**URINARY TRACT INFECTION (UTI)**

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## Overview

A urinary tract infection (UTI) is an infection in any part of the urinary system. The urinary system includes the kidneys, ureters, bladder and urethra. Most infections involve the lower urinary tract — the bladder and the urethra.

Women are at greater risk of developing a UTI than are men. If an infection is limited to the bladder, it can be painful and annoying. But serious health problems can result if a UTI spreads to the kidneys.

Health care providers often treat urinary tract infections with antibiotics. You can also take steps to lower the chance of getting a UTI in the first place.

Symptoms

UTIs don't always cause symptoms. When they do, they may include:

* A strong urge to urinate that doesn't go away
* A burning feeling when urinating
* Urinating often, and passing small amounts of urine
* Urine that looks cloudy
* Urine that appears red, bright pink or cola-colored — signs of blood in the urine
* Strong-smelling urine
* Pelvic pain, in women — especially in the center of the pelvis and around the area of the pubic bone

In older adults, UTIs may be overlooked or mistaken for other conditions.

### Types of urinary tract infections

Each type of UTI may result in more-specific symptoms. The symptoms depend on which part of the urinary tract is affected.

| **Part of urinary tract affected** | **Signs and symptoms** |
| --- | --- |
| Kidneys | * Back or side pain * High fever * Shaking and chills * Nausea * Vomiting |
| Bladder | * Pelvic pressure * Lower belly discomfort * Frequent, painful urination * Blood in urine |
| Urethra | * Burning with urination * Discharge |

### When to see a doctor

Contact your health care provider if you have symptoms of a UTI.

## Causes

UTIs typically occur when bacteria enter the urinary tract through the urethra and begin to spread in the bladder. The urinary system is designed to keep out bacteria. But the defenses sometimes fail. When that happens, bacteria may take hold and grow into a full-blown infection in the urinary tract.

The most common UTIs occur mainly in women and affect the bladder and urethra.

* **Infection of the bladder.** This type of UTI is usually caused by Escherichia coli (E. coli). E. coli is a type of bacteria commonly found in the gastrointestinal (GI) tract. But sometimes other bacteria are the cause.

Having sex also may lead to a bladder infection, but you don't have to be sexually active to develop one. All women are at risk of bladder infections because of their anatomy. In women, the urethra is close to the anus. And the urethral opening is close to the bladder. This makes it easier for bacteria around the anus to enter the urethra and to travel to the bladder.

* **Infection of the urethra.** This type of UTI can happen when GI bacteria spread from the anus to the urethra. An infection of the urethra can also be caused by sexually transmitted infections. They include herpes, gonorrhea, chlamydia and mycoplasma. This can happen because women's urethras are close to the vagina.

## Risk factors

UTIs are common in women. Many women experience more than one UTI during their lifetimes.

Risk factors for UTIs that are specific to women include:

* **Female anatomy.** Women have a shorter urethra than men do. As a result, there's less distance for bacteria to travel to reach the bladder.
* **Sexual activity.** Being sexually active tends to lead to more UTIs. Having a new sexual partner also increases risk.
* **Certain types of birth control.** Using diaphragms for birth control may increase the risk of UTIs. Using spermicidal agents also can increase risk.
* **Menopause.** After menopause, a decline in circulating estrogen causes changes in the urinary tract. The changes can increase the risk of UTIs.

Other risk factors for UTIs include:

* **Urinary tract problems.** Babies born with problems with their urinary tracts may have trouble urinating. Urine can back up in the urethra, which can cause UTIs.
* **Blockages in the urinary tract.** Kidney stones or an enlarged prostate can trap urine in the bladder. As a result, risk of UTIs is higher.
* **A suppressed immune system.** Diabetes and other diseases can impair the immune system — the body's defense against germs. This can increase the risk of UTIs.
* **Catheter use.** People who can't urinate on their own often must use a tube, called a catheter, to urinate. Using a catheter increases the risk of UTIs. Catheters may be used by people who are in the hospital. They may also be used by people who have neurological problems that make it difficult to control urination or who are paralyzed.
* **A recent urinary procedure.** Urinary surgery or an exam of your urinary tract that involves medical instruments can both increase the risk of developing a UTI.

## Complications

When treated promptly and properly, lower urinary tract infections rarely lead to complications. But left untreated, UTIs can cause serious health problems.

Complications of a UTI may include:

* Repeated infections, which means you have two or more UTIs within six months or three or more within a year. Women are especially prone to having repeated infections.
* Permanent kidney damage from a kidney infection due to an untreated UTI.
* Delivering a low birth weight or premature infant when a UTI occurs during pregnancy.
* A narrowed urethra in men from having repeated infections of the urethra.
* Sepsis, a potentially life-threatening complication of an infection. This is a risk especially if the infection travels up the urinary tract to the kidneys.

## Prevention

These steps may help lower the risk of UTIs:

* **Drink plenty of liquids, especially water.** Drinking water helps dilute the urine. That leads to urinating more often — allowing bacteria to be flushed from the urinary tract before an infection can begin.
* **Try cranberry juice.** Studies that look into whether cranberry juice prevents UTIs aren't final. However, drinking cranberry juice is likely not harmful.
* **Wipe from front to back.** Do this after urinating and after a bowel movement. It helps prevent the spread of bacteria from the anus to the vagina and urethra.
* **Empty your bladder soon after having sex.** Also drink a full glass of water to help flush bacteria.
* **Avoid potentially irritating feminine products.** Using them in the genital area can irritate the urethra. These products include deodorant sprays, douches and powders.
* **Change your birth control method.** Diaphragms, unlubricated condoms or condoms treated with spermicide can contribute to bacterial growth.

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## Diagnosis

Tests and procedures used to diagnose urinary tract infections include:

* **Analyzing a urine sample.** Your health care provider may ask for a urine sample. The urine will be looked at in a lab to check for white blood cells, red blood cells or bacteria. You may be told to first wipe your genital area with an antiseptic pad and to collect the urine midstream. The process helps prevent the sample from being contaminated.
* **Growing urinary tract bacteria in a lab.** Lab analysis of the urine is sometimes followed by a urine culture. This test tells your provider what bacteria are causing the infection. It can let your provider know which medications will be most effective.
* **Creating images of the urinary tract.** Recurrent UTIs may be caused by a structural problem in the urinary tract. Your health care provider may order an ultrasound, a CT scan or MRI to look for this issue. A contrast dye may be used to highlight structures in your urinary tract.
* **Using a scope to see inside the bladder.** If you have recurrent UTIs, your health care provider may perform a cystoscopy. The test involves using a long, thin tube with a lens, called a cystoscope, to see inside the urethra and bladder. The cystoscope is inserted in the urethra and passed through to the bladder.

## Treatment

Antibiotics usually are the first treatment for urinary tract infections. Your health and the type of bacteria found in your urine determine which medicine is used and how long you need to take it.

### Simple infection

Medicines commonly used for simple UTIs include:

* Trimethoprim and sulfamethoxazole (Bactrim, Bactrim DS)
* Fosfomycin (Monurol)
* Nitrofurantoin (Macrodantin, Macrobid, Furadantin)
* Cephalexin
* Ceftriaxone

The group of antibiotics known as fluoroquinolones isn't commonly recommended for simple UTIs. These drugs include ciprofloxacin (Cipro), levofloxacin and others. The risks of these drugs generally outweigh the benefits for treating uncomplicated UTIs.

In cases of a complicated UTI or kidney infection, your health care provider might prescribe a fluoroquinolone medicine if there are no other treatment options.

Often, UTI symptoms clear up within a few days of starting treatment. But you may need to continue antibiotics for a week or more. Take all of the medicine as prescribed.

For an uncomplicated UTI that occurs when you're otherwise healthy, your health care provider may recommend a shorter course of treatment. That may mean taking an antibiotic for 1 to 3 days. Whether a short course of treatment is enough to treat your infection depends on your symptoms and medical history.

Your health care provider also may give you a pain reliever to take that can ease burning while urinating. But pain usually goes away soon after starting an antibiotic.

### Frequent infections

If you have frequent UTIs, your health care provider may recommend:

* Low-dose antibiotics. You might take them for six months or longer.
* Diagnosing and treating yourself when symptoms occur. You'll also be asked to stay in touch with your provider.
* Taking a single dose of antibiotic after sex if UTIs are related to sexual activity.
* Vaginal estrogen therapy if you've reached menopause.

### Severe infection

For a severe UTI, you may need IV antibiotics in a hospital.

**Outlook / Prognosis**

**What can I expect if I have a urinary tract infection?**

The outlook for urinary tract infections is good. Most UTIs usually respond very well to treatment. A UTI can be annoying or uncomfortable before you start treatment. However, once a healthcare provider identifies the bacteria and prescribes the appropriate antibiotic, your symptoms should improve quickly.

It’s important to finish all of the antibiotics that your healthcare provider prescribes. If you have frequent UTIs or your symptoms aren’t improving, your provider may test to see if your infection is resistant to antibiotics. Antibiotic-resistant infections may require IV antibiotics or other treatments.

## Lifestyle and home remedies

Urinary tract infections can be painful, but you can take steps to ease discomfort until antibiotics treat the infection. Follow these tips:

* **Drink plenty of water.** Water helps to dilute your urine and flush out bacteria.
* **Avoid drinks that may irritate your bladder.** Avoid coffee, alcohol, and soft drinks containing citrus juices or caffeine until the infection has cleared. They can irritate your bladder and tend to increase the need to urinate.
* **Use a heating pad.** Apply a warm, but not hot, heating pad to your belly to help with bladder pressure or discomfort.

## Alternative medicine

Many people drink cranberry juice to prevent UTIs. There's some indication that cranberry products, in either juice or tablet form, may have properties that fight an infection. Researchers continue to study the ability of cranberry juice to prevent UTIs, but results aren't final.

There's little harm in drinking cranberry juice if you feel it helps you prevent UTIs, but watch the calories. For most people, drinking cranberry juice is safe. However, some people report an upset stomach or diarrhea.

But don't drink cranberry juice if you're taking blood-thinning medication, such as warfarin (Jantovin).

## Preparing for your appointment

Your primary care provider, nurse practitioner or other health care provider can treat most UTIs. If you have frequent UTIs or a chronic kidney infection, you may be referred to a health care provider who specializes in urinary disorders. This type of doctor is called a urologist. Or you may see a health care provider who specializes in kidney disorders. This type of doctor is called a nephrologist.

### What you can do

To get ready for your appointment:

* **Ask if there's anything you need to do in advance,** such as collect a urine sample.
* **Take note of your symptoms,** even if you're not sure they're related to a UTI.
* **Make a list of all the medicines,** vitamins or other supplements that you take.
* **Write down questions to ask** your health care provider.

For a UTI, basic questions to ask your provider include:

* What's the most likely cause of my symptoms?
* Are there any other possible causes?
* Do I need any tests to confirm the diagnosis?
* What factors do you think may have contributed to my UTI?
* What treatment approach do you recommend?
* If the first treatment doesn't work, what will you recommend next?
* Am I at risk of complications from this condition?
* What is the risk that this problem will come back?
* What steps can I take to lower the risk of the infection coming back?
* Should I see a specialist?

Don't hesitate to ask other questions as they occur to you during your appointment.

### What to expect from your doctor

Your health care provider will likely ask you several questions, including:

* When did you first notice your symptoms?
* Have you ever been treated for a bladder or kidney infection?
* How severe is your discomfort?
* How often do you urinate?
* Are your symptoms relieved by urinating?
* Do you have low back pain?
* Have you had a fever?
* Have you noticed vaginal discharge or blood in your urine?
* Are you sexually active?
* Do you use contraception? What kind?
* Could you be pregnant?
* Are you being treated for any other medical conditions?
* Have you ever used a catheter?

**GLOMERULONEPHRITIS**

## Overview

Glomerulonephritis (gloe-MER-u-loe-nuh-FRY-tis) is inflammation of the tiny filters in the kidneys (glomeruli). The excess fluid and waste that glomeruli (gloe-MER-u-lie) remove from the bloodstream exit the body as urine. Glomerulonephritis can come on suddenly (acute) or gradually (chronic).

Glomerulonephritis occurs on its own or as part of another disease, such as lupus or diabetes. Severe or prolonged inflammation associated with glomerulonephritis can damage the kidneys. Treatment depends on the type of glomerulonephritis you have.

## Symptoms

Signs and symptoms of glomerulonephritis may vary depending on whether you have the acute or chronic form and the cause. You may notice no symptoms of chronic disease. Your first indication that something is wrong might come from the results of a routine urine test (urinalysis).

Glomerulonephritis signs and symptoms may include:

* Pink or cola-colored urine from red blood cells in your urine (hematuria).
* Foamy or bubbly urine due to excess protein in the urine (proteinuria).
* High blood pressure (hypertension).
* Fluid retention (edema) with swelling evident in your face, hands, feet and abdomen.
* Urinating less than usual.
* Nausea and vomiting.
* Muscle cramps.
* Fatigue.

### When to see a doctor

Make an appointment with your health care provider promptly if you have signs or symptoms of glomerulonephritis.

## Causes

Many conditions can cause glomerulonephritis. Sometimes the disease runs in families and sometimes the cause is unknown. Factors that can lead to inflammation of the glomeruli include the following conditions.

### Infections

Infectious diseases can directly or indirectly lead to glomerulonephritis. These infections include:

* **Post-streptococcal glomerulonephritis.** Glomerulonephritis may develop a week or two after recovery from a strep throat infection or, rarely, a skin infection caused by a streptococcal bacteria (impetigo). Inflammation occurs when antibodies to the bacteria build up in the glomeruli. Children are more likely to develop post-streptococcal glomerulonephritis than are adults, and they're also more likely to recover quickly.
* **Bacterial endocarditis.** Bacterial endocarditis is an infection of the inner lining of your heart's chambers and valves. It isn't clear whether the inflammation in the kidneys is the result of immune system activity alone or other factors.
* **Viral kidney infections.** Viral infections of the kidney, such as hepatitis B and hepatitis C, cause inflammation of the glomeruli and other kidney tissues.
* **HIV.** Infection with HIV, the virus that causes AIDS, can lead to glomerulonephritis and progressive kidney damage, even before the onset of AIDS.

### Autoimmune diseases

Autoimmune diseases are illnesses caused by the immune system attacking healthy tissues. Autoimmune diseases that may cause glomerulonephritis include:

* **Lupus.** A chronic inflammatory disease, systemic lupus erythematosus can affect many parts of your body, including your skin, joints, kidneys, blood cells, heart and lungs.
* **Goodpasture's syndrome.** In this rare disorder, also known as anti-GBM disease, the immune system creates antibodies to tissues in the lungs and kidneys. It can cause progressive and permanent damage to the kidneys.
* **IgA nephropathy.** Immunoglobulin A (IgA) is an antibody that's a first line of defense against infectious agents. IgA nephropathy occurs when deposits of the antibody accumulate in the glomeruli. The inflammation and subsequent damage may go undetected for a long time. The most common symptom is blood in the urine.

### Vasculitis

Vasculitis is inflammation of blood vessels. Types of vasculitis that can cause glomerulonephritis include:

* **Polyarteritis.** This form of vasculitis affects medium and small blood vessels in many parts of your body, including the kidneys, skin, muscles, joints and digestive tract.
* **Granulomatosis with polyangiitis.** This form of vasculitis, formerly known as Wegener's granulomatosis, affects small and medium blood vessels in your lungs, upper airways and kidneys.

### Sclerotic conditions

Some diseases or conditions cause scarring of the glomeruli that results in poor and declining kidney function. These include:

* **High blood pressure.** Long-term, poorly managed high blood pressure can cause scarring and inflammation of the glomeruli. Glomerulonephritis inhibits the kidney's role in regulating blood pressure.
* **Diabetic kidney disease (diabetic nephropathy).** High blood sugar levels contribute to scarring of the glomeruli and increase the rate of blood flow through the nephrons.
* **Focal segmental glomerulosclerosis.** In this condition, scarring is scattered among some of the glomeruli. This may be the result of another disease, or it may occur for no known reason.

### Other causes

Infrequently, chronic glomerulonephritis runs in families. One inherited form, Alport syndrome, also might impair hearing or vision.

Glomerulonephritis is associated with certain cancers, such as gastric cancer, lung cancer and chronic lymphocytic leukemia.

## Risk factors

Some autoimmune diseases are linked with glomerulonephritis.

## Complications

Glomerulonephritis affects the ability of nephrons to filter the bloodstream efficiently. The breakdown in filtering results in:

* Accumulation of wastes or toxins in the bloodstream.
* Poor regulation of essential minerals and nutrients.
* Loss of red blood cells.
* Loss of blood proteins.

Possible complications of glomerulonephritis include:

* **Acute kidney failure.** Acute kidney failure is the sudden, rapid decline in kidney function, often associated with an infectious cause of glomerulonephritis. The accumulation of waste and fluids can be life-threatening if not treated promptly with an artificial filtering machine (dialysis). The kidneys often resume typical function after recovery.
* **Chronic kidney disease.** Persistent inflammation results in long-term damage and declining function of the kidneys. Chronic kidney disease is generally defined as kidney damage or decreased function for three or more months. Chronic kidney disease may advance to end-stage kidney disease, which requires either dialysis or a kidney transplant.
* **High blood pressure.** Damage to the glomeruli from inflammation or scarring can lead to increased blood pressure.
* **Nephrotic syndrome.** Nephrotic syndrome is a condition in which there is too much blood protein in urine and too little in the bloodstream. These proteins play a role in regulating fluids and cholesterol levels. A drop in blood proteins results in high cholesterol, high blood pressure and swelling (edema) of the face, hands, feet and abdomen. In rare instances, nephrotic syndrome may cause a blood clot in a kidney blood vessel.

## Prevention

There may be no way to prevent some forms of glomerulonephritis. However, here are some steps that might be beneficial:

* Seek prompt treatment of a strep infection with a sore throat or impetigo.
* To prevent infections that can lead to some forms of glomerulonephritis, such as HIV and hepatitis, follow safe-sex guidelines and avoid intravenous drug use.
* Control high blood pressure, which lessens the likelihood of damage to your kidneys from hypertension.
* Control your blood sugar to help prevent diabetic nephropathy.

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## Diagnosis

Glomerulonephritis may be identified with tests if you have an acute illness or during routine testing during a wellness visit or an appointment managing a chronic disease, such as diabetes. Tests to assess your kidney function and make a diagnosis of glomerulonephritis include:

* **Urine test.** A urinalysis can reveal signs of poor kidney function, such as red blood cells and proteins that should not be in urine or white blood cells that are a sign of inflammation. There also may be a lack of the expected levels of waste products.
* **Blood tests.** Analysis of blood samples can reveal higher than expected levels of waste products in the bloodstream, the presence of antibodies that may indicate an autoimmune disorder, bacterial or viral infection, or blood sugar levels indicating diabetes.
* **Imaging tests.** If your doctor detects evidence of kidney disease, he or she may recommend imaging tests that may show an irregularity in the shape or size of the kidney. These tests may be an X-ray, an ultrasound exam or a CT scan.
* **Kidney biopsy.** This procedure involves using a special needle to extract small pieces of kidney tissue to look at under a microscope. A biopsy is used to confirm a diagnosis and to assess the degree and nature of tissue damage.

**Differential Diagnoses**

Following are some important differentials to be considered while making the diagnosis of glomerulonephritis:

* Acute kidney injury
* Crescentic glomerulonephritis
* Diffuse proliferative glomerulonephritis
* Focal segmental glomerulonephritis
* Glomerulonephritis associated with nonstreptococcal infection
* Goodpasture syndrome
* Lupus nephritis
* Membranoproliferative glomerulonephritis
* Poststreptococcal glomerulonephritis
* Rapidly progressive glomerulonephritis

The following renal syndromes frequently mimic the early stages of acute GN:

* Idiopathic hematuria
* Chronic GN with an acute exacerbation
* Anaphylactoid purpura with nephritis
* Familial nephritis

## Prognosis

**Among the Nephritic Spectrum Diseases**

* PSGN has an excellent prognosis, especially in children with complete recovery, usually occurring within 6 to 8 weeks. In adults, around 50% of the patients continue to have reduced renal function, hypertension, or persistent proteinuria.
* Frequently IgA nephropathy has a benign course. Others gradually progress to ESRD, with ESRD frequency increasing with age. Prognosis is predictable, to some extent, based on the Oxford classification. Additionally, on presentation, nephrotic range proteinuria, hypertension, high serum creatinine level, and widespread intestinal fibrosis of the kidneys indicate a poor prognosis.
* Henoch-Schönlein purpura is typically a self-limited illness that demonstrates an excellent prognosis in patients without renal involvement. The majority of patients fully recover in four weeks. The long-term morbidity of Henoch-Schönlein purpura depends on the extent of renal involvement. Approximately 1% of patients with Henoch-Schönlein purpura will develop ESRD and require renal transplantation.
* With timely and avid treatment, pauci-immune GN usually remits (75% of cases). But if left untreated, it carries a very poor prognosis.
* Membranoproliferative glomerulonephritis progresses to ESRD inevitably, despite therapy. Also, the frequency of recurrence is high even after a kidney transplant.

**Among the Nephrotic Spectrum Diseases**

* Minimal change disease has a very good prognosis for all ages if there is a response to corticosteroid therapy. The primary morbidity is related to the adverse effects of the medications
* Approximately a third of patients with membranous nephropathy who have subnephrotic proteinuria respond to conservative management. Spontaneous remission has also been seen in cases of heavy proteinuria. However, in others with features of nephrotic syndrome, remission may take up to 6 months, provided adequate treatment is given.
* Appropriate treatment does slow the progression of HIV-associated nephropathy, but with progression into ESRD, a kidney transplant may be necessary.
* Amyloid light-chain (AL) amyloidosis takes 2 to 3 years for progression towards ESRD, while for amyloid A (AA) amyloidosis, remission can be achieved by identifying and managing the underlying disease.

## Treatment

Treatment of glomerulonephritis and your outcome depend on:

* Whether you have an acute or chronic form of the disease.
* The underlying cause.
* The type and severity of your signs and symptoms.

Some cases of acute glomerulonephritis, especially those that follow an infection with streptococcal bacteria, might improve on their own and require no treatment. If there's an underlying cause — such as high blood pressure, an infection or an autoimmune disease — treatment will be directed to the underlying cause.

In general, the goal of treatment is to protect your kidneys from further damage and to preserve kidney function.

### Therapies for associated kidney failure

Kidney failure is the loss of 85% or more of kidney function. Acute kidney failure due to infection-related glomerulonephritis is treated with dialysis. Dialysis uses a device that works like an artificial, external kidney that filters your blood.

End-stage kidney disease is chronic kidney disease that can only be managed by regular kidney dialysis or a kidney transplant.

## Lifestyle and home remedies

If you have kidney disease, your doctor might recommend certain lifestyle changes:

* Lower your salt intake to prevent or minimize fluid retention, swelling and hypertension.
* Consume less protein and potassium to slow the buildup of wastes in your blood.
* Maintain a healthy weight.
* Take your medications as directed by your health care provider.
* Control your blood sugar level if you have diabetes.
* Quit smoking.

## Coping and support

Living with a chronic illness can tax your emotional resources. If you have chronic glomerulonephritis or chronic kidney failure, you might benefit from joining a support group. A support group can provide both sympathetic listening and useful information.

To find a support group, ask your doctor for a recommendation or contact the National Kidney Foundation to find the chapter nearest you.

## Preparing for your appointment

You'll likely start by seeing your primary care provider. If lab tests reveal that you have kidney damage, you might be referred to a doctor who specializes in kidney problems (nephrologist).

### What you can do

To get ready for your appointment, ask if there's anything you need to do ahead of time, such as limit what you eat and drink. Then make a list of items you'll likely need to discuss with your health care provider:

* **Your symptoms,** including any that seem unrelated to your kidneys or urinary function, and when they began.
* **All your medications and doses,** including vitamins or other supplements that you take.
* **Your key medical history,** including any other medical conditions and family medical history.

Take a family member or friend along, if possible, to help you remember the information you're given.

When you have follow-up appointments after a diagnosis of glomerulonephritis, you may want to ask the following questions:

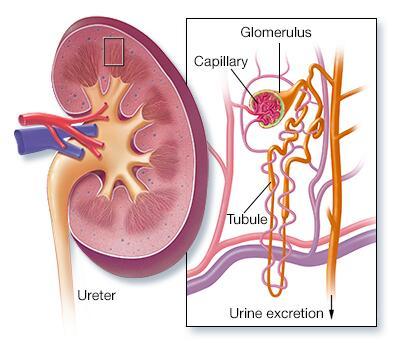
* How well are my kidneys functioning? Has the function changed since the previous exam?
* When should I schedule lab work or another appointment?
* Will I need dialysis?
* What help can I get to manage related conditions, such as support with diet planning or exercise?
* What do I do if I miss a dosage of a prescription?
* When should I call for an appointment or get urgent care?
* Are there brochures or other printed material that I can have? What websites do you recommend?

**Nephrotic syndrome**

## Overview

Nephrotic syndrome is a kidney disorder that causes your body to pass too much protein in your urine.

Nephrotic syndrome is usually caused by damage to the clusters of small blood vessels in your kidneys that filter waste and excess water from your blood. The condition causes swelling, particularly in your feet and ankles, and increases the risk of other health problems.



### Kidney cross section

The kidneys remove waste and excess fluid from your blood through filtering units called nephrons. Each nephron contains a filter (glomerulus) that has a network of tiny blood vessels called capillaries. When blood flows into a glomerulus, tiny molecules — water, essential minerals and nutrients, and wastes — pass through the capillary walls. Large molecules, such as proteins and red blood cells, do not. The filtered solution then passes into another part of the nephron called the tubule. The water, nutrients and minerals your body needs are transferred back to the bloodstream. The excess water and waste become urine that flows to the bladder.

Treatment for nephrotic syndrome includes treating the condition that's causing it and taking medications. Nephrotic syndrome can increase your risk of infections and blood clots. Your doctor might recommend medications and dietary changes to prevent complications.

### Products & Services

## Symptoms

Signs and symptoms of nephrotic syndrome include:

* Severe swelling (edema), particularly around your eyes and in your ankles and feet
* Foamy urine, a result of excess protein in your urine
* Weight gain due to fluid retention
* Fatigue
* Loss of appetite

## When to see a doctor

Make an appointment with your doctor if you have signs or symptoms that worry you.

## Causes

Nephrotic syndrome is usually caused by damage to the clusters of tiny blood vessels (glomeruli) of your kidneys.

The glomeruli filter your blood as it passes through your kidneys, separating things your body needs from those it doesn't. Healthy glomeruli keep blood protein (mainly albumin) — which is needed to maintain the right amount of fluid in your body — from seeping into your urine. When damaged, glomeruli allow too much blood protein to leave your body, leading to nephrotic syndrome.

### Many possible causes

Many diseases and conditions can cause glomerular damage and lead to nephrotic syndrome, including:

* **Diabetic kidney disease.** Diabetes can lead to kidney damage (diabetic nephropathy) that affects the glomeruli.
* **Minimal change disease.** This is the most common cause of nephrotic syndrome in children. Minimal change disease results in abnormal kidney function, but when the kidney tissue is examined under a microscope, it appears normal or nearly normal. The cause of the abnormal function typically can't be determined.
* **Focal segmental glomerulosclerosis.** Characterized by scarring of some of the glomeruli, this condition can result from another disease, a genetic defect or certain medications or occur for no known reason.
* **Membranous nephropathy.** This kidney disorder is the result of thickening membranes within the glomeruli. The thickening is due to deposits made by the immune system. It can be associated with other medical conditions, such as lupus, hepatitis B, malaria and cancer, or it can occur for no known reason.
* **Systemic lupus erythematosus.** This chronic inflammatory disease can lead to serious kidney damage.
* **Amyloidosis.** This disorder occurs when amyloid proteins accumulate in your organs. Amyloid buildup often damages the kidneys' filtering system.

## Risk factors

Factors that can increase your risk of nephrotic syndrome include:

* **Medical conditions that can damage your kidneys.** Certain diseases and conditions increase your risk of developing nephrotic syndrome, such as diabetes, lupus, amyloidosis, reflux nephropathy and other kidney diseases.
* **Certain medications.** Medications that might cause nephrotic syndrome include nonsteroidal anti-inflammatory drugs and drugs used to fight infections.
* **Certain infections.** Infections that increase the risk of nephrotic syndrome include HIV, hepatitis B, hepatitis C and malaria.

## Complications

Possible complications of nephrotic syndrome include:

* **Blood clots.** The inability of the glomeruli to filter blood properly can lead to loss of blood proteins that help prevent clotting. This increases your risk of developing a blood clot in your veins.
* **High blood cholesterol and elevated blood triglycerides.** When the level of the protein albumin in your blood falls, your liver makes more albumin. At the same time, your liver releases more cholesterol and triglycerides.
* **Poor nutrition.** Loss of too much blood protein can result in malnutrition. This can lead to weight loss, which can be masked by edema. You may also have too few red blood cells (anemia), low blood protein levels and low levels of vitamin D.
* **High blood pressure.** Damage to your glomeruli and the resulting buildup of excess body fluid can raise your blood pressure.
* **Acute kidney injury.** If your kidneys lose their ability to filter blood due to damage to the glomeruli, waste products can build up quickly in your blood. If this happens, you might need emergency dialysis — an artificial means of removing extra fluids and waste from your blood — typically with an artificial kidney machine (dialyzer).
* **Chronic kidney disease.** Nephrotic syndrome can cause your kidneys to lose their function over time. If kidney function falls low enough, you might need dialysis or a kidney transplant.
* **Infections.** People with nephrotic syndrome have an increased risk of infections.

## Diagnosis

Tests and procedures used to diagnose nephrotic syndrome include:

* **Urine tests.** A urinalysis can reveal abnormalities in your urine, such as large amounts of protein. You might be asked to collect urine samples over 24 hours.
* **Blood tests.** A blood test can show low levels of the protein albumin and often decreased levels of blood protein overall. Loss of albumin is often associated with an increase in blood cholesterol and blood triglycerides. The creatinine and urea nitrogen levels in your blood also might be measured to assess your overall kidney function.
* **Kidney biopsy.** Your doctor might recommend removing a small sample of kidney tissue for testing. During a kidney biopsy, a needle is inserted through your skin and into your kidney. Kidney tissue is collected and sent to a lab for testing.

## Treatment

Treatment for nephrotic syndrome involves treating any medical condition that might be causing your nephrotic syndrome. Your doctor might also recommend medications and changes in your diet to help control your signs and symptoms or treat complications of nephrotic syndrome.

Medications might include:

* **Blood pressure medications.** Drugs called angiotensin-converting enzyme (ACE) inhibitors reduce blood pressure and the amount of protein released in urine. Medications in this category include lisinopril (Prinivil, Qbrelis, Zestril), benazepril (Lotensin), captopril and enalapril (Vasotec).

Another group of drugs that works similarly is called angiotensin II receptor blockers (ARBs) and includes losartan (Cozaar) and valsartan (Diovan). Other medications, such as renin inhibitors, also might be used, though angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) are generally used first.

* **Water pills (diuretics).** These help control swelling by increasing your kidneys' fluid output. Diuretic medications typically include furosemide (Lasix). Others include spironolactone (Aldactone, Carospir) and thiazides, such as hydrochlorothiazide or metolazone (Zaroxolyn).
* **Cholesterol-reducing medications.** Statins can help lower cholesterol levels. However, it's not clear whether cholesterol-lowering medications can improve the outcomes for people with nephrotic syndrome, such as avoiding heart attacks or decreasing the risk of early death.

Statins include atorvastatin (Lipitor), fluvastatin (Lescol XL), lovastatin (Altoprev), pravastatin (Pravachol), rosuvastatin (Crestor, Ezallor) and simvastatin (Zocor).

* **Blood thinners (anticoagulants).** These might be prescribed to decrease your blood's ability to clot, especially if you've had a blood clot. Anticoagulants include heparin, warfarin (Coumadin, Jantoven), dabigatran (Pradaxa), apixaban (Eliquis) and rivaroxaban (Xarelto).
* **Immune system-suppressing medications.** Medications to control the immune system, such as corticosteroids, can decrease the inflammation that accompanies some of the conditions that can cause nephrotic syndrome. Medications include rituximab (Rituxan), cyclosporine and cyclophosphamide.

## Self care

Changes to your diet might help with nephrotic syndrome. Your doctor might refer you to a dietitian, who might recommend that you do the following:

* Choose lean sources of protein. Plant-based protein is helpful in kidney disease.
* Reduce the amount of fat and cholesterol in your diet to help control your blood cholesterol levels.
* Eat a low-salt diet to help control swelling.
* Reduce the amount of liquid in your diet.

## Preparing for your appointment

Start by seeing your primary care doctor. If your doctor suspects you or your child has a kidney problem, such as nephrotic syndrome, you might be referred to a doctor who specializes in the kidneys (nephrologist).

Here's some information to help you get ready for your appointment.

### What you can do

When you make the appointment, ask if there's anything you need to do in advance, such as restrict your diet. Take a family member or friend along, if possible, to help you remember the information you'll be given.

Make a list of:

* **Your or your child's symptoms** and when they began
* **Key personal information,** including major stresses or recent life changes
* **All medications, vitamins or other supplements** you or your child takes, including doses
* **Questions to ask** your doctor

For nephrotic syndrome, some questions to ask include:

* What's the most likely cause of my or my child's nephrotic syndrome?
* What tests do I or my child need?
* Is this condition likely temporary?
* What are the treatment options? And which do you recommend?
* Are there changes I can make to my or my child's diet? Could consulting a dietitian help?
* How can I best manage this condition with my or my child's other medical conditions?
* Are there brochures or other printed material that I can have? What websites do you recommend?

### What to expect from your doctor

Your doctor is likely to ask you questions, such as:

* Do symptoms come and go, or do you have them all the time?
* How severe are the symptoms?
* Does anything seem to improve the symptoms?

**INFECTIOUS DISEASES**

# About Influenza

## KEY POINTS

* Flu is a contagious respiratory illness caused by influenza viruses
* Flu can cause mild to severe illness
* Most experts believe that flu viruses spread mainly by tiny droplets made when people with flu cough, sneeze, or talk
* The first and most important step in preventing flu is to get a flu vaccine each year.

## Understanding Influenza

Flu is a contagious respiratory illness caused by influenza viruses that infect the nose, throat, and sometimes the lungs. It can cause mild to severe illness, and at times can lead to death. The best way to prevent flu is by getting a flu vaccine each year.

## Symptoms

Flu can cause mild to severe illness, and at times can lead to death. Flu symptoms usually come on suddenly. People who have flu often feel some or all of these signs and symptoms:

* fever\* or feeling feverish/chills
* cough
* sore throat
* runny or stuffy nose
* muscle or body aches
* headaches
* fatigue (tiredness)
* some people may have vomiting and diarrhea, though this is more common in children than adults.

\*It's important to note that not everyone with flu will have a fever.

**Not everyone with flu has symptoms**

Some people with influenza virus infections do not develop any symptoms at all. A household study conducted during the 2017-2023 flu seasons found that 8 percent of people who tested positive for flu did not have symptoms.

## How long it takes for signs to show

### **Period of Contagiousness**

You may be able to spread flu to someone else before you know you are sick, as well as when you are sick with symptoms.

* People with flu are most contagious during the first three days of their illness.
* Some otherwise healthy adults may be able to infect others beginning one day **before**symptoms develop and up to five to seven days **after**becoming sick.
* Some people, including young children and people with weakened immune systems, may be contagious for longer periods of time.

### **Onset of Symptoms**

The time from when a person is exposed and infected with influenza virus to when symptoms begin is about two days but can range from about one to four days.

## People at risk

Anyone can get flu (including healthy people), and serious problems related to flu can happen at any age, but some people are at higher risk of developing serious flu-related complications if they get sick. This includes people 65 years and older, people of any age with certain chronic medical conditions (such as asthma, diabetes, or heart disease), people with a body mass index (BMI) of 40 kg/m2 or higher, those who are pregnant, and children younger than five years.

## How it spreads

Most experts believe that flu viruses spread mainly by tiny droplets made when people with flu cough, sneeze, or talk. These droplets can land in the mouths or noses of people who are nearby. Less often, a person might get flu by touching a surface or object that has flu virus on it and then touching their own mouth, nose or possibly their eyes.

## Prevention

The first and most important step in preventing flu is to get a flu vaccine each year. Flu vaccine has been shown to reduce flu-related illnesses and the risk of serious flu complications that can result in hospitalization or even death. CDC also recommends everyday preventive actions (like staying away from people who are sick (distancing), covering coughs and sneezes, frequent handwashing, and taking steps for cleaner air) to help slow the spread of germs that cause respiratory (nose, throat, and lungs) illnesses like flu. More information is available about core and additional prevention strategies.

## Quick facts

### **U.S annual flu infection rates**

A 2018 CDC study published in Clinical Infectious Diseases looked at the percentage of the U.S. population who got sick with flu using two different methods and compared the findings. Both methods had similar findings, which suggested that on average, about 8 percent of the U.S. population gets sick from flu each season, with a range of between 3 percent and 11 percent, depending on the season.

### **Groups most likely to get sick from flu**

The same CID study found that children are most likely to get sick from flu and that people 65 and older are least likely to get sick from flu. Median incidence values (or attack rate) by age group were 9.3% for children 0-17 years, 8.8% for adults 18-64 years, and 3.9% for adults 65 years and older. This means that children younger than 18 are more than twice as likely to develop a symptomatic influenza virus infection than adults 65 and older.

### **Estimating seasonal flu incidence**

Influenza virus infection is very common, and the number of people infected each season can only be estimated because not everyone will seek medical care or get tested for flu. Statistical estimations are based on CDC-measured flu hospitalization rates that are adjusted to estimate the total number of influenza virus infections in the United States for a given flu season.

The estimates for the number of influenza virus infections are then divided by the census population to estimate how common influenza virus infections are in the population (called seasonal incidence or attack rate).

### **Impact of flu season severity on incidence of flu**

The proportion of people who get sick with flu varies. A paper published in CID found that between 3 percent and 11 percent of the U.S. population gets infected and develops flu symptoms each year. The 3 percent estimate is from the 2011-2012 season, which was an H1N1-predominant season classified as being of low severity. The estimated incidence of flu illness during two seasons was around 11 percent; 2012-2013 was an H3N2-predominant season classified as being of moderate severity, while 2014-2015 was an H3N2 predominant season classified as being of high severity.

| **Table 1. Estimates of the Incidence of Symptomatic Influenza by Season and Age-Group, United States, 2010–2022** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Season** | **Predominant Virus(es)** | **Season Severity** | **Incidence, %, by Age Group** | | | | |
| **0-4 yrs** | **5-17 yrs** | **18-49 yrs** | **50-64 yrs** | **≥65 yrs** |
| **2010-11** | A/H3N2, A/H1N1pdm09 | Moderate | 13.7 | 8.42 | 5.5 | 8.2 | 4.5 |
| **2011-12** | A/H3N2 | Low | 4.7 | 3.7 | 2.6 | 3.2 | 2.3 |
| **2012-13** | A/H3N2 | Moderate | 17.8 | 12.5 | 8.4 | 12.8 | 9.7 |
| **2013-14** | A/H1N1pdm09 | Moderate | 12.7 | 7.4 | 9.6 | 13.7 | 3.8 |
| **2014-15** | A/H3N2 | High | 16.1 | 11.9 | 6.3 | 11.6 | 10.1 |
| **2015-16** | A/H1N1pdm09 | Moderate | 11.0 | 7.7 | 6.7 | 10.5 | 2.9 |
| **2016-17** | A/H3N2 | Moderate | 11.9 | 12.0 | 6.8 | 11.8 | 7.4 |
| **2017-18** | A/H3N2 | High | 17.1 | 13.3 | 9.9 | 18.4 | 10.1 |
| **2018-19** | A/H1N1pdm09, A/H3N2 | Moderate | 15.2 | 12.4 | 7.1 | 11.4 | 4.3 |
| **2019-20** | A/H1N1pdm09, B | Moderate/High | 19.8 | 14.5 | 9.6 | 12.9 | 3.5 |
| **2020-21\*** |  |  |  |  |  |  |  |
| **2021-22** | A/H3N2 | Low | 4.6 | 5.1 | 2.6 | 2.3 | 1.0 |
| **Median** |  |  | 13.7 | 11.9 | 6.8 | 11.6 | 4.3 |

\* The burden estimate for the 2020-2021 season was not calculated due to the uncharacteristically low level of flu activity that season.

### **Complications of Flu**

Complications of flu can include bacterial pneumonia, ear infections, sinus infections and worsening of chronic medical conditions, such as congestive heart failure, asthma, or diabetes.

# Diagnosis for Flu

## KEY POINTS

* Flu is a contagious respiratory illness that can cause fever, cough, sore throat, runny or stuffy nose, body aches, headache, chills and/or fatigue.
* There are multiple tests that can detect flu viruses.
* Although testing is the only way to know if you have flu, your doctor may diagnose you based on your symptoms.

## Symptoms to look out for

Your respiratory illness might be influenza (flu) if you have fever, cough, sore throat, runny or stuffy nose, body aches, headache, chills and/or fatigue. Some people may have vomiting and diarrhea, though this is more common in children. People may be sick with flu and have respiratory symptoms without a fever. Flu viruses usually cause the most illness during the colder months of the year. However, flu can also occur outside of the typical flu season. In addition, other viruses can also cause respiratory illness similar to flu. So, it is impossible to tell for sure if you have flu based on symptoms alone. If your doctor needs to know for sure whether you are sick with flu, there are laboratory tests that can be done.

## Different kinds of flu tests

A number of tests are available to detect flu viruses in respiratory specimens. The most common are called "rapid influenza diagnostic tests (RIDTs)." RIDTs work by detecting the parts of the virus (antigens) that stimulate an immune response. These tests can provide results within approximately 10-15 minutes but may not be as accurate as other flu tests. Therefore, you could still have flu, even though your rapid test result is negative. Other flu tests called "rapid molecular assays" detect genetic material of the flu virus. Rapid molecular assays produce results in 15-20 minutes and are more accurate than RIDTs.

In addition to RIDTs and rapid molecular assays, there are several more accurate flu tests available that must be performed in specialized laboratories, such as hospital and public health laboratories. These tests include reverse transcription polymerase chain reaction (RT-PCR), viral culture, and immunofluorescence assays. All of these tests require that a health care provider swipe the inside of your nose or the back of your throat with a swab and then send the swab for testing. Results may take one to several hours.

## Flu detection for rapid tests

During a flu outbreak, a positive rapid flu test is likely to indicate flu virus infection. However, rapid tests vary in their ability to detect flu viruses, depending on the type of rapid test used, and on the type of flu viruses circulating. Also, rapid tests appear to be better at detecting flu in children than in adults. This variation in ability to detect viruses can result in some people who are infected with flu having a negative rapid test result. This situation is called a false negative test result. Despite a negative rapid test result, your health care provider may diagnose you with flu based on your symptoms and their clinical judgment.

## Health care providers and testing

While your doctor may test you for flu, not everyone who goes to the doctor with flu-like symptoms will be tested. After evaluating you, your doctor may choose to diagnose you with flu without the need for testing based on your symptoms and his or her own clinical judgement.

## COVID-19 and flu co-infection

It is possible to have flu as well as other respiratory illnesses including COVID-19 at the same time. Health experts are still studying how common this can be.

### **Detecting both flu and COVID-19**

There is a test that will check for seasonal flu type A and B viruses and SARS-CoV-2, the virus that causes COVID-19. This test is being used by U.S. public health laboratories for surveillance purposes. Testing for these viruses at the same time will give public health officials important information about how flu and COVID-19 are spreading and what prevention steps should be taken. The test will also help public health laboratories save time and testing materials, and possibly to return test results faster.

The Food and Drug Administration (FDA) has given CDC an Emergency Use Authorization for this new test. Initial test kits were sent to public health laboratories in early August 2020. CDC will continue to manufacture and distribute these kits.

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# Treatment of Flu

## AT A GLANCE

* If you get sick with flu, flu antiviral drugs may be a treatment option.
* Antiviral drugs can make illness milder and shorten the time you are sick. They might also prevent some flu complications, like pneumonia.
* Flu antiviral drugs work best when started early, ideally within two days after your flu symptoms begin.

## Treatment overview

Flu antiviral drugs are prescription medicines (pills, liquid, an inhaled powder, or an intravenous solution) that fight against flu in your respiratory tract. Antiviral drugs are not sold over the counter. You can only get them from a pharmacy if you have a prescription from your doctor or health care provider. Antiviral drugs are different from antibiotics, which fight against bacterial infections. Antibiotics do not work against influenza viruses.

Most people with flu have mild illness and do not need medical care or antiviral drugs. If you get sick with flu symptoms, in most cases, you should stay home and avoid contact with other people except to get medical care.

If, however, you have symptoms of flu and are at increased risk for complications, are very sick with flu or worried about your illness, contact your health care provider right away. CDC recommends early treatment as soon as possible for people who have flu or suspected flu who are at higher risk of serious flu complications, such as people with asthma, diabetes, or heart disease.

Most people not at increased risk for flu complications who get sick with flu do not need to be treated with antiviral drugs.

## Antiviral drugs can help treat flu illness

Antiviral drugs should be started as soon as possible after symptoms begin. Studies show that treatment of flu with antiviral medications works best when started within two days after flu symptoms begin and can lessen symptoms and shorten the time you are sick by about a day. Starting antiviral treatment shortly after symptoms begin also can help reduce some flu complications. However, starting them later can still be helpful, especially if the sick person has a higher-risk health condition or is very sick from flu (for example, hospitalized patients). Follow your doctor's instructions for taking these medications.

## What not to do

### **Antibiotics will not treat flu**

When antibiotics aren't needed, they won't help you, and their side effects could still cause harm. Side effects can range from mild reactions, like a rash, to more serious health problems. These problems can include severe allergic reactions, antimicrobial-resistant infections and *C. diff* infection. *C. diff* causes diarrhea that can lead to severe colon damage and death.

## What to do if you get sick

### ***1. Take flu antiviral drugs, if a health care provider prescribes them.***

### ***2. Take everyday precautions to protect others while sick.***

### ***3. Stay home until you are better.***

Stay home and avoid contact with other people except to get medical care. You can go back to your normal activities when, for at least 24 hours, both are true:

* Your symptoms are getting better overall, **and**
* You have not had a fever (and are not using fever-reducing medication).\*

After these two criteria are met, there are some additional precautions that can be taken to protect others from respiratory illness.

# Treating Flu with Antiviral Drugs

* Flu antiviral drugs are prescription medicines that can be used to treat flu illness.
* They can lessen symptoms and shorten the time you are sick.
* Antiviral drugs work best when started within 1 to 2 days after flu symptoms begin.
* CDC recommends prompt treatment for people who have flu or suspected flu and who are at increased risk of serious flu complications, such as pregnant women, people with asthma and chronic lung disease, diabetes (including gestational diabetes), or heart disease.

## Treatment overview

Flu antiviral drugs are prescription medicines (pills, liquid, an inhaled powder, or an intravenous solution) that fight against flu viruses in your body. Antiviral drugs are not sold over the counter. You can only get them if you have a prescription from a health care provider. Antiviral drugs are different from antibiotics, which fight against bacterial infections. Antiviral drugs for flu only work to treat flu. Flu antiviral drugs are different than antiviral drugs used to treat other infectious diseases such as COVID-19. Antiviral drugs prescribed to treat COVID-19 are not approved or recommended to treat flu.

Treatment of flu with flu antiviral medications works best when started within 1-2 days after flu symptoms begin. Flu antiviral drugs can lessen symptoms and shorten the time you are sick by about a day. Starting antiviral treatment shortly after symptoms begin also can help reduce some flu complications. For adults hospitalized with flu, some studies have reported that early antiviral treatment can reduce the duration of hospitalization and their risk of death.

### **Recommended antiviral drugs for this flu season**

There are four FDA-approved antiviral drugs recommended by CDC to treat flu this season.

* oseltamivir phosphate (available as a generic version or under the trade name Tamiflu®),
* zanamivir (trade name Relenza®),
* peramivir (trade name Rapivab®), and
* baloxavir marboxil (trade name Xofluza®).

#### **Oseltamivir**

Generic oseltamivir and Tamiflu® are available as a pill or liquid suspension and are FDA approved for early treatment of flu in people 14 days and older.

#### **Zanamivir**

Zanamivir is a powdered medication that is inhaled and approved for early treatment of flu in people 7 years and older. **Note**: Zanamivir (trade name Relenza®) is administered using an inhaler device and is not recommended for people with breathing problems like asthma or COPD. Oseltamivir and zanamivir are given twice a day for five days.

#### **Peramivir**

Peramivir is given once intravenously by a health care provider and is approved for early treatment of flu in people 6 months and older.

#### **Baloxavir**

Baloxavir is a pill given as a single dose by mouth and is approved for early treatment of flu in children 5 years to younger than 12 years who do not have any chronic medical conditions, and for all people 12 years and older. **Note**: Baloxavir (trade name Xofluza®) is not recommended for treatment of flu during pregnancy or while breastfeeding, or in outpatients with complicated or progressive illness because there is no information about use of baloxavir in these patients. Baloxavir is also not recommended for treatment of flu in hospitalized patients due to limited data.

### **Who should take antiviral drugs**

It's very important that flu antiviral drugs are started as soon as possible to treat patients who are:

* hospitalized with flu,
* people who are very sick with flu but who do not need to be hospitalized, and
* people who are at increased risk of serious flu complications based on their age or underling health conditions, if they develop flu symptoms. For example, people with asthma and chronic lung disease, diabetes, or heart disease are at higher risk, as well as pregnant women.

Although patients with mild illness who are not at higher risk for flu complications may also be treated with antiviral drugs, most do not need to be.

#### **Children**

### Children and flu antiviral drugs

Parents, if your child gets sick with flu, antiviral drugs offer a safe and effective treatment option. For treatment, flu antiviral drugs should ideally be started within two days after becoming sick and taken according to your doctor's instructions (usually for five days).

Children can take flu antiviral drugs, though this varies by medication. Oseltamivir is recommended by CDC for treatment of flu in children beginning from birth and the American Academy of Pediatrics (AAP) recommends oseltamivir for treatment of flu in children 2 weeks old or older.

* Oseltamivir is available as an oral suspension for children.
* Zanamivir is approved for early treatment of flu in people 7 years and older, though it is not recommended for use in children with underlying respiratory disease, including asthma and other chronic lung diseases.
* Peramivir is approved for early treatment in people 6 months and older.
* Baloxavir is available in a single dose tablet for children 5 years and older.

If your child's health care provider prescribes oseltamivir capsules for your child and your child cannot swallow capsules, but the pediatric liquid suspension is not available, the prescribed capsules may be opened, mixed with a thick sweetened liquid, and given that way.

#### **Pregnancy**

Oral oseltamivir is recommended for treatment of flu during pregnancy because compared to other recommended antiviral medications, it has the most studies available to suggest that it is safe and beneficial during pregnancy. Baloxavir is not recommended during pregnancy or while breastfeeding, as there are no available efficacy or safety data.

## When antiviral drugs should be taken

Antiviral treatment provides the greatest benefit when started soon after flu illness begins. Studies show that flu antiviral drugs work best for treatment when they are started within two days of getting sick. However, starting them later can still be beneficial, especially if the sick person is at higher risk of serious flu complications or is in the hospital with more severe illness. Follow instructions for taking these drugs. Follow your doctor's instructions and the dose, frequency, and duration listed on the label instructions for taking these drugs.

## Possible side effects

Possible side effects vary for each flu antiviral medication. The most common side effects reported for oseltamivir are nausea and vomiting. Zanamivir can cause bronchospasm (difficulty breathing with wheezing), and peramivir can cause diarrhea. Other less common side effects also have been reported. Your health care provider can give you more information about these drugs or you can check the Food and Drug Administration (FDA) website for specific information about antiviral drugs, including the manufacturer's package insert.

## Prevention

Antiviral drugs are not a substitute for getting a flu vaccine. While flu vaccine can vary in effectiveness from season-to-season, a flu vaccine is best way to help **prevent** seasonal flu and its potentially serious complications. Everyone 6 months and older should receive a flu vaccine every year. Antiviral drugs are a second line of defense that can be used to **treat**flu (including seasonal flu and novel influenza viruses) if you get sick.

# HIV and AIDS

## Key facts

* HIV remains a major global public health issue, having claimed an estimated 42.3 million lives to date.  Transmission is ongoing in all countries globally.
* There were an estimated 39.9 million people living with HIV at the end of 2023, 65% of whom are in the WHO African Region.
* In 2023, an estimated 630 000 people died from HIV-related causes and an estimated 1.3 million people acquired HIV.
* There is no cure for HIV infection. However, with access to effective HIV prevention, diagnosis, treatment and care, including for opportunistic infections, HIV infection has become a manageable chronic health condition, enabling people living with HIV to lead long and healthy lives.
* WHO, the Global Fund and UNAIDS all have global HIV strategies that are aligned with the SDG target 3.3 of ending the HIV epidemic by 2030.
* By 2025, 95% of all people living with HIV should have a diagnosis, 95% of whom should be taking lifesaving antiretroviral treatment, and 95% of people living with HIV on treatment should achieve a suppressed viral load for the benefit of the person’s health and for reducing onward HIV transmission. In 2023, these percentages were 86%, 89%, and 93% respectively.
* In 2023, of all people living with HIV, 86% knew their status, 77% were receiving antiretroviral therapy and 72% had suppressed viral loads.

## Overview

Human immunodeficiency virus (HIV) is a virus that attacks the body’s immune system. Acquired immunodeficiency syndrome (AIDS) occurs at the most advanced stage of infection.

