Can Childhood Leukemia Be Found Early?

Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology. 10th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2015.

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Signs and Symptoms of Childhood Leukemia

Many of the symptoms of childhood leukemia can have other causes as well, and most

normal white blood cells. This can lead to:

Infections, which can occur because of a shortage of normal white blood cells.

middle of the chest, such as lymph nodes or the thymus (a small organ in front of the trachea, the breathing tube that leads to the lungs). An enlarged thymus or lymph nodes in the chest can press on the trachea, causing coughing or trouble breathing.

In some cases where the white blood cell count is very high, the leukemia cells can build up in the small blood vessels of the lungs, which can also cause trouble breathing.

Swelling of the face and arms: An enlarged thymus might press on the superior vena cava (SVC), which is a large vein that carries blood from the head and arms back to the heart. This can cause the blood to "back up" in the veins. This is known as **SVC syndrome**. It can result in swelling in the face, neck, arms, and upper chest (sometimes with a bluish-red skin color). Symptoms can also include headaches, dizziness, and a change in consciousness if it affects the brain. The SVC syndrome can be lifethreatening, so it needs to be treated right away.

Headaches, seizures, vomiting: A small number of children have leukemia that has already spread to the brain and spinal cord when it is first found. This can lead to symptoms such as headaches, trouble concentrating, weakness, seizures, vomiting, problems with balance, and blurred vision.

tests-for-cancer.html

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Tests for Childhood Leukemia

- Medical history and physical exam
- Tests to look for leukemia in children
- Lab tests to diagnose and classify leukemia
- Imaging tests

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 applies a numbing cream in an area in the lower part of the back over the spine. The doctor usually also gives the child medicine to make them sleep during the procedure. A small, hollow needle is then put in between the bones of the spine to withdraw some of the fluid, which is then sent to a lab for testing.

In children already diagnosed with leukemia, lumbar punctures might also be used to give <u>chemotherapy</u>³ drugs into the CSF to try to prevent or treat the spread of leukemia to the spinal cord and brain. (This is known as **intrathecal chemotherapy**.)

Lymph node biopsy

This type of biopsy is important in diagnosing lymphomas, but it is rarely needed for children with leukemias.

During this procedure, a surgeon cuts through the skin to remove an entire lymph node (known as an excisional biopsy). If the node is near the skin surface, this is a simple operation. But it is more complex if the node is inside the chest or abdomen. Most often the child will need general anesthesia (where the child is asleep).

Lab tests to diagnose and classify leukemia

All blood, bone marrow, and other samples are sent to a lab for further testing.

Microscopic exams

All of the samples taken (blood, bone marrow, lymph node tissue, or CSF) are looked at with a microscope. The samples might be exposed to chemical stains (dyes) that can cause color changes in some types of leukemia cells.dyeseg s . 0 rg th.7Bi/F2 12 ml9 11anoked atAll of the samples taken (blood, bone marrow, lymph node tissue, or CSF) are looked at cause color changes in some types of leukemia cells.dyeseg s . 0 rg th.7Bi/F2 12 ml9 11anoked atAll of the samples taken (blood, bone marrow, lymph node tissue, or CSF) are looked at

contains a certain number of blood-forming cells and fat cells. Marrow with too many blood-forming cells is said to be **hypercellular**. If too few blood-forming cells are found, the marrow is called **hypocellular**.

Flow cytometry and immunohistochemistry

These tests are used to classify leukemia cells based on certain proteins in or on the cells (known as **immunophenotyping**

the usual 46) – they may be missing some chromosomes or have extra copies of some. This can also affect a child's outlook. For example, in ALL, chemotherapy is more likely to work if the cells have more than 50 chromosomes and is less likely to work if the cells have fewer than 46 chromosomes.

Finding these types of chromosome changes with lab tests can be very helpful in predicting a child's outlook and response to treatment.

Cytogenetics:

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

These tests aren't 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 make sure the blood is clotting properly.

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

Imaging tests

Imaging tests use x-rays, sound waves, magnetic fields, or radioactive particles to make pictures of the inside of the body. Leukemia doesn't 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. For more details, see Imaging Tests⁴.

Chest x-rays

A chest $\underline{x\text{-ray}}^5$ 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 <u>CT scan</u>⁶ isn't usually needed for children with 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.

PET/CT scan: Some machines combine the CT scan with a <u>positron emission</u> tomography (PET) scan⁷, which can provide more information about any abnormal areas that appear on the CT.

Magnetic resonance imaging (MRI) scan

An MRI scan⁸, like a CT scan, makes detailed images of soft tissues in the body. It's most helpful in looking at the brain and spinal cord, so it's 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). This test doesn't expose the child to radiation.

Ultrasound

<u>Ultrasound</u>⁹ 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.)

