key pieces of information:

- The type of rhabdomyosarcoma (embryonal or alveolar)
- The clinical group
- The TNM stage

These factors are then used along with the child's age to divide patients into risk groups, which then are used to determine the best treatment options.

Clinical groups

The clinical group is based on the extent of the disease and how completely it is removed during initial surgery. The groups are defined as follows.

Group I

This group includes children with localized disease (the cancer has not spread to nearby lymph nodes or to distant sites in the body) that is completely removed by surgery. Group I has 2 subgroups:

Group IA: Children in this group had a tumor that was still confined to the muscle or organ where it started and was completely removed by surgery. It had not spread to nearby lymph nodes or distant sites.

Group IB: Children in this group had a tumor that had grown beyond the muscle or organ where it started and into nearby structures, but it was completely removed by surgery. It had not spread to nearby lymph nodes or distant sites.

About 15% of rhabdomyosarcoma patients are in group I.

Group II

This group includes children who have had tumors that have been removed by surgery, but cancer has been found around the edges of the removed specimen, in the nearby lymph nodes, or in both places. In all cases, as much of the cancer has been removed as possible. Group II has 3 subgroups:

Group IIA: In this group, the cancer has not spread to nearby lymph nodes or elsewhere. The surgeon has removed all the cancer that could be seen, but the pathologist has found cancer at the edge of the removed specimen, which means that there is a small amount of cancer left behind.

Group IIB: In this group, the cancer has spread to nearby lymph nodes, but all of the cancer has been removed by surgery.

Group IIC: In this group, the cancer has spread to nearby lymph nodes. The surgeon has removed all the cancer that could be seen (including in the lymph nodes), but the pathologist has found cancer at the edge of the removed specimen, which means that there is a small amount of cancer left behind.

About 20% of patients are in group II.

Group III

These children have tumors that cannot be completely removed, leaving some tumor behind that can be seen with the naked eye. The tumor may have spread to nearby lymph nodes, but there is no sign that it has spread to distant organs. Group III has 2 subgroups:

Group IIIA: The tumor cannot be completely removed by surgery, and only a biopsy of the tumor has been done.

Group IIIB: The tumor cannot be completely removed, but surgery has removed at least half of the tumor.

This group accounts for about 50% of patients with rhabdomyosarcoma.

Group IV

These children have evidence of distant spread at the time of diagnosis to places such as the lungs, liver, bones, bone marrow, or to distant muscles or lymph nodes.

This group contains about 15% of children with rhabdomyosarcoma.

The TNM stage

The TNM stage doesn't depend on the results of surgery, but is based on 3 key pieces of information prior to treatment:

- **T:** The characteristics of the **tumor** (location and size)
- **N:** Whether the cancer has spread to nearby **lymph nodes**
- **M:** Whether it has **metastasized** (spread) to distant parts of the body

These factors are combined to determine an overall stage:

Stage 1

The tumor started in a favorable area:

- The orbit (area near the eye)

- The head and neck area, except for parameningeal sites (next to the membranes covering the brain)
- A genital or urinary site, except the bladder or prostate
- Biliary tract (tubes leading from the liver to the intestines)

The tumor can be any size. It may have grown into nearby areas and/or spread to nearby lymph nodes, but it has not spread to distant sites.

Stage 2

The tumor started in an unfavorable site:

- The bladder or prostate
- An arm or leg
- A parameningeal site (next to the membranes covering the brain)
- Any other site not mentioned in stage 1

The tumor is 5 cm (about 2 inches) or smaller across and there is no evidence that it has spread to nearby lymph nodes or distant sites.

Stage 3

The tumor started in an unfavorable site:

- The bladder or prostate
- An arm or leg
- Aparameningeal site (next to the membranes covering the brain)
- Any other site not mentioned in stage 1

And one of the following applies:

- The tumor is 5 cm across or smaller but has spread to nearby lymph nodes
- The tumor is larger than 5 cm across and may or may not have spread to nearby lymph nodes

In either case, the cancer has not spread to distant sites.

Stage 4

The tumor can have started at any site and can be of any size. It has spread to distant sites such as the lungs, liver, bones, or bone marrow.

Risk groups

Using the information about the type of rhabdomyosarcoma, the clinical group, the TNM stage, and the child's age, doctors classify patients into 3 risk groups. Information about risk groups helps doctors decide how aggressive treatment should be.

Clinical risk groups are defined based on what has been learned from previous research on patients' outcomes. The risk groups discussed here are based on the most current information, but these may change in the future as safer and more effective treatments are developed.

Low-risk group

This group includes:

- Children with TNM stage 1 *embryonal* rhabdomyosarcomas (ERMS) that fall into clinical groups I, II, or III
- Children with stage 2 or 3 ERMS who are in clinical groups I or II

Intermediate-risk group

This group includes:

- Children with stage 2 or 3 ERMS who are in clinical group III
- Children with *alveolar* rhabdomyosarcoma (ARMS) that has not spread to distant sites (stage 1, 2, or 3)

High-risk group

This group includes:

- Children with widespread (stage 4) RMS

Five-year survival rates by risk group

Survival rates are often used by doctors as a standard way of discussing a person's prognosis (outlook). Some people may want to know the survival statistics for those in similar situations, while others may not find the numbers helpful, or may even not want to know them. Whether or not you want to read about the survival statistics below for rhabdomyosarcomas is up to you.

The 5-year survival rate refers to the percentage of patients who live *at least 5 years* after their cancer is diagnosed. Of course, many people live much longer than 5 years (and many are cured).

