

2021

# Anemia and Neutropenia

Low Red and White Blood Cell Counts

Presented with support from: NCCN

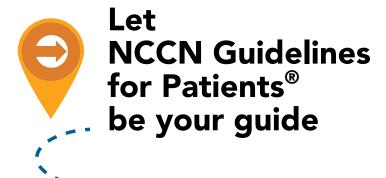






# Anemia and Neutropenia

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- ✓ Step-by-step guides to the cancer care options likely to have the best results
  - ✓ Based on treatment guidelines used by health care providers worldwide
    - ✓ Designed to help you discuss cancer treatment with your doctors

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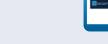
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NCCN Guidelines for Patients®: Anemia and Neutropenia, 2021

# Anemia and Neutropenia

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Blood is a body fluid made up of 4 factors: plasma, red blood cells, white blood cells, and platelets. Blood has many functions, including carrying oxygen and nutrients. This chapter provides a look at the various blood cell types and their functions.

# **Blood basics**

Blood is made up of plasma and cells that float within it. Plasma is the liquid part of the blood, comprised mostly of water. Plasma also contains proteins, hormones, vitamins, and minerals. Blood takes oxygen and nutrients to your body's tissues, and carries away wastes.

Blood cells have important jobs. Red blood cells carry oxygen throughout the body. White blood cells fight infection. Platelets help control bleeding. Plasma transports red blood cells, white blood cells, and platelets.

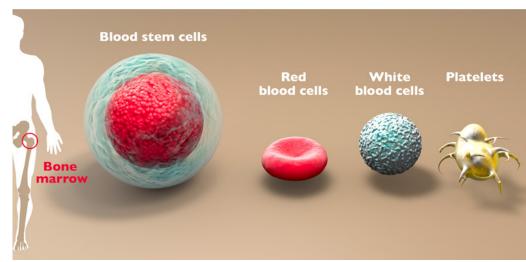
Blood cells don't live forever. Normal red blood cells live for 3 months. Normal white blood cells live for 8 to 14 days. Normal platelets live for about a week (7 days). After cells reach these ages, they die off and are replaced by new cells. Your blood cells are being replaced in your body all the time.

Blood has many functions. These include:

Transport - Blood takes oxygen from the lungs to the cells of the body. It takes carbon dioxide from the body's cells to the lungs where it is breathed out. Blood also carries nutrients, hormones, and waste products around the body.

### Blood stem cells

Bone marrow contains stem cells. A blood stem cell is an immature cell that can develop into a red blood cell, a white blood cell, or a platelet.



- Regulate Blood helps to keep the acid-alkali balance of the body in check. It also plays a part in regulating body temperature. Increasing the amount of blood flowing close to the skin helps the body to lose heat.
- Protect White blood cells attack and destroy invading germs (bacteria) and other pathogens. Blood clots form after an injury, which protects the body from losing too much blood.

# Blood cell types

There are 3 types of blood cells:

- Red blood cells (erythrocytes)
- White blood cells (leukocytes)
- Platelets

### Red blood cells

Red blood cells (RBCs) look like tiny flat doughnuts without holes. They get their color from hemoglobin, an iron-containing protein that picks up oxygen in the lungs. As the blood travels throughout the body, hemoglobin releases oxygen to different body parts. Then, red blood cells pick up carbon dioxide from tissues and organs and carry it back into the lungs for removal.

Red blood cells live for about 120 days. Each day, the body makes new red blood cells. They are made inside part of the bone called bone marrow. Bone marrow produces 7.5 billion red blood cells every hour, or 2 million each second. Your doctor will use a blood test to

check on the size, number, shape, and health of your red blood cells.

If red blood cells are damaged, they are no longer able to carry oxygen and can release toxins. This may lead to kidney damage. Problems with red blood cells may be caused by illness or a lack of iron or vitamins in your diet. Some diseases of the red blood cells are inherited (passed down from one's parents or ancestors). Diseases of the red blood cells include many types of anemia. Anemia is a condition where your body does not make enough healthy red blood cells, resulting in less oxygen in your cells.

### White blood cells

White blood cells (WBCs) are essential to the immune system by helping to fight infections. For example, if a microorganism (bacteria or virus) enters the blood, through a cut or an infection, white blood cells surround and destroy the invading cells.

There are several types of white blood cells:

- Monocytes
- Lymphocytes
- Neutrophils
- Basophils
- Eosinophils

# Monocytes

Monocytes are the largest type of white blood cells. They have a longer lifespan than other white blood cells. Monocytes help to break down bacteria and clean up dead cells.

# Lymphocytes

Lymphocytes are a form of white blood cell. All lymphocytes fight bacteria, viruses, and other potentially harmful invaders. However, some white blood cells have specific jobs.

There are 3 types of lymphocytes:

- B lymphocytes (B cells) make antibodies to help the body fight infections.
- T lymphocytes (T cells) attack foreign cells, cancer cells, and virus-infected cells.
- Natural killer cells (NK cells) kill virusinfected cells or tumor cells. These cells are different in that they can "remember" certain virus cells for many years and fight to keep the body from being infected again.

# **Neutrophils**

Neutrophils kill and digest bacteria and fungi. They are the most numerous type of white blood cell, making up nearly half of all white blood cells. They are the first line of defense when infection strikes.

# Basophils

Basophils sound an alarm when infectious agents invade your blood. They secrete chemicals such as histamine (a marker of allergic disease), which helps control the body's immune response.

# Eosinophils

Eosinophils attack and kill bacteria and parasites (such as worms), and help with allergic responses. These cells are best known for their role in creating allergy symptoms when fighting off invaders (such as pollen).

### **Platelets**

Platelets (thrombocytes) are tiny, plate-shaped cells that form clots. Platelets circulate in the blood. When a damaged blood vessel is found, they bind together to create a clot. Platelets work with proteins called clotting factors to control bleeding inside your body and on your skin. Platelets only survive about 9 days in the bloodstream. They are constantly being replaced by new platelets made in the bone marrow.

# **Plasma**

Plasma is a straw-colored liquid that makes up more than half (60%) of the blood's volume. Plasma contains water, salts, enzymes, antibodies, and other proteins. Plasma serves as a transportation system by bringing nutrients (such as proteins, minerals, vitamins, sugars, and fats) to all parts of the body, and carrying away waste.

This transportation system allows for a constant circulation of white blood cells and antibodies. The circulation in the plasma allows the white blood cells to travel wherever they are needed to fight infections. Also, plasma allows clotting proteins to travel where blood clots are needed. Clotting proteins in the plasma are required for platelets to form blood clots.

### **Bone marrow**

Bone marrow is a spongy substance found in the center of the bones. Bone marrow contains parent cells called stem cells. Stem cells can rapidly divide and clone themselves to form new cells. Healthy bone marrow is needed to make blood cells.

There are two types of bone marrow:

- > Red bone marrow produces blood cells
- Yellow bone marrow stores fat

Red bone marrow is involved in hematopoiesis (blood cell production). Red bone marrow can develop into a variety of different blood cells, including red blood cells and platelets. As you get older, your red bone marrow is gradually replaced with yellow bone marrow. Yellow bone marrow stores fats. Fat is used as an energy source as needed. Yellow bone marrow also contains mesenchymal stem cells (cells that can develop into bone, fat, cartilage, or muscle cells). Over time, most bones in adults contain increasing amounts of yellow bone marrow.

### Stem cells

Stem cells are special cells that can develop into different cell types including new red blood cells, white blood cells, and platelets. Stem cells continually divide and create new cells. The new cells may remain stem cells or form into mature blood cells. Mature blood cells are released from the bone marrow into the bloodstream. Stem cells are the only cell in the body that have the ability to create new cell types.

Stem cells that circulate in the veins and arteries are called peripheral blood stem cells. People recovering from chemotherapy or healthy people treated with certain drugs to stimulate bone marrow cell growth tend to have a large number of peripheral blood stem cells.

# How blood is made

Your body makes millions of blood cells every day. Each cell type lives for a certain period of time. Red blood cells can live for months, while white blood cells live for days or hours. When a blood cell dies, it is broken down by the body. Normally, there is a balance between the number of blood cells created and those that die and are broken down.

Hormones in the bloodstream and chemicals in the bone marrow help to maintain this balance.

- Erythropoietin (a hormone made in the kidneys) increases the creation of red blood cells.
- Thrombopoietin (a hormone made in the liver and kidney) increases the creation of platelets.
- Granulocyte colony-stimulating factor (a chemical produced in the body) increases the creation and release of neutrophils and other white blood cells from the bone marrow.
- Growth factors (a general term for chemicals or hormones) help regulate the number of blood cells created.

# Anemia

Anemia is a condition where your body does not make enough healthy blood cells, resulting in less oxygen being carried to your cells.

There are different types of anemia, including:

- Anemia associated with bone marrow disease or cancer/cancer treatment
- Aplastic anemia
- Hemolytic anemia
- Iron deficiency anemia
- Sickle cell anemia
- Vitamin deficiency anemia

Anemia associated with bone marrow disease or cancer/cancer treatment

Anemia associated with bone marrow disease affects the blood produced in your bone marrow. This anemia includes a variety of diseases, such as leukemia and myelofibrosis. In people with cancer, anemia can also be caused by chemotherapy treatments.

