cancer.org | 1.800.227.2345

Acute Myeloid Leukemia Early Detection, Diagnosis, and Types

Know the signs and symptoms of acute myeloid leukemia (AML). Find out how AML is tested for, diagnosed, and classified.

Detection and Diagnosis

Catching cancer early often allows for more treatment options. Some early cancers may have signs and symptoms that can be noticed, but that is not always the case.

- Can Acute Myeloid Leukemia (AML) Be Found Early?
- Signs and Symptoms of Acute Myeloid Leukemia (AML)
- Tests for Acute Myeloid Leukemia (AML)

Types of AML

Learn how AML is classified and how this may affect your treatment options.

Can Acute Myeloid Leukemia (AML) Be Found Early?

People at increased risk of AML

For many types of cancer, finding the cancer early might make it easier to treat. The American Cancer Society recommends <u>screening tests</u>¹ for early detection of certain cancers in people without any symptoms.

But at this time, no screening tests have been shown to be helpful in finding acute myeloid leukemia (AML) early. AML often develops (and causes symptoms) fairly quickly, so the best way to find AML early is to report any possible symptoms of AML to the doctor right away.

People at increased risk of AML

Some people are known to be at <u>increased risk</u>² of AML because they have certain blood disorders (such as a <u>myelodysplastic syndrome</u>³) or inherited disorders (such as

JO, Dorshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa. Elsevier: 2014.

National Comprehensive Cancer Network. NCCN Practice Guidelines in Oncology: Acute Myeloid Leukemia. V.1.2018. Accessed at www.nccn.org/professionals/physician_gls/pdf/aml.pdf on June 14, 2018.

Stock W, Thirman MJ. Pathogenesis of acute myeloid leukemia. UpToDate. 2018. Accessed at www.uptodate.com/contents/pathogenesis-of-acute-myeloid-leukemia on June 14, 2018.

Last Revised: August 21, 2018

Signs and Symptoms of Acute Myeloid Leukemia (AML)

- General symptoms
- Symptoms caused by low numbers of blood cells
- Symptoms caused by high numbers of leukemia cells
- Bleeding and clotting problems
- Bone or joint pain
- Swelling in the abdomen
- Symptoms caused by leukemia spread

Acute myeloid leukemia (AML) can cause many different signs and symptoms. Some are more common with certain subtypes of AML. Overall, the signs and symptoms of leukemia can affect men or women and do not differ by sex or gender.

General symptoms

People with AML often have several non-specific (general) symptoms. These can include:

- Weight loss
- Fatigue

- Fever
- Night sweats
- · Loss of appetite

These are not just symptoms of AML. More often they are caused by something other than leukemia.

Symptoms caused by low numbers of blood cells

Many signs and symptoms of AML are the result of a shortage of normal blood cells, which happens when the leukemia cells crowd out the normal blood-making cells in the bone marrow. As a result, people don't have enough normal red blood cells, white blood cells, and blood platelets. These shortages show up on blood tests, and they can also cause symptoms.

Symptoms from low red blood cell counts (anemia)

Red blood cells carry oxygen to all of the cells in the body. A shortage of red blood cells can cause:

- Tiredness (fatigue)
- Weakness
- Feeling cold
- Feeling dizzy or lightheaded
- Headaches
- Pale skin
- Shortness of breath

Symptoms from low white blood cell counts

Infections can occur because of a shortage of normal white blood cells (leukopenia), specifically a shortage of infection-fighting white blood cells called neutrophils (a condition called **neutropenia**). People with AML can get infections that don't seem to go away or may get one infection after another. Fever often goes along with the infection.

Although people with AML can have high white blood cell counts due to excess numbers of leukemia cells, these cells don't protect against infection the way normal white blood cells do.