HIV targets the body’s white blood cells, weakening the immune system. This makes it easier to get sick with diseases like tuberculosis, infections and some cancers.

HIV is spread from the body fluids of an infected person, including blood, breast milk, semen and vaginal fluids. It is not spread by kisses, hugs or sharing food. It can also spread from a mother to her baby.

HIV can be prevented and treated with antiretroviral therapy (ART). Untreated HIV can progress to AIDS, often after many years.

WHO now defines Advanced HIV Disease (AHD) as CD4 cell count less than 200 cells/mm3 or WHO stage 3 or 4 in adults and adolescents. All children younger than 5 years of age living with HIV are considered to have advanced HIV disease.

**What’s a retrovirus?**

A retrovirus is a virus that works backward from the way human cells do. Human cells have instructions (DNA) that send a message (RNA) to make building blocks for your body (proteins).

Retroviruses have their instructions written on RNA. When a retrovirus invades your cells, it changes its RNA to look like your cells’ instructions (DNA). Then it cuts your cells’ DNA and inserts its instructions into them. Your cell then acts as though the virus’ instructions are its own.

HIV is a retrovirus. All viruses invade your cells and then use your cells’ “machinery” to make more copies of themselves. HIV not only uses your cells to make more of itself, but it also inserts its instructions into your DNA.

## Signs and symptoms

The symptoms of HIV vary depending on the stage of infection.

HIV spreads more easily in the first few months after a person is infected, but many are unaware of their status until the later stages. In the first few weeks after being infected people may not experience symptoms. Others may have an influenza-like illness including:

* fever
* headache
* rash
* sore throat.

The infection progressively weakens the immune system. This can cause other signs and symptoms:

* swollen lymph nodes
* weight loss
* fever
* diarrhoea
* cough.

Without treatment, people living with HIV infection can also develop severe illnesses:

* tuberculosis (TB)
* cryptococcal meningitis
* severe bacterial infections
* cancers such as lymphomas and Kaposi's sarcoma.

HIV causes other infections to get worse, such as hepatitis C, hepatitis B and mpox.

## Transmission

HIV can be transmitted via the exchange of body fluids from people living with HIV, including blood, breast milk, semen, and vaginal secretions. HIV can also be transmitted to a child during pregnancy and delivery.  People cannot become infected with HIV through ordinary day-to-day contact such as kissing, hugging, shaking hands, or sharing personal objects, food or water.

People living with HIV who are taking ART and have an undetectable viral load will not transmit HIV to their sexual partners. Early access to ART and support to remain on treatment is therefore critical not only to improve the health of people living with HIV but also to prevent HIV transmission.

## Risk factors

Behaviours and conditions that put people at greater risk of contracting HIV include:

* having anal or vaginal sex without a condom;
* having another sexually transmitted infection (STI) such as syphilis, herpes, chlamydia, gonorrhoea and bacterial vaginosis;
* harmful use of alcohol or drugs in the context of sexual behaviour;
* sharing contaminated needles, syringes and other injecting equipment, or drug solutions when injecting drugs;
* receiving unsafe injections, blood transfusions, or tissue transplantation; and
* medical procedures that involve unsterile cutting or piercing; or accidental needle stick injuries, including among health workers.

## Diagnosis

HIV can be diagnosed through rapid diagnostic tests that provide same-day results. This greatly facilitates early diagnosis and linkage with treatment and prevention. People can also use HIV self-tests to test themselves. However, no single test can provide a full HIV positive diagnosis; confirmatory testing is required, conducted by a qualified and trained health worker or community worker. HIV infection can be detected with great accuracy using WHO prequalified tests within a nationally approved testing strategy and algorithm.

Most widely used HIV diagnostic tests detect antibodies produced by a person as part of their immune response to fight HIV. In most cases, people develop antibodies to HIV within 28 days of infection. During this time, people are in the so-called “window period” when they have low levels of antibodies which cannot be detected by many rapid tests, but they may still transmit HIV to others. People who have had a recent high-risk exposure and test negative can have a further test after 28 days.

Following a positive diagnosis, people should be retested before they are enrolled in treatment and care to rule out any potential testing or reporting error. While testing for adolescents and adults has been made simple and efficient, this is not the case for babies born to HIV-positive mothers. For children less than 18 months of age, rapid antibody testing is not sufficient to identify HIV infection – virological testing must be provided as early as birth or at 6 weeks of age. New technologies are now available to perform this test at the point of care and enable same-day results, which will accelerate appropriate linkage with treatment and care.

## Prevention

HIV is a preventable disease.  Reduce the risk of HIV infection by:

* using a male or female condom during sex
* being tested for HIV and sexually transmitted infections
* having a voluntary medical male circumcision
* using harm reduction services for people who inject and use drugs.

Doctors may suggest medicines and medical devices to help prevent HIV infection, including:

* antiretroviral drugs (ARVs), including oral Pre-Exposure Prophylaxis (PrEP) and long acting products
* dapivirine vaginal rings
* injectable long acting cabotegravir.

ARVs can also be used to prevent mothers from passing HIV to their children.

People taking antiretroviral therapy (ART) and who have no evidence of virus in the blood will not pass HIV to their sexual partners. Access to testing and ART is an important part of preventing HIV.

### Antiretroviral drugs given to people without HIV can prevent infection

When given before possible exposures to HIV it is called pre-exposure prophylaxis (PrEP) and when given after an exposure it is called post-exposure prophylaxis (PEP).  People can use PrEP or PEP when the risk of contracting HIV is high; people should seek advice from a clinician when thinking about using PrEP or PEP.

## Treatment

There is no cure for HIV infection. It is treated with antiretroviral drugs, which stop the virus from replicating in the body.

Current antiretroviral therapy (ART) does not cure HIV infection but allows a person’s immune system to get stronger. This helps them to fight other infections.

Currently, ART must be taken every day for the rest of a person’s life.

ART lowers the amount of the virus in a person’s body. This stops symptoms and allows people to live full and healthy lives. People living with HIV who are taking ART and who have no evidence of virus in the blood will not spread the virus to their sexual partners.

Pregnant women with HIV should have access to, and take, ART as soon as possible. This protects the health of the mother and will help prevent HIV transmission to the fetus before birth, or through breast milk.

Advanced HIV disease remains a persistent problem in the HIV response. WHO is supporting countries to implement the advanced HIV disease package of care to reduce illness and death. Newer HIV medicines and short course treatments for opportunistic infections like cryptococcal meningitis are being developed that may change the way people take ART and prevention medicines, including access to injectable formulations, in the future.

**Treatment and care**

The main objective of treatment of HIV infection is to reduce the mortality and morbidity caused by the virus and associated conditions, increasing survival, improving the quality of life and preventing HIV transmission.

HIV treatment involves the use of combined antiretroviral therapy (ART) to effectively suppress the viral load, preserve (or improve) immune function and reduce the risk of opportunistic infections and cancers commonly associated with HIV. People living with HIV are more likely than others to become sick with tuberculosis (TB), which is one of the leading causes of death in this population. HIV suppression with ART also decrease the inflammation caused by the immune activation  associated with chronic HIV infection that contribute with an increased occurrence of cardiovascular, renal, neurological and other end-organ diseases that are prevalent in people living with HIV.

In individuals with advanced HIV disease, the use of certain antimicrobials for prevention and treatment of common opportunistic infections is also an essential part of the care package. Adherence to ART is important to maximize the clinical benefits on mortality and morbidity, and to reduce the risk of drug resistance. ART regimens has evolved in the last years and are more potent, better tolerated and available in fixed-dose combinations for adults adolescents and children, which further support adherence and increase the efficacy and durability of the treatment.

To optimize the programmatic impact of HIV treatment and promote efficiency gains, the use of person-centred, differentiated care models has been adopted by countries, reducing the  HIV disease burden on health systems and improving patient’s quality of care.

**What tests diagnose HIV?**

There are three types of HIV tests: antigen/antibody tests, antibody tests and nucleic acid tests (NATs):

**Antigen/antibody tests**

Antigen tests look for markers on the surface of HIV called p24. Antibody tests look for chemicals your body makes when it reacts to those markers. HIV antigen/antibody tests look for both.

A healthcare provider will take a small sample of blood from your arm with a needle. The blood is sent to a lab and tested for p24 and antibodies to it. An antigen/antibody test is usually able to detect HIV in 18 to 45 days after exposure.

A rapid antigen/antibody test may also be done with a finger prick to draw blood. You’ll need to wait at least 18 days after exposure for this type of test to be able to detect HIV. You may need to take the test up to 90 days after exposure for accurate results. (“Rapid” refers to the amount of time it takes to get test results, not the amount of time after exposure it takes to detect the virus.)

**Antibody tests**

These tests look for antibodies to HIV in your blood or saliva. This can be done with a blood draw from your arm, a finger prick or with a stick that you rub on your gums to collect saliva.

An antibody test can take 23 to 90 days after exposure to detect HIV. Antibody tests done with a blood draw can detect HIV sooner than those done with saliva or blood from a finger prick.

**Nucleic acid tests (NATs)**

NATs look for the HIV virus in your blood. A healthcare provider will take a small sample of blood from your arm with a needle. The blood then is sent to a lab and tested for HIV.

A NAT can typically detect HIV 10 to 33 days after exposure. Note that this test isn’t often used unless you have had a high-risk exposure.

If your test comes back positive, your healthcare provider is likely to recommend other tests to assess your health. These may include a complete blood count (CBC), along with:

* Viral hepatitis screening.
* Chest X-ray.
* Pap smear.
* CD4 count.
* Tuberculosis.

**Are there at-home tests for HIV?**

Yes, there are at-home HIV test kits. Some are rapid tests, where you use a stick with a soft, flexible tip to rub your gums. Then you put the stick in a tube with a special solution to get your results. Results show up in 15 to 20 minutes.

Other at-home tests use a device to prick your finger with a small needle. You put a drop of blood on a card and send the test kit through the mail to a lab to get your results.

If your at-home test result is positive, you should contact your healthcare provider for additional testing to confirm your result.

Who does HIV affect?

It’s a myth that HIV only infects certain people. Anyone can get HIV if they’re exposed to the virus. Having sex without a condom or sharing needles to inject drugs are the most common ways that HIV spreads.

Some populations are statistically more affected by HIV than others. Groups disproportionately affected by HIV include:

* People who are gay, bisexual and men who have sex with men (MSM).
* Certain races such as people who are Black or Hispanic.
* Those who exchange sex for money or other items are also at high risk for HIV infection.

While these aren’t the only populations impacted by HIV, it’s important to consider that they face unique barriers to accessing preventative care, getting tested, and receiving comprehensive treatment. Social stigmas around HIV continue to drive barriers and keep people from accessing high-quality healthcare.

How common is HIV?

The number of new HIV infections has declined. In 2019, 1.2 million people in the US were living with HIV. About 13% of those don’t know they have it, which is why routine testing for HIV is important.

What are the stages of HIV?

HIV has three stages:

Stage 1: Acute HIV

Some people get flu-like symptoms a month or two after they’ve been infected with HIV. These symptoms often go away within a week to a month.

Stage 2: Chronic stage/clinical latency

After the acute stage, you can have HIV for many years without feeling sick. It's important to know that you can still spread HIV to others even if you feel well.

Stage 3: AIDS

AIDS is the most serious stage of HIV infection. In this stage, HIV has severely weakened your immune system and opportunistic infections are much more likely to make you sick.

Opportunistic infections are ones that someone with a healthy immune system could typically fight off. When HIV has advanced to AIDS, these illnesses take advantage of your weakened immune system.

You’re more likely to get certain cancers when you have AIDS. These cancers and opportunistic infections together are called AIDS-defining illnesses.

To be diagnosed with AIDS, you must be infected with HIV and have at least one of the following:

* Fewer than 200 CD4 cells per cubic millimeter of blood (200 cells/mm3).
* An AIDS-defining illness.

What are AIDS-defining illnesses?

AIDS-defining illnesses are opportunistic infections, certain cancers (usually caused by viruses) and some neurological conditions. They include:

* Burkitt lymphoma.
* Candidiasis of bronchi, esophagus, trachea or lungs.
* Chronic intestinal isosporiasis (cystoisosporiasis) that lasts more than a month.
* Coccidioidomycosis, spread outside of your lungs (disseminated/extrapulmonary).
* Chronic intestinal cryptosporidiosis (lasting more than a month).
* Cytomegalovirus disease (other than liver, spleen or lymph nodes), onset at age older than one month.
* Cytomegalovirus retinitis (with loss of vision).
* Encephalopathy attributed to HIV.
* Extrapulmonary cryptococcosis.
* Herpes simplex ulcers (lasting more than a month).
* Herpes simplex bronchitis, pneumonitis or esophagitis (onset at age older than one month).
* Histoplasmosis spread outside the lungs (disseminated/extrapulmonary).
* HIV wasting syndrome.
* Invasive cervical cancer.
* Immunoblastic Lymphoma.
* **Kaposi sarcoma.**
* Multiple or recurrent bacterial infections.
* Mycobacterium avium complex (MAC), spread outside the lungs (disseminated/extrapulmonary).
* Mycobacterium kansasii, spread outside the lungs (disseminated/extrapulmonary).
* Mycobacterium tuberculosis of any site.
* Mycobacterium, other species or unidentified species, spread outside the lungs (disseminated/extrapulmonary).
* Pneumocystis jirovecii pneumonia.
* Primary lymphoma of the brain.
* Progressive multifocal leukoencephalopathy.
* Recurrent pneumonia.
* Recurrent Salmonella septicemia (nontyphoid).
* Toxoplasmosis of the brain (onset at age older than one month).

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* Chest X-ray.
* Pap smear.
* CD4 count.
* Tuberculosis.

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If your at-home test result is positive, you should contact your healthcare provider for additional testing to confirm your result.

**Outlook / Prognosis**

**What can I expect if I have HIV?**

If you’re diagnosed with HIV, it’s important to know that those living with HIV who follow treatment guidelines can live full lives for nearly as long as those without HIV.

If you have a high CD4 count and an undetectable viral load within a year of starting treatment, research suggests you’ll have the best outcomes, as long as you continue your treatment plan.

You can improve your outlook by:

* Getting tested as part of routine healthcare or if you think you’ve been exposed.
* Starting ART soon after being diagnosed.
* Taking your medicine every day.
* Keeping your appointments with your healthcare team.

ART can keep blood levels undetectable but can’t entirely rid your body of the virus (which remains inactive in your cells). If you don’t take your medication every day, the virus can start multiplying again and mutate, which may cause your medications to stop working.

Left untreated, it can take about 10 years for HIV to advance to AIDS. If you progress to AIDS and it goes untreated, you can expect to live about three years more.

For those on treatment, if you have a high CD4 count and undetectable viral load within a year of starting treatment, you can expect to live about as long as someone without HIV. If you have a low CD4 count or a detectable viral load within a year of starting treatment, you may live 10 to 20 years less than someone without HIV.

**Does HIV go away?**

HIV doesn’t go away on its own. It inserts itself into your DNA so your cells think that it’s a part of you. There can be many years without symptoms after initial infection, but HIV can still be damaging your immune system even if you don’t feel sick.

There may be periods while on medication where the virus is not detectable by an HIV test. In these cases, HIV can be hiding in your body, undetected. It can “wake up” and start destroying your cells again in the future.

This is why continuing to take HIV medication, even if you don’t feel sick or the virus is undetectable, is extremely important. Without treatment, HIV will weaken your immune system until you can’t fight off other serious illnesses.

# Tuberculosis

## Key facts

* A total of 1.25 million people died from tuberculosis (TB) in 2023 (including 161 000 people with HIV). Worldwide, TB has probably returned to being the world’s leading cause of death from a single infectious agent, following three years in which it was replaced by coronavirus disease (COVID-19). It was also the leading killer of people with HIV and a major cause of deaths related to antimicrobial resistance.
* In 2023, an estimated 10.8 million people fell ill with TB worldwide, including 6.0 million men, 3.6 million women and 1.3 million children. TB is present in all countries and age groups. TB is curable and preventable.
* Multidrug-resistant TB (MDR-TB) remains a public health crisis and a health security threat. Only about 2 in 5 people with drug resistant TB accessed treatment in 2023.
* Global efforts to combat TB have saved an estimated 79 million lives since the year 2000.
* US$ 22 billion is needed annually for TB prevention, diagnosis, treatment and care to achieve the global target by 2027 agreed at the 2023 UN high level-meeting on TB.
* Ending the TB epidemic by 2030 is among the health targets of the United Nations Sustainable Development Goals (SDGs).

## Overview

Tuberculosis (TB) is an infectious disease caused by bacteria that most often affects the lungs. It spreads through the air when people with TB cough, sneeze or spit.

Tuberculosis is preventable and curable.

About a quarter of the global population is estimated to have been infected with TB bacteria. About 5–10% of people infected with TB will eventually get symptoms and develop TB disease.

Those who are infected but free of disease cannot transmit it. TB disease is usually treated with antibiotics and can be fatal without treatment.

In certain countries, the Bacille Calmette-Guérin (BCG) vaccine is given to babies or small children to prevent TB. The vaccine prevents deaths from TB and protects children from serious forms of TB.

Certain conditions can increase a person’s risk for TB disease:

* diabetes (high blood sugar)
* weakened immune system (for example, from HIV or AIDS)
* being malnourished
* tobacco use
* harmful use of alcohol.

## Symptoms

People with TB infection don’t feel sick and aren’t contagious. Only a small proportion of people who get infected with TB will get TB disease and symptoms. Babies and children are at higher risk.

TB disease occurs when bacteria multiply in the body and affect different organs. TB symptoms may be mild for many months, so it is easy to spread TB to others without knowing it. Some people with TB disease do not have any symptoms.

Common symptoms of TB are:

* prolonged cough (sometimes with blood)
* chest pain
* weakness
* fatigue
* weight loss
* fever
* night sweats

The symptoms people get depend on which part of the body is affected by TB. While TB usually affects the lungs, it can also involve the kidneys, brain, spine and skin.

## Prevention

Follow these steps to help prevent tuberculosis infection and spread:

* Seek medical attention if you have symptoms like prolonged cough, fever and unexplained weight loss as early treatment for TB can help stop the spread of disease and improve your chances of recovery.
* Get tested for TB if you are at increased risk, such as if you have HIV or are in contact with people who have TB in your household or workplace.
* TB preventive treatment (or TPT) prevents infection from becoming disease. If prescribed TPT, complete the full course.
* If you have TB, practice good hygiene when coughing, including avoiding contact with other people and wearing a mask, covering your mouth and nose when coughing or sneezing, and disposing of sputum and used tissues properly.
* Special measures like respirators and ventilation are important to reduce infection in healthcare facilities and other institutions.

## Diagnosis

WHO recommends the use of rapid molecular diagnostic tests as the initial diagnostic test in all persons with signs and symptoms of TB.

Rapid diagnostic tests recommended by WHO include the Xpert MTB/RIF Ultra and Truenat assays. These tests have high diagnostic accuracy and will lead to major improvements in the early detection of TB and drug-resistant TB.

A tuberculin skin test (TST), interferon gamma release assay (IGRA) or newer antigen-based skin tests (TBST) can be used to identity people with infection.

Diagnosing multidrug-resistant and other resistant forms of TB (see multidrug-resistant TB section below) as well as HIV-associated TB can be complex and expensive.

Tuberculosis is particularly difficult to diagnose in children.

## Treatment

Tuberculosis disease is treated with special antibiotics. Treatment is recommended for both TB infection and disease.

The most common antibiotics used are:

* isoniazid
* rifampicin
* pyrazinamide
* ethambutol.

To be effective, medications need to be taken daily for 4–6 months. It is dangerous to stop the medications early or without medical advice as it can prompt TB bacteria in the body to become resistant to the drugs.

TB that doesn’t respond to standard drugs is called drug-resistant TB and requires treatment with different medicines.

## Multidrug-resistant TB (MDR-TB)

Drug resistance emerges when TB medicines are used inappropriately, through incorrect prescription by health care providers, poor quality drugs, or patients stopping treatment prematurely.

MDR-TB is a form of TB caused by bacteria that do not respond to isoniazid and rifampicin, the two most effective first-line TB drugs. MDR-TB is treatable and curable by using other drugs, which tend to be more expensive and toxic.

In some cases, extensively drug resistant TB or XDR-TB can develop. TB caused by bacteria that do not respond to the most effective drugs in MDR-TB treatment regimens can leave patients with very limited treatment options.

MDR-TB remains a public health crisis and a health security threat. Only about 2 in 5 people with multidrug resistant TB accessed treatment in 2023.

In accordance with WHO guidelines, detection of MDR-TB requires bacteriological confirmation of TB and testing for drug resistance using rapid molecular tests or culture methods.

In 2022, new WHO guidelines prioritized a short 6-month all-oral regimen known as BPaLM/BPaL as a treatment of choice for eligible patients. Globally in 2023, 5646 people with MDR/RR-TB were reported to have been started treatment on the BPaLM/BPaL regimen, up from 1744 in 2022. The shorter duration, lower pill burden and high efficacy of this novel regimen can help ease the burden on health systems and save precious resources to further expand the diagnostic and treatment coverage for all individuals in need. In the past, MDR-TB treatment used to last for at least 9 months and up to 20 months. WHO recommends expanded access to all-oral regimens.

## TB and HIV

People living with HIV are 16 (uncertainty interval 14–18) times more likely to fall ill with TB disease than people without HIV. TB is the leading cause of death among people with HIV.

HIV and TB form a lethal combination, each speeding the other's progress. In 2023, about 161 000 people died of HIV-associated TB. The percentage of notified TB patients who had a documented HIV test result in 2023 was 80%, this was the same level as in 2022, but up from 76% in 2021. The WHO African Region has the highest burden of HIV-associated TB. Overall in 2023, only 56% of TB patients known to be living with HIV were on antiretroviral therapy (ART).

WHO recommends a 12-component approach of collaborative TB-HIV activities, including actions for prevention and treatment of infection and disease, to reduce deaths.

## Impact

TB mostly affects adults in their most productive years. However, all age groups are at risk. Over 80% of cases and deaths are in low- and middle-income countries.

TB occurs in every part of the world. In 2023, the largest number of new TB cases occurred in the WHO South-East Asia Region (45%), followed by the African Region (24%) and the Western Pacific Region (17%). Around 87% of new TB cases occurred in the 30 high TB burden countries, with more than two-thirds of the global total in Bangladesh, China, Democratic Republic of the Congo, India, Indonesia, Nigeria, Pakistan and the Philippines.

Globally, about 50% of people treated for TB and their households face total costs (direct medical expenditures, non-medical expenditures and indirect costs such as income losses) that are catastrophic (>20% of total household income), far from the WHO End TB Strategy target of zero. Those with compromised immune systems, such as people living with HIV, undernutrition or diabetes, or people who use tobacco, have a higher risk of falling ill. Globally in 2023, there were estimated 0.96  million new TB cases that were attributable to undernutrition, 0.75 million to alcohol use disorders, 0.70 million to smoking, 0.61 million to HIV infection, and 0.38 million to diabetes.

## Investments to end TB

US$ 22 billion are needed annually for TB prevention, diagnosis, treatment and care to achieve global targets by 2027 agreed on at the 2023 UN high level-TB meeting.

As in the past decade, most of the spending on TB services in 2023 (80%) was from domestic sources. In low- and middle-income countries, international donor funding remains crucial. From 2019 to 2023, there was a decline (of US$ 1.2 billion) in available funding from domestic sources and a very slight increase (of US$ 0.1 billion) in funding provided by international donors. Most of the reduction in domestic funding is largely explained by reductions in domestic funding trends in Brazil, the Russian Federation, India, China and South Africa (BRICS). Financing for TB research and innovation at US$ 1.0 billion in 2022 also continues to fall far short of the global target of US$ 5 billion per year, constrained by the overall level of investment.

# About Tuberculosis

* Tuberculosis (TB) is caused by a bacterium called *Mycobacterium tuberculosis*.
* Two TB-related conditions exist: inactive TB and active TB disease.
* Getting tested and treated for TB can protect yourself, your family and friends, and your community.

## Overview

Tuberculosis (TB) is caused by a bacterium (or germ) called *Mycobacterium tuberculosis*. In the United States, the majority of TB disease cases in people are caused by*Mycobacterium tuberculosis.*Other mycobacteria (such as *Mycobacterium bovis)*can also cause TB disease in people.

TB usually affects the lungs. TB can also affect other parts of the body, such as the brain, the kidneys, or the spine. TB can also affect multiple parts of the body at the same time. For example, TB can affect both the lungs and lymph nodes.

Not everyone infected with TB germs becomes sick. As a result, two TB-related conditions exist: inactive TB (or latent TB infection) and active TB disease.

If not treated properly, TB disease can be fatal.

## Types

### **Inactive TB**

TB germs can live in the body without making you sick. This is called **inactive TB**, or latent TB infection. People with inactive TB are infected with TB germs, but they do not have active TB disease. They do not feel sick, do not have any symptoms, and cannot spread TB to others.

Without treatment, people with inactive TB can develop active TB disease at any time and become sick.

### **Active TB Disease**

TB germs become active if the immune system can’t stop them from growing. When TB germs are active (multiplying in your body), this is called **active TB disease**. People with active TB disease feel sick. They may also be able to spread the germs to people they spend time with every day. Without treatment, active TB disease can be fatal.

# Signs and Symptoms of Tuberculosis

* Symptoms of active tuberculosis (TB) disease depend on where the TB germs are growing in the body.
* Common symptoms of active TB disease include cough, pain in the chest, and coughing up blood or sputum (phlegm).
* People with inactive TB, also called latent TB infection, do not have symptoms of TB disease and cannot spread TB to others.

## Signs and symptoms

### **Active TB Disease**

Symptoms of active TB disease depend on where in the body the TB germs are growing. TB germs usually grow in the lungs (pulmonary TB).

#### **Active TB disease in the lungs may cause symptoms such as:**

* A bad cough that lasts 3 weeks or longer
* Pain in the chest
* Coughing up blood or sputum (phlegm) from deep inside the lungs

#### **Other symptoms of active TB disease are:**

* Weakness or fatigue,
* Weight loss,
* No appetite,
* Chills,
* Fever, and
* Sweating at night.

#### **Symptoms of active TB disease in other parts of the body depend on the area affected:**

* TB disease of the lymph nodes may cause a firm red or purple swelling under the skin.
* TB disease of the kidney may cause blood in the urine.
* TB meningitis (TB disease of the brain) may cause headache or confusion.
* TB disease of the spine may cause back pain.
* TB disease of the larynx may cause hoarseness.

# Tuberculosis: Causes and How It Spreads

* Tuberculosis (TB) germs spread through the air from one person to another.
* TB germs can get into the air when someone with active TB disease coughs, speaks, or sings.
* People nearby may breathe in these germs and become infected.
* People with inactive TB, also called latent TB infection, cannot spread TB germs to others.

## Causes

Tuberculosis (TB) is caused by a bacterium (or germ) called *Mycobacterium tuberculosis*. When a person breathes in TB germs, the germs can settle in the lungs and begin to grow. From there, they can move through the blood to other parts of the body, such as the kidney, spine, and brain.

TB bacteria can live in the body without making you sick. This is called **inactive TB**, or latent TB infection. People with inactive TB are infected with TB germs, but they do not have active TB disease. They do not feel sick, do not have symptoms of TB disease, and cannot spread TB germs to others.

Without treatment, people with inactive TB can develop active TB disease at any time and become sick.

TB germs become active if the immune system can't stop them from multiplying and growing in the body. When TB germs are active (multiplying in your body), this is called **active TB disease**. People with active TB disease feel sick. They may also be able to spread the germs to people they spend time with every day. Without treatment, active TB disease can be fatal.

## How it spreads

TB germs can get into the air when a person with active TB disease of the lungs or throat coughs, speaks, or sings. These germs can stay in the air for several hours, depending on the environment.

TB germs are more likely to spread in indoor areas or other places with poor air circulation (such as a closed vehicle) than in outdoor areas. People nearby may breathe in these germs and become infected.

TB germs are **not** spread by:

* Shaking someone's hand
* Sharing food or drink
* Touching bed linens or toilet seats
* Sharing toothbrushes
* Kissing

## Prevention methods

### **If you have inactive TB, treating it is the best way to prevent active TB disease.**

Without treatment, people with inactive TB can develop active TB disease.

People with weakened immune systems are at very high risk of developing active TB disease once infected with TB germs. It is very important that these people receive treatment for inactive TB to prevent the development of active TB disease.

### **If you have active TB disease of the lungs or throat, you may need to take steps to prevent spreading TB germs to other people.**

If you have TB disease of the lungs or throat, you could be infectious. This means you could spread TB germs to others.

Your health care provider will tell you what steps you can take to keep from spreading TB germs to others. This may include things like covering your mouth with a tissue when you cough or staying home from work or school. After taking your medicine for a few weeks, you will feel better and you may no longer be infectious to others.

## When transmission is possible

Active TB disease in the lungs or throat can be infectious. This means the germs can spread to other people. TB disease in other parts of the body, such as the kidney or spine, is usually not infectious.

People with active TB disease are most likely to spread it to people they spend time with every day. This includes family members, friends, and coworkers or schoolmates.

### Do you think you may have been exposed to TB?

If you think you have been exposed to someone with active TB disease, you should contact your health care provider or local or state health department about getting a TB blood test or TB skin test. Be sure to tell the health care provider when you spent time with the person who has active TB disease.

# Tuberculosis Risk Factors

* Anyone can get tuberculosis (TB), but some people are at higher risk than others.
* You can get TB even if you received the TB vaccine (also known as bacille Calmette-Guérin or BCG vaccine).
* If you are at risk for TB, talk with your health care provider about getting tested.

## Overview

Anyone can get TB. But people at higher risk for TB fall into two categories:

* People at higher risk of **being exposed** to TB germs, and
* People at higher risk of **developing active TB disease**once infected with TB germs.

### Talk to your health care provider about getting tested.‎

If you have recently spent time with someone who has active TB disease you may be at risk for TB. Talk to your health care provider about getting tested.

## Conditions that can increase risk

Some people with weakened immune systems (due to certain medications or health conditions) are at very high risk of developing active TB disease once infected with TB germs. It is very important that these people receive treatment for inactive TB to prevent the development of active TB disease.

Some medications or health conditions can weaken your immune system. These include:

* HIV infection
* Substance use (such as injection drug use)
* Specialized treatment for rheumatoid arthritis or Crohn's disease
* Organ transplants
* Severe kidney disease
* Head and neck cancer
* Diabetes
* Medical treatments such as corticosteroids
* Silicosis
* Low body weight

Babies and young children often have weak immune systems. Children, especially those under age five, have a higher risk of developing TB disease once infected with TB germs.

## Places with increased risk

You have a higher risk of being exposed to TB germs if you:

* Were born in or frequently travel to countries where TB is common, including some countries in Asia, Africa, and Latin America
* Live or used to live in large group settings where TB is more common, such as homeless shelters, prisons, or jails
* Work in places where TB is more likely to spread, such as hospitals, homeless shelters, correctional facilities, and nursing homes

## You may be at risk for TB even if you received the TB vaccine

Bacille Calmette-Guérin (BCG) is a vaccine for TB disease. The vaccine is not generally used in the United States. It is often given to infants and small children in countries where TB is common. It protects children in those countries from getting severe forms of active TB disease, such as TB meningitis.

Tell your health care provider if you have received the TB vaccine, especially if you are getting tested for TB infection because it can cause a false positive TB skin test reaction. TB blood tests are the preferred tests for people who have received the BCG TB vaccine.

# Tuberculosis Vaccine

* Bacille Calmette-Guérin (BCG) is a vaccine for tuberculosis (TB) disease.
* This vaccine is not generally used in the United States.
* The TB vaccine can cause a false positive TB skin test reaction.
* Tell your health care provider if you have received the TB vaccine.

Bacille Calmette-Guérin (BCG) is a vaccine for tuberculosis (TB) disease. The vaccine is not generally used in the United States

Many people born outside the United States have been vaccinated with BCG. It is given to infants and small children in countries where TB is common. It protects children from getting severe forms of active TB disease, such as TB meningitis. The vaccine's protection weakens over time.

Tell your health care provider if you have received the TB vaccine, especially if you are getting tested for TB infection. The vaccine can cause a false positive TB skin test reaction.

TB blood tests are the preferred tests for people who have received the BCG TB vaccine. Unlike the TB skin test, TB blood tests are not affected by BCG TB vaccination.

## Who should receive the vaccine

In the United States, BCG is only considered for people who meet specific criteria and in consultation with a TB expert. Talk to your health care provider if you have questions about the vaccine.

Health care providers can consult their state or local TB control program for questions about BCG vaccination for their patients.

## Common questions

### **Can I have inactive TB or TB disease even if I have received the TB vaccine?**

Yes, a person can have or get TB even if they received the TB vaccine (BCG). The BCG TB vaccine does not always protect people from getting TB.

Contact your health care provider if you think you or someone in your family has been exposed to TB germs.

### **Should people who received the BCG TB vaccine get a TB blood test or TB skin test?**

TB blood tests are the preferred tests for people who have received the BCG TB vaccine. The vaccine can cause a false positive TB skin test reaction. Unlike the TB skin test, TB blood tests are not affected by BCG vaccination.

SEPSIS

## Overview

Sepsis is a serious condition in which the body responds improperly to an infection. The infection-fighting processes turn on the body, causing the organs to work poorly.

Sepsis may progress to septic shock. This is a dramatic drop in blood pressure that can damage the lungs, kidneys, liver and other organs. When the damage is severe, it can lead to death.

Early treatment of sepsis improves chances for survival.

### Products & Services

## Symptoms

### Symptoms of sepsis

Symptoms of sepsis may include:

* Change in mental status.
* Fast, shallow breathing.
* Sweating for no clear reason.
* Feeling lightheaded.
* Shivering.
* Symptoms specific to the type of infection, such as painful urination from a urinary tract infection or worsening cough from pneumonia.

Symptoms of sepsis are not specific. They can vary from person to person, and sepsis may appear differently in children than in adults.

### Symptoms of septic shock

Sepsis may progress to septic shock. Septic shock is a severe drop in blood pressure. Progression to septic shock raises the risk of death. Symptoms of septic shock include:

* Not being able to stand up.
* Strong sleepiness or hard time staying awake.
* Major change in mental status, such as extreme confusion.

## When to see a doctor

Any infection could lead to sepsis. Go to a health care provider if you have symptoms of sepsis or an infection or wound that isn't getting better.

Symptoms such as confusion or fast breathing need emergency care.

## Causes

Any type of infection can lead to sepsis. This includes bacterial, viral or fungal infections. Those that more commonly cause sepsis include infections of:

* Lungs, such as pneumonia.
* Kidney, bladder and other parts of the urinary system.
* Digestive system.
* Bloodstream.
* Catheter sites.
* Wounds or burns.

## Risk factors

Some factors that increase the risk infection will lead to sepsis include:

* People over age 65.
* Infancy.
* People with lower immune response, such as those being treated for cancer or people with human immunodeficiency virus (HIV).
* People with chronic diseases, such as diabetes, kidney disease or chronic obstructive pulmonary disease (COPD).
* Admission to intensive care unit or longer hospital stays.
* Devices that go in the body, such as catheters in the vein, called intravenous, or breathing tubes.
* Treatment with antibiotics in the last 90 days.
* A condition that requires treatment with corticosteroids, which can lower immune response.

## Complications

As sepsis worsens, vital organs, such as the brain, heart and kidneys, don't get as much blood as they should. Sepsis may cause atypical blood clotting. The resulting small clots or burst blood vessels may damage or destroy tissues.

Most people recover from mild sepsis, but the mortality rate for septic shock is about 30% to 40%. Also, an episode of severe sepsis raises the risk for future infections.

## Diagnosis

Doctors often order several tests to try to pinpoint underlying infection.

### Blood tests

Blood samples are used to test for:

Evidence of infection.

Blood-clotting problems.

Abnormal liver or kidney function.

Lower levels of oxygen than the body needs.

Electrolyte imbalances.

### Other lab tests

Other lab tests to find the source of the infection might include samples of:

Urine.

Liquid from the wound.

Mucus and saliva from the respiratory tract.

### Imaging tests

If the site of infection is not readily found, your health care provider may order more tests. Some examples of imaging tests are:

**X-ray.** X-rays can show infections in your lungs.

**Ultrasound.** This machine uses sound waves to produce real-time images on a video screen. Ultrasound can show infections in the gallbladder and kidneys.

**Computerized tomography (CT).** This machine takes X-rays from a variety of angles and combines them to show cross-sectional slices of the inside of the body. Infections in the liver, pancreas or other abdominal organs are easier to see on computed tomography (CT) scans.

**Magnetic resonance imaging (MRI).** This machine uses radio waves and a strong magnet to produce cross-sectional or 3D images. It may be helpful in seeing soft tissue or bone infections.

## Treatment

Early, thorough treatment raises the likelihood of recovery. People who have sepsis need close monitoring and treatment in a hospital intensive care unit. This is because people with sepsis may need lifesaving measures to stabilize breathing and heart action.

### Medications

Different medications are used in treating sepsis and septic shock. They include:

**Antibiotics.** Treatment with antibiotics begins as soon as possible. Broad-spectrum antibiotics, which are effective against a variety of bacteria, are often used first. When blood tests results show which germ is causing the infection, the first antibiotic may get switched out for a second one. This second one targets the germ causing the infection.

**Fluids added to veins.**The use of intravenous fluids begins as soon as possible.

**Vasopressors.** Vasopressors narrow blood vessels and help increase blood pressure. A vasopressor medication may be used if blood pressure is too low even after receiving fluids.

Other medications may be used, such as insulin for blood sugar levels, or painkillers.

### Supportive care

People who have sepsis often get supportive care that includes oxygen. Some people may need a machine help them breathe. If a person's kidneys don't work as well because of the infection, the person may need dialysis.

### Surgery

Surgery may help to remove sources of infection, such as pus, infected tissues or dead tissues.

# Meningitis

## Key facts

Meningitis is a devastating disease that can be deadly and often results in serious long-term health issues.

Meningitis remains a major global public health challenge.

Many organisms can cause meningitis, including bacteria, viruses, fungi and parasites.

Bacterial meningitis is of particular concern. Around 1 in 6 people who get this type of meningitis die and 1 in 5 have severe complications.

Epidemics of meningitis are seen across the world, particularly in sub-Saharan Africa.

Vaccines are the most effective way to deliver long-lasting protection.

## Overview

Meningitis is the inflammation of the tissues surrounding the brain and spinal cord. It can be infectious or non-infectious in origin, can be associated with high risk of death and long-term complications, and requires urgent medical care.

Meningitis remains a significant global health threat. It can be caused by several species of bacteria, viruses, fungi and parasites. Injuries, cancers and drugs cause a small number of cases.

Bacterial meningitis is the most serious type of meningitis. It is a severe, life-threatening condition that can often lead to long-term adverse health consequences. There are four main causes of acute bacterial meningitis:

*Neisseria meningitidis* (meningococcus)

*Streptococcus pneumoniae* (pneumococcus)

*Haemophilus influenzae*

*Streptococcus agalactiae* (group B streptococcus).

These bacteria are responsible for more than half of the deaths from meningitis globally and can cause other severe diseases like sepsis and pneumonia.

Additional important causes of meningitis worldwide include other bacteria species (e.g. *Mycobacterium tuberculosis*, non-typhoidal *Salmonella spp*, Listeria monocytogenes), viruses (e.g. enteroviruses, herpesviruses an arboviruses), fungi (e.g. *Cyptococcus spp.),*and parasites (e.g. some species of amoebae).

## Who is at risk?

Meningitis can affect anyone anywhere, and at any age. The pathogens that cause it can vary, based on a person’s age and immune system, and level of exposure to risk, which can be influenced by their living conditions and geographical location.

Newborn babies are most at risk from Group B streptococcus, whereas children and adolescents are at most risk of meningococcus, pneumococcus and *Haemophilus influenzae*. Pneumococcus and meningococcus also account for most cases of bacterial meningitis among adults.

Immunocompromised and/or people living with HIV are at increased risk of different types of meningitis.

Globally, the highest burden of disease is seen in a region of sub-Saharan Africa, known as the African meningitis belt, which stretches from Senegal to Ethiopia, and is at high risk of recurrent epidemics of meningococcal meningitis.

Meningococcal meningitis outbreaks occur more frequently under special risk conditions, such as crowded settings where people are in close proximity, mining areas, mass gatherings, such as religious or sporting events, settings with refugees or displaced persons, closed institutions, military camps and areas with high migration, such as high-traffic markets and border areas.

## Transmission

The route of transmission varies by organism. Most bacteria that cause meningitis, including meningococcus, pneumococcus and *Haemophilus influenzae*, are carried in the human nose and throat. They are spread from person to person by respiratory droplets or throat secretions. Group B streptococcus is often carried in the human gut or vagina and can spread from mother to child around the time of birth.

Carriage of these organisms is usually harmless and contributes to building up immunity against infection, but the bacteria occasionally invade the body, causing meningitis, sepsis and other forms of invasive disease.

## Signs and symptoms

The symptoms of meningitis can differ based on the cause, how quickly the disease progresses, how long it lasts, brain involvement, and other serious complications like sepsis.

Common symptoms of meningitis are fever, neck stiffness, confusion or altered mental status, headache, sensitivity to light, nausea and vomiting. Less frequent symptoms include seizures, coma and neurological deficits, such as weakness of the limbs.

Infants often have different symptoms compared to adults:

unusual behaviour, such as the child being less active and difficult to wake

irritability

weak, continuous cry

poor feeding

bulging of the soft spot in their head.

Some bacterial pathogens may also account for other symptoms as a result of bloodstream infection, which can quickly lead to sepsis, including cold hands and feet, fast breathing and low blood pressure. A characteristic, non-blanching skin rash may appear with meningococcal sepsis.

## Complications and sequelae

One in 5 people surviving an episode of bacterial meningitis may have long lasting after-effects. These after-effects include hearing loss, seizures, limb weakness, difficulties with vision, speech, language, memory and communication, as well as scarring and limb amputations after sepsis.

## Prevention

Vaccines offer the best protection against common types of bacterial meningitis.

Vaccines can prevent meningitis caused by:

meningococcus

pneumococcus

*Haemophilus influenzae* type b (Hib).

Maternal Group B streptococcus vaccines to prevent invasive GBS disease in infants are in the final stages of clinical development.

Bacterial and viral meningitis can spread from person to person. If you live with someone who has either type of meningitis, you should:

talk to your doctor or nurse about taking antibiotics (in case of bacterial meningitis)

wash hands frequently, especially before eating

avoid close contact and sharing cups, utensils or toothbrushes.

### 1. Vaccination

Licensed vaccines against meningococcal, pneumococcal and *Haemophilus influenzae* disease have been available for many years. These bacteria have several different strains (known as serotypes or serogroups) and vaccines are designed to protect against the most harmful strains. No universal vaccine exists.

Hib vaccine is used in most national childhood immunization programmes globally. WHO also recommends universal use pneumococcal conjugate vaccines (PCV). Meningococcal vaccines include multivalent polysaccharide conjugate vaccines (MMCV), which include 4 to 5 meningococcal serogroups (A,C,W,Y,X); protein-based vaccines, which include meningococcal serogroup B, and combination vaccines combining the latter with 4-valent MMCV. Polysaccharide vaccines are still marketed internationally but are gradually being replaced by MMCV.

In the African meningitis belt, meningococcus serogroup A accounted for 80–85% of meningitis epidemics before the large-scale deployment of a meningococcal A conjugate vaccine starting in 2010. In 2023, the first pentavalent MMCV protecting against serogroups A, C, W, Y and X (Men5CV) was prequalified by WHO and recommended for use in countries of the African meningitis belt. Roll-out of Men5CV has the potential to eliminate meningitis epidemics and make the meningitis belt history.

### 2. Antibiotics for prevention (chemoprophylaxis)

Post-exposure prophylaxis with antibiotics is given to close contacts of individuals with meningococcal disease to eradicate asymptomatic meningococcal carriage in the nose and decrease the risk of transmission.

Identifying mothers whose babies are at risk of getting Group B streptococcal (GBS) disease is recommended in many countries. Mothers at risk of transmitted GBS to their babies are offered intravenous penicillin during labour to prevent their babies developing GBS infection.

## Diagnosis

To diagnose meningitis, a lumbar puncture is needed to examine the cerebrospinal fluid (CSF). This should be done before starting antibiotics; however, if bacterial meningitis is suspected based on the signs and symptoms, a lumbar puncture should never delay antibiotic treatment.

Laboratories will then perform specific tests with CSF or blood to identify the pathogen causing the infection. The tests will also help identify the treatments needed, and specifically for bacterial infections the susceptibility to types of antibiotics, as well as identify the strain(s) of the pathogen responsible and inform public health responses.

## Treatment

Meningitis is a medical emergency and requires urgent medical attention in an appropriate health-care facility.

Antibiotic treatment should be started as soon as possible when bacterial meningitis is suspected. The first dose of antibiotic treatment should not be delayed until the results of the lumbar puncture are available. The choice of antibiotic treatment should consider the age of the patient, presence of immunosuppression, and local prevalence of antimicrobial resistance patterns. In non-epidemic settings, intravenous corticosteroids (e.g., dexamethasone) are initiated with the first dose of antibiotics to reduce the inflammatory response and the risk of neurological sequelae and death,

Those who have lived through meningitiscan have complications such as deafness, learning impairment or behavioural problem and require long-term treatment and care. The ongoing psychosocial impacts of disability from meningitis can have medical, educational, social and human rights-based implications. Access to both services and support for these conditions is often insufficient, especially in low- and middle-income countries.

Individuals and families with members disabled by meningitis should be encouraged to seek services and guidance from local and national organizations of disabled people and other disability focused organizations, which can provide vital advice about legal rights, economic opportunities and social engagement to ensure people disabled by meningitis are able to live full and rewarding lives.

WHO has also developed an Intersectoral global action plan on epilepsy and other neurological disorders to address the many challenges and gaps in providing care and services for people with epilepsy and other neurological disorders that exist worldwide, including those suffering from meningitis sequelae.

## Surveillance

Surveillance, from case detection to investigation and laboratory confirmation, is essential to the control of meningitis. Main objectives include:

detect and confirm outbreaks;

monitor the incidence trends, including the distribution and evolution of serogroups and serotypes;

estimate the disease burden;

monitor the antibiotic resistance profile;

monitor the circulation, distribution, and evolution of specific strains (clones); and

estimate the impact of meningitis control strategies, particularly preventive vaccination programmes.

# About Malaria

Malaria is a serious disease caused by a parasite that infects a certain type of mosquito.

Most people get malaria from the bite of an infective mosquito.

Malaria can be a deadly disease if not diagnosed and treated quickly.

Starting treatment as soon as possible can often prevent severe illness and death.

**MALARIA**

## Overview

Malaria is not endemic in the United States. This means it does not regularly occur or spread in the U.S. In a typical year, the U.S. reports about 2,000 cases of malaria. Most of these cases are in people who contract malaria while traveling to another country where malaria spreads and return to the U.S. On rare occasions, local transmission (spread) occurs because of an imported case of malaria. People do not spread malaria to other people, like the common cold or the flu. Also, malaria is not sexually transmitted.

## Symptoms

Malaria symptoms range from very mild illness to severe disease and even death. Early symptoms can include:

Fever and flu-like illness

Chills

Headache, muscle aches, and tiredness

Nausea, vomiting, and diarrhea may also occur

If not treated quickly, the infection can become severe.

Severe symptoms can include

Kidney failure

Seizures

Mental confusion

Coma

## Causes and Risk

Malaria is a disease caused by a parasite. *Anopheles* mosquitoes are the type of mosquito that transmit malaria from one person to another. Not all *Anopheles* mosquitoes have malaria, but if they bite a person with malaria, they can become infectious. Once they bite another person, this continues the cycle of spreading malaria from mosquito to people.

## Testing and diagnosis

See a healthcare provider as soon as possible if

You are experiencing any of the symptoms of malaria, and

You have traveled in the last year to or from an area where malaria occurs.

Only a healthcare provider can diagnose malaria. A lab test will confirm malaria using a small sample of your blood.

## Treatment

Prescription drugs can treat and cure malaria. The types of drugs and length of treatment depends on

The type of malaria,

Where (geographic location) the person was infected, and

How sick they are when treatment starts.

Other important factors are age and whether the patient is pregnant.

## Prevention

If traveling to an area where malaria spreads, talk with your healthcare provider about medications you can take to prevent malaria.

Avoid areas with high mosquito activity, especially during late evening and at night. This is when *Anopheles* mosquitoes that spread malaria bite.

Use a bug spray approved by the Environmental Protection Agency (EPA).

Wear loose-fitting, long-sleeved shirts and pants and socks.

Keep windows and doors closed or covered with screens to keep mosquitoes out of your house.

Repair broken screens on windows, doors, porches, and patios.

# Symptoms of Malaria

Malaria symptoms range from very mild to severe disease and even death.

Travelers with symptoms of malaria should see a healthcare provider as soon as possible, even if still traveling.

Some people are at higher risk of having serious malaria-related problems if they get sick.

Malaria is a curable disease if diagnosed and treated quickly and correctly.

## Symptoms

Most people begin to feel ill as **early as one week after infection or as late as a year or more.**

Malaria symptoms can include

Fever and flu-like illness

Chills

Headache, muscle aches, and tiredness

Nausea, vomiting, and diarrhea

**See a healthcare provider if you have any these symptoms.**

## Complications

Malaria symptoms may become more severe.

Anemia (low red blood cells) and jaundice (yellow coloring of the skin and eyes).

If not treated right away, the infection can become serious. It may cause kidney failure, seizures, mental confusion, coma, and death.

### **Incubation Period**

The type of mosquito that carries the malaria parasite is an *Anopheles* mosquito. When an infective *Anopheles* mosquito bites you and passes on the malaria parasite, there is a period of time before the first symptoms show. This time between mosquito bite and first sign of symptoms is called the "incubation period."

The incubation period in most cases of malaria ranges from 7 – 30 days. Different species of parasites that cause malaria in humans can cause shorter or longer incubation periods.

In addition, some malaria parasite species can remain dormant (inactive) in the liver for months or years after the initial infection. Later, after returning from an area with malaria, these parasites can then leave the liver and infect red blood cells and cause another episode of illness. Proper diagnosis and treatment can prevent malaria illness caused by these dormant parasites.

# How Malaria Spreads

Most people get malaria from the bite of an infective mosquito, also called a vector.

Most cases of malaria diagnosed in the U.S. are in people who have traveled to or from other countries where malaria is widespread. We call this imported malaria.

Locally acquired, mosquito-transmitted malaria is a rare event in the U.S.

## Causes

Malaria is a disease caused by a parasite.

## How it spreads

Most people get malaria when bitten by an infective mosquito carrying the malaria parasite. Only female *Anopheles* mosquitoes can spread malaria from one person to another. For the *Anopheles* mosquito to become infective, they must bite, or take a blood meal, from a person already infected with the malaria parasites. About one week later, that same mosquito will bite the next person and subsequently inject the parasites via her saliva. And the cycle of infection continues.

In rare occasions, malaria can spread through

Blood transfusions,

Organ transplant,

Sharing needles or syringes contaminated with malaria-infected blood, or

Congenitally, meaning from a mother to her unborn infant before or during delivery.

### **Ways malaria does not spread**

Malaria is not contagious. People can't spread malaria to other people like a cold or the flu. You can't get malaria through casual contact (sitting next to a person with malaria), close physical contact, or even sexual contact.

## Risk factors

Anyone can get malaria. Most cases occur in people who live in countries with widespread malaria. These countries are also called malaria-endemic regions. People from or living in countries with no malaria can become infected when they travel to countries with malaria.

*Plasmodium falciparum* is the parasite species causing malaria that can be severe and life-threatening. It is very common in many countries in Africa south of the Sahara Desert.

## Populations most at risk

Individuals with the most risk of getting very sick and dying from malaria include

People who have little or no recent exposure to malaria parasites. This can include young children and pregnant women or travelers coming from areas with no malaria.

People heavily exposed to the bites of mosquitoes infected with *P. falciparum*.

People living in rural areas who lack access to health care.

Due to these risk factors, an estimated 90% of deaths caused by malaria occur in Africa south of the Sahara Desert. And most of these deaths occur in children under 5 years of age.

# Testing for Malaria

Only a healthcare provider can diagnose malaria.

A lab test will confirm malaria parasite infection using a small sample of your blood.

## Why get tested

Malaria is a serious disease which can become severe if not treated quickly. Quick and accurate diagnosis of malaria is important to ensure treatment begins as soon as possible with the correct medications. Prompt treatment also helps to prevent further infection in the community by breaking the cycle of infection from infected persons via local mosquitoes. Delays in diagnosis and treatment is a leading cause of death in malaria patients in the United States.

**Only a lab test using a small sample of your blood can confirm a malaria diagnosis.**

## When to get tested

If you have traveled to an area in the last year where malaria spreads, you should get tested as soon as you experience symptoms of malaria.

## Types of tests

There are a few diagnostic tests to confirm if you have malaria.

### **Blood smear microscopy**

Blood smear microscopy test is where a small sample of blood is taken from a patient and sent to a laboratory to be examined under a microscope. It is the best way to confirm if a patient has malaria and to determine which species. Only a healthcare provider can order a microscopy test.

### **Rapid diagnostic testing (RDTs)**

Malaria rapid diagnostic tests, or RDTs, are useful test options when reliable microscopic diagnosis is not readily available. Malaria RDTs detect very small pieces from malaria parasites.