# **Aplastic anemia**

In aplastic anemia, normal blood cell production slows or stops. This occurs because bone marrow stem cells are damaged. The number of stem cells also goes down because they are unable to replicate themselves or are being destroyed by a part of the immune system.

You may not have symptoms of anemia right away. Speak with your doctor about treatment options.

# Hemolytic anemia

Hemolytic anemia occurs when red blood cells are destroyed faster than bone marrow can replace them. Hemolytic anemia can be acquired in two ways: either you can inherit it, or you can develop it later in life.

### Sickle cell anemia

Sickle cell anemia is an inherited and serious condition. It is caused by a defective form of hemoglobin that forces red blood cells to assume an abnormal crescent (moon) shape. The irregular blood cells die too soon, resulting in an ongoing shortage of red blood cells.

# Iron deficiency anemia

Iron deficiency anemia is the most common type of anemia. It is caused by a lack of iron in your body. Your bone marrow needs iron to make hemoglobin. Without enough iron, your body can't produce enough hemoglobin for red blood cells.

# Vitamin deficiency anemia

Similar to iron, vitamins (folate, vitamin B12, vitamin C) are essential to making healthy red blood cells. Vitamin deficiency anemia can occur if you do not eat enough foods that have folate, vitamin B12, or vitamin C. It can also occur if your body has trouble absorbing or processing these vitamins.

Symptoms depend on your specific type of anemia. Mild symptoms can be so mild that they go unnoticed. However, as your body loses more iron and the anemia gets worse, symptoms also increase.

Anemia signs and symptoms may include:

- Fatigue
- Weakness
- Pale skin
- Chest pain, fast heartbeat, or shortness of breath
- Headache, dizziness, or lightheadedness
- Cold hands and feet
- Loss of appetite

# Neutropenia

Neutropenia refers to a decrease in neutrophils, the most common type of white blood cell. A low number of white blood cells can lead to frequent or severe infections.

A person with neutropenia may experience:

- Frequent fevers or infections
- Bladder infections that are painful or make you urinate more often
- Lung infections that cause coughing and difficulty breathing
- Mouth sores
- Sinus infections
- Skin infections

More information is provided on neutropenia in the next chapter.

# Thrombocytopenia

Thrombocytopenia refers to a condition where there are not enough platelets found in the blood. Platelets are important; they help your blood clot, which stops bleeding. If there are not enough platelets in your blood, you may experience bruising and excessive bleeding from wounds or injuries to other tissues.

# 1

# Acute lymphoblastic leukemia

Acute lymphoblastic leukemia (ALL) is a fastgrowing blood cancer that starts in diseasefighting lymphocytes of your immune system. In ALL, bone marrow makes too many immature lymphocytes called lymphoblasts. Lymphoblasts can crowd out other blood cells causing blood to not work as it should. Acute leukemias grow faster than chronic leukemias.

ALL can be found in bone marrow, blood, and organs such as the testicles or the central nervous system (CNS).

# Acute myeloid leukemia

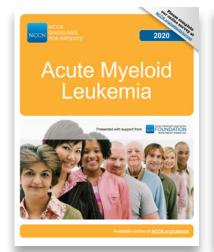
Acute myeloid leukemia (AML) is a fastgrowing cancer of myeloid progenitor cells. Changes in these cells stop myeloid blasts (or myeloblasts) from becoming mature blood cells. As a result, there is a buildup of abnormal blasts in the marrow and blood. In turn, there are not enough red blood cells, platelets, and mature white blood cells.

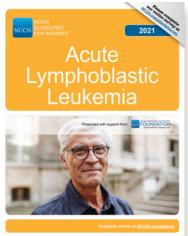
# Myelodysplastic syndromes

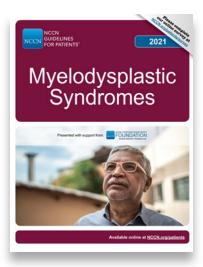
Myelodysplastic syndromes (MDS) are a rare group of bone marrow disorders. In MDS, the body does not make enough healthy blood cells for the bone marrow. Bone marrow is a spongy substance found in the center of the bones. Bone marrow contains parent cells called stem cells. In normal bone marrow, stem cells can rapidly divide and clone themselves to form new cells.

In MDS, some stem cells are abnormal.
Abnormal cells may not develop into normal cells. Instead, abnormal, immature cells crowd out normal cells in the bone marrow.

For more information on blood disorders such as MDS, AML, and/or ALL, read the NCCN Guidelines for Patients: Acute Myeloid Leukemia, Acute Lymphoblastic Leukemia or Myelodysplastic Syndromes, available at NCCN.org/patientguidelines.







# Review

- Blood has many functions. These include transportation, regulation, and protection.
- Blood cells have important jobs. Red blood cells carry oxygen throughout the body. White blood cells fight infection. Platelets help control bleeding. Plasma carries red blood cells, white blood cells, and platelets.
- Platelets work with proteins called clotting factors to control bleeding inside our bodies and on our skin.
- A low number of white blood cells (neutropenia) can lead to frequent or severe infections.



# We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer.

Take our survey to let us know what we got right and what we could do better:

NCCN.org/patients/feedback

# 2 Testing

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In anemia, your body does not make enough healthy red blood cells, resulting in less oxygen being carried to your cells. This chapter reviews tests used to diagnose anemia.

A blood test called a complete blood count (CBC) test is used to diagnose anemia. The test results include the number of red blood cells in a person's body. A red blood cell count is measured in several ways.

Common measurements for a CBC include:

- > Hemoglobin
- Hematocrit

Hemoglobin is a red protein that transports oxygen in the blood. Hematocrit refers to the percentage of blood that is made up of red blood cells.

People with specific cancer types or those who are receiving certain cancer treatments may have regular blood tests. These tests look for anemia and other blood-related problems. If test results show that you have anemia, you may need additional tests to find the cause. Anemia does not always cause symptoms. You may find out you have anemia when checking for another condition.

Your risk for anemia is based on results of blood tests. Blood tests for anemia include a CBC with indices, blood smear, and reticulocyte count and mean corpuscular volume (MCV).

# General health tests

# Family history

Some cancers and other diseases run in families. Your doctor will ask about the health history of family members who are blood relatives. This information is called a family history. Ask family members about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed.

# **Health history**

A health history is a record of all health issues and treatments you have had in your life.

Be prepared to list any illness or injury and when it happened. Bring a list of old and new medicines and any over-the-counter medicines, herbals, or supplements you take. A health history will help determine which treatment is best for you.

### **Medical exam**

A medical exam checks the body for signs of disease.

A health care provider may:

- Check your temperature, blood pressure, pulse, and breathing rate
- Weigh you
- Listen to your lungs and heart
- Look in your eyes, ears, nose, and throat
- Feel and apply pressure to parts of your body to see if organs are of normal size, are soft or hard, or cause pain when touched. Tell your doctor if you feel pain.

Feel for enlarged lymph nodes in your neck, underarm, and groin. Tell the doctor if you have felt any lumps or have any pain.

Doctors should perform a thorough exam along with a complete health history.

# **Blood tests**

# Complete blood count with indices

A complete blood count (CBC) is used to measure the number and physical makeup of cells found in your blood. Your doctor will be specifically interested in red blood cell levels within the hematocrit and hemoglobin in your blood. Hemoglobin is a protein in the red blood cells. Hematocrit measures how much space red blood cells take up in the blood. A low level of either of these is a sign of anemia.

The indices for the CBC include:

- Average red blood cell size
- Hemoglobin amount per red blood cell
- The amount of hemoglobin compared to the size of the cell per red blood cell

If your CBC results indicate anemia, your doctor may ask for further blood testing including a blood smear test.

### **Blood smear**

A blood smear is a blood test used to look for abnormal blood cells. A smear test looks at both your red and white blood cells. It helps define the shape of red blood cells and the presence of abnormal cells.

## Reticulocyte count

A reticulocyte count test measures the number of young red blood cells in the blood. The test shows whether your bone marrow is making red blood cells at the correct rate. This test helps to determine the cause and type of anemia.

## Mean corpuscular volume

Mean corpuscular volume (MCV) measures the average size of red blood cells. This test is especially helpful in identifying iron-deficiency anemia, as red blood cells are smaller than normal.

# Hemorrhage

A hemorrhage refers to a release of blood from a broken blood vessel (either inside or outside the body). A stool guaiac or endoscopy is used to test for hemorrhage. A stool guaiac test (fecal occult test) looks for hidden blood in the stool. The test is performed by taking a small stool sample on guaiac paper and applying a drop or two of hydrogen peroxide. If there is blood present, the sample will immediately turn blue.

An endoscopy is used to look at the upper digestive tract for signs of bleeding. An endoscopy is a nonsurgical test that uses an endoscope (flexible tube with a light and camera) to look inside a person's digestive tract.

# Hemolysis

In hemolytic anemia, your damaged red blood cells grow faster than the bone marrow's ability to make new cells.