In order to get 5-year survival rates, doctors have to look at people who were treated at least 5 years ago. Improvements in treatment since then may result in a more favorable outlook for patients now being diagnosed with Ewing tumors.

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they cannot predict what will happen in any particular person's case. The risk group of a person's cancer is important in estimating their outlook. But many other factors may also affect a person's outlook, such as their age, the location of the tumor, and how well the cancer responds to treatment.

Here are *general* survival statistics based on risk groups. These numbers come from large clinical trials treating children with rhabdomyosarcoma in the 1980s and 1990s.

Low-risk group

Overall, the 5-year survival rate for children in the low risk group is over 90%. Most of these children will be cured.

Intermediate-risk group

For those in the intermediate risk group, the 5-year survival rates range from about 60% to about 80%. The rate varies somewhat by tumor location, stage, and the age of the child.

High-risk group

If the cancer has spread widely, the 5-year survival rate is generally around 20% to 25%. Again, it's important to note that other factors, such as the age of the patient and the site and type of tumor will affect these numbers. For example, children with embryonal rhabdomyosarcoma and limited spread (to only 1 or 2 distant sites) have a higher 5-year survival rate.

Even when taking risk groups and other factors into account, survival rates are at best rough estimates. Your child's doctor can tell you how well these numbers may apply, as he or she is familiar with the aspects of your particular situation.

How is rhabdomyosarcoma treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

General approach to treatment

Treating rhabdomyosarcoma is complex and requires the expertise of many different doctors, nurses, and other health professionals. Pediatric (or medical) oncologists, surgeons, radiation oncologists, and oncology nurses will get together to plan the most effective treatment. In most cases, treatment includes surgery, chemotherapy, and usually radiation therapy as well.

The treatment and prognosis of patients with rhabdomyosarcoma depend to a large extent on the type of rhabdomyosarcoma and on how much of it can be removed with surgery. This is why it's very important for patients to be diagnosed and treated by doctors who have experience with rhabdomyosarcoma. Children with rhabdomyosarcoma are best treated in a cancer center such as those who are members of the Children's Oncology Group, where there is experience and expertise in treating childhood cancers.

All children and adults with rhabdomyosarcoma will be treated with surgery to remove the tumor if it is possible to do so without causing major damage or disfigurement. In some cases, chemotherapy and/or radiation therapy may be used first to try to shrink the tumor. If it shrinks enough, surgery may be done at this point. The goal is to completely remove the tumor, but this is often not possible.

Whether the tumor appears to have been completely removed or not, all patients with rhabdomyosarcoma should receive chemotherapy. Without it, it is very likely that the cancer will recur at distant metastatic sites because small amounts of cancer are almost always present in other parts of the body when the cancer is first diagnosed.

If cancer is left behind after surgery or if the cancer has some less favorable traits and it hasn't spread to distant sites (as is the case most of the time), radiation therapy will also be given.

All of these treatments may have side effects, but many of them can be made less troublesome. Your medical team will help you take care of the side effects and will work closely with nutritionists, psychologists, and social workers to help you understand and deal with the medical problems, stress, and scheduling issues related to the treatment.

Because many of these things can be more complicated for cancer in children, many people will be involved in your child's overall care. As a parent, taking care of a child with cancer can be a very big job. It is important to remember that you will have a lot of help. It is also important for you to know that the health care professionals who treat children with rhabdomyosarcoma are using the experience and knowledge gained from more than 30 years of detailed scientific study of treating this disease.

The next few sections describe in more detail the types of treatments used for rhabdomyosarcomas.

Surgery

Unless the cancer has clearly spread to distant parts of the body, surgery is usually the first step in treating rhabdomyosarcoma. Complete resection (removal) of the main

tumor, along with some surrounding normal tissue, is the goal whenever possible. If there are cancer cells at the edges (margins) of the removed specimen (meaning that some cancer cells may remain in the body at the tumor site), the surgeon may operate again to try to remove the remaining cancer. In some cases, surgery may be done even if it is clear that all of the cancer can't be removed because it may help other treatments (chemotherapy and radiation) to work better.

During surgery, nearby lymph nodes may be biopsied to determine if the cancer has spread to these areas, especially if the main tumor is near the testicles in older boys or is on an arm or leg.

Completely removing head and neck tumors may require special surgical teams with ENT (ear, nose, and throat) surgeons, plastic surgeons, maxillofacial surgeons, and neurosurgeons. If the tumor is large or is in a spot where removing it completely would severely affect the child's appearance or cause other problems, then surgery may be delayed until after a few courses of chemotherapy and possibly radiation therapy to try to shrink it, or it may not be done at all.

What to expect during surgery

The type and extent of surgery can vary a great deal depending on the location and size of the tumor.

The biopsy is generally the first surgery done for rhabdomyosarcoma. How it is done, how long recovery takes, and how it affects later treatment depend on many factors. The type of biopsy used is based on imaging test results, location and size of the tumor, the child's age and health, and the expertise of the doctor. (For a description of biopsy types, see "How is rhabdomyosarcoma diagnosed?")

The main goal of surgery is to completely remove the cancer in an effort to avoid future surgery. But as mentioned before, this is not always an option.

Before any surgery, several issues must be addressed. Someone from the surgical team will talk with your family and examine your child to make sure he or she is physically ready for surgery. Blood will be drawn for lab tests to make sure the bone marrow and other organs are working well and to ensure matched units of blood will be available in case your child needs a transfusion during surgery. A parent or guardian will need to sign consent forms, giving permission for the surgery, anesthesia, and possible blood transfusions.