In the U.S., only a healthcare provider can order an RDT test. A small sample of blood from the patient is collected and applied to the test card's sample pad. RDTs are less sensitive than other lab tests. A blood smear microscopy test must always confirm both positive and negative RDT results in a patient with suspected malaria. Despite these limitations, RDTs can provide results in less than 15 minutes.

### **PCR testing**

PCR tests, or polymerase chain reaction tests, are also available to detect malaria parasites. These tests are more sensitive than routine blood smear microscopy tests or RDTs, but the results take longer, making them less ideal for initial diagnosis and treatment. An advantage is that PCR tests can confirm the exact species of malaria parasite if microscopy testing is not able to do so. This helps guide which medicines to use to treat a patient with malaria.

## How to get tested

See a healthcare provider immediately. They can conduct the most appropriate diagnostic test as soon as possible if they suspect malaria.

## Testing results

If you test positive for malaria, your healthcare provider will start you on medication to treat the disease immediately. The medications prescribed will be based on the type of malaria you have.

If you test negative for malaria, work with your healthcare provider to determine the cause of your symptoms.

# Preventing Malaria While Traveling

You can take medications to prevent malaria.

Check to see if malaria spreads in the region or country you will be visiting before you travel.

Take medications to prevent malaria as prescribed, including the period before travel and after you return from travel.

Avoid mosquito bites even if you are taking medications to prevent malaria.

If you experience symptoms of malaria, especially fever, while traveling or after returning, seek immediate medical attention.

## Overview

Every year, millions of U.S. residents travel to countries where malaria is present. About 2,000 cases of malaria are diagnosed in the U.S. in a typical year, mostly in returned travelers. You can prevent malaria when travelling in areas where malaria spreads by taking medications, called antimalarials, and preventing mosquito bites. There is no vaccine for malaria currently available in the U.S.

## Risk factors

Malaria does not regularly occur in the in the U.S., so there is usually no exposure to the disease here. Travelers, especially to sub-Saharan Africa, regions of South America and Southeast Asia, have the greatest risk of getting malaria and potentially dying from their infection if not diagnosed promptly and appropriately treated. All travelers to countries where malaria is present may be at risk for infection.

U.S.-based travelers going to an area where malaria spreads, even if they had some level of immunity to malaria in the past, are still at risk for infection. It's important to note that acquired immunity to (protection from) malaria weakens the longer you are away from an area where malaria is widespread or endemic. If you have been away from your country of origin, even a short time, you can lose your protective immunity very quickly and should use the same preventative measures as all travelers (preventative medication, mosquito bite prevention, etc.)

## Prevention steps

### **Before you travel**

Before you travel, learn about the health risks and precautions for malaria and other diseases for your destination. Get a detailed itinerary of all the possible destinations or places you may visit during the trip. Check to see if malaria is present and spreads in these locations. CDC's Yellow Book chapter on Malaria Prevention by Country provides detailed information about the specific parts of countries where malaria spreads. It also provides additional information including the species of malaria that occur there, if there is resistance to any of the antimalarial drugs, and the specific medicines that CDC recommends for use for malaria prevention in each country or region.

### **Understand your risk**

To understand your level of risk for getting malaria and if you need to take malaria prevention medications, consider the following

Destination country or region

Specific itinerary, including specific cities, types of accommodation (hotel with AC or open-air tents), season, and style of travel

Pregnancy status, other medical conditions, and current medications you take

Antimalarial drug resistance at your destination

### **Choose the most appropriate malaria prevention measures**

You should discuss with a healthcare provider a detailed itinerary of where you are traveling, your activities, accommodations, and your medical history to understand your risk of malaria and if you need to take medication to prevent malaria.

There are various options of medications available to prevent malaria and based on the country/countries, the urgency of the trip, and how often you prefer to take medication (daily vs. weekly).

If your provider recommends malaria prevention medications, it is important to take them as prescribed, including the period before travel and after you return from travel.

In some areas where only a few cases of malaria occur, CDC recommends preventing mosquito bites as the only way to prevent malaria.

Be aware of counterfeit (fake) or substandard (not made according to U.S. standards) drugs sold in some countries. This includes countries where malaria spreads. These drugs may not be effective. Get all your medications, including antimalarial drugs, in the US, before traveling overseas.

Healthcare providers can reference the Risk Assessment page to ensure they provide appropriate recommendation for all travelers at risk for malaria, including those returning to visit friends and relative.

### **Additional steps to take while traveling**

It is important to take steps to avoid mosquito bites even if you are taking medications as an added layer to prevent malaria.

Steps to prevent mosquito bites

Use Environmental Protection Agency (EPA)-registered insect repellents with one of the active ingredients:

DEET (Insect repellents that contain DEET offer the best protection against mosquito bites.)

Picaridin (known as KBR 3023 and icaridin outside the US)

IR3535

Oil of lemon eucalyptus (OLE)

Para-menthane-diol (PMD)

2-undecanon

Wear loose-fitting, long-sleeved shirts and pants and socks.

Use 0.5% permethrin spray to treat clothing and gear (such as boots, pants, socks, and tents) or buy permethrin-treated clothing and gear.

Do not use permethrin products directly on skin.

Keep windows and doors closed or covered with screens to keep mosquitoes out of your house.

Repair broken screening on windows, doors, porches, and patios.

Sleep in a well-screened or air-conditioned room, or sleep under a permethrin-treated bed net.

### **Know the symptoms of malaria**

Although malaria prevention strategies can be very effective, none will protect 100% of the time. Malaria is *always* a serious disease and may cause death. If you have a fever or flu-like illness either while traveling in an area where malaria spreads or after returning home (for up to one year) seek immediate medical attention. Tell your healthcare provider about your travel history.

### When immediate care is needed‎

If you experience symptoms of malaria, seek immediate medical attention.

### **Blood donation eligibility**

If you recently traveled to an area where malaria is widespread, be sure to understand if you can donate blood.

# Treatment of Malaria

Malaria is a medical emergency and can become life-threatening if not quickly diagnosed and appropriately treated.

Only a healthcare provider can diagnose and treat a patient for malaria.

Prescription drugs, available in the U.S., can cure malaria.

See a healthcare provider if you are sick and have recently been in an area where malaria is widespread.

## Treatment overview

Starting treatment immediately is the best way to treat malaria and prevent serious and life-threatening issues. The type of drugs prescribed, and length of treatment depend on

The type of malaria

The geographic location where the infection likely happened (and likelihood of drug resistance)

Your age

If you are pregnant or breastfeeding

How sick you are at the start of treatment

Patients in the U.S. are typically hospitalized for malaria treatment.

## Treatment options

Healthcare providers can refer to the CDC's Clinical Guidance: Malaria Diagnosis & Treatment in the U.S. for specific information.

# Where Malaria Occurs

Malaria is typically transmitted in tropical and subtropical areas.

Temperature is key to *Anopheles* mosquito survival and the malaria parasite completing its growth cycle within the mosquito.

Generally, in warmer regions closer to the equator, malaria transmission is more intense and can occur year-round.

## Overview

Altitude and climatic factors including temperature, humidity, and rainfall impact where malaria spreads. Malaria is typically transmitted in tropical and subtropical areas, where

*Anopheles* mosquitoes can survive and multiply, and

Malaria parasites can complete their growth cycle in the mosquitoes ("extrinsic incubation period").

Temperature is particularly critical. For example, at temperatures below 20°C (68°F), *Plasmodium falciparum* (which causes severe malaria) cannot complete its growth cycle in the *Anopheles* mosquito. Therefore, it cannot spread in these areas.

In many countries where malaria spreads, you will not find it in all parts of the country. Even within tropical and subtropical areas, you will not find malaria

At very high altitudes,

During colder seasons in some areas,

In deserts (excluding the oases), and

In some countries where spread has been interrupted through successful control/elimination programs.

Generally, in warmer regions closer to the equator, malaria transmission is more intense and year-round.

Most cases of malaria occur in sub-Saharan Africa, but it also occurs in parts of Oceania (such as Papua New Guinea) and in parts of Central and South America and Southeast Asia.

In cooler regions, spread is less intense and more seasonal. There, *P. vivax* might be more prevalent because it is more tolerant of lower average temperatures.

In many temperate areas, such as western Europe and the United States, economic development and public health measures have succeeded in eliminating malaria. However, most of these areas have *Anopheles* mosquitoes that can spread malaria, and reintroduction of the disease remains a risk.

# Lassa Fever

Lassa fever is a viral illness spread by a rat found in parts of West Africa.

People can get Lassa fever by having contact with infected rats or their saliva, urine or droppings.

Lassa fever can spread between people.

Most people with Lassa fever have mild symptoms.

Lassa fever can be deadly.

## What it is

Lassa fever is a severe viral illness that comes on quickly once someone is infected. It is spread by the "multimammate rat" or *Mastomys natalensis* (*Mastomys*), which is found throughout Sub-Saharan Africa. Currently, only West African multimammate rats are known to carry Lassa virus.

Lassa fever is found in parts of West Africa, including Sierra Leone, Liberia, Guinea and Nigeria. People who live in neighboring countries are also at risk because the rat that spreads Lassa fever lives throughout the region.

The first documented case occurred in 1969. Lassa fever is named after the town in Nigeria where the first cases occurred.

### Healthcare providers:

Review guidance on emergency services, screening, testing, infection control and PPE for viral hemorrhagic fevers, like Lassa fever, here: VHFs for Healthcare Providers

## Signs and symptoms

About 8 in 10 people who are infected have mild symptoms and are not diagnosed.

### **Mild symptoms include:**

Slight fever

Feeling tired and weak

Headache

### **In some people, the disease may cause more serious symptoms like:**

Bleeding

Difficulty breathing

Vomiting

Facial swelling

Pain in the chest, back, and abdomen

Shock

## How long it takes for signs to show

Signs and symptoms of Lassa fever typically occur 1 to 3 weeks after a person is infected.

## Complications

Lassa fever can lead to hearing loss, with about 1 out of 3 cases experiencing various levels of deafness. Deafness can occur in both mild and severe cases of Lassa fever. In many cases, the hearing loss is permanent.

If a pregnant woman is infected, there is a high risk of miscarriage. In these cases, about 95% of fetuses do not survive.

## Exposure risks

Although Lassa fever is found in West Africa, there's a risk of Lassa virus infection wherever the multimmamate rat is found.

## How it spreads

Lassa fever is caused by infection with the Lassa virus, which is spread by rodents. These rodents breed quickly and carry the virus in their urine and droppings. They often live in areas where peoples' food supplies are stored.

People mostly get Lassa fever by eating or breathing in the virus, for example:

Touching contaminated objects

Eating food that has the virus

Getting the virus in open cuts or sores

Eating rodents

Breathing in air that has infected urine or droppings

This may occur when cleaning or sweeping.

Infection can also occur after coming in contact with the body fluids of an infected person. People with Lassa fever are not contagious until after their symptoms begin. Lassa fever is not spread through casual contact, such as hugging, shaking hands, or sitting near someone.

The Lassa virus can spread in health care settings when not using proper personal protective equipment (PPE) or properly sterilizing equipment.

## Prevention

If you go to West Africa, prevent Lassa fever by keeping away from rats. You can also:

Put food away in rat-proof containers and keep the home clean.

Avoid eating these rats.

Trap rats in and around homes.

Healthcare providers caring for patients with Lassa fever, should take precautions like:

Wearing protective clothing (masks, gloves, gowns, and goggles)

Properly sterilizing equipment

Taking infection control measures

Isolating infected patients until they are cured

### Controlling rodents at home

Decreasing rat populations at home in high-risk areas helps control and prevent Lassa fever.

## Diagnosis

Diagnosing Lassa fever can be difficult because symptoms vary and are similar to symptoms caused by other diseases. Healthcare workers should contact their health department if they suspect Lassa fever in a returning traveler.

Diagnostic testing can be done in a laboratory with a high level of biosafety and enhanced infection prevention and control precautions.

The ability to diagnose Lassa fever in areas where it is commonly found can be difficult. This is due to limited laboratory capacity to test patient samples easily and safely.

## Treatment

Ribavirin, an antiviral drug, has been used to successfully treat patients with Lassa fever. It is most effective when given soon after a patient becomes sick. Patients should also receive supportive care, including rest, hydration, and treatment of symptoms.

# Cholera

Cholera is a bacterial disease spread through contaminated water and food.

Cholera can cause severe diarrhea, dehydration, and even death if the disease goes untreated.

People living in places with unsafe drinking water, poor sanitation, and inadequate hygiene are at highest risk of cholera.

## What it is

Cholera is an infection of the intestines caused by the bacterium *Vibrio cholerae*. You can get cholera from drinking water or eating food containing cholera bacteria.

Most people who get cholera don't get sick. However, cholera **can cause life-threatening watery diarrhea** and vomiting. Every year, an estimated 1.3 to 4 million people around the world get cholera, and between 21,000 to 143,000 people die.

With early and proper treatment, even severely ill patients can survive cholera.

## Signs and symptoms

People can get cholera from drinking water or eating food containing cholera bacteria.

Cholera can cause severe diarrhea which, left untreated, can lead to dehydration, even death.

## Early symptoms

People with cholera often will have mild symptoms, or no symptoms at all, and get better on their own. About 1 in 10 people will develop severe symptoms that can be life-threatening.

Early symptoms of cholera include:

Watery diarrhea, sometimes described as "rice-water stools" because they are milky white

Vomiting

Leg cramps

Restlessness or irritability

Symptoms usually appear 2-3 days after someone drinks or eats something containing cholera bacteria. Symptoms can show up within a few hours or up to 5 days.

During a cholera outbreak, people with acute watery diarrhea (3 or more loose stools a day) should seek care.

## Later symptoms

Losing body fluids quickly from diarrhea and vomiting can cause dehydration. Patients with severe cholera may have lost more than 10% of body weight by the time they seek medical care.

If untreated, severe dehydration can lead to kidney failure, shock, coma, and death.

Symptoms of dehydration include:

Rapid heart rate

Loss of elasticity in the skin

Dry mucous membranes

Low blood pressure

With early and proper treatment, even people with severe cholera can survive.

**CAUSES**

People usually get cholera from drinking water or eating food contaminated with cholera bacteria.

People traveling to or living in places with unsafe drinking water, poor sanitation, and inadequate hygiene are at the highest risk of getting cholera.

Learn what you can do to protect yourself from getting sick with cholera.

## What causes it

### Fact

‎Diarrhea from someone with cholera contains cholera bacteria. If you are caring for someone with cholera, take steps to keep yourself and others from getting sick.

People can get cholera by drinking water or eating food contaminated with cholera bacteria. Cholera can spread quickly in areas where sewage and drinking water aren't adequately treated.

Cholera bacteria also can live in brackish (slightly salty) and coastal waters. Eating raw shellfish like shrimp and crab can be a source of cholera.

Cholera is not likely to spread from person to person or from casual contact with someone with cholera.

Learn how to protect yourself and others if you are going to or living in a place where cholera is present.

## How it spreads

Large outbreaks often are related to contaminated water supplies or food from street vendors.

In some countries, people moving to urban centers strain water and sanitation systems.

For decades, some regions in Asia, Africa, and Latin America have faced an ongoing cholera pandemic. The African continent has the highest cholera case fatality rates.

## Understanding risk

People who are more likely to be exposed to cholera include healthcare personnel treating cholera patients, cholera response workers, and travelers to an area where cholera is present.

About 1 in 10 people will develop severe symptoms of cholera that can be life-threatening. Cholera can be fatal for up to 50 percent of people with severe disease. People more likely to have severe cholera include those with:

Blood type O

Chronic medical conditions

Achlorhydria (an absence of hydrochloric acids, or HCI, in the stomach)

People without access to rehydration therapy and medical services also are more likely to have severe disease from cholera.[VIEW ALLCholera](https://www.cdc.gov/cholera/site.html)

## Who is at risk

People living in areas with unsafe drinking water, poor sanitation, and inadequate hygiene are at highest risk of getting cholera.

U.S. residents can get cholera while traveling abroad and sometimes become ill after returning home. Some travelers have gotten sick after bringing contaminated seafood home with them from abroad.

## How it spreads

People usually get cholera from drinking water or eating food that contains traces of poop from someone with cholera. The disease can spread quickly in areas where sewage and drinking water aren't adequately treated.

Cholera bacteria also can live in brackish (slightly salty) and coastal waters. Eating raw shellfish can cause cholera.

Cholera is not likely to spread from person to person or from casual contact with someone with cholera.

## Prevention

Using treated water helps prevent cholera.

If you plan to travel, check if cholera is common or ongoing in the area you are visiting. If cholera is present, washing your hands with soap and safe water, drinking treated water, and getting vaccinated against cholera are among the steps that can help prevent you from getting sick.

People can get cholera from drinking water or eating food containing cholera bacteria.

Cholera can cause life-threatening watery diarrhea and vomiting.

Take steps to reduce your risk of getting cholera if you're going to an area where the disease is present.

## Prevention tips

### Keep in mind

In addition to these five prevention measures, visit a doctor or travel clinic to talk about cholera vaccination if you're going to an area where cholera is present, or where the water and food are unsafe to drink and eat.

### **If you're going to an area with cholera...**

#### **1. Drink and use safe water**

Use bottled water with unbroken seals to drink, brush your teeth, wash and prepare food, and make ice or beverages. If bottled water is not available, use water that has been properly chlorinated, boiled, or filtered.

If treating with a chlorine product:

Treat your water with one of the locally available chlorine treatment products for drinking water and follow the instructions on the label.

If boiling:

If a chlorine treatment product isn't available, boiling is an effective way to make water safe. Bring water to a rolling boil for 1 minute.

**Note:** Boiled water is at risk for recontamination and should be safely stored in a clean, covered container.

If filtering:

Use a filter with a pore size of less than or equal to 0.3 microns and treat the water with a disinfectant such as chlorine, chlorine dioxide, or iodine.

**Note:** Filtered water is at risk for recontamination and should be safely stored in a clean, covered container. Additional treatment with a chlorine product is recommended.

#### **2. Wash your hands often with soap and safe water...**

Before, during, and after preparing food

Before and after eating food or feeding your children

After using the toilet

After cleaning your child's bottom

After taking care of someone who is sick with diarrhea

**Note:** If you don't have access to soap and safe water, use an alcohol-based hand sanitizer with at least 60% alcohol.

#### **3. Use toilets**

Use toilets or safely managed sanitation facilities to get rid of poop. This includes disposing of your children's poop.

Wash your hands with soap and safe water after going to the bathroom.

If you don't have access to a toilet:

Poop at least 30 meters (100 feet) away from any body of water, including wells, and then bury your poop.

Dispose of plastic bags containing poop in latrines or at collection points if available. Or bury the bags in the ground.

Do not put plastic bags in chemical toilets.

Dig new latrines or temporary pit toilets at least a half-meter (1.6 feet) deep and at least 30 meters (100 feet) away from any body of water.

#### **4. Boil it, peel it, or leave it**

Eat foods that have been thoroughly cooked and are still hot and steaming, or fruits and vegetables that you have peeled yourself.

Avoid eating raw vegetables and fruits that can't be peeled.

Be sure to cook seafood, especially shellfish, until it is very hot all the way through.

#### **5. Clean up safely**

Clean and disinfect kitchenware and areas where you prepare food with soap and safe water. Allow them to dry completely.

Bathe and wash clothes or diapers 30 meters (100 feet) from drinking water sources.

Clean and disinfect toilets and surfaces contaminated with poop. Clean surfaces with a soap solution to remove poop, then disinfect using a solution of 1 part of household bleach to 9 parts of water.

When finished cleaning, safely dispose of soapy water and disinfection solutions by pouring them into a drain, toilet, or latrine.

Dirty rags can be cleaned with hot water and soap and allowed to fully dry. Wash your hands again with soap and safe water after cleaning and disinfecting.

## Treatment and recovery

If you think you or a family member might have cholera, get medical attention immediately. Dehydration can occur quickly and replacing lost fluids is essential. For babies with watery diarrhea, continue feeding them breast milk or formula to help them stay hydrated.

Treatment for cholera can include:

Rehydration therapy

Antibiotics

Zinc supplementation for children

## Treatment options

### **Oral Rehydration Therapy**

The most important treatment for cholera is rehydration therapy to replace fluids lost through diarrhea and vomiting. Rehydration therapy can include ORS, intravenous fluids, and electrolytes. With timely rehydration therapy, more than 99% of cholera patients survive.

### **ORS**

Many people can be completely rehydrated by drinking ORS, which is made with a prepackaged powder of salts and minerals and mixed with water that has been boiled or treated.

ORS powder is available in many pharmacies and stores. During cholera outbreaks, governments and nongovernmental agencies often distribute ORS powder.

If you think you might have cholera, start drinking ORS immediately, including on your way to a healthcare facility.

Some people who are severely dehydrated may require fluids through an IV. They still should drink ORS as soon as possible.

### **Other fluids**

If you don't have ORS, you can drink safe water, broth, or other fluids. Do **not drink** fluids with a high sugar content like**juice, soft drinks**, or **sports drinks**. Sugary drinks can make diarrhea worse.

Babies with watery diarrhea should continue to be fed breast milk or formula to help them stay hydrated.

### **Antibiotics**

In addition to rehydration therapy, antibiotics may be recommended for severely ill patients and others depending on their symptoms and medical conditions. Antibiotics can help decrease how long someone is sick. However, **antibiotics should be used along with aggressive rehydration.**

### **Zinc supplementation for children**

When available, children ages 6 months to 5 years with suspected cholera should be started on zinc supplementation immediately.

## When to get vaccinated

### If you are traveling

Visit a doctor or travel clinic to talk about cholera vaccination if you're going to an area where cholera is present, or where the water and food are unsafe to drink and eat.

You should consider getting vaccinated against cholera if you're traveling to or living in a place where:

Cholera is present

There's a cholera outbreak

The water is unsafe to drink or use

There's a humanitarian crisis with a high risk of cholera

If vaccination is recommended, visit a doctor or travel clinic to discuss your options.

Cholera vaccines are not 100% effective. Follow CDC's cholera prevention tips to help stay safe when visiting or living in an area with cholera.

## Different cholera vaccine

#### **Vaxchora**

Vaxchora is the only cholera vaccine approved for use in the United States. The FDA approved Vaxchora for people ages 2-to-64 years traveling to an area where cholera is present. The vaccine, a single dose taken by mouth, should be given at least 10 days before traveling.

Vaxchora's manufacturer reports the vaccine reduces the chance of moderate and severe diarrhea in people ages 18-45 years by 90% at 10 days after vaccination, and by 80% at 3 months. It is unknown how long protection lasts beyond 3 months.

#### **Dukora and Euvichol-Plus**

Two oral cholera vaccines have been approved by the World Health Organization (WHO). These vaccines are not available in the United States. They are:

Dukoral

Euvichol-Plus/Euvichol

#### **Cholera Vaccines Approved by FDA or WHO**

| **Vaccine name (Manufacturer)** | **Number of doses recommended** | **Recommended age** | **How long vaccination is effective** | **Available in the U.S.?** |
| --- | --- | --- | --- | --- |
| Vaxchora (Emergent BioSolutions) | 1 dose | 2-64 years | At least 3–6 months | Yes |
| Dukoral (SBL Vaccines) | 2 doses, given 1-6 weeks apart  (Children ages 2-5 years need 3 doses, given 1-6 weeks apart) | 2 years and older | 2 years | No |
| Euvichol/Euvichol-Plus (EuBiologics) | 2 doses, given at least 2 weeks apart | 1 year and older | At least 3 years for 2 doses. (One dose provides short-term protection for about one year.) | No |

# About Mpox

Mpox is a disease caused by a virus in the same family as the virus that causes smallpox.

People with mpox often get a rash, along with other symptoms.

Mpox is spread through close contact with infected people or animals.

There is no specific treatment for mpox.

## Overview

Mpox (formerly known as monkeypox) is a disease caused by infection with a virus, known as *Monkeypox virus*. This virus is part of the same family as the virus that causes smallpox. People with mpox often get a rash, along with other symptoms. The rash will go through several stages, including scabs, before healing. Mpox is not related to chickenpox.

Mpox is a zoonotic disease, meaning it can be spread between animals and people. It is endemic, or found regularly, in parts of Central and West Africa. The virus that causes mpox has been found in small rodents, monkeys, and other mammals that live in these areas.

### **Discovery and history**

The virus that causes mpox was discovered in 1958, when two outbreaks of a pox-like disease occurred in colonies of monkeys kept for research. Despite being named "monkeypox" originally, the source of the disease remains unknown. Scientists suspect African rodents and non-human primates (like monkeys) might harbor the virus and infect people.

The first human case of mpox was recorded in 1970, in what is now the Democratic Republic of the Congo. In 2022, mpox spread around the world. Before that, cases of mpox in other places were rare and usually linked to travel or to animals being imported from regions where mpox is endemic.

The World Health Organization renamed the disease in 2022 to follow modern guidelines for naming illnesses. Those guidelines recommend that disease names should avoid offending cultural, social, national, regional, professional or ethnic groups and minimize unnecessary negative effects on trade, travel, tourism or animal welfare. The virus that causes it still has its historic name, however.

## Types

There are two types of mpox, clade I and clade II:

**Clade I**is responsible for the current rise of cases in Central and Eastern Africa. Historically, clade I caused higher numbers of severe illnesses than clade II, with up to 10% of people dying from it. Recent outbreaks have seen much lower death rates of about 1-3.3%.

**Clade II** is the type that caused the global outbreak that began in 2022. Infections from clade II mpox are less severe. More than 99.9% of people survive. Clade II is endemic to West Africa.

Several countries in Central Africa are endemic for clade I mpox, while several countries in West Africa are endemic for clade II mpox.

### **Mpox clade similarities and differences**

We know that both clades and all subclades of mpox can be spread, treated, and prevented the same way, but the risk factors and locations of sustained transmission can be very different.

# Signs and Symptoms of Mpox

People with mpox often get a rash and may have other symptoms like fever, chills, and swollen lymph nodes.

Symptoms usually start within 21 days of exposure.

Visit a healthcare provider if you have a new or unexplained rash, especially after contact with someone who has mpox.

## Symptoms

People with mpox often get a rash that may be located on hands, feet, chest, face, or mouth or near the genitals, including penis, testicles, labia, and vagina, and anus. The incubation period is 3–17 days. During this time, a person does not have symptoms and may feel fine.

The rash will go through several stages, including scabs, before healing.

The rash can initially look like pimples or blisters and may be painful or itchy.

Other symptoms of mpox can include

Fever

Chills

Swollen lymph nodes

Exhaustion

Muscle aches and backache

Headache

Respiratory symptoms (e.g., sore throat, nasal congestion, or cough)

You may experience all or only a few symptoms.

## How long symptoms last

Typically, mpox symptoms start within 21 days of exposure to the virus. If you have flu-like symptoms, you will likely develop a rash 1–4 days later. If you have symptoms, such as a rash, visit a healthcare provider.

A person with mpox can spread it to others from the time symptoms start until the rash has fully healed and a fresh layer of skin has formed.

New data show that some people can spread mpox to others from one to four days before their symptoms appear. It's not clear how many people this has affected during the ongoing global outbreak that began in 2022. There is currently no evidence showing that people who never have symptoms have spread the virus to someone else. CDC will continue to monitor the latest information about how mpox spreads.

## When to talk to your doctor

If you have a new or unexplained rash or have other mpox symptoms, especially after potential exposure:

**Visit a healthcare provider.** If you think you have mpox or have had close personal contact with someone who has mpox, visit a healthcare provider to help them decide if you need to be tested for mpox. If you don't have a provider or health insurance, visit a public health clinic near you.

**Get tested if recommended.** If your healthcare provider decides that you should be tested, they will collect the specimens and send them to a laboratory for testing.

**Avoid close contact.** Until you have talked to your healthcare provider, avoid close contact, including sex or being intimate with anyone.

**Wear a mask.** When you see a healthcare provider, wear a mask.

## Risk of severe disease

Although cases of mpox are not life-threatening, some people may be more likely to get severely ill, including

People with severely weakened immune systems

Children younger than 1

People with a history of eczema

Pregnant women

# What to Do If You Are Sick

If you think you might be sick with mpox, see a healthcare provider as soon as you can.

Most people with mpox recover fully in 2 to 4 weeks without special medicines, but there are ways to treat your symptoms at home.

Some people with mpox may need special medicines, especially if you have a weakened immune system, an active skin condition, or are pregnant or breastfeeding.

Notify your close contacts and take measures to prevent others from getting sick.

## Taking care of yourself

Use gauze or bandages to cover the rash to limit spread to others and to the environment.

Wash hands often with soap and water or use an alcohol-based hand sanitizer, especially after direct contact with the rash.

If you have rash on your hands, be careful when washing or using sanitizer so as not to irritate the rash.

If you have rash on your hands, wear gloves that are non-irritating when handling common objects or touching surfaces in shared spaces. If you can, use disposable gloves that can be discarded after each use (e.g., latex, polyurethane, or nitrile gloves). Reusable gloves should be washed with soap and water between use.

Wear a well-fitting mask around other people until the rash and all other symptoms have resolved.

Eat healthy and get plenty of rest to allow your body to heal.

## Ways to cope

### **Managing your symptoms**

Medicines like ibuprofen (Advil, Motrin) and acetaminophen (Tylenol) can help you feel better. Your healthcare provider may prescribe stronger pain relievers as well.

### If pain becomes severe

Contact your healthcare provider if pain becomes severe and unmanageable at home.

### **Rash care**

The most important thing is to try not to spread the rash to other parts of the body, spread the virus to others, and possibly cause open lesions to become infected by bacteria. To keep this from happening:

Do not touch or scratch the rash.

Don't lance (pop) lesions from the rash. This doesn't speed up recovery.

Don't shave areas with the rash until the scabs have fallen off and a new layer of skin has formed.

If you do accidentally touch the rash, wash your hands with soap and water and avoid touching sensitive areas like your eyes, nose, mouth, genitals and rectum (butthole).

### **Mpox rash relief**

Topical benzocaine/lidocaine gels can be used for temporary relief. Oral antihistamines such as Benadryl and topical creams such as calamine lotion or petroleum jelly may help with itching.

Soaking in a warm bath (using oatmeal or other over-the-counter bath products for itchy skin) may offer some relief to the dry, itchy sensations that can come with the rash.

People who have the rash in or around their anus (butthole) or genitals (penis, testicles, labia, vagina), or perineum (taint) may also benefit from a sitz bath. A sitz bath is a round, shallow basin that can be purchased online or at a pharmacy. Most fit over the rim of a toilet but can also be placed in a bathtub. There is also the option to sit in a bathtub with shallow water. Your healthcare provider may prescribe medication like povidone-iodine or other products to be added to the water in a sitz bath. Adding Epsom salt, vinegar, or baking soda to the water can be soothing.

For rash in the mouth, you can rinse with salt water several times per day. Prescription mouthwashes, sometimes called miracle or magic mouthwash, or local anesthetics like viscous lidocaine can be used to manage pain. Oral antiseptics like chlorhexidine mouthwash can be used to help keep the mouth clean.

## When extra help is needed

If you're very sick with mpox or may be at a higher risk of getting very sick, there are some medications that can be used to treat mpox. These medications are not FDA-approved for mpox and are only available under special permission from FDA. These medications include tecovirimat (TPOXX), cidofovir, brincidofovir, and vaccinia immune globulin.

Your healthcare provider may prescribe these medicines to use alone, in combination with each other, or in combination with other treatments.

People who are severely ill from mpox may have:

Sores that cover 25% or more of their skin

Symptoms of the disease that affect your airway for breathing, heart, or nervous system

Sores around or in the eyes

People who may be at higher risk of becoming severely ill from mpox include:

People with severely weakened immune systems, including with HIV that isn't controlled, those with certain cancers or organ transplants, and people taking medicines that make your immune system not work as well like chemotherapy or some steroids.

People with active skin conditions like atopic dermatitis, eczema, psoriasis, or Darier disease

Women who are pregnant or breastfeeding

People under the age of 18

Talk to your healthcare provider to see if you are eligible to receive these medications.

These anti-viral medications aren't for people who have milder mpox symptoms or aren't at high risk of becoming severely ill because they may have less benefit, and medications have potential side effects. Using these medications also can increase the chance that the virus that causes mpox will develop resistance to the treatment. If that happens, these medications may not work for people who are severely ill with mpox.

## Preventing spread to others

If you have mpox, you are advised to stay at home (isolate) if you have mpox symptoms, including until your mpox rash has healed and a new layer of skin has formed. Staying away from other people, avoiding close physical contact, and not sharing things you have touched with others will help prevent the spread of mpox.

Wash hands often with soap and water or use an alcohol-based hand sanitizer, especially after direct contact with the rash. People with mpox should clean and disinfect the spaces they occupy regularly to limit household contamination.

If you cannot isolate completely while you are sick, take precautions to limit the risk of spreading mpox to others such as:

Use gauze or bandages to cover the rash to limit spread to others and to the environment.

If you have rash on your hands, wear non-irritating gloves when handling common objects or touching surfaces in shared spaces

Wear a well-fitting mask when you're around others.

Disinfect surfaces in shared bathrooms or rooms between each use.

Avoid sharing objects (e.g., towels, washcloths, drinking from the same glass).

Cover upholstered furniture and porous materials that cannot be washed.

Mpox can also spread to animals, so staying away from pets, livestock and other animals is important.

Also, it's especially important to not travel if you have fever, mouth sores, or respiratory symptoms such as sore throat, nasal congestion, or cough. Learn more at Preventing Mpox While Traveling.

### **Notifying close contacts**

If you have been diagnosed with mpox, it's important to notify your close contacts that they may have been exposed to mpox as soon as possible. This allows them to:

Watch for signs and symptoms

Get tested for mpox

Isolate if they have symptoms

Consider getting vaccinated if exposed less than 14 days ago, ideally within 4 days of exposure. Vaccination provides the best chance to prevent the disease or make it less severe.

By letting your close contacts know they may have been exposed to mpox, you are helping to protect them and everyone around them.

#### **Who are close contacts?**

A close contact is anyone who was exposed to someone with mpox symptoms through:

Having sex; this includes oral, anal, or vaginal sex.

Touching or coming in close contact with the rash of a person with mpox.

Being hugged, cuddled, kissed, or having other prolonged skin-to-skin contact.

Sharing cups, utensils, towels, clothing, bedding, blankets, or other personal objects and materials used by someone with mpox.

#### **Make a list of close contacts to notify**

Who were/are your sex partners?

Who lives with you (including family members, roommates, or overnight guests)?

Who have you recently had prolonged skin-to-skin contact with? Consider the following:

In-person meetings or gatherings you attended.

People you have met with recently (i.e., for a home visit, at a restaurant, for drinks, for dancing, for exercise, or for a party).

People you played contact sports with (for example, basketball or wrestling).

Appointments with health care providers, including dentists.

People who have provided you services, such as childcare providers, house cleaners, barbers, hairdressers, nail salon workers, massage therapists, adult care workers, etc.

People you work or volunteer with outside of the home.

#### **What to say**

If you are feeling a little uncertain about notifying your contacts, it can be helpful to prepare beforehand to make sure the communication goes smoothly. Below are few tips that may be useful:

Think through how you would want to be notified in the same situation.

Consider safety and privacy. If texting, messaging, or emailing, consider whether other people might be able read your communication. If you are notifying by phone, first ask your contact if they are in a place where they can speak privately.

Saying the words out loud can help you think through what you want to say and how you want to say it before you reach out.

Consider the person and prepare how you would want to calmly react to the different types of responses you might get.

An example of what you can say to your close contacts could be:

"Hi. I need to talk to you about something important. Do you have a few minutes to talk privately? I was diagnosed with mpox (or tested positive) on [xxx date]. Mpox can spread through close or intimate contact. Since we spent time together on [xxx date], I wanted to let you know. You should check for symptoms and get tested ASAP if you have symptoms.

#### **Other options for notifying close contacts**

If you are unable to notify your close contacts yourself, there are other options available to you:

**Health Department Assistance.** You may be contacted by a public health professional from your local health department, typically called a disease intervention specialist or DIS. A DIS may reach out to you to discuss your diagnosis, answer any questions you have, and, if you want help, confidentially notify your contacts. They will protect your privacy and not disclose anything about you. When they notify your contacts, they will connect them to services that they may need, including medical care, testing, treatment, and/or vaccines, as appropriate. However, some health departments may not be able to provide this service depending on local resources.

**Anonymous Notification Services.** You can use a reputable, online service that can notify your contacts of their possible exposure to mpox while protecting your anonymity. You can first explore the site to learn more about how they protect your privacy and the language that will be used in the notification. This site also will let your contacts know where they can obtain additional information about mpox.

Choose the method of notifying your contacts that you are most comfortable with. You can use different methods for different contacts. The important thing is to make sure that your contacts have the information they need in time to make decisions about their health and prevent spreading mpox to others.

# Preventing Mpox

Talk to a healthcare provider to learn if the mpox vaccine is recommended for you.

Avoid direct or skin-to-skin contact with people who have a rash that looks like mpox.

Don't use objects or materials a person with mpox has used.

Avoid wild animals in areas where mpox occurs regularly.

Wash hands often and learn steps to lower your risk of mpox during sex or at social gatherings.

## Prevention steps and strategies

### **Get vaccinated!**

Photo of a person's arm with a blue bandage where a vaccine was given.

A vaccine is available to prevent mpox. Talk to a healthcare provider to learn if it's recommended for you.

The JYNNEOS vaccine is recommended for prevention of mpox. Getting both doses provides the best protection. You should get two doses 4 weeks apart.

Even if it has been longer than 4 weeks since you got the first vaccine dose, you should get the second dose as soon as possible.

If you are a close contact of someone who's been diagnosed with mpox, you should get vaccinated as soon as possible after exposure to someone with mpox. Get vaccinated if you were exposed less than 14 days ago, ideally within 4 days, for the best chance to prevent the disease or make it less severe if you do get mpox.

If you previously recovered from mpox, you do not need the vaccine.

Check with your healthcare provider if the mpox vaccine is recommended for you.

Contact your healthcare provider, local pharmacy, or local health department for mpox vaccine availability.

### **Lower your risk of mpox during sex or at a social gathering**

If you are at risk for mpox but haven't received your two-dose vaccine yet, consider temporarily changing activities that involve close personal contact (such as sex).

Avoid any rash you see on others and consider minimizing skin-to-skin contact. This is particularly important at a rave, party, or club where there is minimal clothing and where there is direct, personal, often skin-to-skin contact.

Condoms (latex or polyurethane) may protect your anus (butthole), mouth, penis, or vagina from exposure to mpox. However, condoms alone may not prevent all exposures to mpox since the rash can occur on other parts of the body.

### **Avoid close, skin-to-skin contact with people who have a rash that looks like mpox and animals that carry the virus**

This might include skin with what appears to be a rash, pimples, blisters, or scabs.

The rash might appear on the hands, feet, chest, face, or mouth and other areas like on the genitals (penis, testicles, labia, vagina). Do not touch the rash or scabs of a person with mpox.

Do not kiss, hug, cuddle, or have sex with someone with mpox.

Avoid direct contact with someone who may have mpox, including kissing, hugging, and massage.

### **Avoid contact with animals where mpox occurs regularly**

In areas where mpox is endemic (found regularly), particularly in Central or West Africa, avoid contact with live or dead wild animals that can carry the virus that causes mpox, such as rodents and primates. Direct contact with infected animals can spread the virus.

### **Avoid contact with objects and materials that a person with mpox has used**

Do not share eating utensils, dishes, plates, or cups with a person with mpox.

Do not handle or touch the bedding, towels, or clothing of a person with mpox.

If you or someone you live with has mpox, follow steps for Cleaning and Disinfecting your Home.

### **Wash your hands often.**

Wash your hands often with soap and water, or use an alcohol-based hand sanitizer, especially before eating or touching your face and after you use the bathroom.

Handwashing is one of the best ways to protect you, your family, and your friends from getting sick.

### When to visit a healthcare provider‎

Watch for symptoms of mpox for 21 days from the date of your last exposure. If you have symptoms, such as a rash, visit a healthcare provider.

# Mpox Vaccination

The virus that causes mpox is related to the virus that causes smallpox. JYNNEOS is a 2-dose vaccine developed to protect against mpox and smallpox.

People need to get both doses of the vaccine for the best protection against mpox.

The second dose should be given 4 weeks after the first dose. However, if it has been longer than 4 weeks since you got the first dose, get the 2nd dose as soon as possible.

Whether or not you've been vaccinated, continue to reduce your risk of getting mpox.

## Overview

Vaccination is an important tool in stopping the spread of mpox. If you have certain risk factors that make you eligible, you can help protect yourself from mpox by getting the mpox vaccine. Contact your healthcare provider, local pharmacy, or local health department to find mpox vaccine in your area.

People who are vaccinated should continue to avoid close, skin-to-skin contact with someone who has mpox.

At this time, getting more than 2 mpox vaccine doses (a "booster") isn't recommended. If you've already had both recommended doses, you don't need any more, even if you've been exposed to someone with mpox.

If you've recovered from mpox, CDC does not recommend that you get JYNNEOS vaccine doses at this time. While it is possible for people who have recovered from mpox to get mpox, it's very rare (less than 0.001%). If they did get mpox again, the illness was generally milder than the first time.

### Countries experiencing person-to-person clade I mpox spread

CDC has vaccination recommendations for people traveling to countries with clade I outbreaks. **As of June 2, 2025,** these countries include Burundi, Central African Republic, Democratic Republic of the Congo, Ethiopia, Kenya, Malawi, Republic of the Congo, Rwanda, South Sudan, Tanzania, Uganda, and Zambia.

## Who should get vaccinated

### **CDC recommends vaccination if:**

You had known or suspected exposure to someone with mpox

You had a sex partner in the past 2 weeks who was diagnosed with mpox

You are a gay, bisexual, or other man who has sex with men (MSM), or a person who has sex with gay, bisexual, or other MSM who in the past 6 months has had any of the following:

A new diagnosis of one or more sexually transmitted diseases (e.g., chlamydia, gonorrhea, or syphilis)

More than one sex partner

You have had any of the following in the past 6 months:

Sex at a commercial sex venue (like a sex club or bathhouse)

Sex related to a large commercial event or in a geographic area (city or county for example) where mpox virus transmission is occurring

You have a sex partner with any of the above risks

You anticipate experiencing any of the above scenarios

If you are traveling to a country with a clade I mpox outbreak and anticipate any of the following activities during travel:

Sex with a new partner

Sex at a commercial sex venue (e.g., a sex club or bathhouse)

Sex in exchange for money, goods, drugs, or other trade

Sex in association with a large public event (e.g., a rave, party, or festival)

You are at risk for occupational exposure to orthopoxviruses (e.g., certain people who work in a laboratory or a healthcare facility).

### **You should NOT get the vaccine if:**

You had a severe allergic reaction (such as anaphylaxis) after getting a previous dose of the JYNNEOS vaccine or to a vaccine component.

Talk to your healthcare provider if you had an allergic reaction to the antibiotics gentamicin or ciprofloxacin, or chicken or egg protein.

## How the vaccine is given

The vaccine can be given to you subcutaneously, which means that the vaccine will be injected in the fat layer underneath the skin on the back of your upper arm (the area above the tricep muscle).

Or, the vaccine may be given between the top layers of your skin. This is called an intradermal vaccination. It can be placed in your forearm or other areas, including your upper back just below the shoulder blade or the skin of your shoulder above the deltoid muscle.

You and your provider can discuss which method to use.

Intradermal vaccination may leave a mark that others can see on your forearm. If that concerns you, you have several options:

Ask for the vaccine to be given to you subcutaneously.

Ask to get the vaccine in the skin of your upper back (just below the shoulder blade) or the skin of your shoulder (the area above the deltoid muscle).

If you have ever had keloid scars (thick, raised scars), ask for the vaccine to be given to you subcutaneously. If you are under 18 years of age, you should be given the vaccine subcutaneously. Getting the vaccine intradermally or subcutaneously is equally effective against mpox.

Although findings suggest that the first dose of JYNNEOS vaccine gives some protection against mpox, two doses are recommended to provide stronger protection. Whether you get the vaccine subcutaneously or intradermally, you should still get two doses. The second dose should be given 4 weeks (28 days) after the first dose. If you can't get your second dose on time, you should get it as soon as possible to complete the series.

### **How long it takes for the vaccine to work**

You can start to have an immune response after the first dose of JYNNEOS, but it takes two weeks after the second dose to be the most protected.

It's not known how long protection might last, or if protection might decrease over time. CDC is analyzing the current data and conducting studies to enhance the knowledge on how well the JYNNEOS vaccine works during the current mpox outbreak, as well as how long protection might last. These studies will be used to make future vaccine recommendations.

## Possible side effects

Not everyone has side effects, but some people do. The most common side effects after JYNNEOS vaccination are pain, redness, and itching at the spot where the vaccine is given. You might also experience fever, headache, tiredness, nausea, chills, and muscle aches. These are signs that your immune system is responding, not that you're getting sick.

When JYNNEOS vaccine is given intradermally, some people have reported less pain after vaccination but more side effects like itching, swelling, redness, thickening of the skin, and skin discoloration at the spot where the vaccine was given. Some of these side effects may last for several weeks. If you have concerns about receiving the vaccine intradermally, you can ask for the vaccine to be given to you subcutaneously in the fat layer underneath the skin on the back of your upper arm (triceps).

## Finding and paying for the vaccine

### **Where you can get vaccinated**

In some large cities, mpox vaccines may be available at the health department, public health clinics, hospitals, pharmacies or even at large social gatherings or venues.

In other areas, mpox vaccines may only be available from the health department.

Contact your healthcare provider, local pharmacy, or local health department for mpox vaccine availability.

### **Vaccine cost**

The cost of JYNNEOS vaccine may be covered by some health insurance plans.

Federal agencies are working to incorporate JYNNEOS vaccine into their programs to support broad access to this vaccine, including among people who are uninsured and underinsured.

# Yellow Fever

Yellow fever virus is transmitted to people primarily through the bite of infected mosquitoes.

Illness ranges from a fever with aches to severe liver disease with bleeding and yellowing skin and eyes.

A vaccine is available for at risk travelers.

You can also reduce your risk by avoiding mosquito bites.

## Overview

Yellow fever virus is spread to people by the bite of an infected mosquito. It is found in tropical and subtropical areas of Africa and South America. Yellow fever is a very rare cause of illness in U.S. travelers.

Illness ranges from a fever with aches and pains to severe liver disease with bleeding and yellowing skin and eyes (jaundice). Yellow fever is diagnosed based on laboratory testing, a person’s symptoms, and travel history.

There is no medicine to treat yellow fever. To prevent getting sick from yellow fever, protect yourself from mosquito bites and get vaccinated, if vaccination is recommended for you.

# Yellow Fever: Causes and How It Spreads

Yellow fever is caused by a virus primarily spread to people through the bite of infected mosquitoes.

Yellow fever virus is maintained in the environment between mosquitoes and non-human primates, like monkeys.

If infected, people can spread the virus to mosquitoes and rarely to other people though exposure to infected blood.

## Primary cause

Yellow fever is caused by a virus that is found in Africa and South America.

The virus belongs to a group of viruses called flaviviruses. Other flaviviruses cause disease in people, including dengue virus, West Nile virus, St. Louis encephalitis virus, and Japanese encephalitis virus.

## How it spreads

People can become infected with the virus when mosquitoes feed on infected primates (e.g., other people or monkeys) and then bite them.

In the forested areas, yellow fever virus primarily circulates between forest-dwelling mosquitoes and non-human primates, such as monkeys. People can become infected when visiting or working in forested areas where the virus is circulating.

When outbreaks occur in the urban environment, the virus primarily circulates between urban-dwelling mosquitos (primarily *Aedes*species) and people.

People infected with yellow fever virus have high enough levels of virus in their blood (viremia) during the first few days of illness to transmit the virus to mosquitoes.

Because of the high level of virus in blood, spread through blood transfusion and organ transplantation could occur.

There is one case of a mother with yellow fever virus whose infant became infected during delivery (i.e., perinatal transmission); the infant died due to yellow fever.

The virus is not spread from person-to-person through coughing, sneezing, or touching.

Prevent getting sick with yellow fever by preventing mosquito bites and getting vaccinated before traveling, if vaccination is recommended for you.

# Preventing Yellow Fever

Yellow fever virus is spread through the bite of an infected mosquito.

Yellow fever occurs in tropical and subtropical areas of Africa and South America.

The best way to prevent yellow fever is to prevent mosquito bites and get vaccinated before traveling, if vaccination is recommended for you.

## Prevention tips

Yellow fever virus is spread to people through the bite of an infected mosquito. Mosquitoes bite during the day and night. Yellow fever occurs in tropical and subtropical areas of Africa and South America.

The best way to prevent yellow fever is to protect yourself from mosquito bites and get vaccinated before traveling, if vaccination is recommended for you.

Use insect repellent

Wear long-sleeved shirts and pants

Treat clothing and gear with 0.5% permethrin

Choose lodging with air conditioning, screens on windows and doors, or use a mosquito net if you will be sleeping outdoors

# Yellow Fever Vaccine

Vaccine is recommended for people aged 9 months or older who are traveling to or living in areas at risk for yellow fever virus in Africa and South America.

Typically, one dose of the vaccine is safe and provides life-long protection against yellow fever.

Some people may have an increased risk of developing a reaction to the vaccine.

Talk to your healthcare provider to know if you should receive yellow fever vaccine before you travel.

## Yellow fever vaccine recommendations

Yellow fever vaccine is recommended for people who are 9 months old or older and who are traveling to or living in areas at risk for yellow fever virus in Africa and South America.

The vaccine is a live, weakened form of the virus. For most people, a single dose of yellow fever vaccine provides long-lasting protection, and a booster dose of the vaccine is not needed. However, travelers going to areas with ongoing outbreaks may consider getting a booster dose of yellow fever vaccine if it has been 10 years or more since they were last vaccinated. Certain countries might require you to get the vaccine; visit Travelers' Health for information on specific country requirements.

Talk to your healthcare provider to determine if you need a yellow fever vaccination or a booster shot before your trip to an area at risk for yellow fever.

## Reactions to yellow fever vaccine

Reactions to yellow fever vaccine are generally mild and include headaches, muscle aches, and low-grade fevers. Rarely, people develop severe, sometimes life-threatening reactions to the yellow fever vaccine, including:

Allergic reaction with difficulty breathing or swallowing (anaphylaxis)

Swelling of the brain, spinal cord, or the surrounding tissues (encephalitis or meningitis)

Guillain-Barré syndrome, a nervous system disorder in which a person's own immune system damages the nerve cells causing muscle weakness, and sometimes, paralysis.

Internal organ dysfunction or failure

If you recently received the yellow fever vaccination and develop fever, headache, tiredness, body aches, vomiting, or diarrhea, see your healthcare provider.

### **Am I at greater risk of a vaccine reaction?**

Some people might have an increased risk of developing a reaction to the vaccine (**precaution**) but may still benefit from being vaccinated. A few people should ***not*** get the vaccine because they have a greater risk of developing a severe reaction to the vaccine (**contraindication**). Tell your healthcare provider if you have one of the following precautions or contraindications to vaccination.

#### **Precautions**

Between 6 and 8 months old

Over 60 years old

Pregnant

Breastfeeding

#### **Contraindications**

Allergic to the vaccine or something in the vaccine (like eggs)

Aged 6 months or younger

Organ transplant recipients

Diagnosed with a malignant tumor

Diagnosed with thymus disorder associated with abnormal immune function

Diagnosed with a primary immunodeficiency

Using immunosuppressive and immunomodulatory therapies

Showing symptoms of HIV infection or CD4+ T-lymphocytes less than 200/mm3 (less than 15% of total lymphocytes in children aged 6 years or younger)

# Clinical Features and Diagnosis of Yellow Fever

Yellow fever is a mosquito-borne illness endemic to tropical and subtropical areas of Africa and South America.

Yellow fever can be a mild febrile illness to severe, sometimes fatal disease, with hepatitis and hemorrhagic manifestations.

Molecular and serologic testing for yellow fever can be performed at CDC.

Contact your state or local health department to request testing if you have a patient with suspected yellow fever. Obtain a yellow fever vaccination history prior to testing.

## Clinical considerations

Yellow fever virus is a mosquito-borne flavivirus endemic in tropical areas of Africa and South America. Although most infections are asymptomatic, clinical disease ranges from a mild febrile illness to severe disease with hepatitis and hemorrhagic manifestations. Preliminary diagnosis of yellow fever is based on the patient’s clinical features, vaccination status, and travel history, including destination, time of year, and activities.

## Signs and symptoms

In its mildest form, yellow fever is a self-limited infection characterized by sudden onset of fever and headache without other symptoms.

Other patients experience an abrupt onset of a high fever (up to 104°F [40°C]), chills, severe headache, generalized myalgias, lumbosacral pain, anorexia, nausea, vomiting, and dizziness. The patient appears acutely ill, and examination might demonstrate bradycardia in relation to the elevated body temperature (Faget’s sign). The patient is usually viremic during this period, which lasts for approximately 3 days.

Many patients recover uneventfully, but in approximately 15% of infected persons, the illness recurs in more severe form within 48 hours following the viremic period. Symptoms include fever, nausea, vomiting, epigastric pain, jaundice, renal insufficiency, and cardiovascular instability. Viremia generally is absent during this phase of symptom recrudescence. A bleeding diathesis can occur, with hematemesis, melena, metrorrhagia, hematuria, petechiae, ecchymoses, epistaxis, and oozing blood from the gingiva and needle-puncture sites. Physical findings include scleral and dermal icterus, hemorrhages (e.g., hematemesis, melena, petechiae, ecchymoses), and epigastric tenderness without hepatic enlargement.