Symptoms from low blood platelet counts

Platelets normally help stop bleeding. A shortage of blood platelets (called thrombocytopenia) can lead to:

- Bruises (or small red or purple spots) on the skin
- Excess bleeding
- Frequent or severe nosebleeds
- Bleeding gums
- Heavy periods (menstrual bleeding) in women

Symptoms caused by high numbers of leukemia cells

The cancer cells in AML (called blasts) are bigger than normal white blood cells and have more trouble going through tiny blood vessels. If the blast count gets very high, these cells can clog up blood vessels and make it hard for normal red blood cells (and oxygen) to get to tissues. This is called **leukostasis**. Leukostasis is rare, but it is a medical emergency that needs to be treated right away. Some of the symptoms are like those seen with a stroke, and include:

- Headache
- Weakness in one side of the body
- Slurred speech
- Confusion
- Sleepiness

When blood vessels in the lungs are affected, people can have shortness of breath. Blood vessels in the eye can be affected as well, leading to blurry vision or even loss of vision.

Bleeding and clotting problems

Patients with a certain type of AML called acute promyelocytic leukemia (APL) might have problems with bleeding and blood clotting. They might have a nosebleed that won't stop, or a cut that won't stop oozing. They might also have calf swelling from a blood clot called a **deep vein thrombosis (DVT)** or chest pain and shortness of breath from a blood clot in the lung (called a **pulmonary embolism** or **PE**).

Bone or joint pain

Some people with AML have bone pain or joint pain caused by the buildup of leukemia cells in these areas.

Swelling in the abdomen

Leukemia cells may build up in the liver and spleen, making them larger. This may be noticed as a fullness or swelling of the belly. The lower ribs usually cover these organs, but when they are enlarged the doctor can feel them.

Symptoms caused by leukemia spread

Spread to the skin

If leukemia cells spread to the skin, they can cause lumps or spots that may look like common rashes. A tumor-like collection of AML cells under the skin or other parts of the body is called a chloroma, granulocytic sarcoma, ormyeloid sarcoma. Rarely, AML will first appear as a chloroma, with no leukemia cells in the bone marrow.

Spread to the gums

Certain types of AML may spread to the gums, causing swelling, pain, and bleeding.

Spread to other organs

Less often, leukemia cells can spread to other organs. Spread to the brain and spinal cord can cause symptoms such as:

- Headaches
- Weakness
- Seizures
- Vomiting
- Trouble with balance
- Facial numbness
- Blurred vision

On rare occasions AML can spread to the eyes, testicles, kidneys, or other organs.

Enlarged lymph nodes

Rarely, AML can spread to lymph nodes (bean-sized collections of immune cells throughout the body), making them bigger. Affected nodes in the neck, groin, underarm areas, or above the collarbone may be felt as lumps under the skin.

Although any of the symptoms and signs above may be caused by AML, they can also be caused by other conditions. Still, if you have any of these problems, especially if they don't go away or are getting worse, it's important to see a doctor so the cause can be found and treated, if needed.

References

Appelbaum FR. Chapter 98: Acute leukemias in adults. In: Niederhuber JE, Armitage JO, Dorshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa. Elsevier: 2014.

Kebriaei P, de Lima M, Estey EH, Champlin R. Chapter 107: Management of Acute Leukemias. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology.* 10th ed. Philadelphia, Pa:

Tests for Acute Myeloid Leukemia (AML)

- Types of samples used to test for acute myeloid leukemia (AML)
- Lab tests to diagnose acute myeloid leukemia (AML) and learn more about it
- Imaging tests for AML

Medical history and physical exam

The doctor will want to get a thorough **medical history**, focusing on your symptoms and how long you have had them. They might also ask about other health problems, as well as about possible risk factors¹ for leukemia.

During the **physical exam**, the doctor will check your eyes, mouth, skin, lymph nodes, liver, spleen, and nervous system, and will look for areas of bleeding or bruising, or possible signs of infection.

If there is reason to think you might have problems caused by low levels of blood cells (anemia, infections, bleeding or bruising, etc.), the doctor will most likely order blood tests to check your blood cell counts. You might also be referred to a **hematologist**, a doctor who specializes in diseases of the blood (including leukemia).