If you are suspected of having hemolytic anemia, your doctor may request one of the following tests:

- Direct antiglobulin test (DAT)
- Disseminated intravascular coagulation (DIC) panel
- Haptoglobin
- Indirect bilirubin
- Lactate dehydrogenase (LDH)

# Direct antiglobulin test

A direct antiglobulin test is used to diagnose hemolytic anemia caused by your immune system. Your immune system is your body's defense system. It makes proteins called antibodies to attack invading cells. Hemolytic anemia stimulates your immune system to make antibodies that mistakenly attack your own red blood cells.

# Disseminated intravascular coagulation panel

Disseminated intravascular coagulation (DIC) is a serious condition where clotting proteins in the blood become overactive. This may disrupt normal blood flow to organs and can lead to organ failure. Tests are used to detect DIC, evaluate how severe it is, and monitor effects over time. Many factors are used to diagnose DIC. They include signs and symptoms, presence of an underlying condition, physical examination, and medical history.

# Hemolysis

Hemolysis is a rupture or destruction of red blood cells.



Normal red blood cell (erythrocyte)



Spherocyte (erythrocytes that are sphere-shaped)



Rupturing of erythrocyte, and the release of contents into blood plasma

# Haptoglobin

Haptoglobin is a protein that binds with hemoglobin to help transport oxygen. A haptoglobin test measures the amount of haptoglobin in your blood.

### Indirect bilirubin

Bilirubin is a yellowish pigment created during the breakdown of red blood cells. A bilirubin test measures the levels of bilirubin in your blood. Higher than normal results for indirect bilirubin point to a diagnosis of hemolytic anemia (red blood cells are destroyed faster than they can be made).

Higher than normal levels of bilirubin may indicate different types of liver or bile duct problems. Occasionally, higher bilirubin levels may be caused by an increased rate of destruction of red blood cells (hemolysis). Hemolysis refers to when your body is getting rid of too many red blood cells.

# Lactate dehydrogenase

Lactate dehydrogenase (LDH) helps to turn sugar into energy. LDH is found in many of the organs and tissues in the body, including the liver, heart, pancreas, kidneys, skeletal muscles, lymph tissue, and blood cells. An LDH test is used to find out if you have any tissue damage.

# **Nutritional tests**

### Iron

An iron test may be performed if your doctor suspects too little iron (deficiency) or too much iron (overload). The test is performed by drawing a blood sample and sending it to a lab to be tested.

# **Total iron-binding capacity**

A total iron-binding capacity (TIBC) test is used to see how well transferrin transports iron through your blood. Transferrin moves iron through the blood to various tissues such as the liver, spleen, and bone marrow. The TIBC test determines whether there is too much or too little of the transferrin protein in your bloodstream.

### **Ferritin**

Ferritin is a protein in the blood that contains iron. A ferritin test is used to find out how much iron is stored in your body. If a ferritin test result shows lower than normal results, you may have iron deficiency.

### **B12** and folate

Vitamin B12 and folate are nutrients only found in the food you eat. Vitamin B12 and folate tests measure vitamin levels in the liquid portion of the blood (serum or plasma) to detect deficiencies.

# Kidney function tests

### Glomerular filtration rate

Glomeruli are tiny filters in the kidneys that clean out waste from the blood. A glomerular filtration rate (GFR) is a blood test used to estimate how much blood passes through the glomeruli each minute. Creatinine will also be tested in the blood sample. Creatinine is waste product created by a breakdown of creatine in the muscles. Creatine is a chemical produced by the body that helps to supply energy to muscles.

A GFR rate is determined by identifying your blood creatinine level with other factors such as:

- Age
- Ethnicity
- Sex
- Height
- Weight

A GFR is a blood test that looks at how well your kidneys are working.

# Hormone issues

# Hypogonadism

Hypogonadism is a condition that affects both males (gonads/testes) and women (ovaries). During this condition, the body does not produce enough of the hormone (testosterone for men or estrogen for women). Testosterone helps to regulate fertility, muscle mass, fat distribution, and red blood cell production. Estrogen helps to develop and maintain the female reproductive system and characteristics, such as breasts and pubic hair. Treatment for hypogonadism may include hormone replacement therapy and assisted reproduction.

# Adrenal dysfunction

Adrenal insufficiency (Addison's disease) refers to a disorder that occurs when your adrenal glands do not produce enough hormones (cortisol and aldosterone). Your adrenal glands are located above the kidneys. Cortisol is released by the adrenal glands to help support your body to deal with stressful situations. Aldosterone helps to balance sodium and potassium in your blood. Too much aldosterone can cause you to lose potassium and retain sodium.

Tests used to measure the levels of cortisol and aldosterone in your body include:

- Adrenocorticotrophic hormone (ACTH) stimulation test - used to diagnose adrenal insufficiency
- Insulin-induced hypoglycemia test used to determine how the adrenal glands are responding to stress

# Hyperthyroidism

Hyperthyroidism occurs when your body becomes overactive from producing too much of the thyroid hormones, thyroxine (T4) and triiodothyronine (T3). Thyroxine supports digestion, heart and muscle function, brain development, and maintenance of bones. Triiodothyronine helps the body with important functions such as growth and development, metabolism, body temperature, and heart rate.

During hyperthyroidism, you may have a fast heartbeat, increased appetite, anxiety, sensitivity to heat, or sudden weight loss.

Hyperthyroidism most commonly occurs in three ways:

- Thyroiditis
- Thyroid nodule
- Graves disease

Thyroiditis is caused by antibodies that attack the thyroid. This leads to inflammation and damage to the thyroid cells. Thyroiditis is often caused by autoimmune diseases such as juvenile diabetes (type-1) and rheumatoid arthritis.

Thyroid nodules are found in both hypothyroidism and hyperthyroidism. These nodules are often benign. Under hyperthyroidism, nodules may increase your thyroid's size or produce too much T4 thyroid hormone.

Graves' disease is an autoimmune disorder that causes hyperthyroidism, or overactive thyroid. With this disease, your immune system attacks the thyroid and causes it to make more thyroid hormone than your body needs.

# Hypothyroidism

During hypothyroidism, your thyroid gland cannot make enough hormones to function well. A slow production of hormones leads to a slowing of your metabolism. A slow metabolism will cause weight gain.

Hashimoto thyroiditis is the most common type of hypothyroidism. It refers to when your body attacks its own immune system. This attack causes the thyroid to stop producing hormones, which leads to hypothyroidism.

# Anemia and chronic inflammation

## C-reactive protein

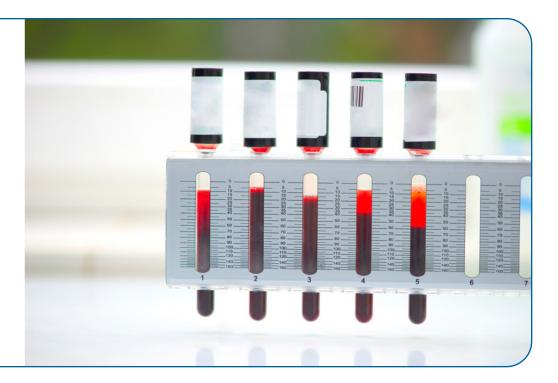
C-reactive protein (CRP) is found in blood plasma. CRP increases when there's inflammation in your body. A CRP test is used to check for inflammation. Inflammation is an indication of infection or a chronic inflammatory disease, such as rheumatoid arthritis, lupus, or heart disease.

**Erythrocyte sedimentation rate** 

An erythrocyte sedimentation rate (ESR) is a blood test that measures how quickly erythrocytes (red blood cells) settle at the bottom of a test tube. Red blood cells normally settle slowly. Inflammation is indicated by a faster-than-normal rate.

Inflammation may prevent your body from using stored iron to make enough healthy red blood cells.

An ESR test measures how quickly red blood cells settle at the bottom of the test tube.



# Review

- Doctors use a blood test called a complete blood count (CBC) test to diagnose anemia.
- A CBC is used to measure the number and physical makeup of cells found in your blood.
- Hemolytic anemia occurs when a person's red blood cells are damaged at higher rates than the bone marrow can create new cells.
- Glomeruli are tiny filters in the kidneys that clean out waste from the blood. A glomerular filtration rate (GFR) is a blood test used to estimate how much blood passes through the glomeruli each minute.



# Create a medical binder

A medical binder or notebook is a great way to organize all of your records in one place.

- Make copies of blood tests, imaging results, and reports about your specific type of cancer. It will be helpful when getting a second opinion.
- Choose a binder that meets your needs.
   Consider a zipper pocket to include a pen, small calendar, and insurance cards.
- Create folders for insurance forms, medical records, and tests results. You can do the same on your computer.
- Use online patient portals to view your test results and other records. Download or print the records to add to your binder.
- Organize your binder in a way that works for you. Add a section for questions and to take notes.
- Bring your medical binder to appointments.
   You never know when you might need it!

# **3**Anemia

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Overview

If you have anemia, your body's cells may not be receiving enough oxygen. There are many forms of anemia, each with its own cause and symptoms. This chapter will provide information on anemia caused by cancer or chemotherapy treatment.