You will be given instructions about what your child can eat and do before and after surgery. The medical team will need to know if your child has any allergies, especially to medicines. The team will calculate the dose of anesthesia based on your child's body size.

Your child may not be allowed to eat or drink for several hours before the surgery. This is done to avoid potential complications related to having food in the stomach while under anesthesia.

An intravenous (IV) access line will be started in a vein (usually in the arm). If an IV line is already in place, this site may be used to give the anesthesia and a second IV line may be started after anesthesia is given to reduce discomfort. Your child will be given a hospital gown, be placed on a stretcher, and taken to the pre-operative holding area. Anesthesia may be started in this area or the operating room.

If the diagnosis was not confirmed by a biopsy before the main operation, the surgeon may first take only a small sample of the tumor. The sample is given to a pathologist right away to look at and determine if it is cancerous or not. If the pathologist can determine that it is cancerous while your child is still on the operating table, the surgeon may remove the entire tumor and may also remove some of the nearby lymph nodes to check for spread of the cancer.

Other procedures may also be done at this time. A bone marrow aspiration and biopsy may be done, and a central venous access line (a thin catheter) may be inserted into one of the large vessels in the chest to deliver chemotherapy and other medicines later. If the surgeon suspects the disease has spread to another part of the body, a second incision to get a piece of the possible metastatic tumor may be done as well.

Once the procedure is finished, your child will be taken to the recovery area and closely monitored until fully awake. Your child will then be returned to his or her hospital room.

Possible risks and side effects

Possible complications of surgery depend on the location and extent of the operation and the child's health beforehand. Serious complications, although rare, can include problems with anesthesia, excessive bleeding, wound infections, and pneumonia. Most children will have some pain for a while after the operation, although this can usually be helped with medicines if needed.

Some operations may result in few physical changes other than a scar, while more involved operations may lead to changes in appearance or may require physical rehabilitation.

For more information on surgery as a treatment for cancer, see our document, *Surgery*.

Chemotherapy

All children with rhabdomyosarcoma will probably be treated with chemotherapy at some point. Even if it is thought that the cancer was completely removed by surgery, without chemotherapy it is likely to come back.

Chemotherapy is the use of drugs to treat cancer. Chemotherapy is *systemic* therapy, meaning that the drug enters the bloodstream and reaches throughout the body to destroy cancer cells. This makes chemotherapy useful for killing rhabdomyosarcoma cells that have spread to the lymph nodes, bone marrow, liver, lungs, or other organs.

Following surgery, any tiny deposits of rhabdomyosarcoma that remain can often be destroyed by chemotherapy. If larger areas of tumor remain after surgery (or if surgery

couldn't be done for some reason), chemotherapy (along with radiation) can often shrink these areas. In some cases this may allow further surgery to completely remove the remaining tumor.

Drugs used to treat rhabdomyosarcoma

There are many chemotherapy drugs. Some of them can be taken by mouth, but most are injected into a vein. The drugs used depend to some extent on which risk group the child is in (described in the section "How is rhabdomyosarcoma staged?").

The main drugs used to treat children in the low-risk group are vincristine and dactinomycin (also known as actinomycin-D). This combination is often referred to as VA. In some cases cyclophosphamide may be added as well. This 3-drug combination is referred to as VAC.

The VAC regimen is the most common combination used for the intermediate-risk group. Irinotecan or topotecan may be added as well. Other drugs used to treat rhabdomyosarcoma include ifosfamide, etoposide, and doxorubicin.

The same drugs are also used for children in the high-risk group (which includes most children with metastatic disease), but these drugs have not been shown to be as successful in this group. New drugs and drug combinations are continually being studied by the Soft Tissue Sarcoma Committee of the Children's Oncology Group and other researchers. It is hoped that they will improve the survival rate in the high-risk group.

Doctors give chemotherapy in cycles, which usually consist of treatment on 1 or 2 days in a row, followed by days off to allow the body time to recover. For rhabdomyosarcoma, chemotherapy is typically given once a week for the first few months, and then less frequently. The total length of chemotherapy is usually in the range of 6 months to a year.

Possible side effects

Chemotherapy drugs work by attacking cells that are dividing quickly, which is why they often work against cancer cells. But other cells in the body, such as those in the bone marrow, the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemotherapy, which can lead to side effects.

Children seem to have an advantage over adults when it comes to chemotherapy. They tend to have less severe side effects and recover from side effects more quickly. This is why doctors can often give them higher doses of chemotherapy to kill the tumor.

The side effects of chemotherapy depend on the type of drugs, the doses, and how long they are taken. Possible side effects can include:

- Hair loss
- Mouth sores
- Loss of appetite

- Nausea and vomiting
- Increased chance of infections (from low white blood cell counts)
- Easy bruising or bleeding (from low blood platelet counts)
- Fatigue (from low red blood cell counts)

These side effects are usually short-term and go away once treatment is finished. Your child's doctor and treating team will watch closely for any side effects that develop. There are often ways to lessen these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting. Be sure to ask your doctor or nurse about medicines to help reduce side effects, and report any side effects your child has so they can be managed effectively.

Along with the risks above, some chemotherapy drugs have specific side effects (although these are relatively uncommon). For example:

Cyclophosphamide and ifosfamide can damage the bladder. This can be avoided or minimized by giving the drugs with plenty of fluids and with a drug called mesna, which helps protect the bladder. These drugs can also cause changes in the menstrual cycle, and can damage the ovaries or testicles, which might affect fertility (the ability to have children).

Vincristine can damage nerves. Some patients may notice tingling and numbness, particularly in the hands and feet.