This is a fairly easy test to have, and it uses no radiation.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/leukemia-in-children/causes-risks-prevention/risk-factors.html</u>
- 2. <u>www.cancer.org/cancer/diagnosis-staging/tests/understanding-your-lab-test-results.html</u>
- 3. www.cancer.org/cancer/types/leukemia-in-children/treating/chemotherapy.html
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- 7. <u>www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/nuclear-medicine-scans-for-cancer.html</u>
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Childhood Leukemia Subtypes

- Acute lymphocytic (lymphoblastic) leukemia (ALL)
- Acute myeloid leukemia (AML)
- Chronic myeloid leukemia (CML)

The type and subtype of leukemia a child has plays a major role in both treatment

about the subtype of your child's leukemia.

Acute lymphocytic (lymphoblastic) leukemia (ALL)

Acute lymphocytic leukemia (ALL) is a fast-growing cancer of lymphocyte-forming cells called

(neutrophils, eosinophils, and basophils).

- **Monoblasts:** These cells normally become white blood cells called **monocytes** and **macrophages**.
- Erythroblasts: These cells mature into red blood cells.
- **Megakaryoblasts:** These cells normally become megakaryocytes, the cells that make platelets.

phase when they are diagnosed.

Accelerated phase of CML

Children whose CML is in accelerated phase may have symptoms such as fever, night sweats, poor appetite, and weight loss. CML in the accelerated phase might not respond as well to treatment as CML in the chronic phase.

Blast phase (also called acute phase or blast crisis) of CML

In this phase, the leukemia cells often spread to tissues and organs outside the bone marrow. Children with CML in this phase often have fever, poor appetite, and weight loss. At this point the CML acts much like an aggressive acute leukemia (AML or, less often, ALL).

For more detailed information on the phases of CML, see <u>Phases of Chronic Myeloid</u> Leukemia⁷.

Hyperlinks

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Prognostic Factors in Childhood Leukemia (ALL or AML)

Generally, children at low risk have a better outlook than those at very high risk. But it's important to know that even children in higher risk groups can often still be cured.

While all of the following are prognostic factors, only certain ones are used to determine which risk group a child is in. (The first 2 factors – age at diagnosis and initial white blood cell count – are thought to be the most important.)

Age at diagnosis

Children between the ages of 1 and 9 with B-cell ALL tend to have better cure rates. Children younger than 1 year and children 10 years or older are considered high-risk patients. The outlook in T-cell ALL isn't affected much by age.

Initial white blood cell (WBC) count

Children with ALL who have very high WBC counts (greater than 50,000 cells per cubic millimeter) when they are diagnosed are at higher risk and need more intensive treatment.

ALL subtype

Children with early B-cell ALL subtypes generally do better than those with mature B-cell (Burkitt) leukemia. The outlook for T-cell ALL seems to be about the same as that for B-cell ALL as long as treatment is intense enough.

Sex

Girls with ALL may have a slightly higher chance of being cured than boys, but as treatments have improved in recent years, this difference has shrunk.

Number of chromosomes in the leukemia cells (ploidy)

Normal human cells have 46 chromosomes. Children are more likely to be cured if their leukemia cells have more than 50 chromosomes (called **hyperdiploidy**), especially if there is an extra chromosome 4, 10, or 17. Hyperdiploidy can also be expressed as a DNA index of more than 1.16. Children whose leukemia cells have fewer than 44 chromosomes (known as **hypodiploidy**) have a less favorable outlook.

Chromosome changes (such as translocations)

Translocations occur when chromosomes swap some of their genetic material (DNA). Children whose leukemia cells have a translocation between chromosomes 12 and 21 are more likely to be cured. Those with a translocation between chromosomes 9 and 22 (the Philadelphia chromosome) or 4 and 11 tend to have a less favorable prognosis.

Children with leukemia cells that have translocations between chromosomes 15 and 17 (seen in most cases of APL) or between 8 and 21, or with an inversion (rearrangement) of chromosome 16 have a better chance of being cured. Children whose leukemia cells are missing a copy of chromosome 5 or 7 (known as **monosomy**) or just part of chromosome 5 (known as a **deletion**) tend to have a poorer prognosis.

Children whose leukemia cells have a mutation in the *FLT3* gene tend to have a poorer outlook, although <u>new drugs that target cells with this abnormal gene</u>¹ might lead to better outcomes. On the other hand, children whose leukemia cells have changes in the *NPM1* gene (and not in the *FLT3* gene) seem to have a better prognosis than children without this change. Changes in the *CEBPA* gene are also linked to a better outcome.

Myelodysplastic syndrome or secondary AML

Children who first have a myelodysplastic syndrome² ("smoldering leukemia") or whose

reaction (PCR).

Even when leukemia is in remission, this does not always mean that it has been cured.

Minimal residual disease

Minimal residual disease (MRD) is a term used after treatment when leukemia cells can't be found in the bone marrow using standard lab tests (such as looking at cells under a microscope), but they can still be detected with more sensitive tests (such as flow cytometry or PCR).

In general, children with MRD during or after induction chemotherapy are more likely to have the leukemia relapse (come back) and therefore may need more intense treatment. Children with more MRD have a greater risk of relapse than those with less MRD.

Active disease

Active disease means that either there is evidence that the leukemia is still present during treatment or that the disease has relapsed (come back) after treatment. For a patient to have relapsed, more than 5% of the bone marrow must be made up of blast cells.