Multiple laboratory abnormalities can be observed in patients with yellow fever; these can vary depending on the severity and stage of illness. In the first week of the illness, leukopenia might occur; however, leukocytosis also can occur during the second week of the disease. Bleeding dyscrasias also can occur, together with elevated prothrombin and partial thromboplastin times, decreased platelet count, and presence of fibrin-split products. Hyperbilirubinemia might be present as early as the third day but usually peaks toward the end of the first week of illness. Elevations of serum transaminase levels occur in severe hepatorenal disease and might remain elevated for up to 2 months after onset.

## Diagnostic testing

Laboratory diagnosis of yellow fever generally is accomplished by testing serum to detect virus-specific immunoglobulin (Ig) M and neutralizing antibodies. It is important to obtain a yellow fever vaccination history, as IgM antibodies to yellow fever vaccine virus can persist for several years following vaccination and available tests cannot differentiate antibodies raised against wild-type virus and vaccine. Serologic cross-reactions occur with other flaviviruses (e.g., West Nile or dengue viruses), so positive results should be confirmed with a more specific test (e.g., plaque-reduction neutralization test).

Early in the illness (during the first 3-4 days), yellow fever virus or viral RNA often can be detected in the serum by virus isolation or nucleic acid amplification testing (e.g., reverse transcription-polymerase chain reaction [RT-PCR]). However, by the time overt symptoms are recognized, the virus is not detectable. Viral RNA can be detected a little longer, typically in the first week after illness onset. Because of the transient viremia, negative virus isolation and RT-PCR results does not rule-out the diagnosis of yellow fever. Immunohistochemical staining of formalin-fixed material can detect yellow fever virus antigen in histopathologic specimens.

In fatal cases, nucleic acid amplification, histopathology with immunohistochemistry, and virus culture of biopsy or autopsy tissues can be positive. Only a few state laboratories or other specialized laboratories, including those at CDC, are capable of doing these specialized tests.

To submit specimens for testing, please contact your state or local health department. They can assist you with determining if samples should be sent to the CDC Arbovirus Diagnostic Laboratory for further testing. Specimens should be submitted to CDC through state health departments. All results will be sent from CDC to the appropriate state health department.

# Treatment and Prevention of Yellow Fever

There is no specific treatment for yellow fever; clinical management is supportive.

Monitor patients closely for severe complications.

Counsel travelers at risk for yellow fever about vaccination and using personal protective measures to prevent mosquito bites.

## Treatment

There is no specific treatment for yellow fever; clinical management is supportive. Treatment for symptoms can include rest, fluids, and use of analgesics and antipyretics. Patients should be advised to avoid aspirin containing drugs or other nonsteroidal anti-inflammatory drugs which might increase the risk of bleeding. Patients who develop more severe symptoms should be hospitalized for close observation and supportive treatment.

## Prevention

YF can be prevented through vaccination. A live-attenuated yellow fever virus vaccine (YF-VAX) is available in the United States.

Regardless of vaccination status, travelers should be advised to use personal protective measures to decrease exposure to infected mosquitoes. This includes using insect repellent, wearing long-sleeved shirts and pants, and treating clothing and gear with 0.5% permethrin. Travelers should choose a hotel or lodging with air conditioning or screens on windows and doors.

People infected with yellow fever virus are viremic and potentially infectious to mosquitoes shortly before the onset of fever and up to 5 days after onset. Therefore, patients with yellow fever should be advised to protect themselves against mosquito bites for up to 5 days after symptom onset.

DENGUE FEVER

## Overview

Dengue (DENG-gey) fever is a mosquito-borne illness that occurs in tropical and subtropical areas of the world. Mild dengue fever causes a high fever and flu-like symptoms. The severe form of dengue fever, also called dengue hemorrhagic fever, can cause serious bleeding, a sudden drop in blood pressure (shock) and death.

Millions of cases of dengue infection occur worldwide each year. Dengue fever is most common in Southeast Asia, the western Pacific islands, Latin America and Africa. But the disease has been spreading to new areas, including local outbreaks in Europe and southern parts of the United States.

Researchers are working on dengue fever vaccines. For now, in areas where dengue fever is common, the best ways to prevent infection are to avoid being bitten by mosquitoes and to take steps to reduce the mosquito population.

## Symptoms

Many people experience no signs or symptoms of a dengue infection.

When symptoms do occur, they may be mistaken for other illnesses — such as the flu — and usually begin four to 10 days after you are bitten by an infected mosquito.

Dengue fever causes a high fever — 104 F (40 C) — and any of the following signs and symptoms:

Headache

Muscle, bone or joint pain

Nausea

Vomiting

Pain behind the eyes

Swollen glands

Rash

Most people recover within a week or so. In some cases, symptoms worsen and can become life-threatening. This is called severe dengue, dengue hemorrhagic fever or dengue shock syndrome.

Severe dengue happens when your blood vessels become damaged and leaky. And the number of clot-forming cells (platelets) in your bloodstream drops. This can lead to shock, internal bleeding, organ failure and even death.

Warning signs of severe dengue fever — which is a life-threatening emergency — can develop quickly. The warning signs usually begin the first day or two after your fever goes away, and may include:

Severe stomach pain

Persistent vomiting

Bleeding from your gums or nose

Blood in your urine, stools or vomit

Bleeding under the skin, which might look like bruising

Difficult or rapid breathing

Fatigue

Irritability or restlessness

### When to see a doctor

Severe dengue fever is a life-threatening medical emergency. Seek immediate medical attention if you've recently visited an area in which dengue fever is known to occur, you have had a fever and you develop any of the warning signs. Warning signs include severe stomach pain, vomiting, difficulty breathing, or blood in your nose, gums, vomit or stools.

If you've been traveling recently and develop a fever and mild symptoms of dengue fever, call your doctor.

## Causes

Dengue fever is caused by any one of four types of dengue viruses. You can't get dengue fever from being around an infected person. Instead, dengue fever is spread through mosquito bites.

The two types of mosquitoes that most often spread the dengue viruses are common both in and around human lodgings. When a mosquito bites a person infected with a dengue virus, the virus enters the mosquito. Then, when the infected mosquito bites another person, the virus enters that person's bloodstream and causes an infection.

After you've recovered from dengue fever, you have long-term immunity to the type of virus that infected you — but not to the other three dengue fever virus types. This means you can be infected again in the future by one of the other three virus types. Your risk of developing severe dengue fever increases if you get dengue fever a second, third or fourth time.

## Risk factors

You have a greater risk of developing dengue fever or a more severe form of the disease if:

**You live or travel in tropical areas.** Being in tropical and subtropical areas increases your risk of exposure to the virus that causes dengue fever. Especially high-risk areas include Southeast Asia, the western Pacific islands, Latin America and Africa.

**You have had dengue fever in the past.** Previous infection with a dengue fever virus increases your risk of severe symptoms if you get dengue fever again.

## Complications

Severe dengue fever can cause internal bleeding and organ damage. Blood pressure can drop to dangerous levels, causing shock. In some cases, severe dengue fever can lead to death.

Women who get dengue fever during pregnancy may be able to spread the virus to the baby during childbirth. Additionally, babies of women who get dengue fever during pregnancy have a higher risk of pre-term birth, low birth weight or fetal distress.

## Prevention

### Vaccine

Dengue fever vaccines may be available for people ages 6 to 60. Dengue vaccination is a series of two or three doses, depending on the vaccine you get, over the course of months. These vaccines are for use by people who live where the viruses that cause dengue are common, and who have already had dengue fever at least once.

The vaccines are not available in the continental United States. But in 2019, the U.S. Food and Drug Administration approved a dengue vaccine called Dengvaxia for people ages 9 to 16 who have had dengue fever in the past and who live in U.S. territories and freely associated states where dengue fever is common.

### Prevent mosquito bites

The World Health Organization stresses that the vaccine is not an effective tool on its own to reduce dengue fever in areas where the illness is common. Preventing mosquito bites and controlling the mosquito population are still the main methods for preventing the spread of dengue fever.

If you live in or travel to an area where dengue fever is common, these tips may help reduce your risk of mosquito bites:

**Stay in air-conditioned or well-screened housing.** The mosquitoes that carry the dengue viruses are most active from dawn to dusk, but they can also bite at night.

**Wear protective clothing.** When you go into mosquito-infested areas, wear a long-sleeved shirt, long pants, socks and shoes.

**Use mosquito repellent.** Permethrin can be applied to your clothing, shoes, camping gear and bed netting. You can also buy clothing made with permethrin already in it. For your skin, use a repellent containing at least a 10% concentration of DEET.

**Reduce mosquito habitat.** The mosquitoes that carry the dengue virus typically live in and around houses, breeding in standing water that can collect in such things as used automobile tires. You can help lower mosquito populations by eliminating habitats where they lay their eggs. At least once a week, empty and clean containers that hold standing water, such as planting containers, animal dishes and flower vases. Keep standing water containers covered between cleanings.

## Diagnosis

Diagnosing dengue fever can be difficult because its signs and symptoms can be easily confused with those of other diseases — such as chikungunya, Zika virus, malaria and typhoid fever.

Your doctor will likely ask about your medical and travel history. Be sure to describe international trips in detail, including the countries you visited and the dates, as well as any contact you may have had with mosquitoes.

Your doctor may also draw a sample of blood to be tested in a lab for evidence of infection with one of the dengue viruses.

## Treatment

No specific treatment for dengue fever exists.

While recovering from dengue fever, drink plenty of fluids. Call your doctor right away if you have any of the following signs and symptoms of dehydration:

Decreased urination

Few or no tears

Dry mouth or lips

Lethargy or confusion

Cold or clammy extremities

The over-the-counter (OTC) drug acetaminophen (Tylenol, others) can help reduce muscle pain and fever. But if you have dengue fever, you should avoid other OTC pain relievers, including aspirin, ibuprofen (Advil, Motrin IB, others) and naproxen sodium (Aleve). These pain relievers can increase the risk of dengue fever bleeding complications.

If you have severe dengue fever, you may need:

Supportive care in a hospital

Intravenous (IV) fluid and electrolyte replacement

Blood pressure monitoring

Transfusion to replace blood loss

## Preparing for your appointment

You'll likely start by seeing your primary care provider. But you might also be referred to a doctor who specializes in infectious diseases.

Because appointments can be brief, and because there's often a lot of ground to cover, it's a good idea to be well prepared for your appointment. Here's some information to help you get ready, and what to expect from your doctor.

### What you can do

**Write down any symptoms you're experiencing,** including any that may seem unrelated to the reason for which you scheduled the appointment.

**Write down key personal information.** List your international travel history, with dates and countries visited and medications taken while traveling. Bring a record of your immunizations, including pre-travel vaccinations.

**Make a list of all your medications.** Include any vitamins or supplements you take regularly.

**Write down questions to ask your doctor.** Preparing a list of questions can help you make the most of your time with your doctor. List your questions from most important to least important in case time runs out.

For dengue fever, some basic questions to ask your doctor include:

What's the most likely cause of my symptoms?

What kinds of tests do I need?

What treatments are available?

How long will it be before I'm feeling better?

Are there any long-term effects of this illness?

Do you have any brochures or other printed material that I can take home with me? What websites do you recommend?

### What to expect from your doctor

Be prepared to answer questions from your doctor, such as:

When did your symptoms begin?

Have your symptoms been continuous or occasional?

How severe are your symptoms?

Does anything seem to make your symptoms better or worse?

Where have you traveled in the past month?

Were you bitten by mosquitoes while traveling?

Have you been in contact recently with anyone who was ill?

# Meningococcal Disease

Meningococcal disease is serious and can be deadly in hours.

Early diagnosis and antibiotic treatment are important.

People spread meningococcal bacteria through close or lengthy contact with other people.

Anyone can get meningococcal disease, but certain people are at increased risk.

Vaccines offer the best protection against meningococcal disease.

## What it is

Meningococcal disease is a name for any infection caused by bacteria called *Neisseria meningitidis*.

## Types

The two most common types of meningococcal infections are **meningitis**and **bloodstream infections**.

With meningococcal meningitis, the bacteria infect the lining of the brain and spinal cord and cause swelling.

With a meningococcal bloodstream infection, the bacteria enter the blood and damage the walls of the blood vessels. This causes bleeding in the skin and organs.

# Meningococcal Disease Symptoms and Complications

Meningitis and bloodstream infections are the two most common types of meningococcal infections.

Both are serious and can be deadly in a matter of hours.

Symptoms of meningococcal disease can first appear as a flu-like illness and rapidly worsen.

Seek medical attention immediately for symptoms of meningococcal disease.

## Symptoms

### **Meningococcal meningitis**

The **most common symptoms** of meningitis include:

Fever

Headache

Stiff neck

There are often additional symptoms, such as

Altered mental status (confusion)

Nausea

Photophobia (eyes being more sensitive to light)

Vomiting

#### **Symptoms in babies**

Babies may not have the classic symptoms listed above. If they do, it may be difficult to notice the symptoms.

Instead, babies may

Appear to be slow or inactive

Be irritable

Feed poorly

Have a bulging anterior fontanelle (the soft spot of the skull)

Have abnormal reflexes

Vomit

### **Bloodstream infection**

Symptoms of a bloodstream infection may include:

Cold hands and feet

Diarrhea or nausea with or without vomiting

Fatigue (feeling tired)

Fever and chills

Rapid breathing

Severe aches or pain in the muscles, joints, chest, or abdomen (belly)

In the later stages, a dark purple rash

## Complications and when to seek help

Even with antibiotic treatment, 10 to 15 in 100 people with meningococcal disease will die.

One in 5 survivors will have **long-term disabilities**, such as:

Brain damage

Deafness

Loss of limb(s)

Nervous system problems

# Risk Factors for Meningococcal Disease

Anyone can get meningococcal disease, but certain people are at increased risk.

A person's risk can vary due to many factors.

CDC recommends meningococcal vaccination for preteens and teens, as well as people at increased risk for meningococcal disease.

## What increases risk

Factors that increase someone's risk for meningococcal disease include:

Age

Certain medical conditions

Certain medicines

Close or lengthy contact with someone with meningococcal disease

Places and settings where people work, live, and travel

## People at increased risk

### **Age**

Infants, teens and young adults, and older adults have the highest rates of meningococcal disease in the United States. Specifically, healthcare providers more commonly diagnose meningococcal disease in

Children younger than 1 year old

Teens and young adults ages 16 through 23 years old

Adults 65 years and older

## Conditions that can increase risk

Certain medical conditions weaken the immune system and increase someone's risk for meningococcal disease:

Complement component deficiencies

Functional and anatomic asplenia

HIV infection

### **Complement component deficiencies**

Complement component deficiencies refer to disorders of the 'complement system,' which helps the body fight off infections. People may have deficiencies of complement components like C3, C5-9, properdin, factor H, and factor D.

These disorders are **very rare and usually genetic**.

### **Functional and anatomic asplenia**

The spleen is an important organ for fighting meningococcal infections because it helps produce antibodies and filter bacteria. People can have one of two types of asplenia:

**Anatomic asplenia**: Not having a spleen (if it was surgically removed)

**Functional asplenia**: Having a spleen that doesn't work like it should

People with sickle cell anemia have functional asplenia.

### **HIV infection**

A **low CD4 count** or **high viral load**increases risk for meningococcal disease for people with HIV.

### Fact sheet: What people with HIV need to know

This fact sheet describes common outcomes of meningococcal disease, a rare but very serious illness. People with HIV are at increased risk for meningococcal disease and should get a meningococcal conjugate vaccine.

## Behaviors that can increase risk

### **Receiving medicines**

People who receive **complement inhibitors** such as eculizumab (Soliris®) and ravulizumab (Ultomiris™) are at increased risk for meningococcal disease.

Healthcare providers most commonly prescribe complement inhibitors for four rare medical conditions:

Atypical hemolytic uremic syndrome, a blood disorder

Generalized myasthenia gravis, a disorder that leads to muscle weakness

Neuromyelitis optica spectrum disorder, a disorder of the brain and spinal cord

Paroxysmal nocturnal hemoglobinuria, a blood disorder

### Complement inhibitors increase meningococcal disease risk

Neither vaccination nor preventive antibiotics can prevent all cases of meningococcal disease in people who receive complement inhibitors. If you take a complement inhibitor and have symptoms of meningococcal disease, get medical care right away. Tell the healthcare provider you are taking a complement inhibitor.

### **Having close or lengthy contact**

People with close or lengthy contact with someone with meningococcal disease are at increased risk of getting sick, especially

Anyone with direct contact with the patient's oral secretions, such as a kissing partner

People in the same household

Roommates

## Places with increased risk

Where people **work, live, and travel**can also increase their risk for meningococcal disease.

The following groups can be at increased risk:

**Microbiologists**who work with the bacteria that cause meningococcal disease

**College students**, compared to other teens and young adults

**Military recruits**, likely due to age and living in a crowded setting (i.e., military training facilities)

**Travelers**to the meningitis belt in sub-Saharan Africa

## Causes

*N. meningitidis*are bacteria that can live in the back of the nose and throat. About 1 in 10 people have these bacteria in their throat and aren't sick.

Sometimes the bacteria move to other parts of the body and cause infection.

### **Spread to others**

People spread meningococcal bacteria to others by **sharing respiratory and throat secretions** (saliva or spit).

Generally, it takes **close or lengthy** **contact**to spread the bacteria.

Example of close contact: Kissing

Example of lengthy contact: Living together

They aren't as contagious as germs that cause the common cold or the flu.

## Prevention

### **Vaccination**

The best way to prevent meningococcal disease is to get vaccinated. CDC recommends meningococcal vaccination for

All preteens and teens

Children and adults at increased risk for meningococcal disease

# Meningococcal Vaccination

CDC recommends meningococcal vaccination for all preteens and teens, as well as other children and adults at increased risk.

Meningococcal vaccines are the best way to protect against meningococcal disease, but side effects can occur.

Talk to a vaccine provider if you have questions about meningococcal vaccines.

## Overview

There are 3 types of meningococcal vaccines used in the United States:

Meningococcal conjugate or MenACWY vaccines

Serogroup B meningococcal or MenB vaccines

Pentavalent or MenABCWY vaccines

## Why getting vaccinated is important

Meningococcal disease is uncommon but can cause serious illness and death in people of all ages. Meningococcal vaccines help protect against meningococcal disease.

## Who should and shouldn't get vaccinated

### **Vaccine recommendations**

CDC recommends meningococcal vaccination for

All preteens and teens

Children 2 months through 10 years old at increased risk

Adults 19 years and older at increased risk

### **Allergies, reactions: Talk with a vaccine provider**

Talk to a vaccine provider about your vaccination history and a specific vaccine's ingredients. There may be times when someone shouldn't get a meningococcal vaccine, like if they:

Had a life-threatening allergic reaction after the vaccine

Have a life-threatening allergy to any part of the vaccine

### Feeling sick?

Generally, vaccination is fine during mild illnesses like a cold. A vaccine provider can advise on whether to get vaccinated or wait until you feel better.

## How well they work

Vaccines that help protect against meningococcal disease work well but can't prevent all cases.

## Possible side effects

Most people who get a meningococcal vaccine don't have any problems with it. Like with medicines, there is a chance of side effects with vaccines. These are usually mild and go away on their own within a few days, but serious reactions are possible.

**MenACWY vaccines**

 Redness or soreness where the vaccine provider gave the shot

 Muscle pain

 Headache

 Feeling tired

**MenB and MenABCWY vaccines**

 Redness, soreness, or swelling where the vaccine provider gave the shot

 Feeling tired

 Headache

 Muscle or joint pain

 Fever or chills

 Nausea or diarrhea

If problems occur after MenACWY vaccination, they usually last for 1 or 2 days.

If problems occur after MenB or MenABCWY vaccination, they usually last for 3 to 5 days.

## Finding and paying for vaccines

### **Vaccination locations**

#### **Children and teens**

Meningococcal vaccines are part of the routine childhood immunization schedule. Therefore, they are regularly available for children at

Pediatric and family practice offices

Community health clinics

Public health departments

#### **Adults**

For adults, a healthcare provider's office or pharmacy are usually the best places to receive recommended vaccines. If your healthcare provider doesn't have meningococcal vaccines, ask for a referral.

Federally funded health centers can also provide services if you don't have a regular source of health care. Locate one near you.

### **Antibiotics**

Close contacts of someone with meningococcal disease should receive antibiotics to prevent them from getting sick. A healthcare provider or health department generally decides who should get preventive antibiotics.

### **Re-infection**

Although rare, people can get meningococcal disease more than once. People who get meningococcal disease twice should get tested to see if they have an underlying immune deficiency (weakened immune system).

## Testing and diagnosis

Meningococcal disease can be **difficult to diagnose**because the signs and symptoms are often similar to other illnesses.

Healthcare providers who suspect meningococcal disease will collect samples of blood or cerebrospinal fluid (fluid near the spinal cord). They then send the samples to a lab for testing.

If bacteria are in the samples, laboratory workers can culture (grow) them. This helps healthcare providers know what's causing the infection and which antibiotic will work best.

Other tests can sometimes detect and identify the bacteria if the cultures don't.

## Treatment and recovery

Healthcare providers treat meningococcal disease with antibiotics. A patient will **get antibiotics right away**if a healthcare provider thinks they have meningococcal disease. Antibiotics help reduce the risk of dying.

Depending on how serious the infection is, people with meningococcal disease **may need other treatments**, including:

Breathing support

Medications to treat low blood pressure

Surgery to remove dead tissue

Wound care for parts of the body with damaged skin

TYPHOID FEVER

## Overview

Typhoid fever, also called enteric fever, is caused by salmonella bacteria. Typhoid fever is rare in places where few people carry the bacteria. It also is rare where water is treated to kill germs and where human waste disposal is managed. One example of where typhoid fever is rare is the United States. Places with the highest number of cases or with regular outbreaks are in Africa and South Asia. It is a serious health threat, especially for children, in places where it is more common.

Food and water with the bacteria in it cause typhoid fever. Close contact with a person who is carrying the salmonella bacteria also can cause typhoid fever. Symptoms include:

High fever.

Headache.

Stomach pain.

Constipation or diarrhea.

Most people who have typhoid fever feel better about a week after they start treatment to kill bacteria, called antibiotics. But without treatment, there is a small chance of death from typhoid fever complications. Vaccines against typhoid fever can provide some protection. But they can't protect against all cases of illness caused by other strains of salmonella. Vaccines can help lower risk of getting typhoid fever.

## Symptoms

Symptoms are likely to start slowly, often showing up 1 to 3 weeks after exposure to the bacteria.

### Early illness

Early symptoms include:

Fever that starts low and increases throughout the day, possibly reaching as high as 104 degrees Fahrenheit (40 degrees Celsius).

Chills.

Headache.

Weakness and fatigue.

Muscle aches.

Stomach pain.

Diarrhea or constipation.

Rash.

People also may have a cough, loss of appetite and sweating.

### Later illness

A few weeks after symptoms start, the illness can cause problems in the intestines. People may have:

Stomach pain.

Very swollen stomach.

An infection caused by gut bacteria spreading throughout the body, called sepsis.

In very serious cases, people may:

Become confused.

Not be able to pay attention to anything around them.

Not be able to react to the world around them.

These are life-threatening complications.

In some people, symptoms may return up to a few weeks after the fever has gone away.

## When to see a doctor

See a health care provider right away if you think you might have typhoid fever.

If you get sick while traveling in a foreign country, know who to call for a list of providers. For some that might be the closest embassy or consulate.

If you have symptoms after you return home, consider seeing a provider who focuses on international travel medicine or infectious diseases. This might help get typhoid fever diagnosed and treated more quickly.

## Causes

A bacteria strain called Salmonella enterica serotype typhi causes typhoid fever. Other strains of salmonella bacteria cause a similar disease called paratyphoid fever.

People pick up the bacteria most often in places where outbreaks are common. The bacteria passes out of the body in the stool and urine of people who are carrying the bacteria. Without careful hand-washing after going to the bathroom, the bacteria can move from the hands to objects or other people.

The bacteria also can spread from a person who carries the bacteria. It can spread on food that isn't cooked, such as raw fruits without a peel. In places where water isn't treated to kill germs, you can pick up the bacteria from that source. This includes drinking water, using ice made from untreated water, or by drinking unpasteurized milk or juice.

### Typhoid carriers

Even after antibiotic treatment, a small number of people who recover from typhoid fever still have the bacteria living in their bodies. These people are known as chronic carriers. They no longer have symptoms of the disease. But they still shed the bacteria in their stools and spread it.

## Risk factors

Typhoid fever is a serious worldwide threat and affects millions of people each year. Places with the highest number of cases or with regular outbreaks are in Africa and South Asia. But cases are recorded worldwide, often due to travelers to and from these areas.

If you live in a country where typhoid fever is rare, you're at increased risk if you:

Work in or travel to areas where typhoid fever is established, especially if you travel to visit family or friends. People visiting loved ones may have higher social pressure to drink or eat foods that present a higher risk.

Work as a clinical microbiologist handling Salmonella enterica serotype typhi bacteria.

Have close contact with someone who is infected or has recently been infected with typhoid fever.

## Complications

### Damage to the intestines

Typhoid fever complications can include damage and bleeding in the intestines. Typhoid fever also can cause cells in the walls of the small intestine or large bowel to die off. This allows the contents of the gut to leak into the body. That can cause severe stomach pain, vomiting and infection throughout the body called sepsis.

Damage to the intestines can develop in the later part of the illness. These life-threatening complications require immediate medical care.

Other possible complications include:

Inflammation of the heart muscle, called myocarditis.

Inflammation of the lining of the heart and valves, called endocarditis.

Infection of major blood vessels, called mycotic aneurysm.

Pneumonia.

Inflammation of the pancreas, called pancreatitis.

Kidney or bladder infections.

Infection and inflammation of the membranes and fluid surrounding the brain and spinal cord, called meningitis.

Psychiatric problems, such as delirium, hallucinations and paranoid psychosis.

## Prevention

People can get a vaccination against typhoid fever. This is an option if you live where typhoid fever is common. It is also an option if you plan to travel to a place where the risk is high.

Where typhoid fever is common, access to treated water helps avoid contact with the Salmonella enterica serotype typhi bacteria. Management of human waste also helps people avoid the bacteria. And careful hand-washing for people who prepare and serve food is also important.

### Vaccines

Two vaccines are available in the United States for people age 2 and older.

One is given as a single shot at least one week before travel.

One is given orally in four capsules, with one capsule to be taken every other day.

The effectiveness of these vaccines wears off over time. So repeat immunization is needed.

Because the vaccine won't provide complete protection, follow these guidelines when traveling to high-risk areas:

**Wash your hands.** Frequent hand-washing in hot, soapy water is the best way to control infection. Wash before eating or preparing food and after using the toilet. Carry an alcohol-based hand sanitizer for times when soap and water aren't available.

**Avoid using untreated water.** Contaminated drinking water is a problem in areas where typhoid fever is common. For that reason, drink only bottled water or canned or bottled carbonated beverages, wine and beer. Carbonated bottled water is safer than noncarbonated bottled water. Ask for drinks without ice. Use bottled water to brush your teeth, and try not to swallow water in the shower.

**Avoid raw fruits and vegetables.** Because raw produce may have been washed in contaminated water, avoid fruits and vegetables that you can't peel, especially lettuce. To be safe, you may want to avoid raw foods.

**Choose hot foods.** Avoid food that's stored or served at room temperature. Freshly made, steaming hot foods may be less risky than uncooked foods.

**Know where the health care providers are.** Find out about medical care in the areas you'll visit. Carry a list of the names, addresses and phone numbers of health care providers.

### Prevent infecting others

If you're recovering from typhoid fever, these measures can help keep others safe:

**Take your antibiotics.** Follow your health care provider's instructions for taking your antibiotics and be sure to finish the entire prescription.

**Wash your hands often.** This is the single most important thing you can do to keep from spreading the infection to others. Use hot, soapy water and scrub thoroughly for at least 30 seconds, especially before eating and after using the toilet.

**Avoid handling food.** Avoid preparing food for others until your health care provider says you're no longer contagious. If you work with food, you may need to take a test to show you aren't shedding typhoid bacteria. If you work in health care, you also may need to show you aren't shedding the bacteria

## Diagnosis

### Medical and travel history

Your health care provider may suspect typhoid fever based on your symptoms, and your medical and travel history. The diagnosis is often confirmed by growing the Salmonella enterica serotype typhi in a sample of your body fluid or tissue.

### Body fluid or tissue culture

A sample of your blood, stool, urine or bone marrow is used. The sample is placed in an environment where bacteria grow easily. The growth, called a culture, is checked under a microscope for the typhoid bacteria. A bone marrow culture often is the most sensitive test for Salmonella typhi.

A culture test is the most common diagnostic test. But other testing may be used to confirm typhoid fever. One is a test to detect antibodies to typhoid bacteria in your blood. Another test checks for typhoid DNA in your blood.

## Treatment

Antibiotic therapy is the only effective treatment for typhoid fever.

### Commonly prescribed antibiotics

The medicine you get to treat typhoid fever may depend on where you picked up the bacteria. Strains picked up in different places respond better or worse to certain antibiotics. These medicines may be used alone or together. Antibiotics that may be given for typhoid fever are:

**Fluoroquinolones.** These antibiotics, including ciprofloxacin (Cipro), may be a first choice. They stop bacteria from copying themselves. But some strains of bacteria can live through treatment. These bacteria are called antibiotic resistant.

**Cephalosporins.** This group of antibiotics keeps bacteria from building cell walls. One kind, ceftriaxone, is used if there is antibiotic resistance.

**Macrolides.** This group of antibiotics keeps bacteria from making proteins. One kind called azithromycin (Zithromax) can be used if there is antibiotic resistance.

**Carbapenems.** These antibiotics also prevent bacteria from building cell walls. But they focus on a different stage of that process than the cephalosporins. Antibiotics in this category may be used with severe disease that doesn't respond to other antibiotics.

### Other treatments

Other treatments include:

**Drinking fluids.** This helps prevent the dehydration caused by a long fever and diarrhea. If you're very dehydrated, you may need to receive fluids through a vein.

**Surgery.** If the intestines are damaged, you may need surgery to repair them.

## Preparing for your appointment

Call your health care provider if you have symptoms of typhoid fever. This is especially important if you or a close companion recently traveled to a place that has a high risk of typhoid fever. If your symptoms are severe, go to an emergency room or call 911 or your local emergency number.

Here's some information to help you get ready and know what to expect from your health care provider.

### Information to gather in advance

**Pre-appointment restrictions.** At the time you make your appointment, ask if there are restrictions you need to follow in the time leading up to your visit. Your health care provider will not be able to confirm typhoid fever without a blood test. The provider may suggest actions you can take to lower the risk that you'll spread the bacteria to someone else.

**Symptom history.** Write down any symptoms you're experiencing and for how long.

**Recent exposure to possible sources of infection.** Be prepared to describe international trips in detail, including the countries you visited and the dates you traveled.

**Medical history.** Make a list of your key medical information, including other conditions for which you're being treated and any medications, vitamins or supplements you're taking. Your provider also will need to know your vaccination history.

**Questions to ask your health care provider.** Write down your questions in advance so that you can make the most of your time with your provider.

For typhoid fever, possible questions to ask your provider include:

What are the possible causes for my symptoms?

What kinds of tests do I need?

Are treatments available to help me recover?

I have other health problems. How can I best manage these conditions together?

How long do you expect a full recovery will take?

When can I return to work or school?

Am I at risk of any long-term complications from typhoid fever?

Don't hesitate to ask any other related questions you have.

### What to expect from your doctor

Your provider is likely to ask you a number of questions. Being ready to answer them may reserve time to go over any points you want to talk about in-depth. Your provider may ask:

What are your symptoms and when did they begin?

Have your symptoms gotten better or worse?

Did your symptoms briefly get better and then come back?

Have you recently traveled abroad? Where?

Did you update your vaccinations before traveling?

Are you being treated for any other medical conditions?

Are you currently taking any medications?

# Hepatitis E

Hepatitis E is a liver disease caused by the hepatitis E virus (HEV).

Hepatitis E is common in many parts of the world where sanitation is poor.

Most people recover fully from hepatitis E without any complications.

Hepatitis E can only be diagnosed with laboratory tests.

## About hepatitis E

Hepatitis E is a liver infection caused by HEV. Most people with hepatitis E fully recover and have no long-term liver problems from their infection.

Hepatitis E is common in many parts of the world where sanitation is poor. It is not common in the United States, where people have access to clean drinking water. Most cases in the US involve people who have recently traveled to countries where hepatitis E is common.

## Types

Most people fully recover from acute hepatitis E without any complications. In rare cases, some people with compromised immune systems develop chronic hepatitis E.

## Signs and symptoms

Many people with hepatitis E, especially young children, do not have any symptoms. Others may experience one or more of these symptoms:

Dark urine or clay-colored stools

Feeling tired

Fever

Joint pain

Loss of appetite

Nausea, stomach pain, throwing up

Yellow skin or eyes (jaundice)

If symptoms occur, they usually appear anywhere from 2 to 6 weeks after exposure to HEV.

## At-risk populations

Travelers to areas of the world with poor sanitation are at greatest risk for getting hepatitis E. Certain populations are at risk for more severe outcomes due to hepatitis E, such as long-term liver problems and liver failure, including:

Pregnant women.

People who have had solid organ transplants.

People with compromised immune systems.

## How it spreads

HEV is found in the stool of people infected with the virus. It's spread when someone unknowingly ingests the virus — even in microscopic amounts.

In countries with poor sanitation, people most often get hepatitis E from drinking water contaminated by feces from people who are infected with the virus. In the US and other countries where hepatitis E is not common, people have gotten sick with hepatitis E after eating raw or undercooked pork, venison (deer), wild boar meat, or shellfish.

## Prevention

No vaccine is available in the US to protect against hepatitis E. However, you can lower your risk for HEV infection by drinking only purified water when visiting countries where hepatitis E is common and by avoiding raw or undercooked pork, venison, and wild boar meat.

## Screening, testing, and diagnosis

Hepatitis E can only be diagnosed with laboratory tests. If you are having symptoms of hepatitis E, see your doctor.

## Treatment and recovery

There is no specific treatment for hepatitis E. Most people recover from hepatitis E with rest and by managing their symptoms with the help of their doctor.

# Sleeping Sickness (African Trypanosomiasis)

Sleeping sickness, also known as human African trypanosomiasis (HAT), is a disease caused by a parasite.

You can get the parasite that causes sleeping sickness from the bite of a tsetse fly in sub-Saharan Africa.

Sleeping sickness is a serious disease. Diagnosis and treatment can be lifesaving.

## Overview

Sleeping sickness (i.e., human African trypanosomiasis or HAT) is caused by the parasite *Trypanosoma brucei*. A parasite is an organism (a living thing) that lives on or inside another organism. Sleeping sickness spreads through the bite of a tsetse fly (*Glossina*species), found only in rural, sub-Saharan Africa. The disease causes death if left untreated. There are two types of sleeping sickness. Each one is named for the region in Africa where it was historically found.

### **Types**

There are two types of sleeping sickness:

#### **West African sleeping sickness**

Spread by bites from a tsetse fly carrying the parasite *T. b. gambiense*.

Disease is slow to progress (a few months to a year or more after exposure).

Found in rural parts of Central and West Africa.

The World Health Organization (WHO) publishes the number of West African sleeping sickness cases reported each year to its website.

#### **East African sleeping sickness**

Spread by bites from a tsetse fly carrying the parasite *T. b. rhodesiense.*

Disease progresses in severity very quickly (one to several weeks after exposure).

Found in rural parts of Eastern and Southern Africa and less commonly reported than West African sleeping sickness.

The World Health Organization (WHO) publishes the number of East African sleeping sickness cases reported each year to its website.

## Causes

Two subspecies of the *Trypanosoma brucei* parasite cause sleeping sickness or human African trypanosomiasis (HAT).

West African sleeping sickness is spread by the parasite *T. b. gambiense*. East African sleeping sickness is spread by the parasite *T. b. rhodesiense*.

These parasites are only found in sub-Saharan Africa and spread by the bite of the tsetse fly (*Glossina*species). The percentage of tsetse flies carrying these parasites is low.

East African sleeping sickness is found in Eastern and Southeastern Africa and caused around 5% of cases in 2022.

Western African sleeping sickness is found in central Africa and limited areas of West Africa. It is the most common type, making up 95% of cases in 2022.

## How it spreads

You can get sleeping sickness from the bite of an infective tsetse fly.

Tsetse flies live in:

Rural areas

Woodlands and thickets in the East African savannah

Forests and vegetation along streams in central and West Africa

Tsetse flies bite during daylight hours. Both male and female flies can spread the parasite that causes the disease.

### **Other causes**

Pregnant women can occasionally pass the *T. b. gambiense* parasite that causes West African sleeping sickness to their unborn baby.

Although rare, the condition may also spread through:

Sexual contact

Blood transfusion

Organ transplantation

Accidental laboratory exposure

However, such cases are poorly documented.

## Risk factors

Sleeping sickness affects people in rural areas of African countries. Travelers to urban areas in those countries are at low risk.

People at higher risk include:

Hunters

Villagers with infected cattle herds

Tourists and others working in or visiting game parks

Your risk of infection increases with the number of times you are bitten by the tsetse fly. This is because most flies are not infective.

Tsetse flies that spread sleeping sickness are found only in sub-Saharan Africa.

## Signs and symptoms

Sleeping sickness occurs in two stages. The first stage typically causes mild, flu-like symptoms. The second stage causes more severe symptoms that affect your brain and central nervous system. Symptoms of each stage take longer to appear in West African sleeping sickness.

If you recently traveled to east or west Africa and were bitten by a tsetse fly, you could have sleeping sickness. Some people who have sleeping sickness develop a red sore, called a chancre, within two days to two weeks of an infected tsetse fly bite but chancres are not always present or noticed.

Sleeping sickness occurs in two stages. The specific symptoms and duration of each stage can vary depending on whether you have East or West African sleeping sickness. However, many of the signs and symptoms are common to both stages, making it difficult to distinguish between the two stages by clinical features alone.

### **East African sleeping sickness**

#### **First stage, 1 – 3 weeks**

The first stage starts when you are bitten by an infective tsetse fly and the parasite enters your bloodstream.

#### **Second stage, a few weeks – two months**

The second stage of infection begins as the parasite infects your brain and central nervous system.

If you have East African sleeping sickness, you are more likely to experience issues with your endocrine system (thyroid, adrenal glands), hormones, and cardiac issues (myocarditis or inflammation of the heart).

### **West African sleeping sickness**

#### **First stage, 1 month – 1 year**

West African sleeping sickness disease progresses more slowly. Your symptoms in the first stage may be minimal or irregular in the first few months and can take a few months to a year to be apparent.

#### **First stage symptoms**

The first stage of sleeping sickness generally causes mild symptoms:

Raised, red sore (chancre) at the site of the bite (appears within 2 – 14 days; not always present or noticed; more common with East African sleeping sickness)

Headache

Fevers that come and go

General discomfort (malaise), weakness, and fatigue

Itchy, irritated skin

Achy muscles and joint pain

Loss of appetite or weight loss

Swollen lymph nodes in the armpits, groin, or inner and upper arm near your elbow

#### **Second stage, one year or more**

West African sleeping sickness can take longer than a year to progress to the second stage of infection. If you don't get treatment, your symptoms can become worse. You can die within months of the second stage of infection.

#### **Second stage symptoms**

The second stage of sleeping sickness affects your brain and central nervous system, causing more severe symptoms:

Sleep/wake cycle reversal (sleepy during the day, awake at night)

Unusual anxiety

Unstable or fluctuating (labile) emotions

Hallucinations (experiencing things that don't exist) or delirium (mental state of confusion)

Sensory disturbances (sensitive skin, loss of sensation, itching, visual problems)

Tremors (ataxia) or slurred speech

Seizures

Coma (prolonged unconsciousness)

## Risk factors

Sleeping sickness affects people in rural areas of African countries. Travelers to urban areas in those countries are at low risk.

People at higher risk include:

Hunters

Villagers with infected cattle herds

Tourists visiting and others working in game parks

Tsetse flies that spread sleeping sickness live only in some African countries. Most flies in these rural areas are not carrying the parasite that causes sleeping sickness. However, the more often you are bitten, the more you are at risk of infection.

You cannot contract the disease in the U.S.

## How it spreads

You can get sleeping sickness from the bite of an infective tsetse fly.

Occasionally, a pregnant woman may pass the parasite *Trypanosoma brucei* to her unborn baby.

Although rare and not well documented, the parasite may also spread through

Sexual contact

Blood transfusion

Organ transplantation

Accidental laboratory exposure

## Prevention

There is no vaccine or drug available to prevent sleeping sickness.

The best way to prevent infection is to prevent bites from the tsetse fly:

Wear protective, neutral-colored clothing, including long pants, long-sleeved shirts, and socks.

Inspect vehicles for tsetse flies before entering.

Avoid bushes.

Use insect repellant.

The best way to prevent sleeping sickness is to avoid contact with the tsetse fly. If you're traveling to sub-Saharan Africa, and specifically regions where sleeping sickness is common, residents may be able to provide advice about places infested with the tsetse flies to avoid.

To prevent bites from the tsetse fly

Wear protective, neutral-colored clothing.

Tsetse flies can bite through thin fabric; therefore, it's recommended you wear medium-weight clothing.

They are attracted to bright and very dark colors.

Inspect vehicles for tsetse flies before entering.

They are attracted to moving vehicles.

Avoid bushes.

The tsetse fly is less active during the hottest period of the day. It rests in bushes but will bite if disturbed.

Use insect repellant.

Permethrin-treated clothing and insect repellant are not particularly effective against tsetse flies, but they will prevent other insect bites that can cause illness.

## Diagnosis

There are several tests that can diagnose sleeping sickness. Talk with your healthcare provider right away if you have traveled to rural areas of the countries in Africa where sleeping sickness spreads and are experiencing any of the symptoms or think you may have sleeping sickness.

It is difficult to diagnose sleeping sickness in the first stage of infection. Early signs and symptoms are not unique to sleeping sickness. Finding the parasite in a sample of your body fluid or tissue is important for diagnosis but may be challenging. Tests are often not sensitive enough to find the parasite in the first stage of infection unless there are a lot of parasites present.

There are several tests that can diagnose sleeping sickness. Talk with your healthcare provider immediately if you think you have sleeping sickness.

## Testing

To diagnose you with either kind of sleeping sickness, your provider must find the parasite in a sample of your body fluid or tissue.

### **West African sleeping sickness**

It can be difficult to detect the parasite that causes West African sleeping sickness with routine testing of your blood. Therefore, your provider will often look for the parasite in a sample from your lymph node under a microscope. The parasite may also be found in your spinal fluid during the second stage of the disease.

### **East African sleeping sickness**

If you have symptoms of East African sleeping sickness, your healthcare provider can usually find the parasite by looking at a sample of your blood under a microscope. The parasite may also be found in your spinal fluid during the second stage of the disease.

## Treatment

If diagnosed with sleeping sickness, start medical treatment as soon as possible. Your laboratory results should guide your treatment.

Hospitalization is usually necessary for treatment. Follow-up care may require lumbar puncture (spinal tap) every six months or sooner, if symptoms return, for two years.

Start medical treatment of sleeping sickness as soon as possible once diagnosed. Your healthcare provider will base your treatment on whether you have East or West African sleeping sickness. Treatment also depends on your stage of infection—specifically, whether the parasite has entered your central nervous system yet.

Hospitalization is usually necessary for treatment. Your follow-up care may require a lumbar puncture (spinal tap) every six months or sooner, if symptoms appear, for two years.

### **Treating East African sleeping sickness**

The drugs used to treat East African sleeping sickness are not commercially available in the United States. Physicians can consult with CDC's parasitic diseases staff to obtain these drugs.

#### **First stage**

Your provider will prescribe medication as indicated for the first stage of East African sleeping sickness, which may include Suramin or possibly fexinidazole.

#### **Second stage**

Your provider will prescribe medication as indicated for the second stage of East African sleeping sickness, which may include Melarsoprol or possibly fexinidazole.

### **Treating West African sleeping sickness**

#### **First stage**

There are drugs available in the United States to treat the first stage of West African sleeping sickness.

Depending on your age and weight, your healthcare provider will prescribe pentamidine or fexinidazole.

#### **Second stage**

Treatment for the second stage of West African sleeping sickness depends on your age and severity of infection.

Your provider will prescribe either nifurtimox eflornithine combination therapy (NECT) or fexinidazole.

## Recovery

After treatment, your healthcare provider should monitor you for two years. If your symptoms return, your provider should test you for the parasite that causes African sleeping sickness.

**Poliomyelitis (POLIO)**

## Overview

Polio is an illness caused by a virus that mainly affects nerves in the spinal cord or brain stem. In its most severe form, polio can lead to a person being unable to move certain limbs, also called paralysis. It can also lead to trouble breathing and sometimes death. The disease also is called poliomyelitis.

A vaccination effort throughout the world has led to only a small number of cases to occur around the world in recent years. But poliovirus still spreads within areas with low vaccination rates.

The U.S. Centers for Disease Control and Prevention (CDC) publishes travel notices of countries where there is a higher risk of polio. Countries at a higher risk of polio are generally in Africa, the Middle East, and southern and central Asia.

Vaccinated adults who plan to travel to an area where polio is spreading should get a booster dose of inactivated poliovirus vaccine (IPV). Immunity after a booster lasts a lifetime.

## Symptoms

Most people infected with the virus that causes polio, called poliovirus, don't get symptoms.

### Abortive polio

About 5% of people with the poliovirus get a mild version of the disease called abortive poliomyelitis. This leads to flu-like symptoms that last 2 to 3 days. These include:

Fever

Headache

Muscle aches

Sore throat

Stomachache

Loss of appetite

Nausea

Vomiting

### Nonparalytic polio

A more severe form of the disease, called nonparalytic polio, affects about 1% of those infected. While the illness lasts longer than a few days, it doesn't cause paralysis. Besides having more-severe flu-like symptoms, nonparalytic polio symptoms may include:

Neck pain or stiffness

Aches or stiffness in the arms or legs

Severe headache

A second phase of symptoms may follow, or a person may seem to be getting better for a few days before a second phase starts. These symptoms include:

Stiffness of the spine and neck

Decreased reflexes

Muscle weakness

### Paralytic polio

This most serious form of the disease is rare. The disease begins much like nonparalytic polio. But it progresses to more-severe signs and symptoms, including:

Intense pain

Extreme sensitivity to touch

Tingling or pricking sensations

Muscles spasms or twitching

Muscles weakness progressing to a limp paralysis

Any combination of limbs may experience paralysis. But paralysis of one leg is most common, followed by paralysis of one arm.

Depending on the severity of disease, other signs or symptoms may include:

Paralysis of muscles involved in breathing

Difficulty swallowing

### Post-polio syndrome

Post-polio syndrome is the appearance of new signs or symptoms or the progression of problems. This usually happens decades after having polio. Common signs and symptoms include:

Progressive muscle or joint weakness and pain

Fatigue

Muscle wasting

Breathing or swallowing problems

Sleep-related breathing disorders, such as sleep apnea

Lowered tolerance of cold temperatures

### When to see a doctor

Signs and symptoms of polio are similar to other viral diseases that affect the nervous system. It's important to get a timely and accurate diagnosis.

If you had polio before, see your health care provider if you have new or worse signs or symptoms.

## Causes

Polio is caused by the poliovirus. It mainly targets nerve cells in the spinal cord and brain stem that control muscle movement. Nerve cells controlling sensation are generally not affected.

The naturally-occurring poliovirus, called the wild-type poliovirus, has been eliminated in most countries and causes few cases of polio. Another version of the virus, called the vaccine-derived poliovirus (VDPV), is more widespread and now causes most infections worldwide. VDPV exists mainly in a few countries that use an oral vaccine with a weakened poliovirus.

The weakened virus in the oral vaccine doesn't itself cause polio, and vaccinated people rarely contract VDPV. Instead, VDPV is a new version of the virus that develops within a community or region where not enough people are vaccinated.

Even though the weakened virus in the oral vaccine doesn't cause illness, it can spread. If most people in a community are vaccinated, the spread of the weakened virus is controlled. If many people aren't vaccinated, the weakened virus can move through a community for a long time. This gives the virus the chance to change, or mutate, and behave like the wild-type virus that causes illness.

Infections from VDPV have been reported in the United States. In each case, the person was either not vaccinated or had a significantly weakened immune system. One case in New York in 2022 was in a county with a lower-than-average polio vaccination rate. Samples from wastewater showed that VDPV was spreading in some communities.

Since 2000, polio vaccination in the United States has used an injected vaccine with an inactivated poliovirus that doesn't create the risk for VDPV.

### How polio spreads

People carrying the poliovirus — even people who don't get sick — can pass along the virus in feces, also called stool, or droplets from sneezing or coughing. The virus enters another person through the mouth. The virus can spread easily. For example, the virus can spread if people haven't washed their hands after coughing, using the toilet or before eating.

The virus also may be in water contaminated with feces carrying the poliovirus.

## Risk factors

Polio mainly affects children. But anyone who hasn't been vaccinated is at risk of getting the disease.

## Complications

Severe disease that affects the ability to breathe can cause death. Long-term complications for people who recover may include:

Permanent paralysis

Muscle shortening that causes deformed bones or joints

Chronic pain

Post-polio syndrome

## Prevention

The most effective way to prevent polio is vaccination.

### Polio vaccine

The CDC recommends four doses of inactivated poliovirus vaccine (IPV) at the following ages:

2 months

4 months

Between 6 and 18 months

Between ages 4 and 6 when children are just entering school

If your child is missing a dose, talk to your health care provider about a catch-up schedule for vaccination.

### Adult vaccination

In the U.S., most adults have immunity to the poliovirus because of childhood vaccination. And U.S. adults have little chance of being exposed to the virus. But adults who are traveling to or living in a region with high rates of spreading poliovirus should receive more vaccinations.

If you had a complete course of vaccination, you should get a one-time IPV booster. You should get three IPV doses if you aren't vaccinated, didn't receive a complete vaccination or are unsure of your vaccination status.

The IPV schedule for adults is a second dose 1 to 2 months after the first dose. Then the third dose is 6 to 12 months after the second dose. Talk to your health care provider if you know you have an incomplete vaccination history.

### Vaccine safety

IPV is safe for people with weakened immune systems, although it's not certain how protective the vaccine is in cases of severe immune deficiency. Common side effects are pain and redness at the injection site.

IPV can cause an allergic reaction in some people. Because the vaccine has trace amounts of the antibiotics streptomycin, polymyxin B and neomycin, it may cause a reaction in people allergic to one of these antibiotics. A person who has a severe reaction to a first dose of IPV won't get more doses.

Signs and symptoms of an allergic reaction usually occur within minutes to a few hours after the shot. Watch for:

Skin reactions, including hives and itching and flushed or pale skin

Low blood pressure (hypotension)

Narrowing of the airways and a swollen tongue or throat, which can cause wheezing and trouble breathing

A weak and fast pulse

Nausea, vomiting or diarrhea

Dizziness or fainting

If you or your child has an allergic reaction after any vaccination, get medical help right away.

## Diagnosis

Health care providers often recognize polio by symptoms, such as neck and back stiffness or abnormal reflexes or muscle weakness. To confirm the diagnosis, a lab test of a stool sample can detect the poliovirus. The virus can be found in a throat sample only during the first week of illness. So a throat sample is a less reliable source for testing.

A test of the fluid surrounding the brain and spinal cord, or cerebrospinal fluid, may be used to rule out other diseases of the nervous system.

## Treatment

Because no cure for polio exists, the focus is on increasing comfort, speeding recovery and preventing complications. Depending on the severity of disease, supportive treatments may include:

Bed rest

Pain relievers

Hot moist packs to control muscle pain and spasms

Portable ventilators to help with breathing

Physical therapy exercises to prevent bone deformity and loss of muscle function

Splints or other devices to encourage good position, or alignment, of the spine and limbs

## Preparing for your appointment

The signs and symptoms of moderate to severe polio — beyond typical flu-like symptoms — need attention right away. Questions that you might be prepared to answer for yourself or on behalf of your child include the following:

When did the symptoms begin?

Have the symptoms progressed or changed since you first became ill?

Has anything improved or worsened the symptoms?

Have you traveled recently? Where?

Do you know of any possible exposure to an infectious disease?

If you traveled, what vaccinations did you get before travel?

# Schistosomiasis

Schistosomiasis is a disease caused by parasitic worms.

The parasites that cause schistosomiasis live in certain types of freshwater snails.

Schistosomiasis spreads when you come into contact with unsafe water that contains these snails.

## Overview

Schistosomiasis, also known as bilharzia, is a disease caused by parasitic worms. More than 200 million people worldwide are infected. Schistosomiasis is one of the neglected tropical diseases (NTDs). It is the second most dangerous parasitic disease after malaria. The parasites that cause schistosomiasis live in certain types of freshwater snails. Although schistosomes are in the United States, they are not the species that infect people.

The infectious form of the parasite, called cercariae, comes out of the snail into the water. You can become infected if your skin comes in contact with unsafe freshwater.

Most human infections are caused by these species:

*Schistosoma mansoni*

*S. haematobium*

*S. japonicum*

Less common infections are caused by these species:

*S. mekongi*

*S. intercalatum*

## Signs and symptoms

Most people have no symptoms at the early phase of infection. Some have a rash or itchy skin in the first few days.

Within 1 – 2 months of infection, symptoms may include:

Fever

Chills

Cough

Muscle aches

Repeated infections in children can cause:

Anemia (lack of red blood cells)

Malnutrition (lack of nutrients)

Learning difficulties

You can also develop chronic (long-term) symptoms if you do not treat the infection. The eggs cause inflammation or scarring when traveling to the intestine, liver, or bladder.

If you think you have schistosomiasis, see your healthcare provider.