# Overview

Anemia is a condition where your body does not make enough healthy red blood cells, resulting in less oxygen being carried to your cells. There are many types and causes of anemia. Mild anemia is a common and treatable condition that can occur in anyone. Anemia may also be a sign of a more serious condition. It may result from chronic bleeding in the stomach, chronic inflammation from an infection, kidney disease, cancer, or an autoimmune disease.

Anemia is a very common side effect of chemotherapy. Anemia most often results in fatigue and lightheadedness. If your anemia is severe, you may be treated with a blood transfusion, iron supplements, or medications to stimulate red blood cell production (called erythropoietin stimulating agents).

Fatigue is common with cancer. Anemia may make fatigue worse. Anemia can also impact your cancer treatment. Severe anemia caused by chemotherapy may result in a delay in treatments, or a need to reduce the chemotherapy dose. Any delay in treatment may cause it to be less effective.

Causes of anemia during chemotherapy include:

- Chemotherapy drugs
- Bleeding
- Cancer type
- Kidney damage

# Anemia

Anemia is a condition where the blood does not have enough healthy red blood cells.

Normal level of red blood cells

Anemia level of red blood cells

# **Tests**

You will receive blood tests before and after chemotherapy treatments to measure your red blood cell count and hemoglobin. Blood tests will provide information on size and number of cells. These tests can help further define your anemia.

For a list of additional tests for anemia, see Guide 1.

# Complete blood count with indices

A complete blood count (CBC) is used to measure the number and physical makeup of cells found in your blood. Your doctor will be specifically interested in red blood cell levels within the hematocrit and hemoglobin in your blood. Hemoglobin is a protein in the red blood cells. Hematocrit measures how much space red blood cells take up in the blood. A low level of either of these is a sign of anemia.

Guide 1 Testing for anemia	
Needed	Complete blood count (CBC) with indices
	Blood smear morphology
	Reticulocyte count
	Mean corpuscular volume (MCV)
In some cases	Hemorrhage
	Hemolysis
	Nutritional
	Inherited
	Renal dysfunction
	Radiation-induced myelosuppression
	Hormone dysfunction
	Anemia and chronic inflammation

The indices for the CBC include:

- Average red blood cell size
- Hemoglobin amount in each red blood cell
- The amount of hemoglobin compared to the size of each red blood cell

If your CBC results indicate anemia, you may need further testing.

### **Blood smear**

A blood smear is a blood test used to look for abnormal blood cells. A smear test looks at both your red and white blood cells. It helps define the shape of red blood cells and the presence of abnormal cells.

# Reticulocyte count

A reticulocyte count test measures the number of young red blood cells in the blood. The test shows whether your bone marrow is making red blood cells at the correct rate. This test helps to determine the cause and type of anemia.

# Mean corpuscular volume

Mean corpuscular volume (MCV) measures the average size of red blood cells. This test is especially helpful in identifying iron-deficiency anemia (too little iron), as red blood cells are smaller than normal.

There are many types and causes of anemia in addition to chemotherapy. Further testing may be needed to identify what is causing the anemia.

# Treatment overview

Treatment depends on the type of anemia and the cause. Iron supplements may be used to treat iron deficiency. Vitamin B supplements may be used for low vitamin levels. Blood transfusions may be used for blood loss. And, certain medications may be used to induce blood creation.

# Erythropoietic therapy

Erythropoiesis-stimulating agents (ESAs) are used to treat anemia due to chronic kidney disease, chemotherapy, or certain treatments for HIV (human immunodeficiency virus). ESAs can help reduce the need for blood transfusions during chemotherapy treatment. ESAs stimulate the bone marrow to make more red blood cells. Epoetin alfa (Procrit® and Epogen®) and darbepoetin alfa (Aranesp®) are examples of erythropoiesis-stimulating agents.

You may receive ESA treatment if you have anemia and any of the following:

- Cancer or chronic kidney disease
- Palliative treatment for cancer
- Myelosuppressive chemotherapy
- Do not want or cannot have a blood transfusion

Things to consider before using ESAs:

- ESAs may increase the risk of blood clots in your veins (venous thromboembolism)
- ESAs may cause too much of an increase in hemoglobin, which puts you at higher

- 3
- risk for heart attack, stroke, heart failure, and death
- ESAs may cause the tumor to grow in people with certain cancer types

# Red blood cell transfusion

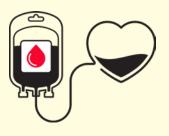
The fastest way to increase red blood cells is with a red blood cell transfusion (blood transfusion). A blood transfusion is a routine procedure where donated blood is given to you through a vein in your arm.

A blood transfusion typically takes 1 to 4 hours, depending on how much is needed and what part of the blood you need. You should expect to receive regular blood tests to check your blood counts. In some cases, you may need to get more than one blood transfusion.

Before your first blood transfusion, you will be evaluated for the severity of your anemia. If you are not experiencing symptoms and do not have other major health issues, no treatment is necessary. Your doctor will re-test your blood at various times during treatment.

If your red blood cell numbers continue to decline due to recent chemotherapy or radiation therapy, and you have no other major health issues, your doctor will recommend treatment with a red blood cell transfusion. Before your blood transfusion, you will be tested for any issues with your heart, lungs, and brain.

If you have symptoms of anemia, you will be tested for the following health concerns before starting treatment:



# **Transfusions**

A transfusion is a common procedure to replace blood or blood components (red blood cells or platelets). It is given to you through an intravenous line (IV), a tiny tube that is inserted into a vein with a small needle.

- The whole process can take about 1 to 4 hours, depending on how much blood is needed.
- Most transfusions use blood from a donor.
   Some choose a family member or friend to donate blood.
- Blood transfusions are usually very safe.
   Donated blood is carefully tested, handled, and stored.
- Most people's bodies handle blood transfusions very well. But, like any medical procedure, there are some risks. Speak with your doctor for specific information about your risks.
- Chemotherapy can affect how bone marrow makes new blood cells. Some people getting treatment for cancer might need a transfusion of red blood cells or platelets.

- 3
- Heart disease or chest pain
- Fast or labored breathing
- Lightheadedness
- Fatigue
- Fainting

# Iron monitoring

Iron is important in maintaining body functions such as producing hemoglobin, the molecule in your blood that carries oxygen. Iron is also necessary to maintain healthy cells, skin, hair, and nails. If it is found that your iron levels are low, your doctor may treat you with an intravenous (IV) iron supplement. Side effects caused by IV iron may include feeling flushed, headaches, and joint or muscle aches days after treatment.

An iron panel is used to test for the level of iron in your blood. Tests include serum iron and serum ferritin tests. A total iron-binding capacity test will also measure iron levels.

### Serum iron

Serum iron is a test that measures the amount of iron that is bound to transferrin and serum ferritin.

# Total iron-binding capacity

Total iron-binding capacity (TIBC) is used to measure the amount of iron that can be bound by proteins in the blood. Transferrins are glycoproteins that support the movement of iron through blood plasma.

### Serum ferritin

Ferritin is a protein that stores iron and releases it when necessary. A serum ferritin test is considered the most accurate to diagnose iron deficiency anemia.

Iron deficiency anemia is treated based on your ferritin level and transferrin saturation (absorption):

- If you have an absolute iron deficiency, you may be treated with an IV or oral supplement.
- If you have a functional iron deficiency and are receiving erythropoiesisstimulating agents (ESAs), you may receive an IV iron supplement with erythropoietic therapy (ESAs).
- If you may have a functional iron deficiency, work with your doctor to determine if any iron supplement is needed.
- If you do not have an iron deficiency, no treatment will be provided.

In all instances, you will receive routine blood tests to check your iron levels.

# Review

- Anemia is a condition where your body does not make enough healthy blood cells, resulting in less oxygen being carried to your cells.
- Severe anemia caused by chemotherapy may result in a delay in treatments, or a need to reduce the chemotherapy dose.
- The fastest way to increase red blood cells is with a red blood cell transfusion.
- ESAs stimulate the bone marrow to make more red blood cells.



# Anemia

Anemia occurs when the body cannot produce enough red blood cells to move oxygen towards tissues and organs.

- Anemia can cause breathing difficulties, cold fingers and toes, pale skin, and frequent headaches.
- Anemia can affect people of all ages, races, and ethnicities. Some types of anemia are very common, and some are very rare.
- Causes of anemia may include blood loss or too few red blood cells. Factors that may cause too few red blood cells include diet, medical conditions, or genetic disorders.
- If the anemia is due to a poor diet, eating more dark leafy green vegetables, nuts, dried fruit, red meat, grains, citrus fruits, and beans may help.
- Anemia symptoms can also be risk factors for other diseases and disorders. This means the anemia could possibly be overlooked or misdiagnosed.
- Work with your doctor to determine the cause of anemia. You are more likely to stay healthy and avoid other serious health conditions in the long run.

# **4** Neutropenia

- 32 Overview
- 32 Causes
- 33 Review



Neutropenia refers to a low white blood count. A low number of white blood cells leads to immunosuppression (a reduced ability to fight infections). Immunosuppression can be caused by certain diseases or treatments like chemotherapy or radiation. This chapter presents an overview of neutropenia.