Recent studies have shown that children under the age of 3 years are more likely to have liver damage from the chemotherapy. Doctors now use lower and very specific doses for any child younger than 3 years old.

Some chemotherapy drugs may also increase the risk of developing a second type of cancer, usually a form of leukemia, years after the rhabdomyosarcoma is cured. This is rare, however, and the importance of chemotherapy in treating rhabdomyosarcoma far outweighs this risk.

For more extensive information on chemotherapy, see the separate our document, *Understanding Chemotherapy: A Guide for Patients and Families*.

Radiation therapy

Radiation therapy (radiotherapy) uses high-energy radiation to kill cancer cells. It is often an effective way to kill cancer cells that cannot be removed during surgery.

Radiotherapy is most useful if some of the main tumor is still left after surgery (group II or III) or if completely removing the tumor would mean loss of an important organ, like the eye or bladder, or would be disfiguring. It is not usually needed for children with embryonal rhabdomyosarcomas that can be completely removed by surgery (group I).

Usually radiation therapy is given to any area of remaining disease after 6 to 12 weeks of chemotherapy. An exception is when a tumor near the meninges (linings of the brain) has

grown into the skull bones, into the brain itself, or into the spinal cord. In these patients radiation therapy is started right away.

Radiotherapy cannot be given to the whole body to treat metastases, but it can be given to certain areas of known disease to reduce any symptoms the cancer may be causing.

Radiation therapy is much like getting an x-ray, although the dose of radiation is much higher. Radiation is usually given daily over many weeks. For each session, your child will lie on a special table while a machine delivers the radiation from a precise angle. The treatment is not painful. Each session lasts about 15 to 30 minutes, with most of the time being spent making sure the radiation is aimed correctly. The actual treatment time each day is much shorter. Some younger children may be given medicine to make them drowsy before each treatment.

Newer radiation techniques

Several newer techniques may allow doctors to more accurately aim treatment at the tumor while reducing the radiation exposure to nearby healthy tissues. These techniques may offer better chances of increasing the success rate and reducing side effects. Many doctors now recommend using these approaches when they are available.

Three-dimensional conformal radiation therapy (3D-CRT): 3D-CRT uses special computers to precisely map the location of the tumor. Depending on where the tumor is, your child may be fitted with a plastic mold resembling a body cast to keep him or her in the same position so that the radiation can be aimed more accurately. Radiation beams are then shaped and aimed at the tumor from several directions, which makes the radiation less likely to damage nearby normal tissues.

Intensity modulated radiation therapy (IMRT): IMRT is an advanced form of 3D therapy. In addition to shaping the beams and aiming them at the tumor from several angles, the intensity (strength) of the beams can be adjusted to limit the dose reaching the most sensitive normal tissues. This allows doctors to deliver an even higher dose to the cancer areas. Many major hospitals and cancer centers now use IMRT.

Brachytherapy (internal radiation therapy): Another newer approach is to insert a radioactive pellet into or near the tumor. The radiation from the pellet travels only a short distance, so the tumor gets most of the radiation. This approach is especially useful in treating some bladder, vaginal, and head and neck area tumors. Some early studies suggest that this may be a good way to preserve the function of these organs in many children.

Other newer techniques, such as stereotactic radiotherapy and proton beam radiotherapy, are discussed briefly in the section, "What's new in rhabdomyosarcoma research and treatment?"

Possible side effects

The side effects of radiation therapy depend on the dose of radiation and where it is aimed.

Short-term side effects can include fatigue and increased numbers of infections. Effects on skin areas that receive radiation can range from hair loss and mild sunburn-like changes to more severe skin reactions. If the abdomen or pelvis gets radiation, nausea, vomiting, and diarrhea are common. In some cases there may be damage to the bladder or bowel. Radiation to the head and neck can cause mouth sores and loss of appetite.

Small children's brains are very sensitive to radiation, so doctors try to avoid using radiation to the head whenever possible. Side effects of brain radiation therapy usually become most serious 1 or 2 years after treatment and may include headaches and problems such as memory loss, personality changes, and trouble learning at school.

Other long-term problems can include scar tissue formation and the slowing of bone growth. Depending on the age of the child and what parts of the body get the radiation, this could result in deformities or a lack of growth to full height. Radiotherapy may also raise the risk of cancer many years later in the areas that got radiation (see "Possible long-term side effects of treatments").

To lower the risk of serious long-term effects from radiation, doctors use the lowest dose of radiation therapy that is still effective.

For more detailed information on radiation therapy, see our document, *Understanding Radiation Therapy: A Guide for Patients and Families*.

High-dose chemotherapy and stem cell transplants

A stem cell transplant (sometimes referred to as a bone marrow transplant) makes it possible to use much larger doses of chemotherapy than would normally be possible. Chemotherapy drugs kill rapidly dividing normal cells (such as those in the bone marrow, where new blood cells are made) as well as cancer cells. Higher doses of these drugs might be more effective in treating some cancers, but they are not given because the severe damage to the bone marrow would cause life-threatening shortages of blood cells.

A stem cell transplant gets around this problem by taking out and saving some of the patient's own blood-forming stem cells (either from the blood or bone marrow) before high-dose chemotherapy and then putting them back into the blood after chemotherapy is over, where they will travel to the bone marrow. This allows the normal marrow to regrow.

Stem cell transplants are used to treat some aggressive childhood cancers, but so far it is not clear if they can help rhabdomyosarcoma patients. Because of the severe side effects they can cause, most doctors recommend they be used only as part of a clinical trial.

For more detailed information on stem cell transplants, see our document, *Bone Marrow and Peripheral Blood Stem Cell Transplants*.