Let them know:

If and where you've traveled recently

How long you were there

If you may have touched unsafe water

## Exposure risks

You might get schistosomiasis if your skin touches freshwater from canals, rivers, streams, ponds, or lakes in places where it is common. Please refer to WHO's map on where schistosomiasis currently spreads.

### **Africa**

Southern and sub-Saharan Africa (high risk)

North Africa's Maghreb region

Egypt and Sudan's Nile River valley

### **Asia**

Southern China

Southeast Asia

Cambodia

Indonesia

Laos

Philippines

### **Europe**

Corsica (ongoing transmission or spread)

### **The Americas**

South America

Brazil

Suriname

Venezuela

Caribbean (low risk)

Antigua & Barbuda

Dominican Republic

Guadeloupe

Martinique

Montserrat

Puerto Rico

Saint Lucia

### **The Middle East**

Iran

Iraq

Saudi Arabia

Yemen

## How it spreads

Schistosomiasis spreads in six steps:

*Schistosoma* eggs enter freshwater when people with schistosomiasis urinate (pee) or defecate (poop) in the water.

The eggs hatch, infect a specific type of freshwater snail, develop, and multiply inside the snails.

The *Schistosoma*parasite leaves the snail and enters the water, where it can live for about 48 hours.

The parasite enters the skin of people who are in contact with unsafe water.

Within weeks, the parasites turn into adult worms in the blood vessels of the body.

The female worms produce eggs that travel to the bladder or intestine and come out in urine or stool (poop).

## Prevention

The most effective ways to prevent schistosomiasis include:

Do not get into or touch unsafe freshwater.

Drink safe water.

Water for bathing

Boil you bath water.

Add 1 mg of chlorine per liter of water and let sit for 30 minutes.

Let water sit for 24 hours before bathing.

There is no vaccine available to prevent schistosomiasis. There are steps you can take to lower your chances of getting it.

### **Do not get in freshwater**

Do not swim, wade, or bathe in freshwater in regions where schistosomiasis is common. The ocean and chlorinated swimming pools are safe.

### **Drink safe water**

You will not get schistosomiasis from drinking unsafe water. However, if the parasites touch your mouth or lips through drinking the water, you might get infected.

Boil water from canals, lakes, rivers, streams, or springs for at least 1 minute before you drink it. You can also filter the water. Boiling water will kill harmful parasites, bacteria, or viruses. Iodine treatment alone **does not guarantee** safe water.

### **Prepare your bath water**

You can take steps to make your bath water safe.

Boil your bath water until it is vigorously bubbling for at least a minute to remove anything harmful. Wait until the water cools down before getting in to prevent burning yourself.

Add 1 mg of chlorine for every 1 liter of water. Let the water sit for 30 minutes before bathing.

Water that has been in a storage tank for at least 1 to 2 days should be safe for bathing.

### **Dry yourself well**

Dry yourself well with a towel after a short exposure to unsafe water. The drying may help prevent the Schistosoma parasite from getting into your skin. **Do not** **rely on this method to prevent schistosomiasis.**

## Controlling Schistosomiasis

Control efforts in countries where schistosomiasis is particularly dangerous focus on:

Reducing the number of people getting infected

Getting rid of the snails the parasites live in

Providing appropriate water and sanitation

Draining and removing sewage can reduce or stop the spread of schistosomiasis. Public health officials say that stopping schistosomiasis is possible in areas with less spread.

Mass treatment of whole communities and targeted treatment of school-age children is also used to control the spread.

However, these methods have some problems. Chemicals to remove the snails can harm other animals in the water. If water treatment is not continuous, the snails could return. In areas where schistosomiasis can also infect animals, water runoff from pastures with infected animals can make freshwater unsafe.

## Diagnosis

Your health care provider may take a stool or urine sample to see if you have the parasite. They can also use a blood sample to test for infection. You should wait 6 – 8 weeks to give samples after contacting unsafe water. This window of time helps with accuracy.

## Treatment and recovery

Safe and effective drugs are available for treating schistosomiasis. Praziquantel is the recommended treatment drug. See your healthcare provider for diagnosis and treatment.

# Guinea Worm

Guinea worm disease (GWD) is caused by the parasite *Dracunculus medinensis.*

A parasite is an organism (a living thing) that lives on or inside another organism.

The disease affects communities in remote parts of Africa that do not have safe water to drink.

There is no treatment nor a vaccine for Guinea worm disease.

## Overview

Dracunculiasis, also known as Guinea worm disease (GWD), is an infection caused by the parasite *Dracunculus medinensis.* GWD is a neglected tropical disease (NTD) transmitted to people mostly by consuming unsafe water. Unfiltered drinking water from ponds or other stagnant surface water sources can contain near-microscopic crustaceans called copepods (tiny "water fleas") that are infected with Guinea worm larvae (immature forms of the Guinea worm).

## Signs and symptoms

People do not usually have GWD symptoms until about one year after infection. Then, a mature pregnant female worm full of larvae creates a blister on the skin through which she will emerge and expel her larvae when she comes in contact with water. A few days to hours before the worm, which can measure up to 3 feet (1 meter) in length, comes out of the skin, a person may develop fever, swelling, and pain in the area. Most worms come out of people's legs and feet, though worms can come out of other body parts, too.

**Challenges**

People in remote rural communities who have GWD often lack access to healthcare. When the adult female worm comes out of the skin, it can be very painful, disabling, and take a long time to remove. The emerging worm can cause a wound that may develop a secondary infection.

## People at risk

Anyone who consumes drinking water from a pond or other stagnant water source contaminated with infected copepods is at risk for infection. People's risk for disease can vary. People do not get immunity after GWD, which means they can get it again.

GWD transmission also has a seasonal pattern.

## How it spreads

Water contact triggers the Guinea worm to release a milky white liquid that contains hundreds of thousands of immature larvae into the water. In ponds and other stagnant water sources, these larvae are then consumed by copepods. People might become infected with Guinea worms by consuming unfiltered drinking water from such water sources containing infected copepods. People and animals might also become infected by eating certain aquatic animals (e.g., fish or frogs) that have swallowed infected copepods. People and animals infected with GWD can then spread the disease when the worm matures and is ready to emerge from the body if they enter ponds and other stagnant water sources that others drink from.

## Prevention

Guinea worm is a disease that has been prioritized for eradication by the World Health Organization. There were an estimated 3.5 million Guinea worm cases occurring annually in 20 African and Asian countries in 1986, but today, through the Guinea Worm Eradication Program (GWEP), only a handful of countries continue to have the disease. GWEP undertakes several water-related and other measures to prevent GWD:

Surveillance and case containment

Safe water practices, including distribution of cloth and pipe filters to remove copepods, and advocacy for installation or rehabilitation of safe drinking water supplies like borehole wells

Vector control

Health education and community mobilization

## Quick facts

There were 14 human GWD cases reported in 2023 in Chad, South Sudan, Mali, Cameroon, and Central African Republic.

There were 714 animal GWD infections reported in 2023, which is a slight increase compared to 2022 following expanded surveillance activities.

WHO has certified 200 countries free from Guinea worm. The six countries that have not yet been certified as free from Guinea worm are Angola, Chad, Ethiopia, Mali, South Sudan, and Sudan.

## Treatment and recovery

There is no drug to treat Guinea worm infection. Once part of the worm begins to come out of the wound, it is important that all of the worm is removed to prevent complications. Anti-inflammatory medicine can help reduce pain and swelling, and antibiotic ointment can help prevent infections.

## Vaccines

There is no vaccine to prevent Guinea worm infection.

Chickenpox (Varicella)

Chickenpox is an illness caused by the varicella-zoster virus. It brings on an itchy rash with small, fluid-filled blisters. Chickenpox spreads very easily to people who haven't had the disease or haven't gotten the chickenpox vaccine. Chickenpox used to be a widespread problem, but today the vaccine protects children from it.

The chickenpox vaccine is a safe way to prevent this illness and the other health problems that can happen during it.

## Symptoms

The rash caused by chickenpox appears 10 to 21 days after you're exposed to the varicella-zoster virus. The rash often lasts about 5 to 10 days. Other symptoms that may appear 1 to 2 days before the rash include:

Fever.

Loss of appetite.

Headache.

Tiredness and a general feeling of being unwell.

Once the chickenpox rash appears, it goes through three phases:

Raised bumps called papules, which break out over a few days.

Small fluid-filled blisters called vesicles, which form in about one day and then break and leak.

Crusts and scabs, which cover the broken blisters and take a few more days to heal.

New bumps keep showing up for several days. So you may have bumps, blisters and scabs at the same time. You can spread the virus to other people for up to 48 hours before the rash appears. And the virus stays contagious until all broken blisters have crusted over.

The disease is by and large mild in healthy children. But sometimes, the rash can cover the whole body. Blisters may form in the throat and eyes. They also may form in tissue that lines the inside of the urethra, anus and vagina.

### When to see a doctor

If you think you or your child might have chickenpox, call your health care provider. Often, chickenpox can be diagnosed with an exam of the rash and other symptoms. You may need medicines that can help fight off the virus or treat other health problems that can happen because of chickenpox. To avoid infecting others in the waiting room, call ahead for an appointment. Mention that you think you or your child may have chickenpox.

Also, let your provider know if:

The rash spreads to one or both eyes.

The rash gets very warm or tender. This might be a sign that the skin is infected with bacteria.

You have more serious symptoms along with the rash. Watch for dizziness, new confusion, fast heartbeat, shortness of breath, shakiness, loss of the ability to use muscles together, a cough that becomes worse, vomiting, stiff neck or a fever higher than 102 F (38.9 C).

You live with people who've never had chickenpox and haven't gotten the chickenpox vaccine yet.

Someone in your household is pregnant.

You live with someone who has a disease or takes medicines that affect the immune system.

## Causes

A virus called varicella-zoster causes chickenpox. It can spread through direct contact with the rash. It also can spread when a person with chickenpox coughs or sneezes and you breathe in the air droplets.

## Risk factors

Your risk of getting infected with the virus that causes chickenpox is higher if you haven't already had chickenpox or if you haven't had the chickenpox vaccine. It's extra important for people who work in child care or school settings to be vaccinated.

Most people who have had chickenpox or have gotten the vaccine are immune to chickenpox. If you've been vaccinated and still get chickenpox, symptoms are often milder. You may have fewer blisters and mild or no fever. A few people can get chickenpox more than once, but this is rare.

## Complications

Chickenpox is often a mild disease. But it can be serious and can lead to other health problem including:

Infected skin, soft tissues, bones, joints or bloodstream caused by bacteria.

Dehydration, when the body runs too low on water and other fluids.

Pneumonia, an illness in one or both lungs.

Swelling of the brain called encephalitis.

Toxic shock syndrome, a dangerous complication of some illnesses caused by bacteria.

Reye's syndrome, a disease that causes swelling in the brain and liver. This can happen in children and teens who take aspirin during chickenpox.

In very rare cases, chickenpox could lead to death.

### Who's at risk?

People who are at higher risk of chickenpox complications include:

Newborns and infants whose mothers never had chickenpox or the vaccine. This includes children under age 1, who have not yet had the vaccine.

Teens and adults.

Pregnant women who haven't had chickenpox.

People who smoke.

People with cancer or HIV who are taking medication that has an effect on the immune system.

People with a chronic condition, such as asthma, who take medicine that calms immune response. Or those who have had an organ transplant and take medicine to limit the immune system's action.

### Chickenpox and pregnancy

Low birth weight and limb problems are more common in babies born to women who are infected with chickenpox early in their pregnancies. When a pregnant person catches chickenpox in the week before birth or within a couple of days after giving birth, the baby has a higher risk of getting a life-threatening infection.

If you're pregnant and not immune to chickenpox, talk to your health care provider about these risks.

### Chickenpox and shingles

If you've had chickenpox, you're at risk of a complication called shingles. The varicella-zoster virus stays in your nerve cells after the chickenpox rash goes away. Many years later, the virus can turn back on and cause shingles, a painful cluster of blisters. The virus is more likely to come back in older adults and people who have weaker immune systems.

The pain of shingles can last long after the blisters go away, and it can be serious. This is called postherpetic neuralgia.

In the United States, the Centers for Disease Control and Prevention (CDC) suggests you get the shingles vaccine, Shingrix, if you're 50 or older. The agency also suggests Shingrix if you're 19 or older and you have a weaker immune system because of diseases or treatments. Shingrix is recommended even if you've already had shingles or you've gotten the older shingles vaccine, Zostavax.

Other shingles vaccines are offered outside of the United States. Talk to your provider for more information on how well they prevent shingles.

## Prevention

The chickenpox vaccine, also called the varicella vaccine, is the best way to prevent chickenpox. In the United States, experts from the CDC report that two doses of the vaccine prevent illness over 90% of the time. Even if you get chickenpox after receiving the vaccine, your symptoms may be much milder.

In the United States, two chickenpox vaccines are licensed for use: Varivax contains only the chickenpox vaccine. It can be used in the United States to vaccinate people age 1 or older. ProQuad combines the chickenpox vaccine with the measles, mumps and rubella vaccine. It can be used in the United States for children ages 1 to 12. This is also called the MMRV vaccine.

In the United States, children receive two doses of the varicella vaccine: the first between ages 12 and 15 months and the second between ages 4 and 6 years. This is part of the routine vaccination schedule for children.

For some children between the ages of 12 and 23 months, the MMRV combination vaccine may raise the risk of fever and seizure from the vaccine. Ask your child's health care provider about the pros and cons of using the combined vaccines.

Children 7 to 12 years old who haven't been vaccinated should receive two doses of the varicella vaccine. The doses should be given at least three months apart.

People age 13 or older who haven't been vaccinated should receive two catch-up doses of the vaccine at least four weeks apart. It's even more important to get the vaccine if you have a higher risk of getting exposed to chickenpox. This includes health care workers, teachers, child-care employees, international travelers, military personnel, adults who live with young children and all nonpregnant women of childbearing age.

If you don't remember whether you've had chickenpox or the vaccine, your provider can give you a blood test to find out.

Other chickenpox vaccines are offered outside the United States. Talk to your health care provider for more information on how well they prevent chickenpox.

Do not get the chickenpox vaccine if you're pregnant. If you decide to get vaccinated before pregnancy, don't try to get pregnant during the series of shots or for one month after the last dose of the vaccine.

Other people also shouldn't get the vaccine, or they should wait. Check with your health care provider about whether you should get the vaccine if you:

Have a weaker immune system. This includes people who have HIV or take medicines that have an effect on the immune system.

Are allergic to gelatin or the antibiotic neomycin.

Have any kind of cancer or are getting cancer treatment with radiation or medicines.

Recently received blood from a donor or other blood products.

Talk to your provider if you're not sure whether you need the vaccine. If you plan on getting pregnant, ask your provider if you're up to date on your vaccines.

### Is it safe and effective?

Parents often wonder whether vaccines are safe. Since the chickenpox vaccine became available, studies have found that it's safe and it works well. Side effects are often mild. They include pain, redness, soreness and swelling at the site of the shot. Rarely, you might get a rash at the site or a fever.

## Diagnosis

Most often, health care providers find out you have chickenpox based on the rash.

Chickenpox also can be confirmed with lab tests, including blood tests or a tissue study of samples of affected skin.

## Treatment

In otherwise healthy children, chickenpox often needs no medical treatment. Some children may be able to take a type of medicine called an antihistamine to calm itching. But for the most part, the disease just needs to run its course.

### If you're at high risk of complications

For people who are at high risk of complications from chickenpox, providers sometimes prescribe medicines to shorten the length of the illness and to help lower the risk of complications.

If you or your child is at high risk of complications, your provider may suggest antiviral medicine to fight the virus, such as acyclovir (Zovirax, Sitavig). This medicine may lessen the symptoms of chickenpox. But they work best when given within 24 hours after the rash first appears.

Other antiviral drugs, such as valacyclovir (Valtrex) and famciclovir, also might make the illness less severe. But these may not be approved or right for everyone. In some cases, your provider may suggest that you get the chickenpox vaccine after you've been exposed to the virus. This can prevent the disease or help make it less severe.

### Treating complications

If you or your child gets complications, your provider will figure out the right treatment. For example, antibiotics can treat infected skin and pneumonia. Brain swelling, also called encephalitis, is often treated with antiviral medicine. Treatment in the hospital may be needed.

## Lifestyle and home remedies

To help ease the symptoms of mild chickenpox, you can follow these self-care tips.

### Try not to scratch

Scratching the skin can cause scarring and slow healing. It also can raise the risk that the sores will get infected. If your child can't stop scratching, trim your child's fingernails. It also may help to put gloves on a child's hands, especially at night.

### Relieve the itch and other symptoms

The chickenpox rash can be very itchy, and broken blisters called vesicles sometimes sting. For relief of these and other symptoms, you can try:

A cool bath with added baking soda, aluminum acetate or uncooked oatmeal. Or you could add colloidal oatmeal, a finely ground oatmeal that is made for soaking.

Calamine lotion dabbed on the itchy spots.

A soft, bland diet if chickenpox sores form in the mouth.

Antihistamines such as diphenhydramine (Benadryl) for itching. But ask your provider if your child can safely take antihistamines.

Acetaminophen (Tylenol) for a mild fever.

Call your provider if a fever lasts longer than four days and is higher than 102 F (38.9 C). And don't give aspirin to children and teenagers who have chickenpox. This can lead to a serious medical problem called Reye's syndrome.

Talk with your provider before you give any type of nonsteroidal anti-inflammatory drug (NSAID), such as ibuprofen (Advil, Motrin IB, others), to someone who has chickenpox. Some studies suggest this type of medicine may lead to skin infections or tissue damage.

## Preparing for your appointment

Call your family health care provider if you or your child has symptoms of chickenpox. Here's some information to help you get ready for your appointment.

### Information to gather in advance

**Pre-appointment safety measures.** Ask if you or your child should follow any restrictions before the checkup, such as staying away from other people.

**Symptom history.** Write down any symptoms you or your child has had, and for how long.

**Recent exposure to people who might have had chickenpox.** Try to remember if you or your child has been exposed to anyone who might have had the disease in the last few weeks.

**Key medical information.** Include any other health problems and the names of any medicines you or your child is taking.

**Questions to ask your provider.** Write down your questions so you can make the most of your time at the checkup.

Questions to ask your provider about chickenpox include:

What is the most likely cause of these symptoms?

Are there any other possible causes?

What treatment do you suggest?

How soon before the symptoms get better?

Are there home remedies or self-care steps that could help relieve the symptoms?

Am I or is my child contagious? For how long?

How do we lower the risk of infecting others?

Feel free to ask any other questions.

### What to expect from your doctor

Your provider may ask:

What symptoms have you noticed, and when did they first appear?

Do you know anyone who has had symptoms of chickenpox within the last few weeks?

Have you had or has your child had a chickenpox vaccine? How many doses?

Are you or is your child being treated? Or have you recently been treated for other medical problems?

Do you or your child take any medicines, vitamins or supplements?

Is your child in school or child care?

Are you pregnant or breastfeeding?

### What you can do in the meantime

Rest as much as possible. Try not to touch skin with chickenpox on it. And think about wearing a face mask over the nose and mouth in public. Chickenpox is highly contagious until skin blisters have fully crusted.

# COVID-19

COVID-19 (coronavirus disease 2019) is a disease caused by the SARS-CoV-2 virus.

It can be very contagious and can spread quickly.

As of June 1, 2024, nearly 1.2 million people have died of COVID-19 in the U.S.

## Learn about COVID-19 and how it spreads

### **About COVID-19**

COVID-19 most often causes respiratory symptoms that can feel much like a cold, the flu, or pneumonia. COVID-19 may attack more than your lungs and respiratory system. Other parts of your body may also be affected by the disease. Most people with COVID-19 have mild symptoms, but some people become severely ill.

Some people, including those with minor or no symptoms, will develop Post-COVID Conditions – also called "Long COVID."

### **How COVID-19 spreads**

COVID-19 spreads when an infected person breathes out droplets and very small particles that contain the virus. Other people can breathe in these droplets and particles, or these droplets and particles can land on others' eyes, nose, or mouth. In some circumstances, these droplets may contaminate the surfaces they touch.

Anyone infected with COVID-19 can spread it, even if they do **NOT**have symptoms. COVID-19 can even spread from people to animals in some situations.

### **Risk factors for severe iIlness from COVID-19**

Some people are more likely than others to get very sick if they get COVID-19. This includes people who:

are older

are immunocompromised (have a weakened immune system)

have certain disabilities or

have underlying health conditions

Understanding your COVID-19 risk and the risks that might affect others can help you make decisions to protect yourself and others.

### **About variants**

Viruses are constantly changing, including the virus that causes COVID-19. These changes occur over time and can lead to the emergence of variants that may have new characteristics, including different ways of spreading. Slowing the spread of the virus, by protecting yourself and others, can help slow new variants from developing.

### **Prevention**

There are many actions you can take to help protect you, your household, and your community from COVID-19. CDC's Respiratory Virus Guidance provides actions you can take to lower the risk of COVID-19 transmission (catching and spreading COVID-19) and lower the risk of severe illness if you get sick.

## Signs and Symptoms

The following list does not include all possible symptoms. Symptoms may change with new COVID-19 variants and can vary depending on vaccination status. Possible symptoms include:

Fever or chills

Cough

Shortness of breath or difficulty breathing

Sore throat

Congestion or runny nose

New loss of taste or smell

Fatigue

Muscle or body aches

Headache

Nausea or vomiting

Diarrhea

CDC will continue to update this list as we learn more about COVID-19.

### **Feeling Sick?**

Stay home and away from others (including people you live with who are not sick) if you have symptoms that aren't better explained by another cause.

Seek health care promptly for testing and/or treatment if you have risk factors for severe illness; treatment may help lower your risk of severe illness.

## When to seek emergency help

Look for emergency warning signs\* for COVID 19:

Trouble breathing

Persistent pain or pressure in the chest

New confusion

Inability to wake or stay awake

Depending on skin tone, lips, nail beds and skin may appear pale, gray, or blue.

If someone is showing any of these signs, call 911 or call ahead to your local emergency facility. Notify the operator that you are seeking care for someone who has or may have COVID-19.

*\*This list does not include all possible symptoms. Please call your medical provider for any other symptoms that are severe or concerning to you.*

## Difference between flu and COVID-19

Influenza (Flu) and COVID-19 are both contagious respiratory illnesses, but they are caused by different viruses. COVID-19 is caused by infection with a coronavirus named SARS-CoV-2, and flu is caused by infection with one of the influenza viruses. You cannot tell the difference between flu and COVID-19 by symptoms alone because some of the symptoms are the same.

Some nucleic acid amplification tests (NAATs), including PCR tests, can differentiate between flu and COVID-19 at the same time. If one of these tests is not available, many testing locations provide flu and COVID-19 tests separately.

## About Long COVID

Long COVID is defined as a chronic condition that occurs after SARS-CoV-2 infection and is present for at least 3 months. Long COVID includes a wide range of symptoms or conditions that may improve, worsen, or be ongoing.

### Anyone can get Long COVID

Long COVID occurs more often in people who had severe COVID-19 illness, but anyone who gets COVID-19 can experience it, including children.

Most people with Long COVID experience symptoms days after first learning they had COVID-19, but some people who later develop Long COVID do not know when they were infected. People can be reinfected with SARS-CoV-2 multiple times. Each time a person is infected with SARS-CoV-2, they have a risk of developing Long COVID. Long COVID symptoms and conditions can emerge, persist, resolve, and reemerge over weeks and months. These symptoms and conditions can range from mild to severe, may require comprehensive care, and can even result in a disability.

While rates of new cases of Long COVID have decreased since the beginning of the COVID-19 pandemic, it remains a serious public health concern as millions of U.S. adults and children have been affected by Long COVID.

## Who is at risk

While anyone who gets COVID-19 can develop Long COVID, studies have shown that some groups of people are more likely to develop Long COVID than others, including (not a comprehensive list):

Women

Hispanic and Latino people

People who have experienced more severe COVID-19 illness, especially those who were hospitalized or needed intensive care

People with underlying health conditions and adults who are 65 or older

People who did not get a COVID-19 vaccine

### **Health inequities affect populations at risk for Long COVID**

Health inequities from disability, economic, geographic, and other social factors disproportionately affect some groups of people. These inequities can increase the risk of negative health outcomes and impact from Long COVID.

## Prevention

CDC emphasizes core strategies to lower health risks from COVID-19, including severe outcomes such as hospitalization and death. Preventing severe outcomes from COVID-19 illness helps prevent Long COVID. Steps you can take to protect yourself and others include:

Staying up to date on COVID-19 vaccination.

Practicing good hygiene (practices like handwashing that improve cleanliness)

Taking steps for cleaner air

When you may have a respiratory virus:

Use precautions to prevent spread

Seek healthcare promptly for testing and/or treatment if you have risk factors for severe illness; treatment may help lower your risk of severe illness

### Vaccination can prevent Long COVID

Research shows COVID-19 vaccination is the best available tool to prevent Long COVID, including in children.

## Testing and diagnosis

Long COVID is not one illness. There is no laboratory test that can determine if your symptoms or conditions are due to Long COVID. A positive SARS-CoV-2 test is not required for a Long COVID diagnosis. Your healthcare provider considers a diagnosis of Long COVID based on:

Your health history

If you had a diagnosis of COVID-19 by a positive test, symptoms, or exposure

A health examination

Clinical evaluations and results of routine blood tests, chest X-rays, and electrocardiograms may be normal in someone with Long COVID. People experiencing Long COVID should seek care from a healthcare provider to create a personal medical management plan and improve their symptoms and quality of life. Talk to your healthcare provider if you think you or your child has Long COVID.

## Similar conditions

Some people experiencing Long COVID symptoms have symptoms similar to those reported by people with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and other poorly understood chronic illnesses that may occur after other infections. These unexplained symptoms or conditions may be misunderstood by healthcare providers, which can result in a delay in diagnosis and people receiving the appropriate care or treatment.

## What CDC is doing

CDC is working with other federal agencies to better understand and address the long-term impacts of Long COVID, who gets Long COVID, and why. CDC supports these goals by:

Partnering with state and local jurisdictions

Supporting healthcare providers

Promoting and conducting research

## Research

Studies are in progress to learn more about Long COVID and identify further measures to help prevent Long COVID. CDC and partners use multiple approaches to support and conduct research that estimates:

How many people experience Long COVID and why

Which groups of people are disproportionately impacted by Long COVID

How new variants may affect Long COVID

The role that COVID-19 vaccination plays in preventing Long COVID

Each approach helps CDC and its partners better understand Long COVID and how healthcare providers can treat or support patients living with these long-term effects. CDC posts data on Long COVID and provides analyses. The most recent CDC data and analyses on Long COVID can be found on the U.S. Census Bureau's Household Pulse Survey. CDC will continue to share information with healthcare providers to help them evaluate and manage these conditions.

## 1. Rheumatoid Arthritis (RA)

## Prognosis

* RA is chronic and progressive, with improved outcomes due to early diagnosis and modern therapies.
* Without treatment, many patients experience disability and decreased quality of life; early, aggressive therapy can preserve joint function and reduce long-term complications.
* Cardiovascular disease, respiratory disease, and infection are leading causes of increased mortality in RA patients.

## Risk Factors

* Non-modifiable: Female sex, age 30-60, family history, HLA-DRB1 genotype.
* Modifiable: Smoking (strongest environmental risk), obesity, poor dental hygiene, certain infections.

## Prevention

* No way to fully prevent RA, but reducing modifiable risks—including smoking cessation, weight management, and good dental health—may help lower risk or delay onset.

## Chronic Disease Management

* Medication: Early initiation of disease-modifying antirheumatic drugs (DMARDs) such as methotrexate; biologics for severe or refractory cases.
* Symptom Control: NSAIDs and corticosteroids (short term).
* Rehabilitation: Physical therapy, exercise, and occupational therapy to maintain joint flexibility and function.
* Ongoing Monitoring: Regular lab and imaging assessments, cardiovascular risk monitoring.
* Lifestyle: Balance rest and activity, address comorbidities.

## Preventive Guidelines

* Influenza and pneumococcal vaccination due to increased infection risk.
* Screen for cardiovascular disease, osteoporosis, and other comorbidities.
* Regular dental care to minimize systemic inflammation.

## 2. Systemic Lupus Erythematosus (SLE)

## Prognosis

* SLE is highly variable; most patients experience flares and remissions.
* 10-year survival rates are now about 90% in high-resource settings.
* Higher risk of organ damage and mortality with renal, cardiovascular, or CNS involvement.

## Risk Factors

* Demographics: Predominantly women, especially of childbearing age; higher prevalence in nonwhite populations.
* Genetic: Family history, certain HLA types.
* Environmental: UV sunlight, infections, smoking, some medications.

## Prevention

* No proven strategy for full primary prevention.
* Limit UV exposure, avoid smoking, and recognize early symptoms for secondary prevention.

## Chronic Disease Management

* Core Medications: Antimalarials (hydroxychloroquine) for all, corticosteroids and/or immunosuppressants as needed.
* Targeted Therapies: Biologics (e.g., belimumab) for refractory disease.
* Lifestyle: UV protection, vitamin D correction, infection prevention.
* Comorbidity Management: Address cardiovascular, bone health, and infection risks proactively.

## Preventive Guidelines

* Use lowest steroid dose possible.
* Routine monitoring for cardiovascular disease, osteoporosis, and infections.
* Vaccinate for influenza and pneumococcus; screen for TB before biologics or immunosuppression.
* Annual cancer screenings per age and risk profile.

# Systemic Lupus Erythematosus (SLE)

Systemic lupus erythematosus is a chronic, multisystem, inflammatory disorder of autoimmune etiology, occurring predominantly in young women. Manifestations may include arthralgias and arthritis, Raynaud syndrome, malar and other rashes, pleuritis or pericarditis, renal or central nervous system involvement, and autoimmune cytopenias. Diagnosis requires clinical and serologic criteria. Treatment of severe, ongoing, active disease requires corticosteroids and immunosuppressants.

The incidence of systemic lupus erythematosus (SLE) is approximately 10-fold higher in women (usually of child-bearing age) than men. SLE is more common and severe among Black and Asian patients than among White patients. It can affect patients of any age, including neonates. In some countries, the prevalence of SLE rivals that of rheumatoid arthritis.

SLE may be precipitated by currently unknown environmental triggers that cause autoimmune reactions in genetically predisposed people. Some medications (eg, hydralazine, procainamide, isoniazid, tumor necrosis factor [TNF] inhibitors) cause a reversible lupus-like syndrome.

## Symptoms and Signs of SLE

Clinical findings vary greatly. SLE may develop abruptly with fever and multisystem involvement or insidiously over months or years with episodes of arthralgias and malaise. Manifestations referable to any organ system may appear. Periodic exacerbations (flares) may occur.

### Joint manifestations

Joint symptoms, ranging from intermittent arthralgias to acute polyarthritis, occur in approximately 90% of patients and may precede other manifestations by years. Most lupus polyarthritis is nondestructive and nondeforming. However, in long-standing disease, deformities without bone erosions may develop (eg, the metacarpophalangeal and interphalangeal joints may rarely develop reducible ulnar drift or swan-neck deformities without bony or cartilaginous erosions [Jaccoud arthritis]) because of ligamentous laxity. Bony erosions might be detected in patients with overlap of SLE and rheumatoid arthritis (sometimes referred to as rhupus).

As in many other chronic diseases, the prevalence of fibromyalgia is increased, which may cause diagnostic confusion in patients with periarticular and generalized pain and fatigue.

### Skin and mucous membrane manifestations

Skin lesions include a persistent malar butterfly erythema (flat or raised) that typically does not affect the nasolabial folds. The absence of papules and pustules and presence of skin atrophy help distinguish SLE from rosacea.

A variety of other erythematous, firm, maculopapular lesions can occur elsewhere, including exposed areas of the face and neck, upper chest, and elbows. Skin blistering and ulceration are rare, although recurrent ulcers on mucous membranes (particularly the central portion of the hard palate near the junction of the hard and soft palate, the buccal and gum mucosa, and the anterior nasal septum) are common; findings can sometimes mimic toxic epidermal necrolysis.

Generalized or focal and reversible alopecia is common during active phases of SLE. Panniculitis can cause subcutaneous nodular lesions (sometimes called lupus panniculitis or profundus). Vasculitic skin lesions may include mottled erythema on the palms and fingers, periungual erythema, nail-fold infarcts, urticaria, and palpable purpura. Petechiae may develop secondary to thrombocytopenia. Photosensitivity is common.

Lupus erythematosus tumidus is characterized by pink to violaceous nonscarring plaques and/or nodules, some annular, in light-exposed areas.

Chilblain lupus is characterized by tender, bright red to reddish blue nodules on the toes, fingers, nose, or ears that occur in cold weather. Some patients with SLE also have features of lichen planus.

Raynaud syndrome due to vasospasm in the fingers and toes causes characteristic blanching and cyanosis and might be associated with digital ischemia; however, unlike in systemic sclerosis, digital ulcers are uncommon in SLE.

### Cardiopulmonary manifestations

Cardiopulmonary symptoms commonly include recurrent pleurisy, with or without pleural effusion. Pneumonitis is rare, although minor impairments in pulmonary function are common. Diffuse alveolar hemorrhage occasionally occurs and is associated with a poor prognosis. Other complications include pulmonary emboli, pulmonary hypertension, and shrinking lung syndrome.

Cardiac complications include pericarditis (most commonly) and myocarditis. Serious, rare complications are coronary artery vasculitis and valvular involvement including Libman-Sacks endocarditis. Accelerated atherosclerosis is an increasingly recognized cause of morbidity and mortality. Congenital heart block can develop in neonates whose mother has the antibodies against Ro (SSA) and is less common if the mother has only antibodies against La (SSB).

### Lymphoid tissue

Generalized adenopathy is common, particularly among children, young adults, and African American patients. Splenomegaly can also occur.

### Neurologic manifestations

Neurologic symptoms can result from involvement of any part of the central or peripheral nervous system or meninges. Mild cognitive impairment is common. There may also be headaches, personality changes, ischemic stroke, subarachnoid hemorrhage, seizures, psychoses, aseptic meningitis, peripheral and cranial neuropathies, transverse myelitis, choreoathetosis, or cerebellar dysfunction.

Differentiation between corticosteroid-induced psychosis and neuropsychiatric lupus can be challenging because neither is associated with marked abnormalities in the cerebrospinal fluid (CSF) or on routine imaging.

### Renal manifestations

Renal involvement can develop at any time and may be the only manifestation of SLE (see Lupus Nephritis). It may be asymptomatic or progressive and fatal.

Renal disease can range in severity from a focal glomerulitis to a diffuse, potentially fatal membranoproliferative glomerulonephritis. Common manifestations include proteinuria (most often), an abnormal urinary sediment manifested by red blood cell casts, hypertension, and edema. Early lupus glomerulonephritis may be misdiagnosed as asymptomatic urinary tract infection.

### Obstetric manifestations

Obstetric manifestations include early and late fetal loss. In patients with antiphospholipid antibodies, the risk of recurrent late miscarriages is increased. Pregnancy can be successful, particularly after 6 to 12 months of remission, but SLE flares are common during pregnancy and especially during the postpartum period. Planned pregnancy should be timed for when disease is in remission.

During pregnancy, the patient should be monitored closely for any disease flare or thrombotic events by a multidisciplinary team that includes an obstetrician who specializes in high-risk pregnancies. Women who are SSA antibody-positive should have weekly fetal ultrasonography between week 18 and week 26 to assess for congenital heart block.

### Hematologic manifestations

Hematologic manifestations include anemia (anemia of chronic disease, autoimmune hemolytic anemia), leukopenia (usually lymphopenia, neutropenia, or both), and thrombocytopenia (usually mild but sometimes life-threatening autoimmune thrombocytopenia). Recurrent arterial or venous thrombosis, thrombocytopenia, and a high probability of obstetric complications occur in patients with antiphospholipid antibodies. Thromboses account for some of the complications of SLE, including obstetric complications.

Macrophage activation syndrome is a rare but potentially life-threatening complication that can occur.

### Gastrointestinal manifestations

Gastrointestinal manifestations can result from bowel vasculitis or impaired bowel motility. In addition, pancreatitis can rarely result from SLE.

Manifestations may include abdominal pain resulting from serositis, nausea, vomiting, manifestations of bowel perforation, protein-losing enteropathy, and pseudo-obstruction.

SLE rarely causes parenchymal liver disease.

## Diagnosis of SLE

* Clinical criteria
* Cytopenias
* Autoantibodies

SLE should be suspected in patients, particularly young women, with any of the symptoms and signs. However, early-stage SLE can mimic other systemic rheumatic diseases, including rheumatoid arthritis if joint symptoms predominate. Mixed connective tissue disease includes, by definition, features of SLE as well as possibly features of systemic sclerosis, rheumatoid-like polyarthritis, and myositis. Infections (eg, bacterial endocarditis, histoplasmosis) can mimic SLE and may develop as a result of treatment-caused immunosuppression. Disorders such as sarcoidosis and paraneoplastic syndromes can also mimic SLE.

Laboratory testing may differentiate SLE from other systemic rheumatic diseases. Initial laboratory testing should include the following:

* Antinuclear antibodies (ANA)
* Extractable nuclear antigens (ENAs) if ANA test is positive, including anti–double-stranded (ds) DNA (anti-dsDNA), anti-Smith, anti-U1 RNP, anti-Ro/SSA, and anti-La/SSB antibodies
* Complement C3 and C4 levels
* Complete blood count (CBC)
* Urinalysis with urinary sediment
* Chemistry profile including renal and liver enzymes

In clinical practice, some clinicians rely on the classification criteria for SLE developed by the European League Against Rheumatism/American College of Rheumatology Patients are eligible for these criteria only if they have a positive ANA result ≥ 1:80. The 2019 EULAR/ACR classification criteria include clinical and immunologic domains, and each criterion is assigned a weight of 2 to 10. If the patient's score is 10 or more, and at least 1 clinical criterion is fulfilled, disease is classified as SLE. However, a positive ANA does not indicate a diagnosis of lupus. A positive ANA test in the presence of fatigue and generalized myofascial pain without other clinical or laboratory findings is rarely significant.

### ANA testing

Testing for ANA (preferably by indirect immunofluorescence rather than by a solid-phase assay) is an appropriate initial test for patients with suspected SLE; a positive ANA test (usually in high titer: > 1:80) occurs in > 95% of people with SLE. However, a positive ANA test can also occur in rheumatoid arthritis, other systemic rheumatic diseases, autoimmune thyroid disease, multiple sclerosis, cancers, and even in the general population. The false-positive rate varies from approximately 3% with ANA titers of 1:320 to approximately 30% for ANA titers of 1:40 among healthy controls. Medications such as hydralazine, procainamide, and tumor necrosis factor inhibitors can cause positive ANA results as well as a drug-induced lupus; the symptoms typically resolve after the medication is stopped. Positive ANA should prompt more specific testing such as anti-dsDNA antibodies; anti-dsDNA is highly specific for SLE ([3](https://www.msdmanuals.com/professional/musculoskeletal-and-connective-tissue-disorders/systemic-rheumatic-diseases/systemic-lupus-erythematosus-sle#0180261d-8107-47e5-a438-8ece777d4a52)).

### Other ANA and anticytoplasmic antibodies

The ANA test is very sensitive, but it is not specific for SLE; thus, evidence of other autoantibodies is used to aid in diagnosis. The other autoantibodies are often referred to as extractable nuclear antigens and include dsDNA, Smith (Sm), ribonucleoprotein (RNP), Ro (SSA), and La (SSB).

Ro is predominantly cytoplasmic; anti-Ro antibodies are occasionally present in patients with ANA-negative SLE presenting with subacute cutaneous lupus erythematosus. Anti-Ro is the causal antibody for neonatal lupus and congenital heart block.

Anti-Sm is highly specific for SLE but, like anti-dsDNA, is not sensitive.

Anti-RNP occurs in patients with SLE, mixed connective tissue disease, and occasionally other systemic rheumatic disorders and systemic sclerosis.

### Other tests

Leukopenia (usually lymphopenia and neutropenia) is common. Hemolytic anemia may occur, but low hemoglobin and red blood cell counts are more often due to the anemia of chronic disease. Thrombocytopenia in SLE may be difficult or impossible to differentiate from idiopathic thrombocytopenic purpura except that patients have other features of SLE and/or SLE-specific antibodies (anti-dsDNA or anti-Sm). False-positive serologic tests for syphilis occur in 5 to 10% of patients with SLE. These test results may be associated with the lupus anticoagulant and a prolonged partial thromboplastin time (PTT). Abnormal values in 1 or more of these assays suggest the presence of antiphospholipid antibodies (e.g., anticardiolipin antibodies), which should then be measured directly by enzyme-linked immunosorbent assay (ELISA). Antiphospholipid antibodies are associated with arterial or venous thrombosis, mild thrombocytopenia, and, during pregnancy, spontaneous abortion or late fetal death but may be present in asymptomatic patients.

Other blood tests help monitor disease severity and determine the need for treatment. Serum complement levels (C3, C4) are often depressed in active disease and are usually lowest in patients with active nephritis. Erythrocyte sedimentation rate (ESR) is elevated frequently during active disease. C-reactive protein levels are not necessarily elevated; high levels raise the concern for infection and/or serositis.

Complete spirometry tests and an electrocardiogram are recommended in patients with respiratory symptoms.

### Renal involvement

Screening for renal involvement begins with urinalysis with urinary sediment. Red blood cell (RBC) and/or white blood cell casts suggest active nephritis. Urinalysis should be done at regular intervals (eg, every 3 to 6 months), even for patients in apparent remission and without previous renal involvement, because kidney disease is usually asymptomatic. Proteinuria can be estimated by the urine protein/creatinine ratio or measured in a 24-hour urine collection.

Renal biopsy is indicated in patients whose protein excretion is > 500 mg/day and who have hematuria (thought to be glomerular) or RBC casts and is helpful in evaluating the status of renal disease (ie, active inflammation vs chronic changes) and in guiding therapy. Classification of lupus nephritis is based on histologic findings on renal biopsy Repeat renal biopsy should be considered in some patients because switching from one class of lupus nephritis to another is common in patients with SLE.

Patients with chronic renal insufficiency and mostly sclerotic glomeruli are not likely to benefit from aggressive immunosuppressive therapy.

## Treatment of SLE

* Hydroxychloroquine (an antimalarial) for all patients with SLE
* Nonsteroidal anti-inflammatory drugs (NSAIDs) as needed in addition to antimalarials for mild disease
* Corticosteroids, other immunosuppressants, and antimalarials for severe disease

To guide therapy, SLE should be classified as mild to moderate (eg, fever, arthritis, pleurisy, pericarditis, rash) or severe (eg, hemolytic anemia, severe thrombocytopenic purpura, massive pleural and pericardial involvement, diffuse alveolar hemorrhage or pneumonitis, nephritis, acute vasculitis of the extremities or gastrointestinal tract, florid central nervous system [CNS] involvement).

The antimalarial hydroxychloroquine is indicated for all patients with SLE regardless of disease severity because it decreases disease flares and decreases mortality. Hydroxychloroquine may also reduce thrombotic events especially in patients with associated antiphospholipid syndrome. It must be avoided if there is an absolute contraindication because of adverse events (eg, ocular toxicity). In addition, it should be used with caution if there is a history of glucose-6-phosphate dehydrogenase (G6PD) deficiency.

Patients require routine monitoring during treatment to assess disease activity and response to therapy. In addition to clinical follow-up, disease activity can be assessed with the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) and the British Isles Lupus Assessment Group (BILAG) index.

### Mild to moderate disease

Arthralgias are usually controlled with NSAIDs. However, chronic NSAID use is discouraged because of gastrointestinal adverse effects (eg, peptic ulcer disease) and potential coronary and renal toxicity (eg, interstitial nephritis, papillary necrosis). Topical agents (eg, corticosteroids, tacrolimus) can be used for skin disease, usually under the guidance of dermatology.

Antimalarials, such as hydroxychloroquine, are useful for joint and skin manifestations. Hydroxychloroquine reduces the frequency of SLE flares and decreases mortality, and is therefore used in virtually all patients with SLE. The dose is 5 mg/kg of actual body weight orally once a day with a maximum dose of 400 mg/day. Baseline ophthalmologic examination should be done before starting therapy to exclude retinopathy because chronic hydroxychloroquine use increases the risk of toxic retinopathy. Ophthalmologic screening should be done yearly to assess for retinal toxicity. Hydroxychloroquine can rarely cause skeletal or cardiac muscle toxicity. Alternatives include oral chloroquine 250 mg once a day and oral quinacrine 50 to 100 mg once a day ([6](https://www.msdmanuals.com/professional/musculoskeletal-and-connective-tissue-disorders/systemic-rheumatic-diseases/systemic-lupus-erythematosus-sle#v37724322)).

Methotrexate (15 to 20 mg orally or subcutaneously once a week), azathioprine (2 mg/kg orally once a day), or mycophenolate mofetil (1 to 1.5 grams orally twice a day) can be added to hydroxychloroquine in patients with uncontrolled mild to moderate disease who would otherwise be candidates for a course of corticosteroids. The ultimate goal is to maintain disease remission either without the need for corticosteroids or with only the lowest dose possible.

Belimumab (10 mg/kg IV every 2 weeks for 3 doses, then 10 mg/kg IV once a month or 200 mg subcutaneously once a week) should be considered if patients have uncontrolled disease or frequent flares, particularly for joint, skin, renal, or nonsevere hematologic manifestations ([2](https://www.msdmanuals.com/professional/musculoskeletal-and-connective-tissue-disorders/systemic-rheumatic-diseases/systemic-lupus-erythematosus-sle#v37724322)). It can be used in addition to hydroxychloroquine and in combination with other medications depending on the specific system involved and severity of disease. Screening and monitoring for depression is required when initiating therapy with belimumab because of a possible risk of new-onset or worsening depression and suicidality.

### Severe disease

Treatment includes induction therapy to control acute severe manifestations followed by maintenance therapy. Corticosteroids are first-line therapy. A combination of a corticosteroid and other immunosuppressants is typically used in active severe disease (ie, lupus nephritis with impaired renal function, myocarditis, or CNS involvement).

The complication for which there is the strongest evidence for treatment efficacy is lupus nephritis. Methylprednisolone 1 g by slow (1-hour) IV infusion on 3 successive days is often the initial treatment, although trial evidence for this pulse corticosteroid therapy is lacking. Then, oral prednisone given in doses of 0.5 to 1 mg/kg once a day (usually 40 to 60 mg once a day) is initiated and the dose is adjusted according to the manifestation of SLE. Corticosteroids should be tapered as soon as allowed by the disease, usually within 6 months, to limit adverse effects. Cyclophosphamide or mycophenolate mofetil (up to 3 g a day orally in 2 doses) is also used for induction therapy along with corticosteroids. Effective birth control (an intrauterine device is typically preferred to hormonal approaches) is required when using mycophenolate mofetil and cyclophosphamide because of the risk of congenital malformations.

Adding belimumab in a dose of 10 mg/kg IV monthly to corticosteroids and mycophenolate or corticosteroids and cyclophosphamide has been shown to lead to a better renal response and complete renal response at 6 months compared to corticosteroids and mycophenolate or corticosteroids and cyclophosphamide alone, especially if extrarenal manifestations are active. Voclosporin in a dose of 23.7 mg orally twice a day in combination with mycophenolate mofetil and a rapidly tapered course of corticosteroid has been shown to lead to better renal outcomes at 1 year than corticosteroids and mycophenolate mofetil alone. Both belimumab and voclosporin are now often being used in combination with mycophenolate to treat lupus nephritis (classes III, IV, and V), but clear guidelines for their use are not yet available.

Cyclophosphamide use for more than 6 months is discouraged because of potential toxicities, including infertility and increased risk of cancer. Once disease control is achieved, patients are transitioned to either mycophenolate mofetil (1 to 1.5 g orally 2 times a day) or azathioprine (0.5 to 1.5 mg/kg orally twice a day) for maintenance. Women of childbearing age for whom cyclophosphamide is being considered should be informed about the risk of gonadal toxicity and offered a fertility consult for ovarian protection or egg harvesting when possible.

In neuropsychiatric lupus, including transverse myelitis, treatment recommendations are based on anecdotal evidence, and options include IV cyclophosphamide or IV rituximab (eg, 1 g on day 1 and day 15 given at 6-month intervals) in addition to a corticosteroid.

First-line therapy for thrombocytopenia and hemolytic anemia includes moderate- or high-dose corticosteroids (typically prednisone 1 mg/kg orally once a day, maximum 80 mg a day) along with an immunosuppressant (azathioprine 2 mg/kg orally once a day or mycophenolate mofetil 1 g orally every 12 hours). IV immune globulin 400 mg/kg once a day for 5 consecutive days or 1 g/kg once a day for 2 days may be useful, particularly if high-dose corticosteroids are contraindicated (eg, in patients with active infection). Rituximab is an alternative option for refractory cases.

Patients with end-stage renal disease can undergo kidney transplantation, as an alternative to dialysis, with a successful outcome, especially if their disease has been in remission.

Improvement of severe SLE often takes 4 to 12 weeks. Thrombosis or embolism of cerebral, pulmonary, or placental vessels requires short-term treatment with heparin and longer treatment with warfarin. If the diagnosis of antiphospholipid syndrome is confirmed, lifelong therapy (usually warfarin) is usually indicated. The initial target international normalized ratio is usually 2 to 3.

Anifrolumab (IgG1κ monoclonal antibody to type I interferon receptor), at a dose of 300 mg IV every 4 weeks, may be added to standard therapy for the management of moderate to severe SLE, particularly in patients with severe skin disease. However, patients with active and severe neuropsychiatric or renal disease were not included in the pivotal trial.

Use of CD19 chimeric antigen receptor (CAR) T-cell therapy for the treatment of refractory SLE shows promise.

### Maintenance therapy

Chronic disease should be treated with the lowest dose of corticosteroids (eg, oral prednisone ≤ 7.5 mg once a day or its equivalent) and other medications that control inflammation (eg, antimalarials, immunosuppressants [mycophenolate mofetil or azathioprine]) to maintain remission. Treatment should be guided by clinical features primarily, although anti-dsDNA antibody titers or serum complement levels may be followed, particularly if they have correlated with disease activity in the past. However, anti-dsDNA antibody titers or serum complement levels may not parallel nonrenal disease flares. Other pertinent blood and urine tests may be used to assess specific organ involvement.

Calcium, vitamin D, and bisphosphonate therapy should be considered in patients taking corticosteroids long term.

If combination immunosuppressive therapy is used, patients should be given prophylaxis for opportunistic infections, such as *Pneumocystis jirovecii* and vaccines against common infections (eg, streptococcal pneumonia, human papillomavirus, influenza, COVID-19).

Photoprotection is also an important measure to help prevent flares. Sunscreens with a sun protection factor (SPF) > 50 that block both UVA and UVB are recommended.

### Coexisting medical conditions and pregnancy

All patients should be closely monitored for atherosclerosis, and cardiovascular risk reduction is a key part of management. Long-term anticoagulation is vital in patients who also have antiphospholipid syndrome and history of thrombosis.

Pregnant women should remain on hydroxychloroquine throughout their pregnancy, and low-dose aspirin is recommended as well. When clinical antiphospholipid syndrome is present, as manifested by prior thrombotic events, full anticoagulation therapy with low molecular weight or unfractionated heparin is advised. If the pregnant woman has positive antiphospholipid syndrome antibodies and prior late-stage fetal loss or recurrent first trimester miscarriages, prophylactic low molecular weight or unfractionated heparin can be considered during pregnancy and 6 weeks postpartum. When the patient has positive serologies but no prior obstetric or thrombotic events, recommendations are less clear. Co-management by a hematologist, an obstetrician who specializes in high-risk pregnancies, and a rheumatologist should be considered when managing these patients.

Mycophenolate mofetil is teratogenic. Because of this teratogenicity and the known poor outcomes related to active SLE during pregnancy, women should ideally conceive after their disease has been in remission for 6 months or longer. If the patient needs to remain on immunosuppression (eg, ongoing maintenance therapy for lupus nephritis), mycophenolate mofetil is usually switched to azathioprine at least 6 months prior to conceiving. Azathioprine and tacrolimus are considered safe during pregnancy.

The choice of contraception method usually is based on multiple factors, including disease activity, risk of thrombosis, and patient preference**Prognosis for SLE**

The course is usually chronic, relapsing, and unpredictable. Remissions may last for years. If the initial acute phase is controlled, even if very severe (eg, with cerebral thrombosis or severe nephritis), the long-term prognosis is usually good.

The 10-year survival in most high-resource countries is almost 90%. Improved prognosis is in part due to earlier diagnosis and more effective therapies. However, despite advanced therapy and improvement of the mortality rate, survival is still considered lower than general population because of premature cardiovascular disease, disease activity, end-stage renal disease, and infection.

## Key Points

* Joint and skin manifestations are common in SLE, but the disorder can also affect various organ systems, such as the heart, lungs, lymphoid tissue, and kidneys and the gastrointestinal, hematologic, reproductive, and nervous systems.
* The European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) criteria can be used to support the diagnosis of SLE.
* Among tests, use the highly sensitive ANA for screening, but use clinical findings and other laboratory tests (eg, anti-dsDNA, anti-Sm) to help support the diagnosis.
* Evaluate all patients for kidney involvement.
* Treat all patients with hydroxychloroquine and, for mild disease, NSAIDs as needed.
* Use corticosteroids for moderate or severe SLE and an additional immunosuppressant for active lupus nephritis, neuropsychiatric lupus, skin manifestations that do not respond to hydroxychloroquine, diffuse alveolar hemorrhage, vasculitis, recurrent serositis, or cardiac manifestations.
* Use corticosteroids at the lowest possible dose and use other medications to maintain remission.