Overview

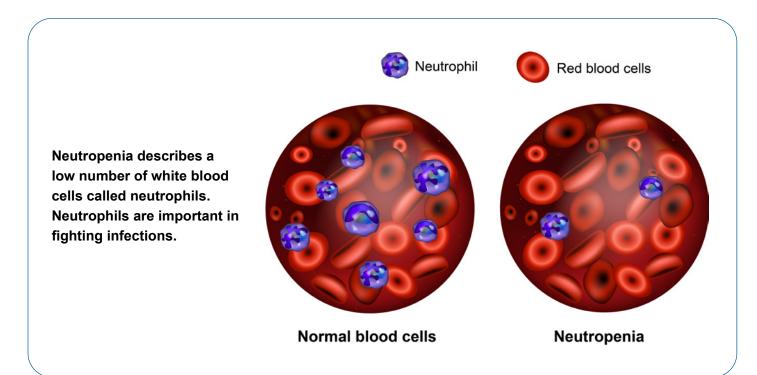
Neutropenia describes a low number of white blood cells called neutrophils. Neutrophils are made in the bone marrow. Neutrophils (a type of white blood cell) are important in fighting infection in the body. Neutrophils make up approximately 40 percent (40%) to 60 percent (60%) of the white blood cells in our bodies.

Neutropenia is common after receiving chemotherapy. This is because chemotherapy kills cancer cells as well as healthy white blood cells. As a result, you will be at increased risk for infections.

Most people are not aware that they have neutropenia. People often find out when they have a blood test performed for other reasons. If the neutropenia is severe, even bacteria normally found in your mouth and intestines can cause serious illness.

# Causes

Neutropenia occurs for a couple of reasons, either neutrophils in the blood are used up or destroyed faster than they can be made, or the bone marrow does not make enough neutrophils.



Neutropenia often occurs between 7 to 12 days after you receive chemotherapy. Timing depends on the type of chemotherapy you receive. A member of your treatment team will let you know when your white blood cell count is likely to be at its lowest. You should carefully watch for signs and symptoms of infection during this time.

## Febrile neutropenia

When someone with neutropenia also develops a fever, it is called febrile neutropenia (FN). With febrile neutropenia, your risk of infection may be higher than normal. This is because a low number of white blood cells leads to a reduced ability to fight infections.

More information is provided in the next chapter about febrile neutropenia.

# Review

- Neutropenia refers to a low white blood cell count. A low number of white blood cells leads to a reduced ability to fight infections.
- Neutropenia is common after receiving chemotherapy. This is because chemotherapy kills cancer cells as well as healthy white blood cells.
- Most people are not aware that they have neutropenia. People often find out when they have a blood test performed for other reasons.
- When someone with neutropenia also develops a fever, it is called febrile neutropenia.

# **5**Febrile neutropenia

35 Overview
36 Before chemotherapy starts
37 Low risk
37 Intermediate risk
38 High risk
39 FN during treatment
40 Review



Febrile neutropenia (FN) is a serious side effect of chemotherapy that may result in delays in treatment or reductions in chemotherapy doses. Febrile neutropenia occurs when a person with neutropenia (very low white blood cell count) develops a fever. This chapter presents an overview of febrile neutropenia.

## Overview

Neutropenia refers to a decrease in the number of white blood cells. White blood cells are the body's main defense against infection. When neutropenia is combined with a fever, it is called febrile neutropenia (FN). This can be a severe complication of chemotherapy treatment that may result in delays or dose reductions of chemotherapy.

Chemotherapy kills fast-growing cells throughout the body, including cancer cells and normal cells. A side effect of chemotherapy is that it can decrease the number of white blood cells in your body. Having a low white blood cell count weakens your immune system, which leads to an increase in your risk of infection.

Neutropenia is common after chemotherapy. It often occurs 7 to 12 days after you receive chemotherapy treatment. Expect your doctor to run blood tests for neutropenia. Also, a member of your care team will let you know when your white blood cell count is likely to be low.

Signs of infection may include the following:

- A fever (temperature of 100.4°F (38°C) or higher)
- Chills or sweating
- Sore throat, sores in the mouth, or a toothache
- Abdominal pain
- Pain near the anus
- Pain or burning when urinating, or frequent urination
- Diarrhea
- > A cough or shortness of breath
- Any redness, swelling, or pain (around a cut, wound, or catheter)
- Unusual vaginal discharge or itching

Carefully watch for any symptoms of infection. Contact your care team if you experience any signs of infection.

## Before chemotherapy starts

## Risk assessment

You will be evaluated for risk of developing febrile neutropenia before your first chemotherapy treatment and throughout your chemotherapy treatments.

Evaluation for risk may include:

- Cancer type
- Dose and type of chemotherapy
- Patient risk factors
- Goal of cancer treatment

## Cancer type

Your cancer type will be considered when discussing your risk for neutropenia. For example, neutropenia is a common side effect in people with leukemia.

## Dose and type of chemotherapy

Chemotherapy kills fast-growing cells throughout the body, including cancer cells and normal cells. Your risk of febrile neutropenia may be increased based on the dose of chemotherapy or the chemotherapy regimen (combination of drugs) you receive.

Chemotherapy doses include:

- High-dose chemotherapy
- Dose-dense chemotherapy
- Standard-dose chemotherapy

High-dose chemotherapy is a high-intensity drug treatment. It can destroy bone marrow and cause severe side effects. A bone marrow

or stem cell transplant is common after highdose chemotherapy.

Dose-dense chemotherapy is given more frequently than normally scheduled, with less time between doses. The purpose of the shortened time between doses is to kill as much of the cancer cells as possible.

Standard-dose chemotherapy is given on a regular schedule (such as monthly). Certain combinations of chemotherapy drugs, even if they are not high-dose or dose-dense can increase the risk of severe neutropenia.

## Patient risk factors

Patient risk factors will be considered when deciding on the best course of treatment. Risk factors for neutropenia complications include age, other health concerns such as lung or heart disease, and previous cancer treatments received.

### Goal of treatment

Work with your care team to define your treatment goal. Your options will vary between cure or palliative care. Palliative care refers to relieving the side effects of chemotherapy or radiation treatment.

## Risk groups

Before starting chemotherapy, you will be placed into a risk group based on your specific risk factors. A risk factor is anything that increases your chance of febrile neutropenia.

Your risk for developing febrile neutropenia will be based on the following:

- Your type of cancer or disease
- Type of chemotherapy planned
- If you have other serious health issues
- Goal of treatment (whether it is to cure or lessen symptoms)

After your risk is determined, you will be placed into one of the following risk groups:

- > Low
- Intermediate
- > High

A low risk means you have a less than 10 percent (10%) chance of developing febrile neutropenia. Intermediate risk means you have a 10 to 20 percent (10% to 20%) chance. If you are at high risk, you have a more than 20 percent (20%) chance of developing it. More information about each of these groups can be found next.

## **Prophylaxis treatment**

Prophylaxis means to prevent and refers to medications given before chemotherapy starts. Prophylaxis treatment includes the use of granulocyte colony-stimulating factors (G-CSFs). G-CSFs stimulate the development of granulocytes (white blood cells). They are used to prevent complications

from neutropenia when you receive myelosuppressive cancer chemotherapy or after a bone marrow transplant.

G-CSFs include the following:

- Filgrastim (Neupogen®) and biosimilar drugs
- Tbo-filgrastim (Granix®)
- Pegfilgrastim (Neulasta®) and biosimilar drugs

## Low risk

If you do not have any symptoms and have no other major health issues, then you are at low risk for febrile neutropenia. Prophylaxis is not needed.

You will be re-evaluated for febrile neutropenia after your first cycle of chemotherapy. If your risk does not change after the first cycle of chemotherapy, you will be tested for any changes to your risk score after each chemotherapy treatment.

## Intermediate risk

If you have an intermediate risk for febrile neutropenia, it refers to having one or more of the following risk factors:

- Prior chemotherapy or radiation therapy
- Persistent neutropenia
- Tumor(s) affecting bone marrow
- Recent surgery and/or open wounds

- Liver failure
- Kidney failure
- 65 years of age or above receiving chemotherapy
- Intensity of chemotherapy treatment

An additional risk factor may include HIV (human immunodeficiency virus).

If you have one or more risk factors, then you may receive G-CSFs. G-CSFs stimulate the development of granulocytes (white blood cells).

For more information on neutropenia risk and treatment options, see Guide 2.

## High risk

If you are at high risk for febrile neutropenia (FN), it means you have more than a 20 percent (20%) chance of developing it.
High-risk febrile neutropenia will be treated with granulocyte colony-stimulating factors (G-CSFs) before your first chemotherapy cycle. G-CSFs are used to stimulate white blood cells. You will also be assessed after each chemotherapy cycle to determine if there are any changes and if further treatment for FN is necessary.

## Guide 2 Febrile neutropenia risk

Intermediate

(10% to 20%)

Risk factors include:

- Prior chemotherapy or radiation therapy
- Persistent neutropenia
- Bone marrow involvement by tumor
- · Recent surgery and/or open wounds
- Liver dysfunction
- Renal dysfunction
- 65 years of age or above receiving full chemotherapy dose intensity

If there are no risk factors, then observe

If one or more risk factors, then consider G-CSFs

## FN during treatment

Sometimes, people develop FN during chemotherapy. This might happen despite prophylaxis or preventive treatment with G-CSFs.