Rhabdomyosarcoma that progresses or recurs after initial treatment

Rhabdomyosarcoma that continues to grow during treatment or that comes back once treatment is finished is often hard to treat. The type of treatment will depend on a number of factors, including the site of the recurrence, type of tumor, and previous treatments used.

For tumors that recur in the same spot as the original tumor, surgery may be used if it is feasible. If radiation therapy wasn't part of the initial treatment, it may be tried as well.

In rare cases, surgery may be used for cancers that recur at distant sites, such as if there is a small recurrence in a lung.

Most often, chemotherapy is the best option for distant spread. This might include some of the drugs listed in the chemotherapy section, as well as newer drugs under study. Because these tumors are hard to treat, clinical trials of newer treatments may be a good option in many cases.

Possible long-term side effects of treatments

Because more children with rhabdomyosarcoma are now surviving longer, it has become possible to look at the long-term effects of their treatment. It's important to discuss what these potential effects might be with your child's medical team before starting treatment.

The possible long-term effects of surgery depend a great deal on the location and extent of the tumor(s). Some operations may result in few physical changes other than a scar, while more involved operations may lead to changes in appearance or may require physical rehabilitation.

Some chemotherapy drugs may damage cells in the ovaries and testicles that can make it difficult or even impossible for patients to have children.

Another unwanted long-term result is the small, but definitely increased, risk of second cancers in survivors who received chemotherapy and radiotherapy. These cancers include bone cancer, leukemia, or other soft tissue tumors. The bone cancers seem to be linked with radiotherapy, while the leukemias are more often seen after treatment with cyclophosphamide and related drugs.

It is important to remember that these second cancers affect only a small number of rhabdomyosarcoma survivors, and these are children who most likely would not have survived the rhabdomyosarcoma without these treatments.

The long-term side effects of radiation therapy may be significant, especially for young children. Bones and soft tissues that are irradiated do not grow very well. Depending on the area getting radiation, this may result in curvature of the spine, a shortened limb, limited motion of a joint, hardening of the surrounding soft tissue, stiffening of the lungs, poor development of the facial bones, cataracts and poor vision of the involved eye, later

problems with sexual function, and other problems. Doctors try to limit these potential side effects as much as possible when planning treatment.

Long-term follow-up care for children

To help increase awareness of late effects and improve follow-up care of childhood cancer survivors throughout their lives, the Children's Oncology Group (COG) has developed long-term follow-up guidelines for survivors of childhood cancers. These guidelines, written for doctors and other health care professionals, describe in detail the suggested long-term follow-up care based on the treatments the child has received. It is very important to discuss possible long-term complications with your child's health care team, and to make sure there is a plan in place to watch for these problems and treat them, if needed. To learn more, ask your child's doctors about the COG survivor guidelines, and see our document, *Childhood Cancer: Late Effects of Cancer Treatment*.

Clinical trials

You may have had to make a lot of decisions since you've been told your child has cancer. One of the most important decisions you will make is deciding which treatment is best. You may have heard about clinical trials being done for this type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you.

Clinical trials are carefully controlled research studies that are done with patients who volunteer for them. These studies are done to get a closer look at promising new treatments or procedures.

If you would like your child to take part in a clinical trial, you should start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of clinical trials that meet your medical needs. You can reach this service at 1-800-303-5691 or on our Web site at www.cancer.org/clinicaltrials. You can also get a list of current clinical trials by calling the National Cancer Institute Cancer Information Service toll free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at www.cancer.gov/clinicaltrials.

Your child will have to meet certain requirements to take part in any clinical trial. If your infant or young child does qualify for a clinical trial, you will have to decide whether or not to enter (enroll) the child into it. Older children, who can understand more, usually must also agree to take part in the clinical trial before the parents' consent is accepted.

Clinical trials are one way to get state-of-the-art cancer care for your child. They are the only way for doctors to learn better methods to treat cancer. Still, they are not right for every child.

You can get a lot more information on clinical trials in our document called *Clinical Trials: What You Need to Know*. You can read it on our Web site or call our toll-free number and have it sent to you.

Complementary and alternative therapies

When your child has cancer you are likely to hear about ways to treat his or her cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to Internet groups and Web sites offer ideas for what might help. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

What exactly are complementary and alternative therapies?

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

Complementary methods: Most complementary treatment methods are not offered as cures for cancer. Mainly, they are used to help the person with cancer feel better. Some methods that are used along with regular treatment are: art therapy or play therapy to reduce stress; acupuncture to help relieve pain; or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not to be helpful, and a few have even been found harmful.

Alternative treatments: Alternative treatments may be offered as cancer cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may pose danger, or have life-threatening side effects. But the biggest danger in most cases is that your child may lose the chance to be helped by standard medical treatment. Delays or interruptions in medical treatments may give the cancer more time to grow and make it less likely that treatment will help.

Finding out more

It is easy to see why parents who have children with cancer think about alternative methods. You want to do all you can to help fight the cancer, and the idea of a treatment with few or no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most of these alternative methods have not been tested and proven to work in treating cancer.

As you consider your child's options, here are 3 important steps you can take:

- Look for "red flags" that suggest fraud. Does the method promise to cure all or most cancers? Are you told not to use regular medical treatments? Is the treatment a "secret" that requires you to take your child to certain providers or to another country?
- Talk to your child's doctor or nurse about any method you are thinking about.

- Contact us at 1-800-227-2345 to learn more about complementary and alternative methods in general and to find out about the specific methods you are looking at.