## 3. Gout

## Prognosis

* Acute attacks are highly treatable, but chronic gout can cause significant morbidity with untreated or poorly controlled disease.
* Effective therapy results in an excellent long-term prognosis.

## Risk Factors

* Elevated serum uric acid (hyperuricemia).
* Male sex; older age.
* Diet rich in purines (e.g., red meat, shellfish), excess alcohol, sugary drinks.
* Obesity, chronic kidney disease, hypertension, metabolic syndrome.
* Certain medications: diuretics, low-dose aspirin, cyclosporine.

## Prevention

* Weight loss and limiting intake of alcohol (especially beer) and high-purine foods.
* Increased consumption of low-fat dairy and vegetables.
* Management of comorbid conditions (hypertension, diabetes).

## Chronic Disease Management

* Acute Flares: NSAIDs, colchicine, corticosteroids.
* Long-term: Urate-lowering therapy (allopurinol, febuxostat) when indicated (recurrent flares, visible tophi, chronic kidney stones).
* Monitoring: Maintain serum urate <6 mg/dL; regular follow-up.

## Preventive Guidelines

* Educate patients on recognizing triggers and managing diet.
* Annual reviews for renal function, metabolic syndrome, and cardiovascular health.
* Lifelong adherence to urate-lowering therapy as needed.

Gout is characterized by painful joint inflammation, most commonly in the first metatarsophalangeal joint, resulting from precipitation of monosodium urate crystals in a joint space. Gout is typically diagnosed using clinical criteria from the American College of Rheumatology. Diagnosis may be confirmed by identification of monosodium urate crystals in synovial fluid of the affected joint. Acute gout may be treated with nonsteroidal anti-inflammatory drugs, corticosteroids, or colchicine. To reduce the likelihood of recurrent flares, patients should limit their consumption of certain purine-rich foods (e.g., organ meats, shellfish) and avoid alcoholic drinks (especially beer) and beverages sweetened with high-fructose corn syrup. Consumption of vegetables and low-fat or nonfat dairy products should be encouraged. The use of loop and thiazide diuretics can increase uric acid levels, whereas the use of the angiotensin receptor blocker losartan increases urinary excretion of uric acid. Reduction of uric acid levels is key to avoiding gout flares. Allopurinol and febuxostat are first-line medications for the prevention of recurrent gout, and colchicine and/or probenecid are reserved for patients who cannot tolerate first-line agents or in whom first-line agents are ineffective. Patients receiving urate-lowering medications should be treated concurrently with nonsteroidal anti-inflammatory drugs, colchicine, or low-dose corticosteroids to prevent flares. Treatment should continue for at least three months after uric acid levels fall below the target goal in those without tophi, and for six months in those with a history of tophi.

## Pathophysiology and Risk Factors

Genetic mutations may be associated with overproduction—or more often underexcretion—of uric acid because of defects in the renal urate transporter system. The prevalence of gout increases with age and peaks at more than 12% in persons older than 80 years. Because female sex hormones increase urinary excretion of uric acid, pre-menopausal women have a substantially lower prevalence of gout compared with men (2.0% vs. 5.9%). Black persons have a higher risk. Consuming alcoholic drinks (particularly beer), meat (especially red meat, wild game, and organ meat), some seafood (e.g., shellfish, some large saltwater fish), fruit juice, and beverages sweetened with high-fructose corn syrup increases the risk of gout. Purine-rich foods such as nuts, oatmeal, asparagus, legumes, and mushrooms do not seem to increase the risk. Consumption of dairy products appears to confer slight protection from gout.

## Clinical Presentation

Gout is typically diagnosed clinically based on the rapid development of monoarticular arthritis marked by swelling and redness usually involving the first metatarsophalangeal joint. The American College of Rheumatology criteria are the most widely used for diagnosis of gout.

Microscopy of joint fluid is used less often, primarily in equivocal cases. In these situations, the diagnosis is established by aspiration of a joint or tophus and identification of needle-shaped monosodium urate crystals, preferably intracellular, with bright, negative birefringence on compensated polarized light microscopy. Ultrasonography, magnetic resonance imaging, and computed tomography are typically not necessary for diagnosis.

The differential diagnosis for acute monoarticular joint swelling includes pseudogout, infection, and trauma. Pseudogout, or calcium pyrophosphate deposition disease, can mimic gout in clinical appearance and may respond to nonsteroidal anti-inflammatory drugs (NSAIDs). Findings of calcium pyrophosphate crystals and normal serum uric acid levels on joint fluid analysis can differentiate pseudogout from gout. Septic arthritis may present without a fever or elevated white blood cell count; arthrocentesis is required to distinguish this condition from acute gout. Gout and septic arthritis can occur concomitantly, but this is rare.Trauma-associated joint swelling is typically identified by the history; however, trauma may result in an acute gout flare caused by increased concentrations of synovial urate. Imaging may be necessary to rule out fracture in a patient with gout-like symptoms after a joint injury.

## Treatment

To achieve rapid and complete resolution of symptoms, treatment of acute gout should commence within 24 hours of symptom onset. Oral corticosteroids, intravenous corticosteroids, NSAIDs, and colchicine are equally effective in treating acute flares of gout. NSAIDs are the first-line treatment. Indomethacin (Indocin) has historically been the preferred choice; however, there is no evidence it is more effective than any other NSAID. Intramuscular ketorolac appears to have similar effectiveness. Any oral NSAID may be given at the maximal dosage and continued for one to two days after relief of symptoms.

Corticosteroids are an appropriate alternative for patients who cannot tolerate NSAIDs or colchicine. Patients with diabetes mellitus can be given corticosteroids for short-term use with appropriate monitoring for hyperglycemia. When gout is limited to a single joint, intra-articular corticosteroid injections may be preferable to systemic corticosteroids because of their lower adverse effect profile. Rebound flares are common after discontinuation of corticosteroid therapy for acute gout. To reduce the risk of a rebound flare, preventive treatment and initiation of a tapered course of corticosteroids over 10 to 14 days is recommended after resolution of symptoms.

Colchicine is another treatment option for acute gout. Generic colchicine, which has been used for decades, did not undergo formal review by the U.S. Food and Drug Administration (FDA) for this indication until 2009, when branded colchicine (Colcrys) was approved. However, Colcrys is expensive, and generic colchicine is no longer available. In addition, colchicine does not have analgesic properties and may be less effective in treating acute flares when given beyond 72 to 96 hours after symptom onset. Common adverse effects include nausea, vomiting, and diarrhea. Colchicine should be used with caution in patients with hepatic or renal impairment.

## Prevention

Serum urate–lowering therapy should be initiated to prevent recurrences in persons with a history of gout and any one of the following: at least two flares per year (one per year in persons with chronic kidney disease stage 2 or greater), tophi, or a history of nephrolithiasis.

Serum urate should be lowered to a target of less than 5 to 6 mg per dL (297 to 357 μmol per L), depending on the crystal and tophaceous burden. Normal serum urate levels do not exclude the diagnosis of gout. They should be monitored periodically to assess preventive therapy in patients with recurrent gout and a history of elevated urate levels. Urate-lowering therapy should be continued for three to six months after a flare if there are no ongoing symptoms. Therapy should continue indefinitely if there are ongoing signs or symptoms (e.g., one or more tophi on examination).

### DIETARY MODIFICATIONS

Weight gain is a significant risk factor for gout in men, whereas weight loss reduces the risk. Intake of high-fructose corn syrup should be restricted because the fructose contributes to increased uric acid production as a byproduct of adenosine triphosphate catabolism. Patients with gout should limit their intake of purine-rich animal protein (e.g., organ meats, beef, lamb, pork, shellfish) and avoid alcohol (especially beer). Purine-rich vegetables do not increase the risk of gout. Consumption of vegetables and low-fat or nonfat dairy products should be encouraged.

### PHARMACOLOGIC OPTIONS

Pharmacologic options for prevention of chronic gout are outlined in Although avoidance of loop and thiazide diuretics has been recommended for patients with hypertension and gout because these agents can increase uric acid levels, a systematic review found only small increases in the risk of gouty flares. Calcium channel blockers and the angiotensin receptor blocker losartan (Cozaar) are associated with a decreased risk of incident gout. Losartan is the only angiotensin receptor blocker with this property.

Historically, urate-lowering medication was thought to worsen acute gout flares, but recent evidence suggests that allopurinol (Zyloprim) can be started during an acute flare if it is used in conjunction with an NSAID and colchicine. Patients receiving a urate-lowering medication should be treated concurrently with an NSAID, colchicine, or low-dose corticosteroid to prevent a flare. Treatment should continue for at least three months after uric acid levels fall below the target goal in those without tophi, or for six months in those with a history of tophi. NSAIDs and corticosteroids should not be used for long periods without a urate-lowering medication because uric acid crystals continue to accumulate and damage the joint, despite a lack of pain or clinical signs of inflammation. If a patient has a gout flare while receiving a urate-lowering agent, the medication should be continued while the flare is treated acutely.

*Allopurinol*. Allopurinol, a xanthine oxidase inhibitor, is a first-line agent to prevent recurrent gout. In patients with gout and chronic kidney disease or congestive heart failure, allopurinol has the added benefit of preventing chronic disease progression. The starting dosage is 100 mg per day, and 300 mg per day is a common maintenance dosage. Dosing is guided by the target serum uric acid level. In patients with chronic kidney disease, low initial doses are recommended with slow titration to achieve target uric acid levels. Dosages higher than 300 mg may be used—even in those with renal impairment—as long as patients are closely monitored for adverse effects. Certain ethnic groups have a higher risk of a severe hypersensitivity skin reaction when starting allopurinol therapy. Screening for human leukocyte antigen-B\*5801 genotype is recommended before initiating treatment in patients of Han Chinese or Thai descent, regardless of kidney function, or in Koreans with chronic kidney disease stage 3 or greater.

*Febuxostat*. Febuxostat (Uloric) is a xanthine oxidase inhibitor that was approved by the FDA in 2009. Although febuxostat is superior to 300 mg allopurinol at lowering serum uric acid levels, it is not more effective at reducing the frequency of gout flares. Febuxostat is considered a first-line agent to prevent recurrent gout, but it is considerably more expensive than allopurinol.

*Colchicine*. Colchicine prevents gout flares at a dosage of 0.6 to 1.2 mg per day. The dose should be adjusted in patients with chronic kidney disease and when used with cytochrome P450 3A4 or P-glycoprotein inhibitors. The long-term adverse effects of colchicine include reversible axonal neuromyopathy (less than 1%). Patients should be advised to stop taking colchicine and tell their physician if they experience leg weakness or pain. Treatment should be discontinued if any signs or symptoms of nerve or muscle damage are present. The rare risk of rhabdomyolysis is increased when colchicine is used concomitantly with statins or clarithromycin (Biaxin), especially in older adults or those with chronic kidney disease; therefore, close monitoring is recommended.

*Probenecid*. Probenecid increases urinary excretion of uric acid and is typically used as a second-line treatment because of numerous drug interactions. Of particular concern, probenecid increases blood levels of methotrexate and ketorolac, which may result in severe toxicity. Probenecid may be used in combination with allopurinol or febuxostat when one drug does not independently lower serum uric acid to target levels. Nephrolithiasis is a common adverse effect that may be avoided by high fluid intake and urine alkalization with potassium citrate.

*Pegloticase*. Pegloticase (Krystexxa) is an intravenous uricase approved by the FDA in 2010. The mechanism of action involves metabolism of uric acid to allantoin. It is a third-line agent and is indicated for treatment of refractory gout. It is usually administered by a rheumatologist and is given every two week.

## 4. Vasculitis

## Prognosis

* Prognosis varies by type, organs involved, and response to treatment.
* With modern therapy, 5-year survival for many forms is >80%, but significant risks remain due to disease and treatment toxicity.

## Risk Factors

* May include genetic predisposition, environmental exposures, infections.
* Often idiopathic (no known cause).

## Prevention

* No primary prevention.
* Early detection and aggressive treatment improve outcomes.
* Manage cardiovascular risks; avoid infectious triggers where possible.

## Chronic Disease Management

* Immunosuppression: Corticosteroids, cyclophosphamide, azathioprine, rituximab (tailored to vasculitis type).
* Maintenance Therapy: Lower-toxicity agents for remission.
* Monitoring: Frequent labs and organ function monitoring to detect relapses and side effects.
* Holistic Approach: Address comorbidities, support rehabilitation needs.

## Preventive Guidelines

* Cardiovascular risk modification (control blood pressure, lipids, glucose).
* Regular vaccination (influenza, pneumococcal) due to immunosuppression.
* Screen for osteoporosis and malignancy according to guideline recommendations.

Vasculitis, also called angiitis or arteritis, is an autoimmune disease that affects your blood vessels, organs, and tissues. Your vessels swell and narrow, which makes it harder for your blood to flow to your tissues and organs. Some vessels could close entirely.

When too little blood reaches your organs and tissues, they can become damaged.

## Vasculitis Symptoms

Vasculitis symptoms can show up in many ways, depending on what part of your body is affected. Still, some general symptoms include:

* Fever
* Weight loss
* Loss of appetite
* Fatigue
* Headache
* General aches and pains

Symptoms related to specific areas of your body include:

* Eyes.Your first sign of vasculitis might be red, itchy, or burning eyes. You could also see double and have temporary or permanent blindness in one or both eyes.
* Skin. You might get rashes, lumps, or open sores if vasculitis affects blood vessels going to your skin.
* Nerves. If your nerves don't get enough blood, you could feel numbness, tingling, pain, and weakness.
* Brain. Vasculitis in your brain may cause a stroke.
* Heart. You could have heart palpitations or even a heart attack if it affects your heart.
* Kidneys. Inflammation in the vessels that supply blood to your kidneys can lead to kidney failure.
* Digestive system. You may feel pain after you eat if vasculitis affects your stomach or intestines. You could also see blood in your stool.
* Ears. Vasculitis can cause your ears to ring. It could also cause dizziness or sudden loss of hearing. You might also get inner ear infections.
* Hands and feet. Vasculitis can cause numbness or weakness in your hands or feet, along with swollen or hardened palms and soles.
* Lungs. If vasculitis affects your lungs, you could have shortness of breath or maybe cough up blood.
* Genitals. Vasculitis in this area can cause ulcers or open sores.
* Nose. Along with sinus infections and a runny nose, you could also get blisters in your nose.
* Mouth. Vasculitis can make your lips and tongue swollen and dry, or your mouth and throat swell.

## Vasculitis Types

Vasculitis is the general term for several conditions that cause blood vessel inflammation. Doctors organize vasculitis into types based on the size of the blood vessels involved. All types of vasculitis can affect anyone, but some are more common in certain age groups.

* Systemic vasculitis is inflammation of your blood vessel walls, which can happen anywhere in your body.
* Exercise-induced vasculitis is a type of small-vessel vasculitis. It restricts vessels in your lower legs after you do intense exercise like running or hiking, particularly in hot weather. Women over 50 get it most often. Symptoms include rashes on your legs that go away in a few days.
* Urticarial vasculitis affects your skin's small blood vessels. The inflammation usually causes patches and hives that can itch, burn, and discolor your skin. If it gets more serious, it may damage other organs, too.
* Leukocytoclastic vasculitis results when waste from immune cells in the walls of your small blood vessels causes inflammation. When the damaged blood vessels become leaky, they cause raised spots on your skin, usually your legs. Most of the time, it affects only your skin. But it can spread to other organs if it's serious.
* ANCA vasculitis targets a certain type of white blood cell in your body and tells these cells to attack small blood vessels. When the blood vessels are invaded, they become swollen and inflamed. ANCA vasculitis can happen in many parts of your body. The inflammation causes different symptoms, depending on where it is.
* IGA vasculitis is the most common type of vasculitis in children. It causes inflammation and bleeding of small blood vessels in your skin, joints, intestines, and kidneys. The most common symptom is a raised skin rash, usually on your legs or buttocks, that looks like bruises. But if IGA vasculitis affects other organs, you could have stomach or joint pain, swelling, and kidney inflammation.
* Cutaneous vasculitis is when you have inflammation and damage to your skin's blood vessels. It's the most common vasculitis doctors see. It shows up as raised patches on your skin.
* Central nervous system (CNS) vasculitis happens when the blood vessel walls in your brain and spine become inflamed. Many conditions can cause it, though your immune system often plays a role. While it's one of the more serious types of vasculitis, it is treatable.
* Rheumatoid vasculitis is a complication of rheumatoid arthritis (RA) that happens when the inflammation that causes joint pain and damage also damages your blood vessels. Rheumatoid vasculitis causes your small- and medium-sized blood vessels to become inflamed and narrow. It most often shows up in skin, nerves, fingers, and toes.
* Other types of vasculitis include giant cell arteritis, polyarteritis nodosa, Takayasu arteritis, Behçet’s disease, and Kawasaki disease.

## Vasculitis Causes

Doctors don’t know exactly what causes many cases of vasculitis. But there are some possible triggers:

* Autoimmune diseases like RA, lupus, or Sjögren's syndrome
* Infections, such as hepatitis B and hepatitis C, that set off an unusual immune system reaction that damages your blood vessels
* Allergic reactions to medications
* Certain blood cancers, like leukemia and lymphoma

## Vasculitis Risk Factors

While anyone can get vasculitis, some things can raise your chances of having certain types of the condition, including:

* Your age. Some types are more common in older people, while others, such as Kawasaki disease, most often affect children.
* A family history of a particular type of vasculitis
* Cocaine use
* Smoking
* Certain medications, such as allopurinol (Zyloprim), hydralazine (Apresoline), minocycline (Dynacin, Minocin, Myrac, Solodyn, Ximino), and propylthiouracil
* COVID-19, hepatitis A, or hepatitis B infections
* Also having other immune disorders
* Your sex. Certain types are more likely to affect people of a particular gender.

How common is it?

Most types of vasculitis are very rare. Fewer than 50 out of 1 million people get vasculitis every year in the U.S.

You're more likely to get it if you're over 50. But your odds are still very low. Only about 300 out of 1 million people older than 50 in the U.S. are diagnosed annually.

## Vasculitis Diagnosis

Your doctor will ask about your medical history and do a physical exam. There's no test just for vasculitis. But because it tends to result from other conditions, you may need tests to look for inflammation and figure out what's causing your symptoms. These tests may include:

* Blood tests. Certain types of blood cells or antibodies can be signs of vasculitis.
* Urine tests. These check for kidney damage.
* Imaging tests. X-rays, MRI scans, CT scans, PET scans, and ultrasounds show inflammation in your blood vessels and organs. You might also have an angiogram, in which your doctor injects dye into your bloodstream. It shows up on X-rays to give a better picture of your blood vessels.
* Heart tests. An echocardiogram tests how well your heart is working.
* Biopsy. Your doctor takes a sample of tissue. A specialist can check it for signs of inflammation or damage.

## Vasculitis Treatment

Which vasculitis treatment your doctor recommends depends on what’s causing it and which organs it affects. It's usually meant to control the inflammation and prevent organ and blood vessel damage.

Medications

Steroids like prednisone are the most common medications prescribed to fight the inflammation vasculitis causes. Your doctor will watch you closely for side effects like high blood pressure, high blood sugar, and bone problems, especially if you take them for a long time.

Other medications, like azathioprine (Azasan, Imuran), cyclophosphamide (Cytoxan), methotrexate (Rheumatrex, Trexall), mycophenolate (CellCept, Myfortic), rituximab (Riabni, Rituxan, Ruxience, Truxima), or tocilizumab (Actemra) can be prescribed along with steroids. Which medication you might need depends on how serious your vasculitis is, whether it's in your organs, and your medical history.

Surgery

Sometimes vasculitis can cause issues that need surgery to repair. For instance, if your blood vessel walls bulge and form an aneurysm, surgery can lower the chances that it will burst. If you have a blocked artery, you could need surgery to restore blood flow to the area. But any kind of organ damage might require surgery.

## Vasculitis Complications

Whether you have complications depends on what type of vasculitis you have and how bad it is. Some serious complications of vasculitis include:

* Organ damage
* Blood clots
* Aneurysm
* Loss of eyesight
* Infection

## Vasculitis Prognosis

There's no cure for vasculitis, but with the right treatment, you can live a long and active life. Most types of vasculitis are lifelong. But successful treatment can give you long periods without symptoms (called remissions).

Your outlook depends on several things, including:

* The type of vasculitis you have
* How quickly you were diagnosed
* Which organs are affected and how seriously
* Other health problems you have

Living with vasculitis  
For many people, the hardest part about vasculitis is managing the side effects of medications. There are steps you can take to manage these and other day-to-day issues:

Learn and understand the disease. Most types of vasculitis have periods of remission and relapse. Stick to your treatment plan and let your doctor know about any new symptoms or health changes.

Exercise regularly. Not only can exercise boost your mood and lower stress, it can help parts of your body that your treatment affects. Regular walking, for instance, can reduce your chances of bone loss, high blood pressure, and diabetes caused by corticosteroids.

Adopt healthy food habits. Focus on fresh fruits and vegetables, whole grains, low-fat dairy products, lean meat, and fish. And limit alcohol, sugar, and fat. A healthful diet can help with medication side effects like thinning bones, high blood pressure, and high blood sugar. If you take corticosteroids, ask your doctors about calcium and vitamin D supplements.

Keep your vaccinations updated to help prevent infections, like pneumonia and the flu, that can stem from your medications.

Surround yourself with support, whether it's from family, friends, or a support group. Your health care team can also refer you to a mental health professional.

## Takeaways

Vasculitis is inflammation of your blood vessels. It thickens your blood vessels, sometimes so much that blood can't flow properly. This can damage your organs and tissues. It's a lifelong disease without a cure, but it can be treated, usually with steroids.

## Vasculitis FAQs

Is vasculitis very serious?

Many types of vasculitis can be serious, specifically when they restrict blood flow. This not only can damage your organs and cause serious issues like aneurysms, but it could also be fatal. Certain kinds of vasculitis can cause vision loss or blindness, if they're not treated.

What does vasculitis look like when it starts?

If your vasculitis has symptoms you can see on your body, it'll likely appear as a rash, or spots of red, purplish red, black, or simply discolored skin. A vasculitis rash can be on your fingers, legs, ankles, or toes. Other signs that can point to vasculitis are swelling in your joints or cramps and bloating.

## 5. Scleroderma (Systemic Sclerosis)

## Prognosis

* Highly variable; limited cutaneous forms generally have a better outcome, while diffuse forms with organ involvement carry a higher risk of morbidity and mortality.
* Prognosis is determined by organ involvement, especially lung, heart, and kidney disease.

## Risk Factors

* Female sex (about 80% of cases).
* Age 30-50 at onset.
* Environmental exposures (silica, solvents), certain medications.
* Genetic factors and specific autoantibodies.

## Prevention

* No primary prevention established.
* Reducing exposure to environmental triggers, smoking cessation, and monitoring for early manifestations in at-risk individuals.

## Chronic Disease Management

* Symptom & Organ Management:
  + Immunosuppressants (mycophenolate, cyclophosphamide) for interstitial lung disease.
  + ACE inhibitors for scleroderma renal crisis.
  + Vasodilators (e.g., calcium channel blockers) for Raynaud phenomenon.
* Therapies: Physical/occupational therapy, pulmonary rehabilitation, mental health support.
* Regular Monitoring: Blood pressure, pulmonary function, bone density.

## Preventive Guidelines

* Early detection and management of renal crisis (BP monitoring, ACE inhibitors).
* Vaccination based on immunosuppressed status.
* Regular cancer and cardiovascular screening due to increased risks.
* Bone density management (vitamin D/calcium supplementation as needed).

## Comparative Table: Key Aspects

| **Disease** | **Prognosis** | **Major Risk Factors** | **Prevention** | **Chronic Management** | **Preventive Guidelines** |
| --- | --- | --- | --- | --- | --- |
| Rheumatoid Arthritis | Variable; early Rx best outcome | Sex, age, genetics, smoking, obesity | No full prevention; modifiable risk reduction | DMARDs, biologics, PT, CVD risk mgmt | Vaccinate, screen CVD/OP |
| Systemic Lupus Erythematosus | Relapsing; most (>90%) survive 10y | Sex, race, genetics, environment | Sun/block, avoid triggers | Antimalarials, steroids, immunoRx, lifestyle | CVD/infection/Osteoporosis |
| Gout | Excellent with therapy | Hyperuricemia, diet, obesity, CKD | Lifestyle, manage comorbids | Urate-lowering Rx, NSAIDs for flares | Diet, urate <6 mg/dL, screens |
| Vasculitis | Improved, still elevated risk | Genetic, environmental, infections | None; early Rx | Immunosuppression, monitor, comorbidity mgmt | Vaccination, CVD/Bone screens |
| Scleroderma | Variable, organ-driven | Sex, age, autoantibodies, exposures | No proven, avoid triggers | Organ-directed Rx, immunosuppressants | BP/bone/cancer monitoring |

Notes:

* “Rx” = therapy; “CVD” = cardiovascular disease; “OP” = osteoporosis; “PT” = physical therapy

# Rheumatoid Arthritis (RA)

Rheumatoid arthritis is an inflammatory arthritis in which joints, usually including those of the hands and feet, are inflamed, resulting in swelling, pain, and often destruction of joints.

* The immune system damages the joints and connective tissues.
* Joints (typically the small joints of the limbs) become painful and have stiffness that persists for more than 60 minutes on awakening and after inactivity.
* Fever, weakness, and damage to other organs may occur.
* Diagnosis is based mainly on symptoms but also on blood tests for rheumatoid factor and anti-cyclic citrullinated peptide (anti-CCP) and on x-rays.
* Treatment can include exercises and splinting, medications (nonsteroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs, and immunosuppressive drugs), and sometimes surgery.

Worldwide, rheumatoid arthritis develops in about 0.5% of the population, regardless of race or country of origin, affecting women 2 to 3 times more often than men. Usually, rheumatoid arthritis first appears between 35 years and 50 years of age, but it may occur at any age. A disorder similar to rheumatoid arthritis can occur in children. The disease is then called juvenile idiopathic arthritis. However, the prognosis for juvenile idiopathic arthritis is often somewhat different.

The exact cause of rheumatoid arthritis is not known. It is considered an autoimmune disease. Components of the immune system attack the soft tissue that lines the joints (synovial tissue) and can also attack connective tissue in many other parts of the body, such as the blood vessels and lungs. Eventually, the cartilage, bone, and ligaments of the joint erode (wear away), causing deformity, instability, and scarring within the joint. The joints deteriorate at a variable rate. Many factors, including genetic predisposition, may influence the pattern of the disease. Unknown environmental factors (such as viral infections and cigarette smoking) are thought to play a role.

Risk factors for rheumatoid arthritis include the following:

* Smoking
* Obesity
* Changes in the microbiome (the group of microorganisms that normally live in a particular part of the body, such as the digestive tract, mouth, and lungs)
* Periodontal disease (periodontitis)

## Symptoms of Rheumatoid Arthritis

People with rheumatoid arthritis may have

* Relatively mild symptoms
* Occasional flare-ups with long periods of remission (in which the disease is inactive)
* A severe, steadily progressive disease, which may be slow or rapid

Rheumatoid arthritis may start suddenly, with many joints becoming inflamed at the same time. More often, it starts subtly, gradually affecting different joints. Usually, the inflammation is symmetric, with joints on both sides of the body affected about equally. Rheumatoid arthritis can affect any joint, but most often the first inflamed are the small joints in the

* Hands
* Wrists
* Fingers
* Feet
* Toes

Other commonly affected joints include the

* Knees
* Shoulders
* Elbows
* Ankles
* Hips

Rheumatoid arthritis can also affect the neck. The lower spine and the joints at the tips of the fingers are not affected.

The inflamed joints are usually painful and often stiff, especially just after awakening (such stiffness generally lasts for more than 60 minutes) or after prolonged inactivity. Some people feel tired and weak, especially in the early afternoon. Rheumatoid arthritis may cause a loss of appetite with weight loss and a low-grade fever.

Affected joints are often tender, warm, and enlarged because of swelling of the soft tissue lining the joint (synovitis) and sometimes fluid within the joint (synovial fluid). Joints can quickly become deformed. Joints may freeze in one position so that they cannot bend or open fully, which leads to a limited range of motion. The fingers may tend to dislocate slightly from their normal position toward the little finger on each hand, causing tendons in the fingers to slip out of place, or may develop other deformities (see swan-neck deformity and boutonnière deformity).

### **When the Fingers Are Abnormally Bent**

| Some disorders, such as rheumatoid arthritis, and injuries can cause the fingers to bend abnormally. In swan-neck deformity, the joint at the base of the finger bends in (flexes), the middle joint straightens out (extends), and the outermost joint bends in (flexes). In boutonnière deformity, the middle finger joint is bent inward (toward the palm), and the outermost finger joint is bent outward (away from the palm). |
| --- |

Swollen wrists can pinch a nerve and result in numbness or tingling due to carpal tunnel syndrome.

Cysts, which may develop behind affected knees, can rupture, causing pain and swelling in the lower legs. Up to 30% of people with rheumatoid arthritis have hard bumps just under the skin (called rheumatoid nodules), usually near sites of pressure (such as the back of the forearm near the elbow).

Rarely, rheumatoid arthritis causes an inflammation of blood vessels (vasculitis). Vasculitis reduces the blood supply to tissues and may cause nerve damage or leg sores (ulcers). Inflammation of the membranes that cover the lungs (pleura) or of the sac surrounding the heart (pericardium) or inflammation and scarring of the lungs or heart can lead to chest pain or shortness of breath. Some people develop swollen lymph nodes (lymphadenopathy), Felty syndrome (a low white blood cell count and an enlarged spleen), Sjögren syndrome (dry mouth and eyes), thinning of the white of the eye (sclera), or red, irritated eyes caused by inflammation (episcleritis).

Rheumatoid arthritis can also affect the neck, making the bones unstable and increasing the risk of the bones putting pressure on (compressing) the spinal cord . Neck involvement is common in longstanding, active rheumatoid arthritis and usually causes headaches and pain and stiffness, sometimes with pain that radiates down the arms or legs.

People with rheumatoid arthritis are at increased risk for early coronary artery disease and bone disease, such as osteopenia and osteoporosis.

## Diagnosis of Rheumatoid Arthritis

* Blood tests
* Imaging tests (x-rays, ultrasound, or magnetic resonance imaging [MRI])
* Examination of joint fluid

In addition to the important characteristic pattern of symptoms, doctors follow established criteria when evaluating a person for rheumatoid arthritis. Doctors suspect rheumatoid arthritis in people who have more than one joint with definite swelling of the joint's lining that is not caused by another disorder. Doctors diagnose rheumatoid arthritis if people have certain combinations of the following criteria:

* Involvement of the joints that are most typical of rheumatoid arthritis
* High blood levels of rheumatoid factor, anti-cyclic citrullinated peptide (anti-CCP) antibodies, or both
* High blood levels of C-reactive protein, a high erythrocyte sedimentation rate (ESR), or both
* Symptoms that have lasted at least 6 weeks

Doctors check blood tests to determine a person's levels of rheumatoid factor and anti-CCP antibodies and usually C-reactive protein, ESR, or both. They also frequently do x-rays of the hands, wrists, and affected joints. X-rays sometimes show characteristic changes in the joints caused by rheumatoid arthritis. Ultrasound and magnetic resonance imaging (MRI) are other imaging tests that can detect joint abnormalities at an earlier stage but are not always needed.

Doctors may also insert a needle into a joint to draw a sample of synovial fluid, the thick fluid that lubricates joints and reduces friction. The fluid is examined to determine whether it is consistent with features of rheumatoid arthritis and to rule out other disorders that cause symptoms similar to rheumatoid arthritis. Synovial fluid needs to be analyzed to establish that a person has rheumatoid arthritis but does not always need to be analyzed whenever a flare-up causes joints to become swollen.

### Blood tests

Many people with rheumatoid arthritis have distinctive antibodies in their blood, such as rheumatoid factor and anti-CCP antibodies. However, doctors do not rely only on blood tests to diagnose rheumatoid arthritis.

**Rheumatoid factor** is present in 70% of people with rheumatoid arthritis. (Rheumatoid factor also occurs in several other diseases, such as cancers, systemic lupus erythematosus, hepatitis, and some other infections. Some people without any disorder, particularly older adults, have rheumatoid factor in their blood.)

**Anti-CCP antibodies** are present in over 75% of people who have rheumatoid arthritis and are almost always absent in people who do not have rheumatoid arthritis. The presence of anti-CCP and rheumatoid factor, especially in people who smoke cigarettes, predicts that their arthritis will be more severe.

**C-reactive protein** levels are often high in people with rheumatoid arthritis. Levels of C-reactive protein (a protein that circulates in the blood) dramatically increase when there is inflammation. High C-reactive protein levels can mean the disease is active.

The **ESR** is increased in 90% of people who have active rheumatoid arthritis. The ESR is another test for inflammation and measures the rate at which red blood cells settle to the bottom of a test tube containing blood. However, similar increases in the ESR, C-reactive protein level, or both occur in many other disorders. Doctors may monitor the ESR or C-reactive protein to help determine whether the disease is active.

Most people with rheumatoid arthritis have mild anemia (an insufficient number of red blood cells). Rarely, the white blood cell count becomes abnormally low. When a person with rheumatoid arthritis has a low white blood cell count and an enlarged spleen, the disorder is called Felty syndrome.

## Treatment of Rheumatoid Arthritis

* Medications
* Lifestyle measures, such as rest, diet, exercise, and stopping smoking
* Physical therapy and occupational therapy
* Sometimes surgery

Treatments include simple, conservative measures in addition to medications and surgical treatments. Simple measures are meant to help the person’s symptoms and include rest, adequate nutrition, and physical treatments. People should take measures that decrease their risk of heart disease, such as stopping smoking and getting treated, if necessary, for high blood pressure and high blood lipids or cholesterol.

### Medications

Because disease-modifying antirheumatic drugs (DMARDs) may actually slow progression of the disease as well as relieve symptoms, they are often started soon after the diagnosis of rheumatoid arthritis is made.

Lifestyle measures

Lifestyle measures play an important role in disease management. These measures include exercising regularly, maintaining a healthy diet, achieving and maintaining a healthy weight, keeping alcohol consumption moderate, stopping smoking, and modifying the worksite if needed for active work participation. Quality sleep is also important, because poor sleep increases pain.

Severely inflamed joints should be rested because using them can aggravate the inflammation. Regular rest periods often help relieve pain, and sometimes a short period of bed rest helps relieve a severe flare-up in its most active, painful stage.

A healthy diet, such as the Mediterranean diet (which is high in fruits and vegetables and low in processed foods), is generally appropriate. A diet rich in fish (omega-3 fatty acids) and plant oils but low in red meat can partially relieve symptoms in some people. Some people may have flare-ups after eating certain foods, and if so, these foods should be avoided, but such flare-ups occur rarely. No specific foods have been proved to cause flare-ups. Many diets have been proposed but have not proved helpful. Fad diets should be avoided.

### Physical treatments

Along with medications to reduce joint inflammation, a treatment plan for rheumatoid arthritis should include nondrug therapies, such as exercise, physical therapy (which includes massage, traction, and deep heat treatments), and occupational therapy (which includes self-help or assistive devices).

Splints can be used to immobilize and rest one or several joints, but some systematic movement of the joints is needed to prevent nearby muscles from weakening and joints from freezing in place.

Inflamed joints should be gently stretched so they do not freeze in one position. Heat therapy can be helpful because heat improves muscle function by reducing stiffness and muscle spasm. As the inflammation subsides, regular, active exercises can help, although a person should not exercise to the point of excessive fatigue. For many people, exercise in warm water may be easier.

Treatment of tight joints consists of intensive exercises and occasionally the use of splints to gradually extend the joint. Cold may be applied to reduce pain caused by temporary worsening in one joint.

People who are disabled by rheumatoid arthritis can use several aids to accomplish daily tasks. For example, specially modified orthopedic or athletic shoes can make walking less painful, and assistive devices such as grippers reduce the need to squeeze the hand forcefully.

### Surgery

If medications have not helped, surgical treatment may be needed. Surgical repair must always be considered in terms of the total disease. For example, deformed hands and arms limit a person’s ability to use crutches during rehabilitation, and seriously affected knees and feet limit the benefits of hip surgery. Reasonable objectives for each person must be determined, and ability to function must be considered. Surgical repair may be performed while the disease is active.

Surgically replacing knee or hip joints is the most effective way to restore mobility and function when the joint disease is advanced. Joints can also be removed or fused together, especially in the foot, to make walking less painful. The thumb can be fused to enable a person to pinch, and unstable vertebrae at the top of the neck can be fused to prevent them from compressing the spinal cord.

Joint repair with prosthetic joint replacement is indicated if damage severely limits function. Total hip replacements and knee replacements are generally successful.

### **Replacing All of a Hip (Total Hip Replacement)**

| Sometimes the whole hip joint must be replaced. The whole hip joint is the top (head) of the thighbone (femur) and the surface of the socket into which the head of the thighbone fits. This procedure is called total hip replacement or total hip arthroplasty. The head of the thighbone is replaced with a ball-shaped part (prosthesis), made of metal. The prosthesis has a strong stem that fits within the center of the thighbone. The socket is replaced with a metal shell lined with durable plastic. |
| --- |

### **Replacing a Knee**

| A knee joint damaged by osteoarthritis may be replaced with an artificial joint. After a general anesthetic is given, the surgeon makes an incision over the damaged knee. The knee cap (patella) may be removed, and the ends of the thigh bone (femur) and shinbone (tibia) are smoothed so that the parts of the artificial joint (prosthesis) can be attached more easily. One part of the artificial joint is inserted into the thigh bone, the other part is inserted into the shinbone, and then the parts are cemented in place. |
| --- |

## Medications for Rheumatoid Arthritis

The main goal of treatment with medications is to reduce inflammation and thereby prevent erosions, progression of the disease, and loss of joint function.

The main categories of medications used to treat rheumatoid arthritis are

* Disease-modifying antirheumatic drugs (DMARDs), which include biologic agents
* Nonsteroidal anti-inflammatory drugs (NSAIDs)
* Corticosteroids

Many of these medications are used in combination. For example, doctors may prescribe two DMARDs together or a corticosteroid plus a DMARD. However, the best combinations of medications are not yet clear. Typically, biologic agents are not used in combination with other biologic agents because these combinations increase the frequency of infections.

All the categories of drugs have potentially serious side effects that must be looked for during treatment.

### Disease-modifying antirheumatic drugs (DMARDs)

DMARDs can be broadly characterized into 3 types:

* Conventional synthetic DMARDs, for example, methotrexate, sulfasalazine, and leflunomide
* Biologic DMARDs, such as tumor necrosis factor [TNF] inhibitors, interleukin [IL]-6, and abatacept
* Targeted synthetic DMARDs, such as tofacitinib and upadacitinib

DMARDs, such as methotrexate, hydroxychloroquine, leflunomide, and sulfasalazine, slow the progression of rheumatoid arthritis and are given to nearly all people with rheumatoid arthritis. Doctors typically prescribe these medications as soon as the diagnosis of rheumatoid arthritis is made. Many take weeks to have an effect. Even if pain is decreased with NSAIDs, a doctor will likely prescribe a DMARD because the disease may otherwise progress even if symptoms are lessened. Combinations of DMARDs may be more effective than single medications. For example, hydroxychloroquine, sulfasalazine, and methotrexate together are more effective than methotrexate alone or the other two together. Also, combining biologic agents with a DMARD is often more effective than using a single medication or certain combinations of DMARDs. For example, methotrexate can be combined with a TNF inhibitor.

### Conventional synthetic DMARDs

Conventional synthetic (nonbiologic) DMARDs slow the progression of rheumatoid arthritis and are given to nearly all people with rheumatoid arthritis. They differ from each other chemically and pharmacologically. There are risks with these medications, and people should be monitored closely for evidence of toxicity.

**Methotrexate** is taken by mouth once weekly. It is anti-inflammatory at the low doses used to treat rheumatoid arthritis. Methotrexate is very effective and begins to work within 3 to 4 weeks, which is relatively rapid for a DMARD. The liver can scar, but this scarring most often can be detected by monitoring with regular blood tests and reversed before major damage develops. People taking methotrexate must refrain from drinking alcohol to minimize the risk of liver damage. Bone marrow suppression (suppression of the production of red blood cells, white blood cells, and platelets) may occur. Blood counts should be tested about every 2 to 3 months in all people taking the medication. Inflammation of the lung (pneumonitis) is rare. Inflammation in the mouth and nausea can also develop. Severe relapses of arthritis can occur after methotrexate is discontinued. Folate (folic acid) tablets may decrease some of the side effects, such as mouth ulcers. Rheumatoid nodules may enlarge with methotrexate therapy.

**Hydroxychloroquine** is given daily by mouth. Side effects, which are usually mild, include rashes, muscle aches, and eye problems. However, some eye problems can be permanent, so people taking hydroxychloroquine must have their eyes checked by an ophthalmologist before treatment begins and every 12 months during treatment. If the medication has not helped after 9 months, it is discontinued. Otherwise, hydroxychloroquine can be continued as long as necessary.

**Sulfasalazine** is initially given by mouth and can relieve symptoms and slow the development of joint damage. Sulfasalazine can also be used in people who have less severe rheumatoid arthritis or added to other medications to boost their effectiveness. The dose is increased gradually, and improvement usually is seen within 3 months. Because sulfasalazine may quickly cause a person's white blood cell count to become very low (neutropenia), blood tests are done after the first 2 weeks and then about every 12 weeks while the person is taking the medication. Like the other DMARDs, it can cause stomach upset, diarrhea, liver problems, blood cell disorders, and rashes. In males, sulfasalazine may cause a low sperm count, which is reversible.

**Leflunomide** is taken daily by mouth and has benefits that are similar to those of methotrexate but it is less likely to cause suppression of blood cell production in the bone marrow, abnormal liver tests, or inflammation of the lungs (pneumonitis). It can be given at the same time as methotrexate. The major side effects are rashes, liver dysfunction, hair loss, diarrhea, and rarely nerve damage (neuropathy).

### Biologic DMARDs

A biologic agent is something made from a living organism, often using cells in a laboratory. Many biologic agents used to treat rheumatoid arthritis are antibodies. Biologic agents used to treat rheumatoid arthritis include abatacept, rituximab, tumor necrosis factor (TNF) inhibitors (adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab), an interleukin-1 receptor blocker (anakinra), and interleukin-6 receptor blockers (tocilizumab and sarilumab).Biologic agents may suppress the inflammation so that corticosteroids can be avoided or given in lower doses. But by interfering with the immune system, biologic agents may increase the risks of infection and certain cancers. Because treatment with biologic agents increases the risk of infection, before starting treatment with a biologic agent people should be up to date on vaccinations TNF is an important part of the body’s immune system, so inhibition of TNF can impair the body’s ability to fight infections, particularly a reactivated tuberculosis infection. These medications should be avoided in people who have active infections and should be discontinued before major surgery. Etanercept, infliximab, and adalimumab can be and are often used with methotrexate. People who have severe heart failure should not take high doses of infliximab.

Side effects of TNF inhibitors include the potential risk of reactivation of infection (particularly tuberculosis and fungal infections), skin cancers other than melanoma, and reactivation of hepatitis B.

**Tocilizumab**, an IL-6 receptor blocker, is given to people who have not been helped by or who cannot tolerate conventional synthetic DMARDs. It can be used alone or sometimes in combination with methotrexate. Side effects include infection (such as tuberculosis), suppression of blood cell production in the bone marrow (neutropenia), anaphylaxis (a life-threatening allergic reaction), and increased liver enzymes. There may be an increased risk of bowel perforation when people who have had diverticulitis use tocilizumab.

**Sarilumab** is an IL-6 receptor blocker, which means it interrupts one of the major chemical pathways involved in inflammation. This medication is given to people who have not been helped by or who cannot tolerate conventional synthetic DMARDs. Sarilumab can cause suppression of blood cell production in the bone marrow (neutropenia), suppression of platelet production in the bone marrow (sometimes with increased susceptibility to bleeding), and increased liver enzymes. Like tocilizumab, there may also be an increased risk of bowel perforation in people who have had diverticulitis.

**Abatacept** is another biologic agent that interferes with the communication between cells that coordinates inflammation. This medication is given to people who have not been helped by or who cannot tolerate conventional synthetic DMARDs. Side effects include lung problems, headache, increased susceptibility to infection, and upper respiratory infection.

**Rituximab** is a biologic agent that decreases the number of B-cell lymphocytes, one of the white blood cells responsible for causing inflammation and for fighting infection. Rituximab is usually reserved for people who do not improve enough after taking methotrexate and a TNF inhibitor. Side effects, as with other immunosuppressive drugs, may include increased risk of infections. In addition, rituximab can cause effects while it is being given, such as rashes, nausea, back pain, itching, and high or low blood pressure. It can cause severe liver damage by reactivating hepatitis B in people who had previously been infected with this virus.

The COVID-19 vaccine may be less effective in people taking rituximab, and people on rituximab may have poorer outcomes if infected with COVID-19. Therefore, doctors now try to reserve rituximab for people who did not respond to other biologic DMARDs and to those with certain lymphatic disorders and cancers.

**Anakinra** is an interleukin-1 (IL-1) receptor blocker, which means it interrupts one of the major chemical pathways involved in inflammation. Side effects include infection and neutropenia. It is rarely used because it is not as effective as other biologics and because it is a daily injection.

### Targeted synthetic DMARDs

Janus kinase inhibitors are small molecule agents that interfere with the communication between cells that coordinate inflammation by inhibiting the enzyme JAK. JAK inhibitors include the following

* **Tofacitinib** is used if a person has taken methotrexate and has not improved enough. Tofacitinib can be used at the same time as methotrexate.
* **Upadacitinib** is given to adults with moderately to severely active rheumatoid arthritis when methotrexate has not been effective enough.
* **Baricitinib** is given to people who have not been helped by or who cannot tolerate TNF inhibitors.

Because treatment with JAK inhibitors increases the risk of infection, including herpes zoster infection, people should be vaccinated against zoster before starting treatment with a JAK inhibitor. Doctors should also discuss the potentially increased risk of major cardiovascular events associated with this class of drugs. Major cardiovascular events include heart attack, stroke, deep vein thrombosis, and pulmonary embolism. Some patients are at higher risk for these side effects, and the risks and benefits should be weighed before using these medications. These medications also increase the risk of nonmelanoma skin cancers and possibly other types of cancers. They can also cause high cholesterol levels.

### Other immunosuppressive agents

Other immunosuppressive agents, including azathioprine or cyclosporine (an immunomodulatory medication), are less effective and are rarely used because of an increased risk of toxicity. Thus, they are used only for people in whom treatment with more traditional DMARDs has not adequately controlled their symptoms.

### Nonsteroidal anti-inflammatory drugs (NSAIDs)

NSAIDs can be used to treat the symptoms of rheumatoid arthritis. They do not prevent the damage caused by rheumatoid arthritis from progressing and thus should not be considered the primary treatment.

NSAIDs can reduce the swelling in affected joints and relieve pain and stiffness. They can be taken by mouth or applied directly to the skin over painful joints. Rheumatoid arthritis, unlike osteoarthritis, causes considerable inflammation. Thus, medications that decrease inflammation, including NSAIDs, have an important advantage over medications such as acetaminophen that reduce pain but not inflammation. However, NSAIDs should generally not be taken by people who have a history of digestive tract (peptic) ulcers—including stomach ulcers or duodenal ulcers—because NSAIDs can upset the stomach and cause ulcers to bleed. Medications called proton pump inhibitors (such as esomeprazole, lansoprazole, omeprazole, pantoprazole, and rabeprazole) can reduce the risk of stomach or duodenal ulcers.

Other possible side effects of NSAIDs may include headache, confusion, elevation of blood pressure, worsening of kidney function, swelling, and decreased platelet function, causing bruising or bleeding. People who get hives, inflammation and swelling in the nose, or asthma after they take aspirin may have the same symptoms after taking other NSAIDs. NSAIDs may increase the risk of heart attacks and strokes. The risk appears to be higher if the medication is used at higher doses and for longer periods of time.

Aspirin is no longer used to treat rheumatoid arthritis because effective doses are often toxic.

The **cyclooxygenase (COX-2) inhibitors** (coxibs, such as celecoxib) are NSAIDs that act similarly to the other NSAIDs but are slightly less likely to damage the stomach and do not affect platelet function and cause bruising or bleeding like the other NSAIDs. However, if a person also takes aspirin, stomach damage is almost as likely to occur as with other NSAIDs. Caution should be taken with use of coxibs and probably all NSAIDs for long periods or by people with risk factors for heart attack and stroke.

### Corticosteroids

Corticosteroids are potent anti-inflammatory drugs that suppress the immune system. Corticosteroids, such as prednisone, are the most dramatically effective medications for reducing inflammation and symptoms of rheumatoid arthritis anywhere in the body.

Consequently, doctors usually reserve corticosteroids for short-term use in the following situations:

* When beginning treatment for severe symptoms (until a DMARD has taken effect)
* In severe flare-ups when many joints are affected

They are also useful in treating rheumatoid inflammation outside of joints, for example, in the membranes covering the lungs (pleura) or in the sac surrounding the heart (pericardium).

Because of the risk of side effects, the lowest effective dose is almost always used. When corticosteroids are injected into a joint, the person does not get the same side effects as when taking a corticosteroid by mouth (orally) or vein (intravenously). Corticosteroids can be injected directly into affected joints for fast, short-term relief of pain and swelling.

When used for a long time, corticosteroids may cause weight gain, high blood pressure, diabetes, thinning and bruising of the skin, glaucoma and other eye problems such as cataracts, and increase the risk of certain infections.

### **Corticosteroids: Uses and Side Effects**

| Corticosteroids are the strongest medications available for reducing inflammation in the body. They are useful in any condition in which inflammation occurs, including rheumatoid arthritis and other connective tissue disorders, multiple sclerosis, and in emergencies such as brain swelling due to cancer, asthma attacks, and severe allergic reactions. When inflammation is severe, use of these medications is often lifesaving.  Corticosteroids can be   * Given by vein (intravenously—especially in emergency situations) * Taken by mouth (orally) * Directly applied to the inflamed area (topically; for example, as eye drops or as skin creams) * Inhaled (as in inhaled versions for the lungs, used to treat disorders such as asthma and COPD) * Injected into a muscle (intramuscularly) * Injected into a joint   For example, corticosteroids can be used as an inhaled preparation for treatment of asthma. They can be used as a nasal spray to treat hay fever (allergic rhinitis). They can be used as eye drops to treat eye inflammation (uveitis). They may be applied directly to an affected area for treatment of certain skin conditions such as eczema and psoriasis. They can be injected into joints inflamed by rheumatoid arthritis or another disorder.  Corticosteroids are prepared synthetically to have the same action as cortisol (or cortisone), a steroid hormone produced by the outer layer (cortex) of the adrenal glands—hence the name “corticosteroid.” Many synthetic corticosteroids are, however, more powerful than cortisol, and most are longer acting. Corticosteroids are chemically related to, but have different effects than, anabolic steroids (such as testosterone) that are produced by the body and sometimes abused by athletes.  Examples of corticosteroids are prednisone, dexamethasone, triamcinolone, betamethasone, beclomethasone, flunisolide, and fluticasone. All of these medications are very strong (although strength depends on the dose used). Hydrocortisone is a milder corticosteroid that is available in over-the-counter skin creams.  Corticosteroids reduce the body’s ability to fight infections by reducing inflammation, typically when they are taken by mouth or given by vein. Because of this side effect, they are used with extreme care when infections are present. Oral and intravenous use may cause or worsen high blood pressure, heart failure, diabetes, peptic ulcers, and osteoporosis. Therefore, corticosteroids are used in such conditions only when their benefit is likely to exceed their risk.  When they are taken by mouth or by injection for more than about 2 weeks, corticosteroids should not be stopped abruptly. This is because corticosteroids inhibit the production of cortisol by the adrenal glands, and this production must be given time to recover. Thus, at the end of a course of corticosteroids, the dose is gradually reduced. It is important for a person who takes corticosteroids to follow the doctor’s instructions on dosage very carefully.  The long-term use of corticosteroids, particularly at higher doses and particularly when given by mouth or vein, invariably leads to many side effects, involving almost every organ in the body. Common side effects include thinning of the skin with stretch marks and bruising, high blood pressure, elevated blood sugar levels, cataracts, puffiness in the face (moon face) and abdomen, thinning of the arms and legs, poor wound healing, stunted growth in children, loss of calcium from the bones (which can lead to osteoporosis), hunger, weight gain, and mood swings. Inhaled corticosteroids and corticosteroids that are applied directly to the skin have far fewer side effects than corticosteroids given by mouth, vein, or injection. |
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## Prognosis for Rheumatoid Arthritis

Rheumatoid arthritis decreases life expectancy; however, this effect has been decreasing over time as treatments improve, and the difference appears to be very small. The major causes of death among patients with rheumatoid arthritis appear to be respiratory conditions (for example, interstitial lung disease and pneumonia), cardiovascular disease, and cancer. Side effects of treatment with immunosuppressive agents (for example, infection and increased cancer risk) may be responsible. Rarely, rheumatoid arthritis resolves spontaneously.