- If you received G-CSFs FN will be treated based on the drug received. If you received filagrastim (Neupogen®) or TBO-filgrastim (Granix®), you will continue this treatment. If you were treated with pegfilgrastim (Neulasta®), no further treatment is needed.
- If you did not receive G-CSFs you will be monitored for changes throughout treatment. If you are at risk for developing an infection-related complication, you will be treated with myeloid growth factors (MGFs). MGFs are naturally made in the body, or they can be made in a lab. They are used to increase the number of blood cells and prevent infections.

You will be tested for febrile neutropenia before and after each chemotherapy cycle.

For more information on when MGFs and G-CSFs are used, please see Guide 3.

Guide 3 Therapeutic use of myeloid growth factors: Febrile neutropenia		
Receiving or received prophylactic G-CSFs	Receiving daily prophylactic filgrastim or tbo-filgrastim	→ Continue G-CSFs
	Received long-lasting prophylactic pegfilgrastim	→ No additional G-CSFs
Did not receive prophylactic G-CSFs	Risk factors not present for an infection-associated complication	→ No therapeutic MGFs
	Risk factors present for an infection- associated complication	→ Therapeutic MGFs

## Review

- Neutropenia refers to a decrease in the number of white blood cells. White blood cells are the body's main defense against infection.
- When neutropenia is combined with a fever, it is called febrile neutropenia (FN).
- Neutropenia is common after receiving chemotherapy and increases your risk for infections.
- You will be evaluated for risk of developing febrile neutropenia before and throughout your chemotherapy treatments.
- Before starting chemotherapy, you will be placed into a risk group based on specific risk factors. A risk factor is anything that increases your chance of febrile neutropenia.
- G-CSFs are used to increase the number of neutrophils and help prevent infections.



## Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.

NCCN.org/patients/response

## 6 Thrombocytopenia

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## Overview

Platelets are an important part of blood.
Platelets work with proteins called clotting factors to control bleeding inside our bodies and on our skin. Platelets are made in your bone marrow along with other kinds of blood cells. They travel through your blood vessels and stick together (clot) to stop bleeding when needed.

When your blood has lower than normal platelets, it is called thrombocytopenia. Thrombocytopenia occurs when your immune system attacks the platelets in your blood.

During thrombocytopenia, serious bleeding can occur inside your body or underneath your skin.

There are many factors that can cause thrombocytopenia, including:

- The bone marrow does not make enough platelets (such as leukemia or blood disorders)
- Infection such as hepatitis C virus, human immunodeficiency virus (HIV), or Epstein-Barr virus
- Platelets become trapped in the spleen (such as cirrhosis of the liver, myelofibrosis, and Gaucher disease)
- Red blood cell transfusions can thin platelet numbers in the blood
- The body may destroy or use up platelets made in the bone marrow (this occurs in many disorders including immune thrombocytopenia, thrombotic thrombocytopenic purpura, and hemolyticuremic syndrome)

 Certain drugs such as heparin, certain antibiotics, ethanol, anticancer drugs, and quinine

Thrombocytopenia can last days to years depending on its cause.

Symptoms of thrombocytopenia may include any of the following:

- Easy or excessive bruising (known as purpura)
- > Bleeding from your gums, skin, or nose
- Heavy menstrual bleeding
- Excessive bleeding during or after birth or surgery
- > Blood in urine or stool
- Red or purple dots on your skin
- Fatigue
- Headaches
- > Enlarged spleen

## Chemotherapy-induced thrombocytopenia

## **Testing**

Thrombocytopenia is common in people with cancer. It can be caused by chemotherapy, radiation treatment, or the disease itself. If you are suspected of having chemotherapy-induced thrombocytopenia (CIT), you will be tested to determine the cause. Required testing will include a complete blood count (CBC) with differential for evaluation of other cytopenias (one or more blood cell types are lower than they should be) and blood smear morphology, including checking for platelet clumping.

## Complete blood count

A CBC measures the levels of red blood cells, white blood cells, and platelets in your blood. Red blood cells carry oxygen throughout your body, white blood cells fight infection, and platelets control bleeding. A CBC looks for many illnesses including anemia, infections, and leukemia.

## Differential

There are 5 types of white blood cells: neutrophils, lymphocytes, monocytes, eosinophils, and basophils. A differential counts the number of each type of white blood cell (WBC). It also checks if the counts are in balance with each other. Your doctor may be able to determine the cause of an abnormal white blood cell count from this test.

### **Blood smear**

In a blood smear test, a drop of blood is placed on a slide so it can be viewed with a microscope. A pathologist will look at cell size, shape, type, and maturity. This test is also used to count the different types of blood cells, which help to define blood cells that are abnormal in shape or size (dysplasia).

A blood smear test may also be used to check for blast cells in the bloodstream. Although blast cells are normally found in the bone marrow, in some cases of MDS, blast cells may be found in the bloodstream.

Additional testing may be required to determine treatment.

## **Treatment**

Treatment for thrombocytopenia depends on its cause and severity. If you do not have chemotherapy-induced thrombocytopenia (CIT), you will be treated for the cause of low platelets as determined from the tests.

If you are found to have CIT, you can expect to be treated with one or more of the following:

- Platelet transfusion
- Reduction in chemotherapy dose or change in treatment
- Clinical trial of TPO-RA
- Romiplostim

## Platelet transfusion

You may receive a platelet transfusion if your platelet count is low. During a transfusion, platelets are given through an intravenous (IV) drip into your vein. The platelets will be from one or more donors. A platelet transfusion is used to stop or prevent bleeding in someone with thrombocytopenia. The transfusion normally takes about 15 to 30 minutes to complete. You can expect an immediate increase in the number of platelets in your blood after a transfusion.

For some, however, the effects may only be temporary and more transfusions may be needed.

## Chemotherapy dose reduction or change in treatment

If your chemotherapy treatment is causing issues with low platelet count, your treatment may be reduced or changed. You will want to weigh the pros and cons of changing or delaying chemotherapy doses with your care team.

## Clinical trial of thrombopoietin receptor agonists

You may be asked to participate in a clinical trial for thrombopoietin receptor agonists (TPO-RAs). TPO-RAs have shown success in increasing platelet counts, decreasing bleeding events, and reducing the need for rescue treatments. Rescue treatments are treatments given when you do not respond to standard therapy.

## Romiplostim

Romiplostim (Nplate®) is an injection drug. It is used to increase the number of platelets (cells that help the blood to clot) to decrease the risk of bleeding. It is a granulocyte colony-stimulating factor (G-CSF). A G-CSF stimulates the bone marrow to make more stem cells.

## After a stem cell transplant

## **Testing**

Hematopoietic cell transplant (HCT) (also referred to as bone marrow transplant or stem cell transplant), destroys cells in the bone marrow and replaces them with new, healthy blood cells. These blood-forming cells are called blood stem cells or hematopoietic stem cells.

The goal of an HCT is to cure cancer by replacing unhealthy blood stem cells with healthy ones. The transplanted healthy cells may also recognize and attack cancer cells.

This is done by first suppressing the normal stem cells and cancer cells with chemotherapy. Then, healthy stem cells from another person are infused. The healthy stem cells will expand to form new cells, and potentially attack any remaining cancer cells.

If you have thrombocytopenia after a hematopoietic cell transplant, you will be tested for the following:

- Nutritional deficiencies
- Medications and supplements suppressing platelet production
- Infection
- Immune thrombocytopenia
- > Primary or secondary graft failure
- Graft-versus-host disease
- Relapse of hematologic malignancy
- Transplant-associated thrombotic microangiopathy

## **Treatment**

6

If you have thrombocytopenia after a hematopoietic cell transplant, your doctor will try to determine the cause. If a clear reason is found, you will be treated based on symptoms.

If there is no clear cause, the following treatments are options:

- Platelet transfusion
- Clinical trial of thrombopoietin receptor agonists (TPO-RAs)

## Review

- Platelets are an important part of blood. Platelets work with proteins called clotting factors to control bleeding inside our bodies and on our skin.
- Thrombocytopenia occurs when your immune system attacks the platelets in your blood.
- During thrombocytopenia, serious bleeding can occur inside your body or underneath your skin.
- If you have chemotherapy-induced thrombocytopenia, treatment options include platelet transfusion, clinical trial, romiplostim, or reduction in chemotherapy.
- A hematopoietic cell transplant (HCT) destroys cells in the bone marrow then replaces them with new, healthy bloodforming cells from another person.

## 7 Myeloid growth factors

47 G-CSF

49 Review



Myeloid growth factors (MGFs) such as granulocyte colony-stimulating factors (G-CSFs) are used to reduce the occurrence of febrile neutropenia (FN) in those receiving myelosuppressive chemotherapy.

Myeloid growth factors (MGFs) help to stimulate the body to produce certain cells. MGFs are naturally made in the body, or they can be made in a lab. They are used to increase the number of blood cells and prevent infections.

Granulocyte colony-stimulating factors (G-CSFs) are MGFs used to reduce the chances for developing febrile neutropenia (FN) in people receiving myelosuppressive chemotherapy (therapy that kills normal cells and cancer cells in the bone marrow).