The choice is yours

You always have a say in how your child is treated. If you want to use a non-standard treatment, learn all you can about the method and talk to your child's doctor about it. With good information and the support of your child's health care team, you may be able to safely use the methods that can help your child while avoiding those that could be harmful.

More treatment information

For more details on treatment options – including some that may not be addressed in this document – the National Cancer Institute (NCI) is a good source of information.

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its Web site (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on www.cancer.gov.

What should you ask your doctor about rhabdomyosarcoma?

It is important for you to understand as much as you can about your child's care, and your child's health care team can help you by answering your questions and concerns. Ask for things to be explained to you until you are sure you understand them.

- What kind of rhabdomyosarcoma does my child have?
- Has my child's tumor spread?
- Are there other tests that need to be done before we can decide on treatment?
- What are the clinical group and stage of my child's cancer, and what do these mean?
- How much experience do you have treating this type of cancer?
- What other doctors will we need to see?
- What treatment options do we have?
- What do you recommend and why?
- What are the short-term risks and side effects to the treatments you suggest?
- What are the likely long-term effects of treatment? Could it affect my child's fertility?
- What should we do to be ready for treatment?

- How long will treatment last? What will it involve? Where will it be done?
- How will treatment affect our daily activities?
- Based on what you've learned about my child's cancer, what is the outlook for cure?
- What would we do if the treatment doesn't work or if the cancer recurs?
- What clinical trials are suitable options for my child?
- What type of follow-up and rehabilitation will my child need after treatment?

You may have other questions as well. For example, you may want to:

- Ask about getting a second opinion as to the best treatment option.
- Find out if the treatment schedule can be arranged so that your child will miss as little school as possible.
- Ask how to explain what is happening with your child so that his brothers, sisters, and friends can understand.
- Ask about support groups that might help you benefit from the experience of other families who have been through this.

What happens during and after treatment for rhabdomyosarcoma?

Your child will probably have to return to the doctor often during chemotherapy for lab tests to look for low blood counts that could lead to bleeding or serious infection. The doctor will also check for other side effects of the treatment. Sometimes your child may need blood transfusions to treat low blood counts or antibiotics to treat infection.

Usually chemotherapy and follow-up testing will be done in the pediatric cancer center, but if you must travel a great distance the specialists involved in your child's care can work with your local doctor to reduce your need to travel.

For several years after treatment, it is very important for your child to have regular follow-up exams with the cancer care team. The doctors will continue to watch for signs of disease, as well as for short-term and long-term side effects of treatment. Doctor visits will be more frequent at first, but the time between visits may get longer as time goes on.

Checkups after treatment of rhabdomyosarcoma include careful physical exams, lab tests, and sometimes imaging tests such as CT and/or MRI scans. If the rhabdomyosarcoma recurs (comes back), it is usually within the first few years after treatment. As time goes by, the risk of recurrence goes down.

If the tumor comes back, or it does not respond to treatment, your child's doctors will discuss with you the various treatment options available (as discussed in "Rhabdomyosarcoma that progresses or recurs after initial treatment").

As mentioned in "How is rhabdomyosarcoma treated?", there are some potential long-term complications from the treatment of this disease, including effects on fertility and a risk of developing another type of cancer at a later time. It's important to talk with your child's doctors to understand what these risks are.

Psychosocial considerations in treating rhabdomyosarcoma

Most cases of rhabdomyosarcoma develop during a very sensitive time in a young person's life. A diagnosis of rhabdomyosarcoma and its treatment may have a profound effect on a person's outward appearance and how they view themselves and their body. It can also affect their ability to do some everyday tasks. This can have an impact on their ability to continue certain school, work, or recreational activities. The effect will probably be greatest during the first year of treatment. The treating center should evaluate the family situation as soon as possible, so that any areas of concern can be addressed.

Some common family concerns include financial stresses, transportation to the cancer center, the possible loss of a job, and the need for home schooling. Many experts recommend that school-aged patients attend school as much as possible. This helps them maintain important social connections and gives them a chance to tell their friends what is happening to them.

Friends can be a great source of support, but patients and parents should know that some people have misunderstandings and fears about cancer. Some cancer centers have a school re-entry program that can help in these situations. In this program, health educators visit the school and inform students about the diagnosis, treatment, and changes that the cancer patient may go through. They also answer any questions from teachers and classmates.

Centers that treat many patients with rhabdomyosarcoma may have programs to introduce new patients to children or teens who have finished their treatment. Seeing another patient with rhabdomyosarcoma doing well after treatment is often helpful. There are also support groups that may be helpful.

Although the psychological impact of this disease in children and teenagers is most obvious, adults with this disease may face many of the same challenges. Adult patients should also be encouraged to take advantage of the cancer centers' physical therapy, occupational therapy, and counseling services.

Moving on

As much as you may want to put the experience behind you once treatment is completed, it is very important to keep good records of your child's medical care during this time. Eventually, your child will grow up, be on his or her own, and have new doctors. It is important that he or she be able to give the new doctors the details of the cancer diagnosis and treatment. Gathering these details soon after treatment may be easier than trying to get them at some point in the future. There are certain pieces of information that your child's doctors should have, even after your child has become an adult. These include:

- A copy of the pathology report from any biopsies or surgeries.
- If there was surgery, a copy of the operative report(s).
- If there were hospitalizations, a copy of the discharge summaries that doctors prepare when patients are sent home.
- A list of the final doses of each chemotherapy drug or other drug your child received. (Certain chemotherapy drugs have specific long-term side effects. If you can get a list of these from the pediatric oncologist, this might also help any new primary care doctor.)
- If there was radiation therapy, a summary of the type and dose of radiation and when and where it was given.