Although the majority of people experience improvement with treatment, less than half of people are likely to experience sustained remissions. At least 10% of people with rheumatoid arthritis are eventually severely disabled despite full treatment. Factors that tend to predict a poorer prognosis include the following:

* Being White, a woman, or both
* Having rheumatoid nodules
* Being older when the disorder begins
* Having inflammation in 20 or more joints
* Being a cigarette smoker
* Obesity
* Having a high erythrocyte sedimentation rate (ESR)
* Having high levels of rheumatoid factor or anti-cyclic citrullinated peptide (anti-CCP) antibodies

## Prevention

### **How do I prevent arthritis?**

Some forms of arthritis happen naturally or because of health conditions you can’t change, so there’s not always a way to prevent it. However, you can lower your chances of developing arthritis by:

* Avoiding tobacco products.
* Following a diet and exercise plan that’s healthy for you.
* Doing low-impact exercise.
* Always wearing proper protective equipment for any activity that could damage your joints.

# Systemic Lupus Erythematosus (SLE)

Systemic lupus erythematosus is a chronic, multisystem, inflammatory disorder of autoimmune etiology, occurring predominantly in young women. Manifestations may include arthralgias and arthritis, Raynaud syndrome, malar and other rashes, pleuritis or pericarditis, renal or central nervous system involvement, and autoimmune cytopenias. Diagnosis requires clinical and serologic criteria. Treatment of severe, ongoing, active disease requires corticosteroids and immunosuppressants.

# symptoms and signs

Clinical findings vary greatly. SLE may develop abruptly with fever and multisystem involvement or insidiously over months or years with episodes of arthralgias and malaise. Manifestations referable to any organ system may appear. Periodic exacerbations (flares) may occur.

### Joint manifestations

Joint symptoms, ranging from intermittent arthralgias to acute polyarthritis, occur in approximately 90% of patients and may precede other manifestations by years. Most lupus polyarthritis is nondestructive and nondeforming. However, in long-standing disease, deformities without bone erosions may develop (e.g., the metacarpophalangeal and interphalangeal joints may rarely develop reducible ulnar drift or swan-neck deformities without bony or cartilaginous erosions [Jaccoud arthritis]) because of ligamentous laxity. Bony erosions might be detected in patients with overlap of SLE and rheumatoid arthritis (sometimes referred to as rhupus).

As in many other chronic diseases, the prevalence of fibromyalgia is increased, which may cause diagnostic confusion in patients with periarticular and generalized pain and fatigue.

### Skin and mucous membrane manifestations

Skin lesions include a persistent malar butterfly erythema (flat or raised) that typically does not affect the nasolabial folds. The absence of papules and pustules and presence of skin atrophy help distinguish SLE from rosacea.

A variety of other erythematous, firm, maculopapular lesions can occur elsewhere, including exposed areas of the face and neck, upper chest, and elbows. Skin blistering and ulceration are rare, although recurrent ulcers on mucous membranes (particularly the central portion of the hard palate near the junction of the hard and soft palate, the buccal and gum mucosa, and the anterior nasal septum) are common; findings can sometimes mimic toxic epidermal necrolysis.

Generalized or focal and reversible alopecia is common during active phases of SLE. Panniculitis can cause subcutaneous nodular lesions (sometimes called lupus panniculitis or profundus). Vasculitic skin lesions may include mottled erythema on the palms and fingers, periungual erythema, nail-fold infarcts, urticaria, and palpable purpura. Petechiae may develop secondary to thrombocytopenia. Photosensitivity is common.

Lupus erythematosus tumidus is characterized by pink to violaceous nonscarring plaques and/or nodules, some annular, in light-exposed areas.

Chilblain lupus is characterized by tender, bright red to reddish blue nodules on the toes, fingers, nose, or ears that occur in cold weather. Some patients with SLE also have features of lichen planus.

Raynaud syndrome due to vasospasm in the fingers and toes causes characteristic blanching and cyanosis and might be associated with digital ischemia; however, unlike in systemic sclerosis, digital ulcers are uncommon in SLE.

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### Cardiopulmonary manifestations

Cardiopulmonary symptoms commonly include recurrent pleurisy, with or without pleural effusion. Pneumonitis is rare, although minor impairments in pulmonary function are common. Diffuse alveolar hemorrhage occasionally occurs and is associated with a poor prognosis. Other complications include pulmonary emboli, pulmonary hypertension, and shrinking lung syndrome.

Cardiac complications include pericarditis (most commonly) and myocarditis. Serious, rare complications are coronary artery vasculitis and valvular involvement including Libman-Sacks endocarditis. Accelerated atherosclerosis is an increasingly recognized cause of morbidity and mortality ([1](https://www.msdmanuals.com/professional/musculoskeletal-and-connective-tissue-disorders/systemic-rheumatic-diseases/systemic-lupus-erythematosus-sle#18598407-07cc-4fa5-a732-8186b768623f)). Congenital heart block can develop in neonates whose mother has the antibodies against Ro (SSA) and is less common if the mother has only antibodies against La (SSB).

### Lymphoid tissue

Generalized adenopathy is common, particularly among children, young adults, and African American patients. Splenomegaly can also occur.

### Neurologic manifestations

Neurologic symptoms can result from involvement of any part of the central or peripheral nervous system or meninges. Mild cognitive impairment is common. There may also be headaches, personality changes, ischemic stroke, subarachnoid hemorrhage, seizures, psychoses, aseptic meningitis, peripheral and cranial neuropathies, transverse myelitis, choreoathetosis, or cerebellar dysfunction.

Differentiation between corticosteroid-induced psychosis and neuropsychiatric lupus can be challenging because neither is associated with marked abnormalities in the cerebrospinal fluid (CSF) or on routine imaging.

### Renal manifestations

Renal involvement can develop at any time and may be the only manifestation of SLE. It may be asymptomatic or progressive and fatal.

Renal disease can range in severity from a focal glomerulitis to a diffuse, potentially fatal membranoproliferative glomerulonephritis. Common manifestations include proteinuria (most often), an abnormal urinary sediment manifested by red blood cell casts, hypertension, and edema. Early lupus glomerulonephritis may be misdiagnosed as asymptomatic urinary tract infection.

### Obstetric manifestations

Obstetric manifestations include early and late fetal loss. In patients with antiphospholipid antibodies, the risk of recurrent late miscarriages is increased. Pregnancy can be successful, particularly after 6 to 12 months of remission, but SLE flares are common during pregnancy and especially during the postpartum period. Planned pregnancy should be timed for when disease is in remission.

During pregnancy, the patient should be monitored closely for any disease flare or thrombotic events by a multidisciplinary team that includes an obstetrician who specializes in high-risk pregnancies. Women who are SSA antibody-positive should have weekly fetal ultrasonography between week 18 and week 26 to assess for congenital heart block.

### Hematologic manifestations

Hematologic manifestations include anemia (anemia of chronic disease, autoimmune hemolytic anemia), leukopenia (usually lymphopenia, neutropenia, or both), and thrombocytopenia (usually mild but sometimes life-threatening autoimmune thrombocytopenia). Recurrent arterial or venous thrombosis, thrombocytopenia, and a high probability of obstetric complications occur in patients with antiphospholipid antibodies. Thromboses account for some of the complications of SLE, including obstetric complications.

Macrophage activation syndrome is a rare but potentially life-threatening complication that can occur.

### Gastrointestinal manifestations

Gastrointestinal manifestations can result from bowel vasculitis or impaired bowel motility. In addition, pancreatitis can rarely result from SLE.

Manifestations may include abdominal pain resulting from serositis, nausea, vomiting, manifestations of bowel perforation, protein-losing enteropathy, and pseudo-obstruction.

SLE rarely causes parenchymal liver disease.

## diagnosis

* Clinical criteria
* Cytopenias
* Autoantibodies

SLE should be suspected in patients, particularly young women, with any of the symptoms and signs. However, early-stage SLE can mimic other systemic rheumatic diseases, including rheumatoid arthritis if joint symptoms predominate. Mixed connective tissue disease includes, by definition, features of SLE as well as possibly features of systemic sclerosis, rheumatoid-like polyarthritis, and myositis. Infections (eg, bacterial endocarditis, histoplasmosis) can mimic SLE and may develop as a result of treatment-caused immunosuppression. Disorders such as sarcoidosis and paraneoplastic syndromes can also mimic SLE.

Laboratory testing may differentiate SLE from other systemic rheumatic diseases. Initial laboratory testing should include the following:

* Antinuclear antibodies (ANA)
* Extractable nuclear antigens (ENAs) if ANA test is positive, including anti–double-stranded (ds) DNA (anti-dsDNA), anti-Smith, anti-U1 RNP, anti-Ro/SSA, and anti-La/SSB antibodies
* Complement C3 and C4 levels
* Complete blood count (CBC)
* Urinalysis with urinary sediment
* Chemistry profile including renal and liver enzymes

In clinical practice, some clinicians rely on the classification criteria for SLE developed by the European League Against Rheumatism/American College of Rheumatology. Patients are eligible for these criteria only if they have a positive ANA result ≥ 1:80. The 2019 EULAR/ACR classification criteria include clinical and immunologic domains, and each criterion is assigned a weight of 2 to 10. If the patient's score is 10 or more, and at least 1 clinical criterion is fulfilled, disease is classified as SLE. However, a positive ANA does not indicate a diagnosis of lupus. A positive ANA test in the presence of fatigue and generalized myofascial pain without other clinical or laboratory findings is rarely significant

### ANA testing

Testing for ANA (preferably by indirect immunofluorescence rather than by a solid-phase assay) is an appropriate initial test for patients with suspected SLE; a positive ANA test (usually in high titer: > 1:80) occurs in > 95% of people with SLE. However, a positive ANA test can also occur in rheumatoid arthritis, other systemic rheumatic diseases, autoimmune thyroid disease, multiple sclerosis, cancers, and even in the general population. The false-positive rate varies from approximately 3% with ANA titers of 1:320 to approximately 30% for ANA titers of 1:40 among healthy controls. Medications such as hydralazine, procainamide, and tumor necrosis factor inhibitors can cause positive ANA results as well as drug-induced lupus; the symptoms typically resolve after the medication is stopped. Positive ANA should prompt more specific testing such as anti-dsDNA antibodies; anti-dsDNA is highly specific for SLE.

### Other ANA and anticytoplasmic antibodies

The ANA test is very sensitive, but it is not specific for SLE; thus, evidence of other autoantibodies is used to aid in diagnosis. The other autoantibodies are often referred to as extractable nuclear antigens and include dsDNA, Smith (Sm), ribonucleoprotein (RNP), Ro (SSA), and La (SSB).

Ro is predominantly cytoplasmic; anti-Ro antibodies are occasionally present in patients with ANA-negative SLE presenting with subacute cutaneous lupus erythematosus. Anti-Ro is the causal antibody for neonatal lupus and congenital heart block.

Anti-Sm is highly specific for SLE but, like anti-dsDNA, is not sensitive.

Anti-RNP occurs in patients with SLE, mixed connective tissue disease, and occasionally other systemic rheumatic disorders and systemic sclerosis.

### Other tests

Leukopenia (usually lymphopenia and neutropenia) is common. Hemolytic anemia may occur, but low hemoglobin and red blood cell counts are more often due to the anemia of chronic disease. Thrombocytopenia in SLE may be difficult or impossible to differentiate from idiopathic thrombocytopenic purpura except that patients have other features of SLE and/or SLE-specific antibodies (anti-dsDNA or anti-Sm). False-positive serologic tests for syphilis occur in 5 to 10% of patients with SLE. These test results may be associated with the lupus anticoagulant and a prolonged partial thromboplastin time (PTT). Abnormal values in 1 or more of these assays suggest the presence of antiphospholipid antibodies (eg, anticardiolipin antibodies), which should then be measured directly by enzyme-linked immunosorbent assay (ELISA). Antiphospholipid antibodies are associated with arterial or venous thrombosis, mild thrombocytopenia, and, during pregnancy, spontaneous abortion or late fetal death but may be present in asymptomatic patients.

Other blood tests help monitor disease severity and determine the need for treatment. Serum complement levels (C3, C4) are often depressed in active disease and are usually lowest in patients with active nephritis. Erythrocyte sedimentation rate (ESR) is elevated frequently during active disease. C-reactive protein levels are not necessarily elevated; high levels raise the concern for infection and/or serositis.

Complete spirometry tests and an electrocardiogram are recommended in patients with respiratory symptoms.

### Renal involvement

Screening for renal involvement begins with urinalysis with urinary sediment. Red blood cell (RBC) and/or white blood cell casts suggest active nephritis. Urinalysis should be done at regular intervals (eg, every 3 to 6 months), even for patients in apparent remission and without previous renal involvement, because kidney disease is usually asymptomatic. Proteinuria can be estimated by the urine protein/creatinine ratio or measured in a 24-hour urine collection.

Renal biopsy is indicated in patients whose protein excretion is > 500 mg/day and who have hematuria (thought to be glomerular) or RBC casts and is helpful in evaluating the status of renal disease (i.e., active inflammation vs. chronic changes) and in guiding therapy. Classification of lupus nephritis is based on histologic findings on renal biopsy. Repeat renal biopsy should be considered in some patients because switching from one class of lupus nephritis to another is common in patients with SLE.

Patients with chronic renal insufficiency and mostly sclerotic glomeruli are not likely to benefit from aggressive immunosuppressive therapy.

## treatment of SLE

* Hydroxychloroquine (an antimalarial) for all patients with SLE
* Nonsteroidal anti-inflammatory drugs (NSAIDs) as needed in addition to antimalarials for mild disease
* Corticosteroids, other immunosuppressants, and antimalarials for severe disease

To guide therapy, SLE should be classified as mild to moderate (eg, fever, arthritis, pleurisy, pericarditis, rash) or severe (eg, hemolytic anemia, severe thrombocytopenic purpura, massive pleural and pericardial involvement, diffuse alveolar hemorrhage or pneumonitis, nephritis, acute vasculitis of the extremities or gastrointestinal tract, florid central nervous system [CNS] involvement).

The antimalarial hydroxychloroquine is indicated for all patients with SLE regardless of disease severity because it decreases disease flares and decreases mortality. Hydroxychloroquine may also reduce thrombotic events especially in patients with associated antiphospholipid syndrome. It must be avoided if there is an absolute contraindication because of adverse events (eg, ocular toxicity). In addition, it should be used with caution if there is a history of glucose-6-phosphate dehydrogenase (G6PD) deficiency.

Patients require routine monitoring during treatment to assess disease activity and response to therapy. In addition to clinical follow-up, disease activity can be assessed with the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) and the British Isles Lupus Assessment Group (BILAG) index ([5](https://www.msdmanuals.com/professional/musculoskeletal-and-connective-tissue-disorders/systemic-rheumatic-diseases/systemic-lupus-erythematosus-sle#v37724322)).

### Mild to moderate disease

Arthralgias are usually controlled with NSAIDs. However, chronic NSAID use is discouraged because of gastrointestinal adverse effects (eg, peptic ulcer disease) and potential coronary and renal toxicity (eg, interstitial nephritis, papillary necrosis). Topical agents (eg, corticosteroids, tacrolimus) can be used for skin disease, usually under the guidance of dermatology.

Antimalarials, such as hydroxychloroquine, are useful for joint and skin manifestations. Hydroxychloroquine reduces the frequency of SLE flares and decreases mortality, and is therefore used in virtually all patients with SLE. The dose is 5 mg/kg of actual body weight orally once a day with a maximum dose of 400 mg/day. Baseline ophthalmologic examination should be done before starting therapy to exclude retinopathy because chronic hydroxychloroquine use increases the risk of toxic retinopathy. Ophthalmologic screening should be done yearly to assess for retinal toxicity. Hydroxychloroquine can rarely cause skeletal or cardiac muscle toxicity. Alternatives include oral chloroquine 250 mg once a day and oral quinacrine 50 to 100 mg once a day.

Methotrexate (15 to 20 mg orally or subcutaneously once a week), azathioprine (2 mg/kg orally once a day), or mycophenolate mofetil (1 to 1.5 grams orally twice a day) can be added to hydroxychloroquine in patients with uncontrolled mild to moderate disease who would otherwise be candidates for a course of corticosteroids. The ultimate goal is to maintain disease remission either without the need for corticosteroids or with only the lowest dose possible.

Belimumab (10 mg/kg IV every 2 weeks for 3 doses, then 10 mg/kg IV once a month or 200 mg subcutaneously once a week) should be considered if patients have uncontrolled disease or frequent flares, particularly for joint, skin, renal, or nonsevere hematologic manifestations. It can be used in addition to hydroxychloroquine and in combination with other medications depending on the specific system involved and severity of disease. Screening and monitoring for depression is required when initiating therapy with belimumab because of a possible risk of new-onset or worsening depression and suicidality.

### Severe disease

Treatment includes induction therapy to control acute severe manifestations followed by maintenance therapy. Corticosteroids are first-line therapy. A combination of a corticosteroid and other immunosuppressants is typically used in active severe disease (ie, lupus nephritis with impaired renal function, myocarditis, or CNS involvement).

The complication for which there is the strongest evidence for treatment efficacy is lupus nephritis. Methylprednisolone 1 g by slow (1-hour) IV infusion on 3 successive days is often the initial treatment, although trial evidence for this pulse corticosteroid therapy is lacking. Then, oral prednisone given in doses of 0.5 to 1 mg/kg once a day (usually 40 to 60 mg once a day) is initiated, and the dose is adjusted according to the manifestation of SLE. Corticosteroids should be tapered as soon as allowed by the disease, usually within 6 months, to limit adverse effects. Cyclophosphamide or mycophenolate mofetil (up to 3 g a day orally in 2 doses) is also used for induction therapy along with corticosteroids. Effective birth control (an intrauterine device is typically preferred to hormonal approaches) is required when using mycophenolate mofetil and cyclophosphamide because of the risk of congenital malformations.

Adding belimumab in a dose of 10 mg/kg IV monthly to corticosteroids and mycophenolate or corticosteroids and cyclophosphamide has been shown to lead to a better renal response and complete renal response at 6 months compared to corticosteroids and mycophenolate or corticosteroids and cyclophosphamide alone, especially if extrarenal manifestations are active. Voclosporin in a dose of 23.7 mg orally twice a day in combination with mycophenolate mofetil and a rapidly tapered course of corticosteroid has been shown to lead to better renal outcomes at 1 year than corticosteroids and mycophenolate mofetil alone. Both belimumab and voclosporin are now often being used in combination with mycophenolate to treat lupus nephritis (classes III, IV, and V), but clear guidelines for their use are not yet available.

Cyclophosphamide use for more than 6 months is discouraged because of potential toxicities, including infertility and increased risk of cancer. Once disease control is achieved, patients are transitioned to either mycophenolate mofetil (1 to 1.5 g orally 2 times a day) or azathioprine (0.5 to 1.5 mg/kg orally twice a day) for maintenance. Women of childbearing age for whom cyclophosphamide is being considered should be informed about the risk of gonadal toxicity and offered a fertility consult for ovarian protection or egg harvesting when possible.

In neuropsychiatric lupus, including transverse myelitis, treatment recommendations are based on anecdotal evidence, and options include IV cyclophosphamide or IV rituximab (eg, 1 g on day 1 and day 15 given at 6-month intervals) in addition to a corticosteroid.

First-line therapy for thrombocytopenia and hemolytic anemia includes moderate- or high-dose corticosteroids (typically prednisone 1 mg/kg orally once a day, maximum 80 mg a day) along with an immunosuppressant (azathioprine 2 mg/kg orally once a day or mycophenolate mofetil 1 g orally every 12 hours). IV immune globulin 400 mg/kg once a day for 5 consecutive days or 1 g/kg once a day for 2 days may be useful, particularly if high-dose corticosteroids are contraindicated (eg, in patients with active infection). Rituximab is an alternative option for refractory cases ([2](https://www.msdmanuals.com/professional/musculoskeletal-and-connective-tissue-disorders/systemic-rheumatic-diseases/systemic-lupus-erythematosus-sle#v37724322)).

Patients with end-stage renal disease can undergo kidney transplantation, as an alternative to dialysis, with a successful outcome, especially if their disease has been in remission.

Improvement of severe SLE often takes 4 to 12 weeks. Thrombosis or embolism of cerebral, pulmonary, or placental vessels requires short-term treatment with heparin and longer treatment with warfarin. If the diagnosis of antiphospholipid syndrome is confirmed, lifelong therapy (usually warfarin) is usually indicated. The initial target international normalized ratio is usually 2 to 3.

Anifrolumab (IgG1κ monoclonal antibody to type I interferon receptor), at a dose of 300 mg IV every 4 weeks, may be added to standard therapy for the management of moderate to severe SLE, particularly in patients with severe skin disease. However, patients with active and severe neuropsychiatric or renal disease were not included in the pivotal trial.

Use of CD19 chimeric antigen receptor (CAR) T-cell therapy for the treatment of refractory SLE shows promise.

### Maintenance therapy

Chronic disease should be treated with the lowest dose of corticosteroids (eg, oral prednisone ≤ 7.5 mg once a day or its equivalent) and other medications that control inflammation (e.g., antimalarials, immunosuppressants [mycophenolate mofetil or azathioprine]) to maintain remission. Treatment should be guided by clinical features primarily, although anti-dsDNA antibody titers or serum complement levels may be followed, particularly if they have correlated with disease activity in the past. However, anti-dsDNA antibody titers or serum complement levels may not parallel nonrenal disease flares. Other pertinent blood and urine tests may be used to assess specific organ involvement.

Calcium, vitamin D, and bisphosphonate therapy should be considered in patients taking corticosteroids long term.

If combination immunosuppressive therapy is used, patients should be given prophylaxis for opportunistic infections, such as *Pneumocystis jirovecii*, and vaccines against common infections (eg, streptococcal pneumonia, human papillomavirus, influenza, COVID-19).

Photoprotection is also an important measure to help prevent flares. Sunscreens with a sun protection factor (SPF) > 50 that block both UVA and UVB are recommended.

### Coexisting medical conditions and pregnancy

All patients should be closely monitored for atherosclerosis, and cardiovascular risk reduction is a key part of management. Long-term is vital in patients who also have antiphospholipid syndrome and history of thrombosis.

Pregnant women should remain on hydroxychloroquine throughout their pregnancy, and low-dose aspirin is recommended as well. When clinical antiphospholipid syndrome is present, as manifested by prior thrombotic events, full anticoagulation therapy with low molecular weight or unfractionated heparin is advised. If the pregnant woman has positive antiphospholipid syndrome antibodies and prior late-stage fetal loss or recurrent first trimester miscarriages, prophylactic low molecular weight or unfractionated heparin can be considered during pregnancy and 6 weeks postpartum. When the patient has positive serologies but no prior obstetric or thrombotic events, recommendations are less clear. Co-management by a hematologist, an obstetrician who specializes in high-risk pregnancies, and a rheumatologist should be considered when managing these patients.

Mycophenolate mofetil is teratogenic. Because of this teratogenicity and the known poor outcomes related to active SLE during pregnancy, women should ideally conceive after their disease has been in remission for 6 months or longer. If the patient needs to remain on immunosuppression (eg, ongoing maintenance therapy for lupus nephritis), mycophenolate mofetil is usually switched to azathioprine at least 6 months prior to conceiving. Azathioprine and tacrolimus are considered safe during pregnancy.

The choice of contraception method usually is based on multiple factors, including disease activity, risk of thrombosis, and patient preference.

## Prognosis for SLE

The course is usually chronic, relapsing, and unpredictable. Remissions may last for years. If the initial acute phase is controlled, even if very severe (eg, with cerebral thrombosis or severe nephritis), the long-term prognosis is usually good.

The 10-year survival in most high-resource countries is almost 90%. Improved prognosis is in part due to earlier diagnosis and more effective therapies. However, despite advanced therapy and improvement of the mortality rate, survival is still considered lower than the general population because of premature cardiovascular disease, disease activity, end-stage renal disease, and infection.

## GOUT

Gout and pseudogout are the two most common crystal-induced arthropathies. Gout (see the image below) is caused by monosodium urate monohydrate crystals; pseudogout is caused by calcium pyrophosphate (CPP) crystals and is more accurately termed calcium pyrophosphate disease (CPPD).

Gout is one of the oldest diseases in the medical literature, known since the time of the ancient Greeks.Pseudogout, which may be clinically indistinguishable from gout, was recognized as a distinct disease entity in 1962.

Crystal deposition can be asymptomatic, but gout and CPPD can develop into debilitating illnesses marked by recurrent episodes of pain and joint inflammation that result from the formation of crystals within the joint space and deposition of crystals in soft tissue.If untreated, these disorders can lead to joint destruction and, in the case of uric acid crystals, kidney damage.

Elevated serum uric acid levels are the principal risk factor for developing gout. lIn study that compared 993 patients with asymptomatic hyperuricemia and 4241 normouricemic patients, the odds ratio (OR) for developing gout was 32 times higher in the hyperuricemic group than in the normouricemic group. The risk was most striking in men with severe hyperuricemia, in whom the OR for developing gout was 624.8.

Although gout is associated with hyperuricemia, gout attacks are triggered not by a particular level of uric acid but typically by acute changes in the level of uric acid. All individuals with gout have hyperuricemia; however, hyperuricemia is also found in patients taking diuretics and even in those taking niacin or low doses of aspirin.

Gout may be either primary or secondary. Primary gout is related to underexcretion or overproduction of uric acid, often associated with a mix of dietary excesses or alcohol overuse and metabolic syndrome. Secondary gout is related to medications or conditions that cause hyperuricemia, such as the following:

* Myeloproliferative diseases or their treatment
* Therapeutic regimens that produce hyperuricemia
* Kidney failure
* Renal tubular disorders
* Lead poisoning
* Hyperproliferative skin disorders
* Enzymatic defects (eg, deficient hypoxanthine-guanine phosphoribosyl transferase, glycogen storage diseases)

Gout is definitively diagnosed on the basis of demonstration of urate crystals in aspirated synovial fluid, in the absence of another etiology for arthritis. Classic radiographic findings are highly suggestive.

Advances in early diagnosis and the availability of definitive treatment have significantly improved the prognosis for patients with gout, as evidenced by the declining incidence of disabling chronic tophaceous gout. However, tophaceous gout may still develop because of misdiagnosis, poor management, medication intolerances, or poor patient adherence.

Gout is managed in the following 3 stages:

* Treating the acute attack
* Providing prophylaxis to prevent acute flares
* Lowering excess stores of urate

Treatment of gout is important to relieve pain; to prevent disease progression; and to prevent deposition of urate crystals in the renal medulla or uric acid crystals in the renal collecting system, which may produce kidney stones or urate nephropathy. Management of pseudogout also involves treatment of the acute attack and prophylaxis. Treatment of the acute phase of pseudogout follows the same approaches as are used in gout, and colchicine is effective for prophylaxis. In contrast with gout, however, no specific therapeutic regimen exists to treat the underlying cause of CPP crystal deposition in pseudogout, except in cases associated with disorders such as hemochromatosis or hyperparathyroidism.

## Pathophysiology

Gout can be considered a disorder of metabolism that allows uric acid or urate to accumulate in blood and tissues. When tissues become supersaturated, the urate salts precipitate, forming monosodium urate crystals. Deposition of these crystals is most commonly reported in synovium, bone, skin, cartilage, tendon, ligament, and kidney, but involvement of a range of other musculoskeletal and non-musculoskeletal tissues also occurs.In addition, the crystals also are less soluble under acid conditions and at low temperatures, such as occur in cool, peripheral joints (eg, the metatarsophalangeal joint of the big toe).

Urate initially precipitates in the form of needlelike crystals. The light-retarding (phase-shifting) characteristics of urate crystals allow them to be recognized by polarizing microscopy Many conditions and drugs have been associated with an increase in plasma (and subsequent synovial) urate levels, particularly metabolic syndrome.A genetic predisposition for hyperuricemia exists; except in rare genetic disorders, however, the development of gout in hyperuricemic individuals appears to be mediated by environmental factors.Gout flares have strong seasonality, with peak frequency in the spring. Serum urate levels also show seasonal variation, but are highest in the summer. However, other factors may contribute to this seasonality; for example, the absolute neutrophil count peaks in the spring (neutrophils play a critical role in the inflammatory response), while cortisol levels drop to their lowest.

Increasing evidence points to a role for the gut microbiome in gout. The gut microbiome is involved in the metabolism of dietary purine, and the composition of the gut microbiome is distinctly different in persons with gout than in healthy individuals. In addition, the gut microbiome shows seasonal variation that may contribute to flares; for example, *Bacteroidales* bacteria are most prevalent in the spring.

Variation in the organisms that comprise the gut microbiome may also help explain why only a minority of individuals with hyperuricemia develop gout; the gut microbiota of persons with asymptomatic hyperuricemia may provide anti-inflammatory mediators, which prevent the appearance of gout flares. A study of gut microbiota found that, compared with individuals with asymptomatic hyperuricemia, patients with gout had more bacteria capable of producing acetate, a molecule that seems to contribute to the development of gout.

The CPP crystals that produce pseudogout comprise a combination of inorganic pyrophosphate and calcium. The inorganic pyrophosphate is produced in large part by ectonucleotide phosphodiesterase pyrophosphatase (ENPP1), a catalytic enzyme found in chondrocytes of cartilage, and the pyrophosphate is exported potently by the membrane transporter ANKH.

A genetic predisposition exists for pseudogout. However, aging, some metabolic diseases (eg, hyperparathyroidism, hemochromatosis, and hypomagnesemia), and any process that leads to osteoarthritis also can be associated with subsequent CPP crystal deposition and pseudogout.

The presence of urate crystals in the soft tissues and synovial tissues is a prerequisite for a gouty attack. However, these crystals can also be found in synovial fluid or on the cartilage surface in the absence of joint inflammation.

A gout attack may be triggered either by release of crystals (eg, from partial dissolution of a microtophus caused by changing serum urate levels) or by precipitation of crystals in a supersaturated microenvironment (eg, release of urate as a consequence of cellular damage). In either situation, it is believed, naked urate crystals then interact with intracellular and surface receptors of local dendritic cells and macrophages, triggering a danger signal to activate the innate immune system.

This interaction may be enhanced by immunoglobulin G (IgG) binding.Triggering of these receptors, including Toll-like receptors, followed by intracellular signaling by the NLRP3 inflammasome, results in the release of interleukin (IL)-1β, which in turn initiates a cascade of proinflammatory cytokines, including IL-6, IL-8, neutrophil chemotactic factors, and tumor necrosis factor (TNF)-α.Neutrophil phagocytosis leads to another burst of inflammatory mediator production.

Chatfield et al reported that the interaction of urate crystals with lysosomes results in the formation of web-like chromatin structures known as neutrophil extracellular traps (NETs) and subsequent cell death (NETosis), via a mechanism independent of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase. The urate crystal–induced NETs are enriched for actin and are resistant to degradation by serum and DNase; they coat the crystals with DNA. Aggregated NETs persist in tissues as gouty tophi.​

Subsidence of an acute gout attack results from multiple mechanisms, including the clearance of damaged neutrophils, change in the properties of urate crystals, and the production of anti-inflammatory cytokines such as IL-1 receptor antagonist (IL-1RA), IL-10, and transforming growth factor (TGF)-β.

## Etiology

Gout develops in the setting of excessive stores of uric acid in the form of monosodium urate. Uric acid is an end-stage by-product of purine metabolism. Humans remove uric acid primarily by renal excretion. When excretion is insufficient to maintain serum urate levels below the saturation level of 6.8 mg/dL, hyperuricemia may develop, and urate can crystallize and deposit in soft tissues.

About 90% of patients with gout develop excess urate stores because of an inability to excrete sufficient amounts of uric acid in the urine (underexcretion). Most of the remaining patients either overconsume purines or produce excessive amounts of uric acid endogenously (overproduction). A few have impaired intestinal elimination of uric acid.

In rare cases, overproduction of uric acid is the result of a genetic disorder, such as the following:

* Hypoxanthine-guanine phosphoribosyltransferase deficiency (Lesch-Nyhan syndrome)
* Glucose-6-phosphatase deficiency (von Gierke disease)
* Fructose 1-phosphate aldolase deficiency
* Superactivity of phosphoribosyl pyrophosphate synthetase (PRPP)

Overproduction of uric acid may also occur in disorders that cause high cell turnover with release of purines that are present in high concentration in cell nuclei. These disorders include myeloproliferative and lymphoproliferative disorders, psoriasis, and hemolytic anemias.Cell lysis from chemotherapy for malignancies, especially those of the hematopoietic or lymphatic systems, can raise uric acid levels, as can excessive exercise and obesity.

Causes of secondary gout due to underexcretion of uric acid include kidney insufficiency, lead nephropathy (saturnine gout), starvation or dehydration, certain drugs, and chronic abuse of ethanol (especially beer and hard liquor).These disorders should be identified and corrected, if possible.

Certain comorbid conditions are associated with a higher incidence of gout, including the following:

* Hypertension
* Diabetes mellitus
* Kidney insufficiency
* Hypertriglyceridemia
* Hypercholesterolemia
* Obesity
* Anemia

A population-based study from Taiwan concluded that proton pump inhibitor (PPI) use increases the risk of gout (adjusted odds ratio 1.3; 95% CI 1.0-1.6). The risk of gout was highest within 30 days of PPI treatment (aOR 1.7; 95% CI 1.4-1.9) and diminished thereafter; was higher in women than in men (adjusted OR 2.2; 95% CI 1.7-2.8); and was higher in individuals age 41-60 years than in older ones (adjusted OR 2.1; 95% CI 1.7-2.7).

A study of 231,208 patients with incident type 2 diabetes mellitus in Taiwan suggested that the risk of gout may be lower in patients receiving sodium-glucose transport protein 2 (SGLT2) inhibitors (especially dapagliflozin) than in those receiving dipeptidyl peptidase 4 (DPP4) inhibitors. The overall gout incidence per 1000 patient-years was 20.26 for SGLT2 inhibitor users and 24.30 for DPP4 inhibitor users.

Foods that are rich in purines include anchovies, sardines, sweetbreads, kidney, liver, and meat extracts. Consumption of fructose-rich foods and beverages (eg, those sweetened with high-fructose corn syrup) is associated with an increased risk of gout in both men and women.Genetics

The heritability of serum urate levels is estimated at 63%.Genome-wide association studies (GWAS) have identified several candidate loci associated with chronically elevated serum urate concentrations and gout. A GWAS of 2.6 million people that included 120,295 people with prevalent gout detected 377 loci, as well as 410 genetically independent signals; a prioritization scheme identified genes that may be involved in the inflammatory process of gout, including genes involved in epigenetic remodeling, cell osmolarity, and regulation of NOD-like receptor protein 3 (NLRP3) inflammasome activity.In particular, 3 genes are noted to have a strong association with hyperuricemia. The locus with the strongest evidence of association is the glucose transporter 9 (*GLUT9)* gene, commonly referred to as the solute carrier 2A9 (*SLC2A9*), the product of which alters the renal excretion of uric acid. Some of the variants are associated with a protective effect, whereas others convey a higher risk of gout.

The urate transporter 1 (*URAT1)* gene is involved with the urate-organic anion exchanger. Several mutations in this gene have been associated with gout.

Polymorphisms in the *ABCG2* gene, which is located on chromosome 4 and codes for an intestinal urate transporter, are strongly associated with high serum uric acid concentrations and gout. Elevation of uric acid levels is greater in men than in women with the minor allele of rs2231142 in *ABCG2*.Although genetic factors have been strongly associated with hyperuricemia, environmental and other state-of-health factors are responsible for the majority of the gout burden in developed countries.A study of 514 male twin pairs did show a strong concordance in hyperuricemia among monozygotic (MZ) twins (53%) as compared with dizygotic (DZ) twins (24%), but it did not show a significant difference between MZ and DZ twins with regard to the lifetime prevalence of gout.

Gout is increasingly regarded as an auto-inflammatory disease rather than a purely metabolic disease, given that most persons with hyperuricemia never develop gout. Auto-inflammatory aspects of gout include the inflammasome and a variants in a number of inflammatory-pathway genes.

### Causes of gout flares

Individual gout flares are often triggered by acute increases or decreases in urate levels that may lead to the production, exposure, or shedding of crystals. Changes in urate levels can result from acute alcohol ingestion, acute overindulgence in foods high in purines, rapid weight loss, dehydration, or trauma.

Similarly, flares can be precipitated by additions of or changes in dosage of medications that raise or lower uric acid levels. Medications that increase uric acid levels via effects on renal tubular transport include the following:

* Loop and thiazide diuretics
* Niacin
* Low-dose aspirin
* Cyclosporine
* Pembrolizumab

​Agents that lower levels of uric acid include the following:

* Radiocontrast dyes
* Xanthine oxidase inhibitors (eg, allopurinol, febuxostat)
* Uricosurics (eg, probenecid)

Vaccination has been associated with increased risk of gout flares. Elevated risk has been reported with recombinant zoster vaccine and other vaccines, but not influenza vaccine.

### Pseudogout

Although the pathophysiology, clinical presentation, and acute-phase treatment of gout and pseudogout are very similar, the underlying causes of the 2 diseases are very different. Many cases of pseudogout in elderly people are idiopathic, but pseudogout has also been associated with trauma and with many different metabolic abnormalities, the most common of which are hyperparathyroidism and hemochromatosis. Other conditions associated with CPPD include rheumatoid arthritis, hypomagnesemia, and osteoporosis.

Several drugs have been implicated as possibly responsible for induction of CPPD. These include thiazide diuretics, loop diuretics, and proton pump inhibitors, which are associated with hypomagnesemia, and bisphosphonates. However, the role of these drugs in CPPD is controversial; they may even be protective.Anecdotal evidence links hyaluronic acid and granulocyte colony-stimulating factor as risk factors. Pseudogout attacks have been reportedly induced by etidronate disodium therapy and angiography.Pseudogout has been recognized as having an underlying genetic component; however, comorbid conditions (such as osteoarthritis) and environmental factors are thought to play a much stronger role.Some disorders that can lead to secondary pseudogout, such as hemochromatosis, do have a clear genetic cause. These patients should be properly evaluated and counseled.

## Prognosis

Gout is associated with considerable morbidity, with acute episodes often causing incapacitation. However, gout that is treated early and properly carries an excellent prognosis if patient adherence to treatment is good.

With early treatment, gout should be totally controlled. If attacks recur, successful uric acid adjustment (requiring lifelong use of urate-lowering medication) usually suppresses further activity. During the first 6-24 months of urate-lowering therapy, acute attacks of gout often occur more frequently.

### Morbidity/mortality

Chronic injury to intra-articular cartilage leaves the joints more susceptible to subsequent joint infections. Draining tophi can become secondarily infected. Untreated chronic tophaceous gout can lead to severe joint destruction and, rarely, renal impairment. Deposition of monosodium urate crystals in the kidney can result in inflammation and fibrosis, leading to reduced renal function or chronic nephropathy.Rarely, gout can produce spinal cord impingement when deposition in tissues produces a local mass.

Acute attacks of pseudogout usually resolve within 10 days. Prognosis for resolutions of acute attacks is excellent. Some patients experience progressive joint damage with functional limitation. CPPD also can cause chronic arthritis that can resemble osteoarthritis or rheumatoid arthritis. Results of a study by Hubert et al suggest that osteoarthritis of the ankle can be a complication of CPPD.Hyperuricemia and gout are associated with an increased overall likelihood of mortality. Whether this is directly attributable to hyperuricemia or gout or to gout-associated diseases (eg, insulin resistance, type 2 diabetes mellitus, abdominal obesity, hypercholesterolemia, or hypertension) has been much debated.

Although no evidence has shown that gout or hyperuricemia causes any of these disorders, elevated urate levels have been shown to correlate with elevated blood pressure in adolescents.Among middle-aged men, hyperuricemia is a significant independent risk factor for death from cardiovascular disease.A meta-analysis found an independent association between gout and cardiovascular mortality as well as all-cause mortality.A review of a national US database found that gout patients who are hospitalized with concurrent cardiac arrhythmia have a likelihood of longer stays in the hospital and higher mortality (adjusted odds ratio for death, 2.06).

Kuo et al demonstrated that gout, but not hyperuricemia, is associated with higher risk of death from all causes and cardiovascular diseases. Analysis of 1383 deaths among 61,527 Taiwanese subjects showed in individuals with gout compared with those who had normal uric acid levels, the hazard ratio (HR) of all-cause mortality was 1.46 and the adjusted HR of cardiovascular mortality was 1.97. Among individuals with hyperuricemia, the HR of all-cause mortality was 1.07 and the adjusted HR of cardiovascular mortality was 1.08.

An analysis of nationwide data on more than 200,000 English patients indicates that individuals with gout are at increased risk for both heart attack and stroke. The rate ratio for myocardial infarction in patients with gout was 1.82. Rate ratios for stroke were 1.71 for all stroke, 1.68 for ischemic stroke, 1.69 for hemorrhagic stroke, and 2.00 for stroke of unspecified type. Risks were elevated in both men and women and were higher in the younger age groups.

Risk for vascular disease is increased in patients with gout, particularly women, according to a retrospective cohort study from the United Kingdom that included 8386 patients with gout and 39,766 matched controls. Multivariate analysis showed that women with gout had a 25% increased risk for any vascular event compared with women without gout (hazard ratio [HR], 1.25) and increased risks for any coronary heart disease (HR, 1.25) and peripheral vascular disease (HR, 1.89).

Men with gout, compared with those without gout, had a small but significantly increased risk for any vascular event (hazard ratio [HR], 1.06) and an increased risk for any coronary heart disease (HR, 1.08) and peripheral vascular disease (HR, 1.18). Unlike women, men with gout were not at greater risk for angina, transient ischemic attack, or stroke.

In contrast, urate-lowering therapy (ULT) in patients with gout has been linked to reduced risk for both cardiovascular (CV) mortality and all-cause mortality. A prospective case-matched cohort study by Chen et al of Taiwanese patients followed for 6.5 years found that patients with gout who received ULT with either allopurinol or benzbromarone had a lower risk of CV disease (HR 0.29) and all-cause mortality (HR 0.47) relative to patients with gout not treated with ULT.

Similarly, Solomon et al reported a reduced risk of a CV event in patients with gout who take colchicine. Their analysis of data from an electronic medical record database on 1002 gout patients, with a median follow-up of 16.5 months, found that the incidence rates of myocardial infarction, stroke, or transient ischemic attack were 35.6 per 1000 person-years for colchicine users and 81.8 for non-users. Adjusted risk of a CV event was 49% lower with colchicine use (HR 0.51) and all-cause mortality was 73% lower (HR 0.55).

A cohort study of 5,924,918 Veterans Affairs patients, 556,521 of them with gout, found that patients with gout, especially those with poor serum urate control, had higher rates of lower extremity amputation than those without gout.However, it is unclear whether the criteria for gout identification used in this study included identification of urate crystals, which many rheumatologists consider essential for the diagnosis of gout. This calls the conclusions of this study into question.

A study using data from the UK Biobank, which included 15, 871 people with gout, found that individuals with gout were at increased risk of contracting COVID-19 (odds ratio [OR] 1.20); when stratified by vaccination status, however, the risk of COVID-19 diagnosis was significant in non-vaccinated patients with gout (OR 1.21) but not in the vaccinated group (OR 1.09). Risk of COVID-related death was higher in women with gout (OR 1.98) but not in men with gout (OR 1.16). The increased risk in women was independent of the metabolic comorbidities of gout (eg, kidney insufficiency, diabetes, hypertension).

However, results of a study using data from The Health Improvement Network in the UK suggested that individuals with gout, especially women, are at higher risk for COVID-19 and severe outcomes even when vaccinated. Compared with the general population, vaccinated patients with gout had adjusted hazard ratios of 1.30 for hospitalization and 1.36 for death; in women, those risks were1.55 and 2.46, respectively.Complications

Complications of gout include the following:

* Severe degenerative arthritis
* Secondary infections
* Urate or uric acid nephropathy
* Increased susceptibility to infection
* Urate nephropathy
* Renal stones
* Nerve or spinal cord impingement
* Fractures in joints with tophaceous gout

Calcification of the atlas transverse ligament has been reported in 44-70% of individuals with calcium pyrophosphate disease (CPPD), with frequency increasing with age. A significantly elevated rate of non-union of type II and III odontoid fractures has been reported in patients with CPPD (90.3%, versus 32% in controls).

## Treatment

To achieve rapid and complete resolution of symptoms, treatment of acute gout should commence within 24 hours of symptom onset. Oral corticosteroids, intravenous corticosteroids, NSAIDs, and colchicine are equally effective in treating acute flares of gout. NSAIDs are the first-line treatment. Indomethacin (Indocin) has historically been the preferred choice; however, there is no evidence it is more effective than any other NSAID. Intramuscular ketorolac appears to have similar effectiveness. Any oral NSAID may be given at the maximal dosage and continued for one to two days after relief of symptoms.

Corticosteroids are an appropriate alternative for patients who cannot tolerate NSAIDs or colchicine. Patients with diabetes mellitus can be given corticosteroids for short-term use with appropriate monitoring for hyperglycemia. When gout is limited to a single joint, intra-articular corticosteroid injections may be preferable to systemic corticosteroids because of their lower adverse effect profile. Rebound flares are common after discontinuation of corticosteroid therapy for acute gout. To reduce the risk of a rebound flare, preventive treatment and initiation of a tapered course of corticosteroids over 10 to 14 days is recommended after resolution of symptoms.

Colchicine is another treatment option for acute gout. Generic colchicine, which has been used for decades, did not undergo formal review by the U.S. Food and Drug Administration (FDA) for this indication until 2009, when branded colchicine (Colcrys) was approved. However, Colcrys is expensive, and generic colchicine is no longer available. In addition, colchicine does not have analgesic properties and may be less effective in treating acute flares when given beyond 72 to 96 hours after symptom onset. Common adverse effects include nausea, vomiting, and diarrhea.Colchicine should be used with caution in patients with hepatic or renal impairment.

## Prevention

Serum urate–lowering therapy should be initiated to prevent recurrences in persons with a history of gout and any one of the following: at least two flares per year (one per year in persons with chronic kidney disease stage 2 or greater), tophi, or a history of nephrolithiasis.

Serum urate should be lowered to a target of less than 5 to 6 mg per dL (297 to 357 μmol per L), depending on the crystal and tophaceous burden. Normal serum urate levels do not exclude the diagnosis of gout. They should be monitored periodically to assess preventive therapy in patients with recurrent gout and a history of elevated urate levels. Urate-lowering therapy should be continued for three to six months after a flare if there are no ongoing symptoms. Therapy should continue indefinitely if there are ongoing signs or symptoms (e.g., one or more tophi on examination).

### DIETARY MODIFICATIONS

Weight gain is a significant risk factor for gout in men, whereas weight loss reduces the risk. Intake of high-fructose corn syrup should be restricted because the fructose contributes to increased uric acid production as a byproduct of adenosine triphosphate catabolism. Patients with gout should limit their intake of purine-rich animal protein (e.g., organ meats, beef, lamb, pork, shellfish) and avoid alcohol (especially beer). Purine-rich vegetables do not increase the risk of gout. Consumption of vegetables and low-fat or nonfat dairy products should be encouraged.

### PHARMACOLOGIC OPTIONS

Pharmacologic options for prevention of chronic gout are outlined in Although avoidance of loop and thiazide diuretics has been recommended for patients with hypertension and gout because these agents can increase uric acid levels, a systematic review found only small increases in the risk of gouty flares. Calcium channel blockers and the angiotensin receptor blocker losartan (Cozaar) are associated with a decreased risk of incident gout. Losartan is the only angiotensin receptor blocker with this property.

Historically, urate-lowering medication was thought to worsen acute gout flares, but recent evidence suggests that allopurinol (Zyloprim) can be started during an acute flare if it is used in conjunction with an NSAID and colchicine. Patients receiving a urate-lowering medication should be treated concurrently with an NSAID, colchicine, or low-dose corticosteroid to prevent a flare. Treatment should continue for at least three months after uric acid levels fall below the target goal in those without tophi, or for six months in those with a history of tophi. NSAIDs and corticosteroids should not be used for long periods without a urate-lowering medication because uric acid crystals continue to accumulate and damage the joint, despite a lack of pain or clinical signs of inflammation. If a patient has a gout flare while receiving a urate-lowering agent, the medication should be continued while the flare is treated acutely.

*Allopurinol*. Allopurinol, a xanthine oxidase inhibitor, is a first-line agent to prevent recurrent gout. In patients with gout and chronic kidney disease or congestive heart failure, allopurinol has the added benefit of preventing chronic disease progression. The starting dosage is 100 mg per day, and 300 mg per day is a common maintenance dosage. Dosing is guided by the target serum uric acid level. In patients with chronic kidney disease, low initial doses are recommended with slow titration to achieve target uric acid levels. Dosages higher than 300 mg may be used—even in those with renal impairment—as long as patients are closely monitored for adverse effects. Certain ethnic groups have a higher risk of a severe hypersensitivity skin reaction when starting allopurinol therapy. Screening for human leukocyte antigen-B\*5801 genotype is recommended before initiating treatment in patients of Han Chinese or Thai descent, regardless of kidney function, or in Koreans with chronic kidney disease stage 3 or greater.

*Febuxostat*. Febuxostat (Uloric) is a xanthine oxidase inhibitor that was approved by the FDA in 2009. Although febuxostat is superior to 300 mg allopurinol at lowering serum uric acid levels, it is not more effective at reducing the frequency of gout flares. Febuxostat is considered a first-line agent to prevent recurrent gout, but it is considerably more expensive than allopurinol.

*Colchicine*. Colchicine prevents gout flares at a dosage of 0.6 to 1.2 mg per day. The dose should be adjusted in patients with chronic kidney disease and when used with cytochrome P450 3A4 or P-glycoprotein inhibitors. The long-term adverse effects of colchicine include reversible axonal neuromyopathy (less than 1%). Patients should be advised to stop taking colchicine and tell their physician if they experience leg weakness or pain. Treatment should be discontinued if any signs or symptoms of nerve or muscle damage are present. The rare risk of rhabdomyolysis is increased when colchicine is used concomitantly with statins or clarithromycin (Biaxin), especially in older adults or those with chronic kidney disease; therefore, close monitoring is recommended.

*Probenecid*. Probenecid increases urinary excretion of uric acid and is typically used as a second-line treatment because of numerous drug interactions. Of particular concern, probenecid increases blood levels of methotrexate and ketorolac, which may result in severe toxicity. Probenecid may be used in combination with allopurinol or febuxostat when one drug does not independently lower serum uric acid to target levels. Nephrolithiasis is a common adverse effect that may be avoided by high fluid intake and urine alkalization with potassium citrate.

*Pegloticase*. Pegloticase (Krystexxa) is an intravenous uricase approved by the FDA in 2010. The mechanism of action involves metabolism of uric acid to allantoin. It is a third-line agent and is indicated for treatment of refractory gout. It is usually administered by a rheumatologist and is given every two weeks at a cost of more than $5,000 per dose.

## Vasculitis

Vasculitis, also called angiitis or arteritis, is an autoimmune disease that affects your blood vessels, organs, and tissues. Your vessels swell and narrow, which makes it harder for your blood to flow to your tissues and organs. Some vessels could close entirely.

When too little blood reaches your organs and tissues, they can become damaged.

## Vasculitis Symptoms

Vasculitis symptoms can show up in many ways, depending on what part of your body is affected. Still, some general symptoms include:

* Fever
* Weight loss
* Loss of appetite
* Fatigue
* Headache
* General aches and pains

Symptoms related to specific areas of your body include:

* Eyes.Your first sign of vasculitis might be red, itchy, or burning eyes. You could also see double and have temporary or permanent blindness in one or both eyes.
* Skin. You might get rashes, lumps, or open sores if vasculitis affects blood vessels going to your skin.
* Nerves. If your nerves don't get enough blood, you could feel numbness, tingling, pain, and weakness.
* Brain. Vasculitis in your brain may cause a stroke.
* Heart. You could have heart palpitations or even a heart attack if it affects your heart.
* Kidneys. Inflammation in the vessels that supply blood to your kidneys can lead to kidney failure.
* Digestive system. You may feel pain after you eat if vasculitis affects your stomach or intestines. You could also see blood in your stool.
* Ears. Vasculitis can cause your ears to ring. It could also cause dizziness or sudden loss of hearing. You might also get inner ear infections.
* Hands and feet. Vasculitis can cause numbness or weakness in your hands or feet, along with swollen or hardened palms and soles.
* Lungs. If vasculitis affects your lungs, you could have shortness of breath or maybe cough up blood.
* Genitals. Vasculitis in this area can cause ulcers or open sores.
* Nose. Along with sinus infections and a runny nose, you could also get blisters in your nose.
* Mouth. Vasculitis can make your lips and tongue swollen and dry, or your mouth and throat swell.

# Symptoms

The symptoms of vasculitis are different depending on the type of vasculitis you have, the blood vessels and organs involved, and whether your condition is serious. Some people may have few symptoms. Other people may become very sick.

Sometimes, the symptoms develop slowly over months. The symptoms may also develop very quickly over days or weeks. Not everyone will experience the common symptoms below. Some people will experience some, but not all of them. General symptoms of vasculitis include:

* Tiredness
* Fever
* General aches and pains
* Loss of appetite
* Weight loss

Others may experience common, more specific problems that are caused by vasculitis.

## What problems can vasculitis cause?

* Ear and nose problems, including sinus infections, inner ear infections, open sores in the nose, a runny nose, dizziness, ringing in the ears, hearing loss, and deafness, may occur.
* Eye problems, including redness, itching, burning, and changes in vision, may also occur. Blindness in one eye may be the first sign of giant cell arteritis. The risk of blindness with giant cell arteritis is higher for people who have had a stroke or have peripheral artery disease.
* gastrointestinal tract problems, such as open sores in the mouth or stomach area, diarrhea, vomiting blood, and pain in the stomach area, are also sometimes caused by vasculitis.
* Genital ulcers, which are open sores in the genital area, may also occur.
* Headache, scalp tenderness, and pain may develop after chewing.
* Heart palpitations, or the feeling that your heart is racing, can occur with vasculitis.
* Joint pain is another common condition caused by vasculitis.
* Lung problems, including shortness of breath, bleeding within the lung, and coughing up blood, may also occur when you have vasculitis.
* Nerve problems, including numbness, tingling, pain, and weakness in various parts of body, can occur. Loss of strength in the hands and feet and shooting pains in the arms and legs can also occur with vasculitis.
* Skin rashes, purple or red spots or bumps, clusters of small dots, splotches, bruises, hives, and itching also sometimes develop.
* Problems with the hands and feet, including swelling or hardening of the palms and soles, or pain, ulcers, and gangrene, can show up in some people.
* Swollen, dry lips or tongue, or swelling in the mouth and throat may occur.
* Problems during pregnancy can develop if a person has vasculitis.