Types of samples used to test for acute myeloid leukemia (AML)

If the doctor thinks you might have leukemia, tests will be done on samples of cells from your blood and bone marrow (the inner parts of some bones, where new blood cells are made). Other tissue and cell samples might also be taken to help guide treatment.

Blood samples

Blood tests are generally the first tests done to look for leukemia. Blood is taken from a vein in your arm.

Bone marrow samples

Leukemia starts in the bone marrow, so checking the bone marrow for leukemia cells is a key part of testing for it. Bone marrow samples are obtained from 2 tests that are usually done at the same time:

- Bone marrow aspiration
- Bone marrow biopsy

The samples are usually taken from the back of the pelvic (hip) bone, but sometimes other bones are used instead. If only an aspiration is to be done, it may be taken from the sternum (breastbone).

For a **bone marrow aspiration**, you lie on a table (either on your side or on your belly). The doctor will clean the skin over the hip and then numb the area and the surface of the bone by injecting a local anesthetic. This may cause a brief stinging or burning sensation. 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. Even with the anesthetic, most people still have some brief pain when the marrow is removed.

A **bone marrow biopsy** is usually done just after the aspiration. A small piece of bone and marrow is removed with a slightly larger needle that is pushed down into the bone. This also might cause some brief pain. Once the biopsy is done, pressure will be applied to the site to help prevent bleeding.

These bone marrow tests are used to help diagnose leukemia, but they might also be repeated later to see how well leukemia is responding to treatment.

Spinal fluid

The cerebrospinal fluid (CSF) surrounds the brain and spinal cord. AML can sometimes spread to the area around the brain and spinal cord. To check for this spread, doctors might remove a sample of CSF for testing (a procedure called a **lumbar puncture** or **spinal tap**). A lumbar puncture is not often used to test for AML, unless a person is having symptoms that could be caused by leukemia spread into the brain and spinal cord.

For this test, you might lie on your side or sit up. The doctor first numbs an area of skin on the lower part of the back over the spine. A small, hollow needle is then inserted between the bones of the spine into the area around the spinal cord to remove some of the fluid.

A lumbar puncture is also sometimes used to deliver <u>chemotherapy</u>² drugs into the CSF to help prevent or treat the spread of leukemia to the spinal cord and brain.

Lab tests to diagnose acute myeloid leukemia (AML) and learn more about it

One or more of the following lab tests may be done on the samples to diagnose AML, to determine the specific subtype of AML, and to learn more about the leukemia.

Complete blood count and peripheral blood smear

The <u>complete blood count (CBC)</u>³ measures the amounts of different cells in the blood, such as the red blood cells, white blood cells, and platelets. The CBC is often done

of AML. (In normal bone marrow, the blast count is 5% or less, and the blood usually doesn't contain any blasts.) AML can also be diagnosed if another lab test shows that the blasts have a chromosome change that occurs only in a specific type of AML, even if the blast percentage doesn't reach 20%.

Other lab tests may also be used to confirm an AML diagnosis or to learn more about it.

Cytochemistry

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

Flow cytometry and immunohistochemistry

For both flow cytometry and immunohistochemistry (IHC), samples of cells are treated with antibodies, which are proteins that stick only to certain other proteins on cells. For IHC, the cells are then looked at with a microscope to see if the antibodies stuck to them (meaning they have these proteins), while for flow cytometry a special machine is used.

These tests are used for **immunophenotyping** – classifying leukemia cells according to the substances (antigens) on their surfaces. Leukemia cells can have different antigens depending on which type of cells they start in and how mature they are, so this information can be helpful in AML classification.