What's new in rhabdomyosarcoma research and treatment?

The treatment of rhabdomyosarcoma has come a long way in the past 30 years, largely due to the work of the Intergroup Rhabdomyosarcoma Study Group (now known as the Soft Tissue Sarcoma Committee of the Children's Oncology Group). However, more work needs to be done.

Better classification of rhabdomyosarcomas

Newer molecular techniques may help better categorize rhabdomyosarcomas and predict which patients will respond best to certain treatments. For example, rather than just looking at the cancer cells under a microscope, researchers have begun to use specialized genetic tests to help classify rhabdomyosarcomas. About 25% of cancers that doctors would usually classify as alveolar rhabdomyosarcoma (ARMS) have been found to lack the typical gene change (the PAX/FKHR fusion gene) seen in ARMS. Some early studies have shown that these cancers seem to act more like embryonal rhabdomyosarcoma (ERMS) than ARMS. ERMS generally requires less intensive treatment than ARMS. If this finding is confirmed in other studies, it may allow doctors to use less intensive treatments on these cancers and still achieve the same results.

Improving standard treatments

A major goal of current research is to more effectively treat all patients, while reducing exposure to intensive treatments (and their side effects) when possible. For example, researchers are studying whether children who have a low risk of the tumor recurring can be successfully treated without using potentially harmful therapies such as the chemotherapy drug cyclophosphamide and radiation therapy.

Because children's bodies are very sensitive to radiation, doctors are looking for ways to limit the doses as much as possible. Newer radiation therapy techniques allow doctors to

aim the radiation more precisely, limiting the amount that reaches normal body tissues. Some of these techniques were described in the section "How is rhabdomyosarcoma treated?", and other approaches are now being studied. For example, in stereotactic radiation therapy, a special machine allows the radiation to be aimed at the tumor from many different angles.

Proton beam radiation is another new approach. Standard radiation beams give off the same amount of radiation at all points in the body as they pass through it. Proton beam radiation uses radioactive particles that travel only a certain distance before releasing most of their energy. Doctors can use this property to limit the radiation reaching normal body tissues. While this new approach seems promising, it is expensive and is only available in a handful of centers around the country at this time.

Doctors are studying adding newer chemotherapy drugs such as irinotecan to the standard VAC chemotherapy regimen in those who have a higher risk of the tumor recurring.

For patients at a high risk of tumor recurrence, the goal is to maximize the early treatment with drugs such as cyclophosphamide and ifosfamide by giving them more frequently (a concept called "interval compression").

Newer treatment approaches

Drugs that target specific parts of cancer cells (as opposed to just attacking fast-growing cells) are now being used to treat some adult cancers. Some of these drugs, such as dasatinib (Sprycel), are now being studied for use in rhabdomyosarcoma as well.

Some other newer drugs also work in ways that are different from standard chemotherapy drugs. Trabectedin (ET-743) and IGF-1 receptor inhibitors are examples of such drugs now being tested in clinical trials.

Researchers are also testing other new ways to treat rhabdomyosarcoma. For example, some researchers are looking at exposing some of the body's own immune system cells, called dendritic cells, to the abnormal PAX-FKHR protein that is found in many ARMS cells. The hope is that the dendritic cells will then cause the immune system to attack these cells, no matter where they are in the body.

Other new approaches, including the use of monoclonal antibodies (manmade versions of immune system proteins), may also prove to be effective against rhabdomyosarcoma.

Eventually, a combination of these approaches may prove to be the best way to treat this disease.

Additional resources

More information from your American Cancer Society

The following information may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-227-2345.

After Diagnosis: A Guide for Patients and Families

Bone Marrow and Peripheral Blood Stem Cell Transplants

Childhood Cancer: Late Effects of Cancer Treatment

Children Diagnosed With Cancer: Dealing with Diagnosis (also available in Spanish)

Children Diagnosed With Cancer: Financial and Insurance Issues

Children Diagnosed With Cancer: Returning to School

Children Diagnosed With Cancer: Understanding the Health Care System (also available in Spanish)

Clinical Trials: What You Need to Know

Family Medical Leave Act (FMLA)

Fertility and Cancer: What Are My Options?

Nutrition for Children With Cancer (also available in Spanish)

Pediatric Cancer Centers (also available in Spanish)

Surgery (also available in Spanish)

Understanding Chemotherapy: A Guide for Patients and Families (also available in Spanish)

Understanding Radiation Therapy: A Guide for Patients and Families (also available in Spanish)

What Happened to You, Happened to Me (children's booklet)

When Your Brother or Sister Has Cancer (children's booklet)

When Your Child's Treatment Ends: A Guide for Families (booklet)

The following books are available from the American Cancer Society. Call us at 1-800-227-2345 to ask about costs or to place your order.

Because... Someone I Love Has Cancer (kids' activity book)

Caregiving: A Step-By-Step Resource for Caring for the Person with Cancer at Home

Jacob Has Cancer: His Friends Want to Help (coloring book for a child with a friend who has cancer)

Let My Colors Out (picture book for young children)

National organizations and Web sites*

American Childhood Cancer Organization (formerly Candlelighters)

Toll-free number: 1-800-366-2223 (1-800-366-CCCF)

Web site: www.candlelighters.org

Cancer Kids

Web site: www.cancerkids.com

CureSearch (National Childhood Cancer Foundation and Children's Oncology Group)

Toll-free number: 1-800-458-6223

Web site: www.curesearch.org

National Cancer Institute

Toll-free number: 1-800-422-6237 (1-800-4-CANCER)

Web site: www.cancer.gov

National Children's Cancer Society, Inc.