Hyperlinks

- 1. www.cancer.org/cancer/types/leukemia-in-children/about/new-research.html
- 2. www.cancer.org/cancer/types/myelodysplastic-syndrome.html

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Survival Rates for Childhood Leukemias

Survival rates are often used by doctors as a standard way of discussing a child's prognosis (outlook). These numbers tell you what portion of children in a similar situation (such as with the same type and subtype of leukemia) are still alive a certain amount of time after they were diagnosed. They can't tell you exactly what will happen in an individual child's case, but they may help give you a better understanding about how likely it is that treatment will be successful. Some people find survival rates helpful, but some people might not.

The **5-year survival rate** refers to the percentage of children who live **at least** 5 years after their leukemia is diagnosed. With acute leukemias (ALL or AML), children who are free of the disease after 5 years are very likely to have been cured, because it's very rare for these cancers to return after this long.

Knowing the type and subtype of leukemia is important in estimating a child's outlook. But a number of other factors, including the child's age and leukemia characteristics, can also affect outlook. Many of these factors are discussed in Prognostic Factors In Childhood Leukemia (ALL or AML). Even when taking these other factors into account, survival rates are at best rough estimates. Your child's doctor can probably tell you how these numbers apply to your child.

Current 5-year survival rates are based on children first diagnosed and treated more

than 5 years ago. Improvements in treatment since then might result in a better outlook for children now being diagnosed.

Acute lymphocytic leukemia (ALL)

The 5-year survival rate for children with ALL has greatly increased over time and is now about 90% overall. In general, children in lower risk groups have a better outlook than those in higher risk groups. But it's important to know that even children in higher risk groups can often still be cured.

Acute myelogenous leukemia (AML)

The overall 5-year survival rate for children with AML has also increased over time, and is now in the range of 65% to 70%. However, survival rates vary depending on the subtype of AML and other factors. For example, most studies suggest that the cure rate for acute promyelocytic leukemia (APL), a subtype of AML, is now higher than 80%, but rates are lower for some other subtypes of AML.

Other childhood leukemias

Accurate survival rates for less common forms of childhood leukemia are harder to find.

Juvenile myelomonocytic leukemia (JMML)

For JMML, 5-year survival rates of about 50% have been reported.

Chronic myeloid leukemia (CML)

For CML, which is rare in children, 5-year survival rates are less helpful, because some children may live for a long time with the leukemia without actually being cured. In the past, 5-year survival rates for CML were reported to be in the range of 60% to 80%. But with the newer, more effective medicines used to treat CML¹ in recent years, survival rates are likely to be higher now.

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1. www.cancer.org/cancer/types/leukemia-in-children/treating/targeted-therapy.html

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Questions to Ask About Childhood Leukemia

It's important to have open, honest discussions with your child's cancer care team. They want to answer all of your questions, no matter how small they might seem. For instance, consider these examples:

If leukemia has just been diagnosed

- What type of leukemia¹ does my child have?
- How will the subtype of the leukemia or any other factors affect my child's prognosis?
- Do we need other tests before we can decide on treatment?
- Will we need to see other doctors?
- How much experience do you have treating this type of leukemia?
- Who else will be on the treatment team, and what do they do?

When deciding on a treatment plan

- What are our treatment choices²?
- What do you recommend and why?
- Should we get a <u>second opinion</u>³? How would we do that? Can you recommend a doctor or cancer center?
- Should we consider a stem cell transplant⁴? When?
- Are there any <u>clinical trials</u>⁵ we should consider?
- How soon do we need to start treatment?
- What should we do to be ready for treatment?
- How long will treatment last? What will it be like?
- How much of the treatment will need to be done in the hospital?
- How will treatment affect our daily lives (school, work, etc.)?
- What are the risks and side effects of the treatments you recommend?
- Which side effects start shortly after treatment, and which ones might develop later on?
- Will treatment affect my child's ability to learn, grow, and develop?
- Will treatment affect my child's future ability to have children?
- What are the chances of curing the leukemia?

During and after treatment

Once treatment begins, you'll need to know what to expect and what to look for. Not all of these questions may apply, but getting answers to the ones that do may be helpful.

- What type of follow-up⁶ will we need after treatment?
- How will we know if the treatment is working?

- Is there anything we can do to help manage side effects?
- What symptoms or side effects should we tell you about right away?
- How can we reach you or someone on your team on nights, weekends, or holidays?
- Who can we talk to if we have questions about costs, insurance coverage, or social support?
- What will our options be if the treatment doesn't work or if the leukemia comes back?
- Do you know of any support groups where we can talk to other families who have been through this?

Along with these sample questions, be sure to write down your own. For instance, you might want to ask about possible long-term risks of cancer or other health problems.

Also keep in mind that doctors are not the only ones who can give you information. Other health care professionals, such as nurses and social workers, may have the answers to some of your questions. You can find out more about speaking with your health care team in <u>The Doctor-Patient Relationship</u>⁷.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/leukemia-in-children/about/what-is-childhood-leukemia.html</u>
- 2. www.cancer.org/cancer/types/leukemia-in-children/treating.html
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