## **G-CSF**

Granulocyte colony-stimulating factors (G-CSFs) stimulate the development of granulocytes (white blood cells). They are used to prevent febrile neutropenia when you receive myelosuppressive cancer chemotherapy or to reduce neutropenia associated with a bone marrow transplant.

G-CSFs include the following:

- > Filgrastim (Neupogen®) and biosimilars
- Tbo-filgrastim (Granix<sup>®</sup>)
- Pegfilgrastim (Neulasta®) and biosimilars

In addition to chemotherapy, MGFs such as G-CSFs are used to treat severe febrile neutropenia caused by radiation treatment.

## **Granulocytes**

Three types of granulocytes include neutrophils, basophils, and eosinophils.



Neutrophil



Basophil



Eosinophil

## How it works

G-CSFs stimulate bone marrow to produce more white blood cells. White blood cells help to reduce the risk of infection after some cancer treatments. G-CSF also helps to move stem cells from bone marrow into the blood. Stem cells are special cells that can develop into different cell types including new red blood cells, white blood cells, and platelets.

G-CSFs are used before a stem cell transplant to help stimulate the bone marrow to produce more normal stem cells. Stem cells are then collected and stored while you receive high-dose chemotherapy. Since high-dose chemotherapy stops bone marrow from producing blood cells, the saved stem cells are necessary to reboot the bone marrow to start making different types of blood cells again. The saved stem cells are infused back into the bloodstream to help with the reboot.

## Bone pain

Bone pain is a common side effect of G-CSFs. It is not clear why. It may be due to the body's inflammatory response (immune system's response to an irritant).

Speak to your care team if you experience bone pain. They may be able to prescribe medication to relieve the pain.

## Keep a pain diary

A pain diary is a written record that helps you keep track of when you have pain, how bad it is, what causes it, and what makes it better or worse. Use a pain diary to discuss your pain with your care team. You might be referred to a specialist for pain management.

Include in your pain diary:

- · The time and dose of all medicines
- When pain starts and ends or lessens
- Where you feel pain
- Describe your pain. Is it throbbing, sharp, tingling, shooting, or burning? Is it constant, or does it come and go?
- Does the pain change at different times of day? When?
- Does the pain get worse before or after meals? Does certain food or drink make it better?
- Does the pain get better or worse with activity? What kind of activity?
- Does the pain keep you from falling asleep at night? Does pain wake you up in the night?
- Rate your pain from 0 (no pain) to 10 (worst pain you have ever felt)
- Does pain get in the way of doing the things you enjoy?

## 7

## Review

- Myeloid growth factors (MGFs) help to stimulate the body to produce certain cells.
- G-CSFs are MGFs used to reduce the chances for developing febrile neutropenia in people receiving myelosuppressive chemotherapy.
- G-CSFs stimulate the development of granulocytes (white blood cells).
- In addition to chemotherapy, MGFs such as G-CSFs are used to treat severe neutropenia caused by radiation treatment.

A major side effect of G-CSF is mild to moderate bone pain in 10 to 30 percent of people.

# 8 Making treatment decisions

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It's important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your doctor.

## It's your choice

In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your doctor.

Treatment decisions are very personal. What is important to you may not be important to someone else.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments like surgery or chemotherapy
- Your feelings about pain or side effects such as nausea and vomiting
- Cost of treatment, travel to treatment centers, and time away from work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor. If you take the time to build a relationship with your doctor, it will help you feel supported

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when considering options and making treatment decisions.

## **Second opinion**

It is normal to want to start treatment as soon as possible. While cancer can't be ignored, there is time to have another doctor review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your second opinion.

## **Support groups**

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn't have support groups for people with cancer, check out the websites listed in this book.

## Questions to ask your doctors

Possible questions to ask your doctors are listed on the following pages. Feel free to use these or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment.

## Questions to ask about diagnosis and testing

- What type of anemia do I have? What does this mean in terms of my prognosis and treatment options?
   What tests do I need? What tests are recommended?
   How soon will I know the results and who will explain them to me?
   Where will the tests take place? How long will the tests take?
- 5. Is there a cancer center or hospital nearby that specializes in blood disorders?
- 6. What will you do to make me comfortable during testing?
- 7. How do I prepare for testing?
- 8. Would you give me a copy of the pathology report and other test results?
- 9. Who will talk with me about the next steps? When?
- 10. Will I start treatment before the test results are in?

## Questions to ask about options

- 1. What will happen if I do nothing?
- 2. How do my age, health, and other factors affect my options?
- 3. Am I a candidate for a blood stem cell transplant?
- 4. Am I a candidate for a clinical trial?
- 5. Which option is proven to work best for my type, age, and other risk factors?
- 6. Does any option offer a cure or long-term cancer control? Are my chances any better for one option than another? Less time-consuming? Less expensive?
- 7. How do you know if treatment is working? How will I know if treatment is working?
- 8. What are my options if my treatment stops working?
- 9. Are there any life-threatening side effects of this treatment? How will I be monitored?

11. Can I stop treatment at any time? What will happen if I stop treatment? How will I know

- 10. What should I expect from this treatment?
- when to stop blood transfusions or antibiotics?

## Questions to ask about treatment

- 1. What is my risk for developing anemia, neutropenia, or thrombocytopenia?
- 2. How often will I receive blood tests to determine my risk?
- 3. What are my treatment options based on my risk? What are the benefits and risks?
- 4. Which treatment do you recommend and why?
- 5. How long do I have to decide?
- 6. Will I have to go to the hospital or elsewhere for treatment? How often? How long is each visit? Will I have to stay overnight in the hospital or make travel plans?
- 7. Do I have a choice of when to begin treatment? Can I choose the days and times of treatment? Should I bring someone with me?
- 8. How much will the treatment hurt? What will you do to make me comfortable?
- 9. How much will this treatment cost me? What does my insurance cover? Are there any programs to help me pay for treatment?
- 10. What type of home care will I need? What kind of treatment will I need to do at home?
- 11. What can I do to prevent or relieve side effects? What will you do?
- 12. Which treatment will give me the best quality of life? Which treatment option will extend my life? By how long?

## Questions to ask your doctors about their experience

1. What is your experience treating neutropenia or anemia? 2. What is the experience of those on your team? 3. Do you only treat blood disorders? What else do you treat? 4. I would like to get a second opinion. Is there someone you recommend? 5. I would like another pathologist or hemopathologist to review my blood samples. Is there someone you recommend? 6. How many patients like me (of my age, gender, race) have you treated? 7. Will you be consulting with experts to discuss my health care? Whom will you consult? 8. How many procedures like the one you're suggesting have you done?

## Websites

## Aplastic Anemia and MDS International Foundation (AAMDSIF)

aamds.org/about/MDS

## American Cancer Society®

cancer.org/cancer/myelodysplastic-syndrome

## **American Society of Hematology**

hematology.org/education/patients

## Be The Match®

bethematch.org

## Blood & Marrow Transplant Information Network

bmtinfonet.org

## The Leukemia and Lymphoma Society

<u>lls.org/disease-information/myelodysplastic-</u> syndromes

## National Bone Marrow Transplant Link

nbmtlink.org

## **National Cancer Institute**

<u>Cancer.gov/types/myeloproliferative/patient/myelodysplastic-treatment-pdq</u>

## National Coalition for Cancer Survivorship

Canceradvocacy.org/toolbox

## National Hospice and Palliative Care Organization

nhpco.org/patients-and-caregivers

## U.S. Centers for Disease Control & Prevention

https://www.cdc.gov/cancer/preventinfections/pdf/neutropenia.pdf

## U.S. Department of Health & Human Services

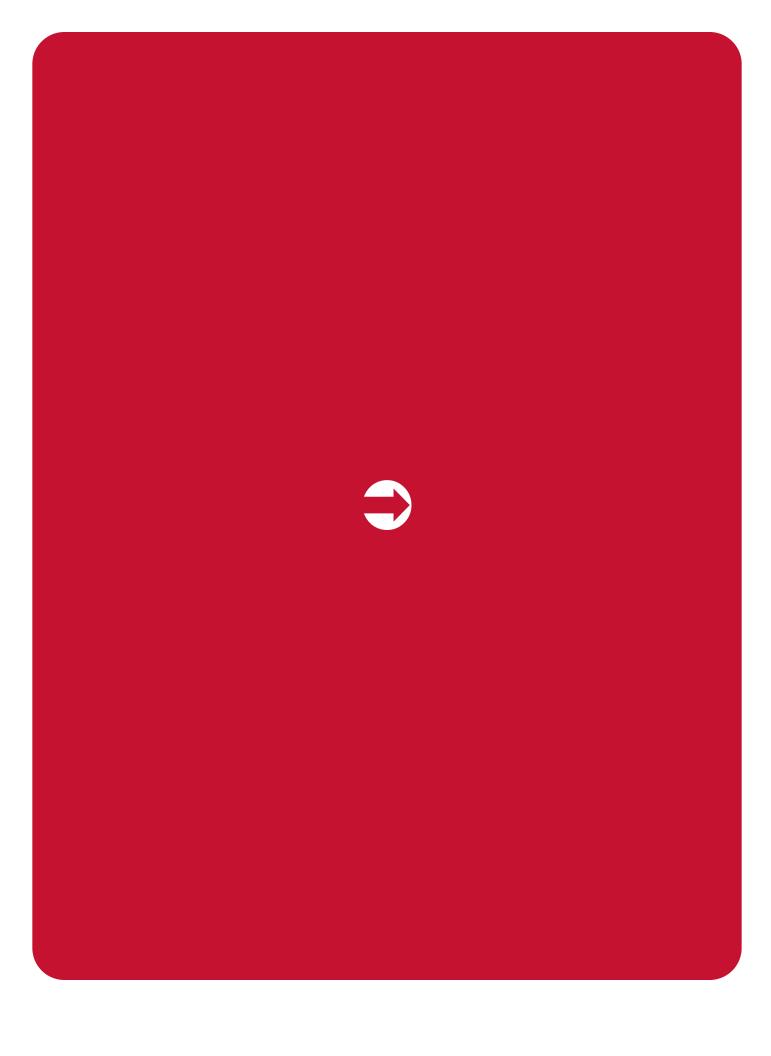
bloodstemcell.hrsa.gov



## Take our <u>survey</u>

And help make the NCCN Guidelines for Patients better for everyone!