Chromosome and gene tests

Some tests look at the chromosomes inside the cells. Chromosomes are long strands of DNA that contain our genes. Normal human cells have 23 pairs of chromosomes, each of which are a certain size and look a certain way. AML cells sometimes have

The results of cytogenetic testing are written in a shorthand form that describes the chromosome changes:

- A **translocation** means parts of two chromosomes have traded places with each other. For example, if chromosomes 8 and 21 have swapped pieces, it would be written as t(8;21).
- An **inversion**, written as inv(16), for example, means that part of the chromosome 16 is now in reverse order but is still attached to the chromosome.
- A **deletion**, written as del(7) or -7, for example, indicates part of chromosome 7 has been lost.
- An additionorduplication, such as +8, for example, means that all or part of chromosome 8 has been duplicated, and too many copies of it are found within the cell.

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

Fluorescent in situ hybridization (FISH): This test looks more closely at cell DNA using special fluorescent dyes that only attach to specific genes or parts of particular chromosomes. FISH can find the chromosome changes (such as translocations) that are visible with a microscope in standard cytogenetic tests, as well as some changes too small to be seen with usual cytogenetic testing.

FISH can be used to look for changes in specific genes or parts of chromosomes. It can be used on regular blood or bone marrow samples without growing them in a lab first. This means the results are often available more quickly than with regular cytogenetic testing.

Polymerase chain reaction (PCR): This is a very sensitive test that can also find some gene and chromosome changes too small to be seen under a microscope. It can be helpful in finding gene changes that are in only a few cells, making it good for finding small numbers of leukemia cells in a sample (like after treatment).

Other molecular and genetic tests

Other types of lab tests can also be done on the samples to look for specific gene or other changes in the leukemia cells. This is sometimes referred to as biomarker testing⁴.

Some of the changes found on these tests can help doctors learn more about the leukemia, and some can even help tell if certain treatments are likely to be helpful. For

example, the AML cells are often tested for changes (mutations) in genes such as *FLT3*, *IDH1*, and *IDH2*. People whose leukemia cells have changes in one of these genes are more likely to be helped by treatment with certain <u>targeted therapy drugs</u>⁵.

To learn more about these lab tests, see <u>Tests Used on Biopsy and Cytology Samples</u> to <u>Diagnose and Classify Cancer</u>⁶.

Imaging tests for AML

Imaging tests⁷ use x-rays, sound waves, magnetic fields, or radioactive particles to create pictures of the inside of the body. Leukemia doesn't usually form tumors, so imaging tests aren't often helpful in diagnosing AML. When imaging tests are done in people with AML, it's most often to look for infections or other problems, rather than to look for leukemia itself. In some cases, imaging tests may be done to help determine the extent of the leukemia, if it's thought it might have spread beyond the bone marrow and blood.

X-rays

Routine chest x-rays may be done if a lung infection is suspected.

Computed tomography (CT) scan

A CT scan uses x-rays to make detailed, cross-sectional images of your body. This test can help show if any lymph nodes or organs in your body are enlarged. It isn't usually needed to diagnose AML, but it may be done if your doctor suspects the leukemia is growing in an organ, like your spleen.

CT-guided needle biopsy: In some cases, a CT can be used to guide a biopsy needle into a suspected abnormality, such as an abscess. For this procedure, you lie on the CT scanning table while the doctor moves a biopsy needle through the skin and toward the mass. CT scans are repeated until the needle is within the mass. A sample is then

the body. With a PET/CT scan, the doctor can compare areas of higher radioactivity on the PET scan with the more detailed appearance of that area on the CT.

Magnetic resonance imaging (MRI)

Like CT scans, MRIs make detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets instead of x-rays.

MRIs are very helpful in looking at the brain and spinal cord, but they are not usually needed in people with AML.

Ultrasound

Ultrasound uses sound waves and their echoes to make pictures of internal organs or masses.

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

Hyperlinks

Prognostic factors for AML

For most types of cancer, determining the stage (extent) of the cancer is very important. The stage is based on the size of the main tumor and how far the cancer has spread. This can be helpful in predicting a person's outlook and deciding on treatment.

Acute myeloid leukemia (AML), on the other hand, does not usually form tumors. It generally is widespread throughout the bone marrow and, in some cases, has spread to other organs, such as the liver and spleen. Therefore AML is not staged like most other cancers. The outlook for a person with AML depends instead on other information, such as the subtype of AML (determined by lab tests), the patient's age, and other lab test results.