Toll-free number: 1-800-532-6459 (1-800-5-FAMILY)

Web site: www.children-cancer.org

National Dissemination Center for Children with Disabilities (NICHCY)

Toll-free number: 1-800-695-0285 (also for TTY)

Web site: www.nichcy.org

Starlight Children's Foundation

Toll-free number: 1-310-479-1212

Web site: www.starlight.org

Teens Living with Cancer

Web site: www.teenslivingwithcancer.org

**Inclusion on this list does not imply endorsement by the American Cancer Society.*

No matter who you are, we can help. Contact us anytime day or night for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

Other publications*

For adults

100 Questions & Answers About Your Child's Cancer, by William L. Carroll and Jessica Reisman. Jones and Bartlett Publishers, 2004.

Cancer & Self-Help: Bridging the Troubled Waters of Childhood Illness, by Mark A. Chester and Barbara K. Chesney. University of Wisconsin Press, 1995.

Care for Children and Adolescents with Cancer: Questions and Answers. National Cancer Institute. Available at: www.cancer.gov/cancertopics/factsheet/NCI/children-adolescents or call 1-800-332-8615.

Childhood Cancer: A Parent's Guide to Solid Tumor Cancers, by Honna Janes-Hodder and Nancy Keene. O'Reilly and Associates, 1999.

Childhood Cancer: A Handbook from St Jude Children's Research Hospital, by Grant Steen and Joseph Mirro (editors). Perseus Publishing, 2000.

Childhood Cancer Survivors: A Practical Guide to Your Future, by Nancy Keene, Wendy Hobbie, and Kathy Ruccione. O'Reilly and Associates, 2000.

Children with Cancer: A Comprehensive Reference Guide for Parents (2nd Edition), by Jeanne Munn Bracken and Pruden Pruden. Oxford University Press, 2005.

Educating the Child With Cancer: A Guide for Parents and Teachers, edited by Nancy Keene. Candlelighters Childhood Cancer Foundation, 2003.

Living with Childhood Cancer: A Practical Guide to Help Families Cope, by Leigh A. Woznick and Carol D. Goodheart. American Psychological Association, 2002.

Surviving Childhood Cancer: A Guide for Families, by Margo Joan Fromer. New Harbinger Publications, 1998.

When Bad Things Happen to Good People, by Harold Kushner. G.K. Hall, 1982.

When Someone You Love Is Being Treated for Cancer. National Cancer Institute. Available at: www.cancer.gov/cancertopics/when-someone-you-love-is-treated, or call 1-800-332-8615.

Young People with Cancer: A Handbook for Parents. National Cancer Institute, 2003. Available at: www.cancer.gov/cancertopics/youngpeople, or call 1-800-332-8615.

Your Child in the Hospital: A Practical Guide for Parents (2nd Edition), by Nancy Keene. O'Reilly & Associates. 1999. (Also available in Spanish.)

Books for teens and children

Although these books are intended for children, younger kids are helped more when an adult reads with and helps the child reflect about what different parts of the book mean to the child.

The Amazing Hannah, Look at Everything I Can Do! by Amy Klett. Candlelighters Childhood Cancer Foundation, 2002. For ages 1 to 6. (Also available in Spanish.)

Chemo, Crazyness and Comfort: My Book about Childhood Cancer by Nancy Keene. Candlelighters Childhood Cancer Foundation, 2002. Can be ordered from www.candlelighters.org. For ages 6 to 12.

Childhood Cancer Survivors: A Practical Guide to Your Future (2nd Edition), by Kathy Ruccione, Nancy Keene, and Wendy Hobbie. Patient Centered Guides, 2006. For older teens.

Going to the Hospital, by Fred Rogers. Paperstar Book, 1997. For ages 4 to 8.

Life Isn't Always a Day at the Beach: A Book for All Children Whose Lives Are Affected by Cancer, by Pam Ganz. High-Five Publishing, 1996. Workbook for ages 6 to 10.

Little Tree: A Story for Children with Serious Medical Problems, by Joyce C. Mills. Magination Press, 2003. For ages 4 to 8.

Living Well With My Serious Illness, by Marge Heegaard. Fairview Press, 2003. For ages 8 to 12.

Me and My Marrow, by Karen Crowe. Published by Fujsawa Healthcare, 1999. For teens.

My Book for Kids with Cansur [sic], by Jason Gaes. Viking Penguin, 1998. For ages 4 to 8.

Oncology, Stupology...I Want to Go Home! by Marilyn K. Hershey. Butterfly Press, 1999. For ages 8 to 12. (Also available in Spanish.)

What About Me? When Brothers and Sisters Get Sick, by Allan Peterkin and Frances Middendorf. Magination Press, 1992. For brothers and sisters (ages 4 to 8) of a child with cancer.

When Someone Has a Very Serious Illness: Children Can Learn to Cope with Loss and Change, by Marge Heegaard. Woodland Press, 1991. For ages 6 to 12.

Why, Charlie Brown, Why? A Story About What Happens When a Friend Is Very Ill, by Charles M. Schultz. Ballantine Publishing Group, 1990. For ages 6 to 12.

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and Rosenberg's *Cancer: Principles and Practice of Oncology*. 8th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2008:2067–2071.

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Wexler LH, Meyer WH, Helman LJ. Rhabdomyosarcoma and the undifferentiated sarcomas. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 5th ed. Philadelphia Pa: Lippincott Williams & Wilkins; 2006:971–1001.

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