**NCCN.org/patients/comments** 



## Words to know

### anemia

A condition in which the number of red blood cells is low.

### blast cell

An immature blood cell.

## blood cell growth factors

Substances that cause new blood cells to grow in the bone marrow.

## blood smear

A test in which a drop of blood is placed on a slide and viewed with a microscope to assess the size, shape, type, and maturity of the blood cells.

## blood stem cell

An immature blood-forming cell from which all other types of blood cells are made. Also called hematopoietic stem cell.

## bone marrow

The soft, sponge-like tissue in the center of most bones where blood cells are made.

## chemotherapy

Treatment with drugs that kill abnormal cells or stop new ones from being made.

## complete blood count (CBC)

A test of the number of blood cells in a sample.

### donor

A person who gives their organs, tissues, or cells to another person.

## erythropoiesis-stimulating agent (ESA)

A drug that tells (stimulates) the bone marrow to make more red blood cells.

## erythropoietin (EPO)

A substance that is made naturally in the body and that tells (stimulates) the bone marrow to make more red blood cells.

## fatigue

Severe tiredness despite getting enough sleep that limits one's ability to function.

## febrile neutropenia (FN)

Fever during a period of significant neutropenia.

## granulocyte colony-stimulating factor (G-CSF)

A substance that helps (stimulates) the bone marrow to make more white blood cells called neutrophils. It is made naturally in the body but can also be made in a lab.

## hematopoiesis

The production of blood cells and platelets, which occurs in the bone marrow.

## hematopoietic stem cell or hematopoietic cell

An immature blood-forming cell from which all other types of blood cells are made. Also called blood stem cell.

## hemoglobin

A protein in red blood cells that carries oxygen.

## high-intensity chemotherapy

Treatment with high doses of strong cancer drugs that are more likely to cause severe side effects.

### hormone

A chemical in the body that activates cells or organs.

## immune response

The action of the body's natural defense against infections and disease in response to foreign substances.

## Words to know

## immune system

The body's natural defense against infection and disease.

### iron

A mineral that is found in red blood cells and that the body needs to make new red blood cells.

## lymphocyte

A type of white blood cell that helps protect the body from infection and disease.

## mean corpuscular volume (MCV)

The average size of your red blood cells.

## mesenchymal stem cells

Stem cells found in bone marrow that are important for making and repairing skeletal tissues, such as cartilage, bone and the fat found in bone marrow.

## myeloid growth factors (MGFs)

Molecules that play important roles in the growth, survival, and differentiation of blood progenitor cells, as well as in the functional activation of mature cells.

## neutropenia

A condition in which the number of white blood cells called neutrophils is low.

## neutrophil

A type of white blood cell that helps fight infections and has small particles (granules).

## platelet

A type of blood cell that helps control bleeding.

## red blood cell (RBC)

A type of blood cell that carries oxygen from the lungs to the rest of the body.

## red blood cell growth factor

A substance that causes new red blood cells to grow in the bone marrow. It is made naturally in the body but can also be made in a lab to use as treatment.

## red blood cell transfusion

A slow injection of red blood cells into a vein.

## regimen

A treatment plan that specifies the dose, schedule, and duration of treatment.

## reticulocyte

Younger (precursor) cells that become mature red blood cells.

### transfusion

A slow injection of whole blood or parts of blood into a vein.

## white blood cell (WBC)

A type of blood cell that helps fight infections in the body.

## white blood cell growth factor

A substance that causes new white blood cells to grow in the bone marrow. It is made naturally in the body but can also be made in a lab to use as treatment.

## **NCCN Contributors**

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hematopoietic Growth Factors, Version 1.2021. It was adapted, reviewed, and published with help from the following people:

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## **NCCN Cancer Centers**

Abramson Cancer Center at the University of Pennsylvania Philadelphia, Pennsylvania 800.789.7366 • pennmedicine.org/cancer

Fred & Pamela Buffett Cancer Center Omaha, Nebraska 402.559.5600 • unmc.edu/cancercenter

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer
Center and Cleveland Clinic Taussig
Cancer Institute
Cleveland, Ohio
800.641.2422 • UH Seidman Cancer Center
uhhospitals.org/services/cancer-services
866.223.8100 • CC Taussig Cancer Institute
my.clevelandclinic.org/departments/cancer
216.844.8797 • Case CCC
case.edu/cancer

City of Hope National Medical Center Los Angeles, California 800.826.4673 • cityofhope.org

Dana-Farber/Brigham and
Women's Cancer Center |
Massachusetts General Hospital
Cancer Center
Boston, Massachusetts
617.732.5500
youhaveus.org
617.726.5130
massgeneral.org/cancer-center

Duke Cancer Institute Durham, North Carolina 888.275.3853 • <u>dukecancerinstitute.org</u>

Fox Chase Cancer Center *Philadelphia, Pennsylvania* 888.369.2427 • foxchase.org

Huntsman Cancer Institute at the University of Utah Salt Lake City, Utah 800.824.2073 huntsmancancer.org

Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance Seattle, Washington 206.606.7222 • seattlecca.org 206.667.5000 • fredhutch.org The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins Baltimore, Maryland 410.955.8964

www.hopkinskimmelcancercenter.org

Robert H. Lurie Comprehensive Cancer Center of Northwestern University Chicago, Illinois 866.587.4322 • cancer.northwestern.edu

Mayo Clinic Cancer Center Phoenix/Scottsdale, Arizona Jacksonville, Florida Rochester, Minnesota 480.301.8000 • Arizona 904.953.0853 • Florida 507.538.3270 • Minnesota mayoclinic.org/cancercenter

Memorial Sloan Kettering Cancer Center New York, New York 800.525.2225 • mskcc.org

Moffitt Cancer Center *Tampa, Florida* 888.663.3488 • moffitt.org

The Ohio State University
Comprehensive Cancer Center James Cancer Hospital and
Solove Research Institute
Columbus, Ohio
800.293.5066 • cancer.osu.edu

O'Neal Comprehensive Cancer Center at UAB Birmingham, Alabama 800.822.0933 • uab.edu/onealcancercenter

Roswell Park Comprehensive Cancer Center Buffalo, New York 877.275.7724 • roswellpark.org

Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine St. Louis, Missouri 800.600.3606 • siteman.wustl.edu

St. Jude Children's Research Hospital/ The University of Tennessee Health Science Center Memphis, Tennessee 866.278.5833 • stjude.org 901.448.5500 • uthsc.edu Stanford Cancer Institute Stanford, California 877.668.7535 • cancer.stanford.edu

UC Davis Comprehensive Cancer Center Sacramento, California 916.734.5959 | 800.770.9261 health.ucdavis.edu/cancer

UC San Diego Moores Cancer Center La Jolla, California 858.822.6100 • cancer.ucsd.edu

UCLA Jonsson Comprehensive Cancer Center Los Angeles, California 310.825.5268 • cancer.ucla.edu

UCSF Helen Diller Family Comprehensive Cancer Center San Francisco, California 800.689.8273 • cancer.ucsf.edu

University of Colorado Cancer Center Aurora, Colorado 720.848.0300 • coloradocancercenter.org

University of Michigan Rogel Cancer Center Ann Arbor, Michigan 800.865.1125 • rogelcancercenter.org

The University of Texas MD Anderson Cancer Center Houston, Texas 844.269.5922 • mdanderson.org

University of Wisconsin Carbone Cancer Center Madison, Wisconsin 608.265.1700 • uwhealth.org/cancer

UT Southwestern Simmons Comprehensive Cancer Center Dallas, Texas 214.648.3111 • utsouthwestern.edu/simmons

Vanderbilt-Ingram Cancer Center Nashville, Tennessee 877.936.8422 • vicc.org

Yale Cancer Center/ Smilow Cancer Hospital New Haven, Connecticut 855.4.SMILOW • yalecancercenter.org

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# Anemia and Neutropenia

2021

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