Knowing the subtype of AML can be very important, as it sometimes affects both a patient's outlook and the best treatment. For example, the acute promyelocytic leukemia (APL) subtype is often <u>treated using drugs</u>¹ that are different from those used for other subtypes of AML. If you're not sure which subtype of AML you have, ask your doctor about it, and about how it might affect your treatment.

Two of the main systems that have been used to classify AML into subtypes are the French-American-British (FAB) classification and the newer World Health Organization (WHO) classification.

The French-American-British (FAB) classification of AML

In the 1970s, a group of French, American, and British leukemia experts divided AML into subtypes, M0 through M7, based on the type of cell the leukemia develops from and how mature the cells are. This was based largely on how the leukemia cells looked under the microscope after routine staining.

FAB subtype	Name
MO	Undifferentiated acute myeloblastic leukemia
M1	Acute myeloblastic leukemia with minimal maturation
M2	Acute myeloblastic leukemia with maturation
M3	Acute promyelocytic leukemia (APL)
M4	Acute myelomonocytic leukemia

AML with myelodysplasia-related changes

AML related to previous chemotherapy or radiation

AML not otherwise specified (This includes cases of AML that don't fall into one of the above groups, and is similar to the FAB classification.)

- AML with minimal differentiation (FAB M0)
- AML without maturation (FAB M1)
- AML with maturation (FAB M2)
- Acute myelomonocytic leukemia (FAB M4)
- Acute monoblastic/monocytic leukemia (FAB M5)
- Pure erythroid leukemia (FAB M6)
- Acute megakaryoblastic leukemia (FAB M7)
- · Acute basophilic leukemia
- Acute panmyelosis with fibrosis

Myeloid sarcoma (also known as granulocytic sarcoma or chloroma)

Myeloid proliferations related to Down syndrome

Undifferentiated and biphenotypic acute leukemias are not strictly AML, but are leukemias that have both lymphocytic and myeloid features. They are sometimes called **mixed phenotype acute leukemias (MPALs)**.

Prognostic factors for AML

The subtype of AML can be important in helping to determine a person's prognosis (outlook). But other factors can also affect why some patients with AML have a better outlook than others. These are called prognostic factors. Prognostic factors help doctors determine a person's risk of the leukemia coming back after treatment, and therefore if they should get more or less intensive treatment. Some of these include:

Chromosome (cytogenetic) abnormalities

AML cells can have many kinds of chromosome changes, some of which can affect a person's prognosis. Those listed below are some of the most common, but there are many others. Not all leukemias have these abnormalities. Patients whose AML doesn't have any of these usually have an outlook that is between favorable and unfavorable.

Favorable abnormalities:

- Translocation between chromosomes 8 and 21 (seen most often in patients with M2)
- Translocation or inversion of chromosome 16
- Translocation between chromosomes 15 and 17 (seen most often in patients with M3)

Unfavorable abnormalities:

- Deletion (loss) of part of chromosome 5 or 7
- Translocation or inversion of chromosome 3
- Translocation between chromosomes 6 and 9
- Translocation between chromosomes 9 and 22
- Abnormalities of chromosome 11 (at the spot q23)
- Loss of a chromosome, so the cell has only 1 copy instead of the normal 2 (known as monosomy)
- Complex changes (those involving 3 or more chromosomes)

Gene mutations

People whose leukemia cells have certain gene mutations may have a better or worse outlook.

For instance, people with AML that has a mutation in the *FLT3* gene tend to have a poorer outlook, although new <u>drugs that target cells with this abnormal gene</u>³ might lead to better outcomes. Mutations in the *TP53*, *RUNX1*, and *ASXL1* genes are also linked with a worse outlook.

On the other hand, people whose leukemia cells have changes in the *NPM1* gene (and no other abnormalities) seem to have a better prognosis than people without this change. Changes in both copies of the *CEBPA* gene are also linked to a better outcome.

Markers on the leukemia cells

If the leukemia cells have the CD34 protein and/or the P-glycoprotein (*MDR1* gene product) on their surface, it is linked to a worse outlook.

Age

the leukemia. A **complete** *molecular* **remission** means there is no evidence of leukemia cells in the bone marrow, even when using very sensitive tests, such as PCR (polymerase chain reaction).

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

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

Hyperlinks

- 1. www.cancer.org/cancer/types/acute-myeloid-leukemia/treating/other-drugs.html
- 2. <u>www.cancer.org/cancer/types/acute-myeloid-leukemia/causes-risks-prevention/what-causes.html</u>
- 3. <u>www.cancer.org/cancer/types/acute-myeloid-leukemia/treating/targeted-therapy.html</u>
- 4. www.cancer.org/cancer/types/myelodysplastic-syndrome.html
- 5. www.cancer.org/cancer/types/acute-myeloid-leukemia/treating/chemotherapy.html

References

Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood*. 2016;127(20):2391-2405.

National Cancer Institute. Physician Data Query (PDQ). Adult Acute Myeloid Leukemia Treatment. 2018. Accessed at www.cancer.gov/types/leukemia/hp/adult-aml-treatment-pdq on June 17, 2018. National Comprehensive Cancer Network.

NCCN Practice Guidelines in Oncology: Acute Myeloid Leukemia. V.1.2018. Accessed at www.nccn.org/professionals/physician_gls/pdf/aml.pdf on June 17, 2018.

Schiffer CA, Gurbuxani S. Classification of acute myeloid leukemia. UpToDate. 2018. Accessed at www.uptodate.com/contents/classification-of-acute-myeloid-leukemia on June 17, 2018.

Last Revised: August 21, 2018

Questions to Ask About Acute Myeloid Leukemia (AML)

It's important to have open and honest communications with your cancer care team about your acute myeloid leukemia (AML). Ask about anything you don't understand or

- How will we know if the treatment is working?
- What type of follow-up⁴ will I need after treatment?
- Is there anything I can do to help manage side effects?
- What symptoms or side effects should I tell you about right away?
- How can I reach you on nights, holidays, or weekends?
- Do I need to eat a special diet during treatment?
- Are there any limits on what I can do?
- Should I exercise? What should I do, and how often?
- Can you suggest a mental health professional I can see if I start to feel overwhelmed, depressed, or distressed?
- What would my options be if the treatment isn't working?
- Where can I find more information and support?

Be sure to write down any questions you have that are not on this list. For instance, you might want specific information about expected recovery times or returning to work. Or you might want to ask if you qualify for any <u>clinical trials</u>⁵.

Keep in mind that doctors aren't the only ones who can give you information. Other health care professionals, such as nurses and social workers, might be able to answer some of your questions. You can find out more about speaking with your health care team in Talking With Your Doctor⁶.

Hyperlinks

- 1. www.cancer.org/cancer/types/acute-myeloid-leukemia/treating.html
- 2. <u>www.cancer.org/cancer/types/acute-myeloid-leukemia/treating/bone-marrow-stem-cell-transplant.html</u>
- 3. www.cancer.org/cancer/managing-cancer/finding-care/seeking-a-second-opinion.html
- 4. <u>www.cancer.org/cancer/types/acute-myeloid-leukemia/after-treatment/follow-up.html</u>
- 5. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
- 6. <u>www.cancer.org/cancer/managing-cancer/finding-care/the-doctor-patient-relationship.html</u>

Last Revised: August 21, 2018

Written by

The American Cancer Society medical and editorial content team (https://www.cancer.org/cancer/acs-medical-content-and-news-staff.html)

Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as editors and translators with extensive experience in medical writing.

American Cancer Society medical information is copyrighted material. For reprint requests, please see our Content Usage Policy (www.cancer.org/about-us/policies/content-usage.html).

cancer.org | 1.800.227.2345