Blood vessels damaged by vasculitis can narrow and block normal blood flow, which may cause problems in other parts of the body. Some problems can be life-threatening. They include:

* Aneurysm or a tear inside the aorta called an aortic dissection
* Arrhythmia
* Coronary heart disease
* Deep vein thrombosis, a type of venous thromboembolism
* Heart attack
* High blood pressure
* Low blood pressure
* Kidney disease
* Myocarditis, a type of heart inflammation
* Stroke and transient ischemic attack (TIA). A TIA, also known as a mini-stroke, occurs if blood flow to a part of the brain is blocked only for a short time. A TIA may happen and may develop into a stroke later.

## Vasculitis Types

Vasculitis is the general term for several conditions that cause blood vessel inflammation. Doctors organize vasculitis into types based on the size of the blood vessels involved. All types of vasculitis can affect anyone, but some are more common in certain age groups.

* Systemic vasculitis is inflammation of your blood vessel walls, which can happen anywhere in your body.
* Exercise-induced vasculitis is a type of small-vessel vasculitis. It restricts vessels in your lower legs after you do intense exercise like running or hiking, particularly in hot weather. Women over 50 get it most often. Symptoms include rashes on your legs that go away in a few days.
* Urticarial vasculitis affects your skin's small blood vessels. The inflammation usually causes patches and hives that can itch, burn, and discolor your skin. If it gets more serious, it may damage other organs, too.
* Leukocytoclastic vasculitis results when waste from immune cells in the walls of your small blood vessels causes inflammation. When the damaged blood vessels become leaky, they cause raised spots on your skin, usually your legs. Most of the time, it affects only your skin. But it can spread to other organs if it's serious.
* ANCA vasculitis targets a certain type of white blood cell in your body and tells these cells to attack small blood vessels. When the blood vessels are invaded, they become swollen and inflamed. ANCA vasculitis can happen in many parts of your body. The inflammation causes different symptoms, depending on where it is.
* IGA vasculitis is the most common type of vasculitis in children. It causes inflammation and bleeding of small blood vessels in your skin, joints, intestines, and kidneys. The most common symptom is a raised skin rash, usually on your legs or buttocks, that looks like bruises. But if IGA vasculitis affects other organs, you could have stomach or joint pain, swelling, and kidney inflammation.
* Cutaneous vasculitis is when you have inflammation and damage to your skin's blood vessels. It's the most common vasculitis doctors see. It shows up as raised patches on your skin.
* Central nervous system (CNS) vasculitis happens when the blood vessel walls in your brain and spine become inflamed. Many conditions can cause it, though your immune system often plays a role. While it's one of the more serious types of vasculitis, it is treatable.
* Rheumatoid vasculitis is a complication of rheumatoid arthritis (RA) that happens when the inflammation that causes joint pain and damage also damages your blood vessels. Rheumatoid vasculitis causes your small- and medium-sized blood vessels to become inflamed and narrow. It most often shows up in skin, nerves, fingers, and toes.
* Other types of vasculitis include giant cell arteritis, polyarteritis nodosa, Takayasu arteritis, Behçet’s disease, and Kawasaki disease.

## Vasculitis Causes

Doctors don’t know exactly what causes many cases of vasculitis. But there are some possible triggers:

* Autoimmune diseases like RA, lupus, or Sjögren's syndrome
* Infections, such as hepatitis B and hepatitis C, that set off an unusual immune system reaction that damages your blood vessels
* Allergic reactions to medications
* Certain blood cancers, like leukemia and lymphoma

## Vasculitis Risk Factors

While anyone can get vasculitis, some things can raise your chances of having certain types of the condition, including:

* Your age. Some types are more common in older people, while others, such as Kawasaki disease, most often affect children.
* A family history of a particular type of vasculitis
* Cocaine use
* Smoking
* Certain medications, such as allopurinol (Zyloprim), hydralazine (Apresoline), minocycline (Dynacin, Minocin, Myrac, Solodyn, Ximino), and propylthiouracil
* COVID-19, hepatitis A, or hepatitis B infections
* Also having other immune disorders
* Your sex. Certain types are more likely to affect people of a particular gender.

## What are the risk factors for vasculitis?

### Age

Vasculitis can develop at any age. However, some types of vasculitis are more common among people at particular ages.

* Buerger’s disease usually affects men younger than age 45 who smoke or have smoked.
* IgA vasculitis is diagnosed more often in children than adults.
* Giant cell arteritis affects adults age 50 and older and is most common in people who are in their 70s and 80s.
* Kawasaki disease is most common in children under age 5.
* Takayasu arteritis is most common in women between ages 20 and 40.

### Family history

Certain types of vasculitis, including the following, may run in families:

* Behçet’s disease
* Granulomatosis with polyangiitis
* Kawasaki disease

### Lifestyle habits

Lifestyle habits that can raise your risk of developing vasculitis include:

* Smoking.
* Using illegal drugs, such as cocaine.

### Medicines

Many medicines, including those listed below, have been linked to a higher risk of vasculitis.

* Hydralazine is used to treat high blood pressure.
* Levamisole is used for infections, but is also commonly added to cocaine.
* Propylthiouracil is used to treat some thyroid disorders.
* Allopurinol is used for gout.
* Tumor necrosis factor inhibitors are used to treat some autoimmune diseases.

Other medical conditions may trigger vasculitis, too.

* Autoimmune disorders, such as lupus, rheumatoid arthritis, and scleroderma can lead to vasculitis.
* COVID-19 can raise the risk of many types of vasculitis or trigger flares (repeat occurrences or worsening of symptoms) in children and adults who have a history of vasculitis.
  + Multisystem inflammatory syndrome (MIS-C) in children, which occurs after a COVID-19 infection, may also lead to vasculitis.
* Hepatitis B or C infections sometimes trigger vasculitis.
* Lymphoma, a cancer of the blood, is another possible vasculitis trigger.

### Race or ethnicity

* Behçet’s disease is most common in people of Turkish descent and is relatively common in other countries in the Mediterranean, the Middle East, Central Asia, China, and Japan. It is relatively uncommon in Northern and Western Europe and the United States.
* Giant cell arteritis is more common in people of Northern European ancestry.
* Kawasaki disease is more common among children of Japanese descent.

### Sex

* Behçet’s disease is more common in men in some countries and more common in women in other countries.
* Buerger’s disease is more common in men.
* Giant cell arteritis affects women 2 to 4 times more often than men.
* Microscopic polyangiitis affects men slightly more often than women.

How common is it?

Most types of vasculitis are very rare. Fewer than 50 out of 1 million people get vasculitis every year in the U.S.

You're more likely to get it if you're over 50. But your odds are still very low. Only about 300 out of 1 million people older than 50 in the U.S. are diagnosed annually.

## Vasculitis Diagnosis

Your doctor will ask about your medical history and do a physical exam. There's no test just for vasculitis. But because it tends to result from other conditions, you may need tests to look for inflammation and figure out what's causing your symptoms. These tests may include:

* Blood tests. Certain types of blood cells or antibodies can be signs of vasculitis.
* Urine tests. These check for kidney damage.
* Imaging tests. X-rays, MRI scans, CT scans, PET scans, and ultrasounds show inflammation in your blood vessels and organs. You might also have an angiogram, in which your doctor injects dye into your bloodstream. It shows up on X-rays to give a better picture of your blood vessels.
* Heart tests. An echocardiogram tests how well your heart is working.
* Biopsy. Your doctor takes a sample of tissue. A specialist can check it for signs of inflammation or damage.

# Diagnosis

Your healthcare provider may be able to diagnose the type of vasculitis that you have and how serious it is. Depending on your symptoms, your provider may recommend that you see a specialist for more tests or procedures.

## Which specialists can diagnose vasculitis?

* Cardiologists specialize in the heart.
* Dermatologists specialize in skin.
* Infectious disease specialists are experts in diagnosis and treatment of infections.
* Nephrologists specialize in the kidneys.
* Neurologists specialize in the brain and nervous system.
* Ophthalmologists specialize in eyes.
* Pulmonologists specialize in the lungs.
* Rheumatologists specialize in joints, muscles, and autoimmune diseases.
* Urologists specialize in the urinary tract and urogenital systems.

## Diagnostic tests and procedures

Diagnosis of vasculitis can be difficult. Some types of vasculitis cannot be diagnosed with a test. Instead, your healthcare provider will diagnose you based on your symptoms or order specific procedures.

* A biopsy collects a small sample of your tissue from a specific blood vessel or an organ. A pathologist, someone with special training in laboratory results, will study the sample for specific signs of tissue damage.
* Blood tests detect levels of certain blood cells and antibodies in your blood.
* A chest X-ray finds out whether vasculitis is affecting your lungs, your large arteries, such as the aorta, or your lung arteries.
* A computed tomography (CT) scan looks for signs of granulomatosis with polyangiitis
* Echocardiography is an ultrasound test to learn how well the heart is working.
* A pathergy test diagnoses Behçet’s disease. In this test, a needle pricks the skin, and sometimes a small amount of saline solution may be injected. The test is positive if a red bump or ulcer develops after 2 days.
* CT coronary angiography looks at your blood vessels for damage, signs of inflammation, blockages, or aneurysms.
* Positron electron tomography (PET) scan, a type of nuclear scan, detects narrowing and damage in the blood vessels.
* Ultrasound
* looks for signs of narrowing and damage in your blood vessels or organs.
* Urinalysis
* checks for kidney damage.
* Fluorescein retinal angiography looks for signs of retinal vasculitis in the eyes.

## Vasculitis Treatment

Which vasculitis treatment your doctor recommends depends on what’s causing it and which organs it affects. It's usually meant to control the inflammation and prevent organ and blood vessel damage.

Medications

Steroids like prednisone are the most common medications prescribed to fight the inflammation vasculitis causes. Your doctor will watch you closely for side effects like high blood pressure, high blood sugar, and bone problems, especially if you take them for a long time.

Other medications, like azathioprine (Azasan, Imuran), cyclophosphamide (Cytoxan), methotrexate (Rheumatrex, Trexall), mycophenolate (CellCept, Myfortic), rituximab (Riabni, Rituxan, Ruxience, Truxima), or tocilizumab (Actemra) can be prescribed along with steroids. Which medication you might need depends on how serious your vasculitis is, whether it's in your organs, and your medical history.

Surgery

Sometimes vasculitis can cause issues that need surgery to repair. For instance, if your blood vessel walls bulge and form an aneurysm, surgery can lower the chances that it will burst. If you have a blocked artery, you could need surgery to restore blood flow to the area. But any kind of organ damage might require surgery.

# Treatment

The goal of vasculitis treatment is usually to slow down the body’s inflammatory attack on your blood vessels. People who have mild vasculitis may find relief with over-the-counter pain medicines. For severe vasculitis, you may be prescribed medicines. With treatment, vasculitis can go into remission, which is a period of time when you don’t have symptoms.

## Medicine

Over-the-counter pain medicines can relieve symptoms of mild vasculitis. For more serious cases, your healthcare provider may prescribe medicines.

* Anti-inflammatory medicine, including non-steroidal anti-inflammatory medicines (NSAIDs) can lower pain and infection-fighting activity in the body. One possible side effect is increased bleeding. Your provider may run liver function and blood tests before prescribing this medicine.
* Corticosteroids lower the activity of the body’s defense system in your blood vessels. For some types of vasculitis, you will need steroids for months or years. Corticosteroids can lower your bone density, raise your blood sugar and blood pressure levels and cause your skin to get thinner.
* Dual endothelin receptor antagonists block the action of a chemical called endothelin that can reduce blood flow.
* Immunomodulators lower the defense system activity (inflammation) that causes symptoms. Possible side effects can include gastrointestinal tract problems.
* Immunosuppressive medicines suppress or weaken the body’s ability to fight germs and sickness. Possible side effects include a higher risk of infection and birth defects.
* Interferon therapy blocks and reduces swelling. Interferons are molecules that the body’s defense system normally makes, but they have also been developed as medicines.
* Interleukin antagonists lower natural infection-fighting activity in the body by blocking a key protein.
* Intravenous immunoglobulin (IVIG) helps control the body’s defensive response. This medicine also fights infection by introducing purified antibodies from healthy donors into the bloodstream.
* Monoclonal antibodies suppress the body’s natural defense system against illness. Possible side effects include fever-like symptoms, stomach pain, and allergic reactions.
* Phosphodiesterase inhibitors increase blood flow by blocking the action of particular enzymes in the body. Possible side effects include headaches, heart palpitations, upset stomach, nausea, and vomiting.
* Tumor necrosis factor inhibitors suppress the body’s defense system by blocking a protein called tumor necrosis factor alpha.

## Procedures or surgery

* Plasmapheresis, a procedure where blood plasma is removed and then replaced with donor plasma or saline to lower plasma antibody levels, may be performed.
* Surgical bypass of the blood vessels may help restore blood flow to some areas in Buerger’s disease. Surgery is rarely used to treat vasculitis.

## Vasculitis Complications

Whether you have complications depends on what type of vasculitis you have and how bad it is. Some serious complications of vasculitis include:

* Organ damage
* Blood clots
* Aneurysm
* Loss of eyesight
* Infection

## Vasculitis Prognosis

There's no cure for vasculitis, but with the right treatment, you can live a long and active life. Most types of vasculitis are lifelong. But successful treatment can give you long periods without symptoms (called remissions).

Your outlook depends on several things, including:

* The type of vasculitis you have
* How quickly you were diagnosed
* Which organs are affected and how seriously
* Other health problems you have

Living with vasculitis  
For many people, the hardest part about vasculitis is managing the side effects of medications. There are steps you can take to manage these and other day-to-day issues:

Learn and understand the disease. Most types of vasculitis have periods of remission and relapse. Stick to your treatment plan and let your doctor know about any new symptoms or health changes.

Exercise regularly. Not only can exercise boost your mood and lower stress, it can help parts of your body that your treatment affects. Regular walking, for instance, can reduce your chances of bone loss, high blood pressure, and diabetes caused by corticosteroids.

Adopt healthy food habits. Focus on fresh fruits and vegetables, whole grains, low-fat dairy products, lean meat, and fish. And limit alcohol, sugar, and fat. A healthful diet can help with medication side effects like thinning bones, high blood pressure, and high blood sugar. If you take corticosteroids, ask your doctors about calcium and vitamin D supplements.

Keep your vaccinations updated to help prevent infections, like pneumonia and the flu, that can stem from your medications.

Surround yourself with support, whether it's from family, friends, or a support group. Your health care team can also refer you to a mental health professional.

## Takeaways

Vasculitis is inflammation of your blood vessels. It thickens your blood vessels, sometimes so much that blood can't flow properly. This can damage your organs and tissues. It's a lifelong disease without a cure, but it can be treated, usually with steroids.

## Vasculitis FAQs

Is vasculitis very serious?

Many types of vasculitis can be serious, specifically when they restrict blood flow. This not only can damage your organs and cause serious issues like aneurysms, but it could also be fatal. Certain kinds of vasculitis can cause vision loss or blindness, if they're not treated.

What does vasculitis look like when it starts?

If your vasculitis has symptoms you can see on your body, it'll likely appear as a rash, or spots of red, purplish red, black, or simply discolored skin. A vasculitis rash can be on your fingers, legs, ankles, or toes. Other signs that can point to vasculitis are swelling in your joints or cramps and bloating.

## Can vasculitis be prevented?

Some types of vasculitis cannot be prevented because they are caused by autoimmune disorders. However, depending on what caused the vasculitis, it is possible to prevent some types from flaring up.

Your healthcare provider may prescribe medicines to reduce symptoms.

* Anticoagulant medicines prevent blood clots from forming. You may need them if you have an aneurysm.
* Beta blockers lower blood pressure. You may need them if you have an aneurysm.
* Statins control or lower high blood cholesterol levels and have anti-inflammatory effects.

Your provider may also recommend healthy lifestyle changes.

* Adopt a heart-healthy lifestyle.
* Avoid illegal drugs, including cocaine. If you use illegal or street drugs, ask your healthcare provider how to get help to stop. You can also call the Substance Abuse and Mental Health Services Administration’s (SAMHSA) National Helpline at 1-800-662-HELP.
* Quit smoking and tobacco. Visit Smoking and Your Heart and the National Heart, Lung, and Blood Institute’s Your Guide to a Healthy Heart. Although these resources focus on heart health, they include basic information about how to quit smoking. For free help and support to quit smoking, you may call the National Cancer Institute’s Smoking Quitline at 1-877-44U-QUIT (1-877-448-7848).

After you are diagnosed with vasculitis, it is important to follow your treatment plan. Your healthcare provider may recommend additional follow up care and medicines to avoid problems.

If vasculitis responds to treatment, it may go into remission (a period of time when you don’t have symptoms).

## Receive routine follow-up care

* Talk to your provider about any new symptoms and other changes in your health, including side effects of your medicines.
* Your provider will see you regularly to check for side effects from medicines used to treat vasculitis, such as corticosteroids.
* If you had Kawasaki disease as a child, you will need follow-up heart testing throughout your life.
* Because of your vasculitis, you may have a higher risk of getting a serious case of COVID-19, especially if you have another serious health condition. Keep your vaccines current and follow hand washing, masking, and social distancing recommendations.

## Watch your condition

To check on your condition, your healthcare provider may recommend some regular tests or procedures.

* Blood tests look for abnormal levels of certain blood cells and antibodies.
* Heart tests may capture images of areas of concern.
  + Cardiac magnetic resonance imaging (MRI) looks for heart and vascular problems caused by vasculitis.
  + A chest X-ray looks for any problems in the lungs, heart, and large blood vessels, such as an aortic aneurysm.
  + Echocardiography (echo) or electrocardiography (EKG) both look for heart problems caused by vasculitis.
  + Myocardial perfusion imaging measures blood supply to your heart. It can also be used to look for heart problems caused by vasculitis.
  + A PET scan checks for aneurysms or heart problems caused by vasculitis.

## Plan for a healthy pregnancy

Most people with vasculitis that is under control or not active can have a healthy pregnancy. However, vasculitis can raise the risk of blood pressure-related disorders in pregnancy and during cesarean delivery. As a result, the risk of miscarriage is higher. Vasculitis can also raise the risk that the baby will not grow as fast in the womb or will be born early. With some types of vasculitis, there is a higher risk of flares in pregnancy.

If you have vasculitis and are thinking about becoming pregnant, it is very important to talk to your healthcare provider and make a plan to manage your condition during pregnancy.

* If your vasculitis is not under control, pregnancy can harm your health. Work together with your provider to bring your vasculitis into remission first. If you become pregnant and did not plan it, talk to your provider as soon as you can.
* If you had Kawasaki disease or another type of vasculitis as a child, tell your provider that you are planning to become pregnant. They will want to regularly check your heart and any blood clotting conditions during pregnancy. Talk to your provider to understand the risk of your child having vasculitis, too.
* Some medicines given to people who have vasculitis can be dangerous to a developing baby, so be sure your healthcare provider knows what you are taking. Your provider may need to adjust your medicines during pregnancy. Do not stop taking medicine without first talking with your provider.
* Vasculitis raises your risk of high blood pressure during pregnancy. The risk of preeclampsia and other high blood pressure-related disorders during pregnancy is also higher. Your provider should watch your blood pressure closely.
* In some cases, flares can occur after birth. Be sure to continue taking your medicine and check in with your provider regularly after your child is born.

## Take steps to prevent vasculitis flares

After vasculitis is treated and goes into remission, you may have flares. You may have the same or different symptoms than when you first had vasculitis. Taking medicines and adopting healthy lifestyle changes to treat other health conditions you have, such as high blood pressure or high blood cholesterol, can help prevent flares.

Part of the goal of vasculitis treatment is avoiding flares.

* Flares may be treated with some of the same medicines used for your initial treatment, including corticosteroids.
* If your vasculitis goes into remission, your healthcare provider may carefully stop your medicines. However, you will still need to be monitored for flares.

## Learn the warning signs of serious complications and have a plan

An aneurysm can lead to a more serious problem like a dissection or rupture, which is a tear in the blood vessel wall. Vasculitis also can lead to other serious heart and blood vessel problems, such as heart attack or stroke.

If you think that you are or someone else is having symptoms of one of these conditions, call 9-1-1 right away. Every minute matters.

### Aneurysm dissection or rupture

Symptoms of a dissection or rupture may include:

* Light-headedness
* Paleness
* Rapid heart rate
* Sudden, strong pain in your stomach area, chest, or back, which can travel upward or downward

### Heart attack

Signs of a heart attack include mild or strong chest pain or discomfort in the center of the chest or upper stomach area. It may last for a few minutes or more, or it may go away and come back. A heart attack can feel like pressure, squeezing, fullness, heartburn, or indigestion. There may also be pain down the left arm.

Women may feel chest pain and pain down the left arm, but are more likely to have symptoms such as shortness of breath, nausea, vomiting, unusual tiredness, and back, shoulder, or jaw pain.

### Stroke

If you think someone may be having a stroke or transient ischemic attack (TIA), act F.A.S.T. and do the following simple test.

F—Face: Ask the person to smile. Does one side of the face droop?

A—Arms: Ask the person to raise both arms. Does one arm drift downward?

S—Speech: Ask the person to repeat a simple phrase. Is his or her speech slurred or strange?

T—Time: If you observe any of these signs, call 9-1-1 immediately. Early treatment is essential.

# Scleroderma

# Scleroderma Risk Factors

## Who’s at the highest risk of developing scleroderma?

Unfortunately, the exact causes of scleroderma are unknown. The research that’s been done suggests that, like many rheumatic and autoimmune diseases, it stems from a problem with our immune systems.

But we do know who is at a higher risk of developing scleroderma:

* **Gender:** It’s much more common in women than men. As many as 80 percent of those diagnosed with scleroderma are women.
* **Age:** Most localized types of scleroderma show up before age 40, and systemic types of scleroderma are typically diagnosed between ages 30 and 50.
* **Race:** localized types of scleroderma are more common in people of European descent than in African-Americans. Choctaw Native Americans and African-Americans have a higher risk of the systemic form of scleroderma than people of European descent.
* **Environmental exposure:** Some environmental influences can put people at greater risk for developing scleroderma. Men exposed to silica appear to have a higher risk for developing scleroderma. Being around certain solvents and taking certain drugs can also increase your potential for developing the disease.

## Genes and Scleroderma

Genetics plays a role in the disease, but it is not passed on from parents to children, and it’s rare for immediate family members of those with scleroderma to get it. It is common for family members, however, to have other autoimmune diseases such as thyroid disease, rheumatoid arthritis or lupus.

Scleroderma is a group of diseases with a common symptom: hardening and tightening of the skin. There are two types of scleroderma: localized and systemic. Localized scleroderma only affects the skin and systemic scleroderma affects the skin, the blood vessels and internal organs.

Scleroderma is a rheumatic disease, which means patients may have inflammation, pain, swelling and stiffness in the joints, tendons, ligaments, bones, muscles and/or tissues. It’s also an autoimmune disease.

Scleroderma affects many more women than men, and it’s typically found in people between the ages of 30 and 50. As many as 300,000 people in the United States have been diagnosed with scleroderma, and as many as 10,000 die each year from the most serious forms of the disease.

# Types of Scleroderma

There are two main categories of scleroderma: localized and systemic. Each category is made up of several conditions.

* **Localized scleroderma:** often affects only the skin and not major organs.
* **Systemic scleroderma:** affects the skin and may affect the tissues under it, including blood vessels and major organs, such as the gastrointestinal tract, heart, lungs or kidneys.

## Three Types of Localized Scleroderma: Localized, Generalized and Linear

The skin is typically the only organ impacted in localized scleroderma. However, the tissue injury may extend into the structures underlying the skin, including the subcutaneous tissue, fascia, muscle or bone. Localized scleroderma skin lesions can get better or even go away.

### **Circumscribed Morphea**

With circumscribed morphea (another name for discolored patches of skin), you may have a single oval patch or you may see a few patches of morphea. The patches vary in size and typically have a red border and a thickened pale-yellow center. These lesions can enlarge when active and then flatten and become asymptomatic with treatment. Deep circumscribed morphea extends into the subcutaneous tissues.

### **Generalized Morphea**

Generalized morphea is seen when there are many patches of morphea (greater than four plaques in many anatomical areas (trunk, arms, head or neck). They are seen as thick, tight patches that can blend into each other. Pansclerotic morphea is a severe form of generalized morphea with involvement of most of the body.

### **Linear Scleroderma**

Linear scleroderma is more common in children 10 and younger. These tight, thick bands can appear on the extremities, the back and front of the trunk, the buttocks or the face. They often appear as a single band in one body area and can be seen mixed with patches of morphea. Linear scleroderma can affect the bones and the muscles. When linear scleroderma appears on the arms or legs, it can cause the child’s limb to under develop, causing disability.

## Three Types of Systemic Sclerosis (Scleroderma): Limited, Diffuse and Sine

Systemic sclerosis (scleroderma) affects the skin as well as what’s underneath, such as blood vessels, muscles and joints, gastrointestinal (GI) tract, kidneys, lungs and heart.

The skin thickening that accompanies systemic scleroderma can cause tightening so there is a loss of flexibility and ease of movement, especially in the fingers. Facial involvement is common and may be mild or it can reduce facial movements, including decreasing the mouth opening.

Scleroderma may cause chronic joint pain, inflammation and swelling in muscles and joints. Most scleroderma patients also experience Raynaud’s phenomenon, an exaggerated response to ambient temperatures, making one sensitive to cold. Raynaud’s phenomenon causes the skin of the fingers to look white or blue with cold temperature exposure or emotional stress. Skin sores or ulcers can occur due to lack of good blood flow in some cases.

### **Limited Scleroderma**

Limited scleroderma is the most common type of scleroderma. The skin hardening and tightening is limited usually just to the fingers and sometimes the hands, forearms or the face. Internal organ damage is less likely in the limited scleroderma type. In general, patients with limited scleroderma have a normal life expectancy. Some have problems with their GI tract, especially heartburn; severe Raynaud’s and musculoskeletal pain; and a small subset can develop pulmonary hypertension that can be life-threatening.

A subtype of limited scleroderma is also known as CREST syndrome. CREST is an acronym for its most prominent clinical features:

* **Calcinosis**: calcium deposits under the skin and sometimes in tissues.
* **Raynaud’s phenomenon**: an exaggerated response to ambient temperatures making the skin of the fingers or toes cold, numb or tingling with color changes.
* **Esophageal dysmotility**: which causes heartburn.
* **Sclerodactyly**: the skin on the fingers becomes thick.
* **Telangiectasias**: enlarged blood vessels that appear as red spots on the fingers, face or other parts of the body.

### **Diffuse Scleroderma**

Diffuse scleroderma is a subtype of scleroderma where excess collagen production causes skin thickening over large areas of the body, usually the fingers, hands, arms, anterior trunk, legs and face. There can be significant associated organ damage, including to the gastrointestinal tract, kidneys, lungs and heart. The tightening of the skin is often associated with dryness and itching. Musculoskeletal pain is common. Life-threatening disease occurs when the lung or heart is severely affected. Acute severe systemic high blood pressure can cause kidney damage.

### **Sine Sclerosis**

Sine sclerosis is systemic scleroderma that has features of systemic organ disease, including Raynaud’s phenomenon, but not the skin symptoms. The symptoms and complications of either limited or diffuse scleroderma can occur, but there is no skin thickening.

# Scleroderma Symptoms

Symptoms of scleroderma may include:

Thickening and swelling of the fingers

Pale fingers that may become numb and tingle when exposed to cold or stress, known as Raynaud's phenomenon

Joint pain

Taut, shiny, darker skin on large areas, which can cause problems with movement

Limited mobility or immobile fingers, wrists or elbows because of the thickening of the skin

Systemic forms of scleroderma are associated with involvement of the internal organs, which may cause:

Calcium bumps on your fingers or other bony areas such as your elbows and knees

Sores on your fingertips and knuckles

A grating noise when you try to move your inflamed joints and tissues

Problems of the esophagus, which can lead to heartburn and trouble swallowing

Scarring of the lungs, which can lead to shortness of breath

Heart failure and abnormal heart rhythms

High blood pressure that affects the kidneys

The specific symptoms and the way scleroderma appears depend on the type of scleroderma. The majority of people with scleroderma, however, will see changes to their skin, typically in the form of body areas that harden and tighten.

Scleroderma can affect small areas of the body — as ovals or straight lines — or it can cover much wider areas and even entire limbs. Since the skin becomes tight, the ability to move might be restricted, and the skin may look shiny.

Scleroderma typically appears as a hardening and tightening of the skin and the connective tissue underneath it. The symptoms of scleroderma may vary and can look quite different in each person. In some people, it only affects the skin, but in others, scleroderma goes much deeper, harming your joints, blood vessels, internal organs and the digestive tract, in addition to the skin. The particular symptoms might just be annoying or they could cause significant problems and pain. For some, the symptoms can be life-threatening.

Most scleroderma patients also experience some pain, which can range from uncomfortable to debilitating.

Early Symptoms of Scleroderma

Two of the symptoms listed above are often early signs of scleroderma. The fingers may become:

Highly sensitive to the cold and change color with cold or emotional stress (the symptoms of Raynaud’s phenomenon)

Stiff and puffy

These symptoms happen because the blood vessels narrow due to spasm. Excess collagen can also damage blood vessels.

If You Believe You Could Have Scleroderma

Since many scleroderma symptoms resemble those of other conditions, and the severity varies from person to person, a doctor should evaluate the problems carefully. If scleroderma is thought to be the cause of the clinical symptoms, referral to a rheumatologist in a scleroderma center is recommended.

# Scleroderma Diagnosis

## How is scleroderma diagnosed?

Many scleroderma symptoms resemble the symptoms of a number of conditions, which means it can take longer to find out if scleroderma is the cause or which of the different types of scleroderma is present. Diagnosing scleroderma becomes a little easier if some of the primary physical symptoms or signs are present, such as Raynaud’s phenomenon or skin that appears to suddenly become puffy, swollen or thick.

There is no single test for scleroderma. It is a clinical diagnosis that requires a thorough exam and history by the doctor. The doctor will start by asking questions about symptoms and previous medical history. He or she will also do a physical exam and may order a biopsy to look at a small sample of the affected skin under a microscope. He or she may also order urine, blood and other tests to see if any internal organs have been affected.

## Specific Tests for Scleroderma

One of the most important tests that a physician performs is a physical examination. A rheumatologist will be able to assess the skin for skin tightening or swelling that is typically seen in patients with scleroderma. As discussed above, patients with scleroderma who have Raynaud’s phenomenon will have characteristic features seen on nailfold capillaroscopy, a simple noninvasive test that looks at the skin near the base of the fingernail with a magnifier to determine if there is capillary (small blood vessels in the skin) loss or distortion such as dilatation.

After a thorough examination, the doctor may also order an antibody nuclear (ANA) test, which will let them know if any autoantibodies (blood proteins) are in the blood. However, because our bodies develop antibodies for other reasons, the results of an ANA test by itself don’t determine a diagnosis of scleroderma. It is important to remember that scleroderma is a clinical diagnosis that takes into account all factors, including the physical examination and all symptoms. A blood test alone cannot diagnose scleroderma. Depending on the clinical situation, additional tests may be done, such as:

* **Pulmonary function tests or breathing tests** to measure how well the lungs are working.
* **CT chest scan** may also be ordered to evaluate the extent of lung involvement.
* **Electrocardiogram (EKG or ECG)** to see if there are changes in the heart muscle tissue due to scleroderma**.** An EKG/ECG records the electrical activity of the heart, shows abnormal rhythms and detects any damage.
* **Echocardiogram** to look at the structure and function of the heart**.** It uses sound waves to take pictures of the heart and valves.
* **X-rays** or special imaging to show any changes in the bones or soft tissues caused by scleroderma**.** It uses a small amount of radiation to take pictures of internal tissues, bones and organs.
* **Motility studies** to assess for gastrointestinal dysmotility**.**

## After You’ve Been Diagnosed with Scleroderma

Once a diagnosis of scleroderma is determined then the type of scleroderma is defined to help determine the best treatment plan that is specific to the system and organ involvement. This plan will take into account the severity and activity of the particular type of scleroderma. Many times scleroderma is mild and not active and treatment is supportive. If it is serious and active there are many options to manage the specific situation.

# Scleroderma Treatment

Scleroderma is a chronic disease that can affect both the patient’s physical and mental health. The key to feeling better is to tailor the scleroderma treatment to meet the specific needs, taking into account symptoms, type of scleroderma, age and overall health of the patient.

Currently, there’s no cure for scleroderma, so doctors will find the treatments that work best to decrease the severity of the specific symptoms and manage or prevent additional complications.

## Treating Scleroderma

Treatment typically focuses on inflammation, autoimmunity, vascular issues and tissue fibrosis (the thickening and scarring of the connective tissue that surrounds the internal organs).

Your treatment may include some or all of the following:

* Getting pain relief through nonsteroidal, anti-inflammatory medications or corticosteroids
* Easing skin itchiness with skin lotions and moisturizers
* Slowing skin thickening and minimizing damage to the internal organs with medication that suppresses the immune system
* Maintaining muscle strength through physical therapy and exercise
* Managing digestive tract function to optimize nutritional intake
* Controlling blood pressure and improving blood flow with medication
* Treating specific symptoms such as heartburn and Raynaud’s phenomenon
* Improving emotional state through counseling and other measures

Surgery may be an option if the complications can’t be resolved with less invasive therapies. For example, if you develop ulcers on your fingers and those ulcers lead to gangrene, it might be necessary to amputate parts of a finger.

Whatever treatment is chosen, the doctor should discuss the benefits, risks and side effects.

## Your Scleroderma Support Team

Scleroderma can impact many important aspects of life, which makes it critical for you to have a reliable team of people to help manage challenges. At different points in time, patients might want support from members of the family and friends or from specialists such as a physical therapist or a personal assistant.

Because scleroderma can change your appearance and make it difficult to do everyday tasks, it might cause stress and worry more than usual. As stress can impact the severity of the disease, it’s important to learn techniques for coping with this condition. Doctors often use a referral to a counselor or a scleroderma support group.

## The Long-Term Prognosis for Scleroderma

Many scleroderma patients, even those with more invasive systemic scleroderma, can expect to have a normal life expectancy. But to remain as healthy as possible, you need to be open with the doctor about how you feel. The doctor should monitor your health closely and deal quickly with any complications that arise.

There are a number of specific issues that are important to consider:

* **Plateaus.** Some patients may have a time when their condition stabilizes. During this time, your skin may improve, and the mobility could increase. This could be a short-term change or might even go into long-term remission.
* **Monitoring.** Patients with systemic scleroderma should be screened regularly to monitor for internal organ complications.
* **Pregnancy.** Patients can get pregnant; however, there likely is a higher chance of miscarrying. During pregnancy, some of the symptoms (such as Raynaud phenomenon) might get better, but others (such as heartburn) could get worse.

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# Osteoarthritis

Osteoarthritis is the most common type of arthritis. It happens when the cartilage that lines your joints is worn down or damaged and your bones rub together when you use that joint. A healthcare provider will help you find a combination of treatments to manage your symptoms.

## Overview

### **What is osteoarthritis?**

Osteoarthritis is the most common type of arthritis (a condition that affects your joints). Healthcare providers sometimes refer to it as degenerative joint disease or OA. It happens when the cartilage that lines your joints is worn down over time and your bones rub against each other when you use your affected joints.

Usually, the ends of bones in your joints are capped in a layer of tough, smooth cartilage. Cartilage is like a two-in-one shock absorber and lubricant — it helps the bones in your joints move past each other smoothly and safely. If you have osteoarthritis, the cartilage in your affected joints wears away over time. Eventually, your bones rub against each other when you move your joints.

Osteoarthritis can affect any of your joints, but most commonly develops in your:

* Hands.
* Knees.
* Hips.
* Neck (cervical spine).
* Lower back (lumbar spine).

#### **Types of osteoarthritis**

A healthcare provider might classify osteoarthritis as one of two types:

* Primary osteoarthritis is the most common form of osteoarthritis that develops in your joints over time. Experts think it’s usually caused by normal wear and tear of using your joints throughout your life.
* Secondary osteoarthritis happens when something directly damages one of your joints enough to cause osteoarthritis. Injuries and traumas are common causes of secondary osteoarthritis. Other types of arthritis can damage the cartilage in your joints enough to cause osteoarthritis, too.

#### **How common is osteoarthritis?**

Osteoarthritis is very common. Experts estimate that more than 80% of adults older than 55 have osteoarthritis, even if some of them never experience symptoms.

Around 60% of people with osteoarthritis have symptoms they can notice or feel.

## Symptoms and Causes

### **What are osteoarthritis symptoms?**

The most common symptoms of osteoarthritis include:

* Pain in a joint (especially when you’re moving it).
* Stiffness.
* Swelling near a joint.
* A decreased range of motion (how far you can move a joint).
* Feeling like a joint isn’t as strong or stable as it usually is.
* A joint looking noticeably different than it used to (joint deformity).

### **What causes osteoarthritis?**

Experts aren’t sure what causes osteoarthritis. Primary osteoarthritis usually develops slowly as you age. As you get older, normal wear and tear on your joints might contribute to their cartilage breaking down.

Anything that directly damages your joints can also cause osteoarthritis, including:

* Sports injuries.
* Falls.
* Car accidents.
* Health conditions that affect your joints, like Ehlers-Danlos syndrome or joint hypermobility syndrome.

Other forms of arthritis (specifically inflammatory arthritis) can cause osteoarthritis, including:

* Rheumatoid arthritis.
* Gout.
* Psoriatic arthritis

#### **Osteoarthritis risk factors**

Anyone can develop osteoarthritis. Adults older than 55 and people who are in postmenopause are more likely to develop osteoarthritis.

People with certain health conditions are more likely to experience osteoarthritis, including:

* Obesity (having a body mass index, or BMI, greater than 30) or overweight (having a BMI over 25).
* Diabetes.
* High cholesterol (hyperlipidemia).
* Some autoimmune diseases that affect your joints.

## Diagnosis and Tests

### **How is osteoarthritis diagnosed?**

A healthcare provider will diagnose osteoarthritis with a physical exam and imaging tests. They’ll look at your joints and ask you when you first noticed any symptoms. Tell them if any activities make your symptoms worse, or if they come and go.

#### **What tests are done to diagnose osteoarthritis?**

Your healthcare provider might use X-rays to take pictures of your joints. They might also use an MRI (magnetic resonance imaging) or CT (computed tomography) scan.

You might need blood tests to rule out other conditions or issues that cause similar symptoms.

## Management and Treatment

### **How is osteoarthritis treated?**

Your healthcare provider will help you find treatments that relieve your osteoarthritis symptoms. There’s no cure for arthritis, and you can’t regrow the cartilage in your affected joints. Your provider will help you find ways to manage your symptoms when you’re experiencing them.

The most common treatments for osteoarthritis include:

* Medication: Over-the-counter (OTC) pain relievers can help reduce pain and inflammation. You might need medication you take by mouth or topical pain relievers (creams, ointments or patches you put on your skin near your affected joints).
* Exercise: Moving your joints can relieve stiffness and strengthen the muscles around them. Low-impact activities like swimming, water aerobics and weight training can all help. Your provider might recommend that you work with a physical therapist.
* Supportive devices: Wearing shoe inserts or a brace can support and stabilize your joints. Using a cane or walker can take pressure off your affected joints and help you move safely.
* Heat and cold therapies: Applying heat or cold to your affected joints might help relieve pain and stiffness. Your provider will tell you how often (and for how long) you should apply a heating pad, ice packs, or a cool compress.
* Complementary therapy: Complementary therapies may work alongside other treatment options. Examples of complementary medicine include acupuncture, massage, meditation, tai chi and dietary supplements. Talk to your provider before you start taking any herbal or dietary supplements.
* Surgery: Most people don’t need surgery to treat osteoarthritis. Your provider might recommend surgery if you’re experiencing severe symptoms and other treatments haven’t worked. You might need a joint replacement (arthroplasty). Your provider or surgeon will tell you what to expect.

## Outlook / Prognosis

### **What can I expect if I have osteoarthritis?**

Most people with osteoarthritis need to manage their symptoms for the rest of their lives. Your healthcare provider will help you find the right combination of treatments to reduce your symptoms.

If you have osteoarthritis, it’s important to stay as active as possible. If joint pain and other symptoms make it too hard for you to move, you may face a greater risk for other serious health conditions like heart disease, diabetes and some types of cancer.

Talk to your healthcare provider if osteoarthritis makes it hard (or impossible) to stay active. They’ll help you find new treatments to manage your symptoms.

## Prevention

### **How can I prevent osteoarthritis?**

The best way to prevent osteoarthritis is to maintain good overall health, including:

* Avoiding tobacco products.
* Doing low-impact exercise.
* Following a diet plan that’s healthy for you.
* Always wearing your seatbelt.
* Wearing proper protective equipment for any activity, sport or work you’re doing.
* Visiting a healthcare provider for regular checkups and as soon as you notice any changes in your joints.

## Living With

### **What can I do to make living with osteoarthritis easier?**

You might need to tweak your routine to make living with osteoarthritis easier. Depending on when you’re experiencing symptoms (and how severe they are), you may need to avoid or modify your activities while you’re managing symptoms. You might work with an occupational therapist if you need help performing your daily tasks. Occupational therapists are healthcare providers who can help you manage physical challenges like arthritis. They may recommend:

* Adaptive equipment, such as grips for opening jars.
* Techniques for doing hobbies, sports or other activities safely.
* Tips for reducing joint pain during arthritic flare-ups.

### **When should I see my healthcare provider?**

Visit a healthcare provider as soon as you notice any symptoms of osteoarthritis. Even minor joint pain can be a sign that you need treatment — especially if it doesn’t get better in a few days.

You can’t repair any cartilage degeneration (breakdown) that’s already happened, but starting osteoarthritis treatment can slow down further damage inside your joints.

Talk to your provider if it feels like your symptoms are coming back more often or are more severe than they used to be. Ask your provider about other treatment options or changes you can make to your existing treatments if you feel like they’re not working as well as they usually do.

### **What questions should I ask my doctor?**

* Do I have osteoarthritis or another type of arthritis?
* Which of my joints are affected?
* Which treatments will I need?
* Will I need surgery?
* Would working with a physical therapist or occupational therapist help me?

## Additional Common Questions

### **At what age does osteoarthritis usually start?**

Osteoarthritis usually affects people older than 55. However, there’s no set timeline or age restriction on when you might experience it. It also doesn’t start the way some health conditions do — there’s not usually an exact starting point your healthcare provider can precisely identify.

It can take a long time for the cartilage in your affected joints to wear down enough to cause pain and stiffness. So, even if you first notice symptoms around age 55, that doesn’t mean osteoarthritis started exactly at that time.

## Osteoporosis

## Overview

Osteoporosis causes bones to become weak and brittle — so brittle that a fall or even mild stresses such as bending over or coughing can cause a break. Osteoporosis-related breaks most commonly occur in the hip, wrist or spine.

Bone is living tissue that is constantly being broken down and replaced. Osteoporosis occurs when the creation of new bone doesn't keep up with the loss of old bone.

Osteoporosis affects men and women of all races. But white and Asian women, especially older women who are past menopause, are at highest risk. Medicines, healthy diet and weight-bearing exercise can help prevent bone loss or strengthen already weak bones.

Symptoms

There typically are no symptoms in the early stages of bone loss. But once your bones have been weakened by osteoporosis, you might have signs and symptoms that include:

* Back pain, caused by a broken or collapsed bone in the spine.
* Loss of height over time.
* A stooped posture.
* A bone that breaks much more easily than expected.

### **When to see a doctor**

You might want to talk to your health care provider about osteoporosis if you went through early menopause or took corticosteroids for several months at a time, or if either of your parents had hip fractures.

Your bones are in a constant state of renewal — new bone is made and old bone is broken down. When you're young, your body makes new bone faster than it breaks down old bone and your bone mass increases. After the early 20s this process slows, and most people reach their peak bone mass by age 30. As people age, bone mass is lost faster than it's created.

How likely you are to develop osteoporosis depends partly on how much bone mass you attained in your youth. Peak bone mass is partly inherited and varies also by ethnic group. The higher your peak bone mass, the more bone you have "in the bank" and the less likely you are to develop osteoporosis as you age.

## Risk factors

A number of factors can increase the likelihood that you'll develop osteoporosis — including your age, race, lifestyle choices, and medical conditions and treatments.

### **Unchangeable risks**

Some risk factors for osteoporosis are out of your control, including:

* **Your sex.** Women are much more likely to develop osteoporosis than are men.
* **Age.** The older you get, the greater your risk of osteoporosis.
* **Race.** You're at greatest risk of osteoporosis if you're white or of Asian descent.
* **Family history.** Having a parent or sibling with osteoporosis puts you at greater risk, especially if your mother or father fractured a hip.
* **Body frame size.** Men and women who have small body frames tend to have a higher risk because they might have less bone mass to draw from as they age.

### **Hormone levels**

Osteoporosis is more common in people who have too much or too little of certain hormones in their bodies. Examples include:

* **Sex hormones.** Lowered sex hormone levels tend to weaken bone. The fall in estrogen levels in women at menopause is one of the strongest risk factors for developing osteoporosis. Treatments for prostate cancer that reduce testosterone levels in men and treatments for breast cancer that reduce estrogen levels in women are likely to accelerate bone loss.
* **Thyroid problems.** Too much thyroid hormone can cause bone loss. This can occur if your thyroid is overactive or if you take too much thyroid hormone medicine to treat an underactive thyroid.
* **Other glands.** Osteoporosis has also been associated with overactive parathyroid and adrenal glands.

### **Dietary factors**

Osteoporosis is more likely to occur in people who have:

* **Low calcium intake.** A lifelong lack of calcium plays a role in the development of osteoporosis. Low calcium intake contributes to diminished bone density, early bone loss and an increased risk of fractures.
* **Eating disorders.** Severely restricting food intake and being underweight weakens bone in both men and women.
* **Gastrointestinal surgery.** Surgery to reduce the size of your stomach or to remove part of the intestine limits the amount of surface area available to absorb nutrients, including calcium. These surgeries include those to help you lose weight and for other gastrointestinal disorders.

### **Steroids and other medicines**

Long-term use of oral or injected corticosteroid medicines, such as prednisone and cortisone, interferes with the bone-rebuilding process. Osteoporosis has also been associated with medications used to combat or prevent:

* Seizures.
* Gastric reflux.
* Cancer.
* Transplant rejection.

### **Medical problems**

The risk of osteoporosis is higher in people who have certain medical problems, including:

* Celiac disease.
* Inflammatory bowel disease.
* Kidney or liver disease.
* Cancer.
* Multiple myeloma.
* Rheumatoid arthritis.

### **Lifestyle choices**

Some bad habits can increase your risk of osteoporosis. Examples include:

* **Sedentary lifestyle.** People who spend a lot of time sitting have a higher risk of osteoporosis than do those who are more active. Any weight-bearing exercise and activities that promote balance and good posture are good for your bones, but walking, running, jumping, dancing and weightlifting seem particularly helpful.
* **Excessive alcohol consumption.** Regular consumption of more than two alcoholic drinks a day increases the risk of osteoporosis.
* **Tobacco use.** The exact role tobacco plays in osteoporosis isn't clear, but it has been shown that tobacco use contributes to weak bones.

## Complications

Bone breaks, particularly in the spine or hip, are the most serious complications of osteoporosis. Hip fractures often are caused by a fall and can result in disability and even an increased risk of death within the first year after the injury.

In some cases, broken bones in the spine can occur even if you haven't fallen. The bones that make up your spine, called vertebrae, can weaken to the point of collapsing, which can result in back pain, lost height and a hunched-forward posture.

## Prevention

Good nutrition and regular exercise are essential for keeping your bones healthy throughout your life.

### **Calcium**

Men and women between the ages of 18 and 50 need 1,000 milligrams of calcium a day. This daily amount increases to 1,200 milligrams when women turn 50 and men turn 70.

Good sources of calcium include:

* Low-fat dairy products.
* Dark green leafy vegetables.
* Canned salmon or sardines with bones.
* Soy products, such as tofu.
* Calcium-fortified cereals and orange juice.

If you find it difficult to get enough calcium from your diet, consider taking calcium supplements. However, too much calcium has been linked to kidney stones. Although yet unclear, some experts suggest that too much calcium, especially in supplements, can increase the risk of heart disease.

The Health and Medicine Division of the National Academies of Sciences, Engineering, and Medicine recommends that total calcium intake, from supplements and diet combined, should be no more than 2,000 milligrams daily for people older than 50.

### **Vitamin D**

Vitamin D improves the body's ability to absorb calcium and improves bone health in other ways. People can get some of their vitamin D from sunlight, but this might not be a good source if you live in a high latitude, if you're housebound, or if you regularly use sunscreen or avoid the sun because of the risk of skin cancer.

Dietary sources of vitamin D include cod liver oil, trout and salmon. Many types of milk and cereal have been fortified with vitamin D.

Most people need at least 600 international units (IU) of vitamin D a day. That recommendation increases to 800 IU a day after age 70.

People without other sources of vitamin D and especially with limited sun exposure might need a supplement. Most multivitamin products contain between 600 and 800 IU of vitamin D. Up to 4,000 IU of vitamin D a day is safe for most people.

### **Exercise**

Exercise can help you build strong bones and slow bone loss. Exercise will benefit your bones no matter when you start, but you'll gain the most benefits if you start exercising regularly when you're young and continue to exercise throughout your life.

Combine strength training exercises with weight-bearing and balance exercises. Strength training helps strengthen muscles and bones in your arms and upper spine. Weight-bearing exercises — such as walking, jogging, running, stair climbing, skipping rope, skiing and impact-producing sports — affect mainly the bones in your legs, hips and lower spine. Balance exercises such as tai chi can reduce your risk of falling especially as you get older.

# Fibromyalgia

### **What is fibromyalgia?**

Fibromyalgia is a long-term (chronic) health condition that causes pain and tenderness throughout your body. It causes musculoskeletal pain and fatigue.

People with fibromyalgia usually experience symptoms that come and go in periods called flare-ups. Sometimes, it can feel exhausting and challenging to navigate living with fibromyalgia. The peaks and valleys between feeling good and suddenly having a flare-up of symptoms can feel overwhelming. Fibromyalgia is real, and so is how you feel.

Experts don’t know what causes fibromyalgia, but studies have found that certain health conditions, stress and other changes in your life might trigger it. You might be more likely to develop fibromyalgia if one of your biological parents has it.

Any new pain in your body is often the first sign of fibromyalgia — especially in your muscles. Trust your instincts and listen to your body. Visit a healthcare provider if you’re experiencing new pain, fatigue and other symptoms — even if it feels like they come and go.

#### **Who is affected by fibromyalgia?**

Anyone can develop fibromyalgia. It affects people of any age, including children. Around 4 million people in the U.S. are living with fibromyalgia.

Women and people older than 40 are more likely to be diagnosed with fibromyalgia.

## Symptoms and Causes

****Fibromyalgia can cause physical, mental and emotional symptoms.

### **What are fibromyalgia symptoms?**

The two most common symptoms of fibromyalgia are pain and fatigue. You may experience:

* Muscle pain or tenderness.
* Fatigue.
* Face and jaw pain (temporomandibular joint disorders).
* Headaches and migraines.
* Digestive problems, including diarrhea and constipation.
* Bladder control issues.

Fibromyalgia can cause mental and emotional symptoms, including:

* Memory problems (sometimes called “fibro fog” or “brain fog”).
* Anxiety.
* Depression.
* Insomnia and other sleep disorders.

### **What causes fibromyalgia?**

Experts don’t know what causes fibromyalgia.

Certain genes you inherit from you biological parents might make you more likely to develop fibromyalgia. Studies have found a link between biological parents who have fibromyalgia and their children — this might mean it’s passed down through families.

People with fibromyalgia are usually more sensitive to pain than most people. Experts haven’t found the direct link yet, but they think genetic mutations in the genes responsible for forming the neurotransmitters in your brain that broadcast and receive pain signals to your body might cause fibromyalgia.

#### **What are the risk factors for fibromyalgia?**

Even though experts can’t say for sure what causes fibromyalgia, some health conditions and other issues are risk factors for developing it. Fibromyalgia risk factors include:

* Your age: People older than 40 are more likely to develop fibromyalgia. But it can affect anyone, including children.
* Your sex: Women are twice as likely to experience fibromyalgia.
* Chronic illnesses: People with conditions like osteoarthritis, depression, anxiety disorders, chronic back pain and irritable bowel syndrome are more likely to develop fibromyalgia.
* Infections: Some people develop fibromyalgia after having an infection, especially if they experience severe symptoms.
* Stress: The amount of stress you experience can’t be measured on a test, but too much stress can affect your health.
* Traumas: People who’ve experienced a physical or emotional trauma or a serious injury sometimes develop fibromyalgia.

#### **What triggers a fibromyalgia flare-up?**

Certain events or changes in your life can trigger a fibromyalgia flare-up. Everyone is different, and what triggers symptoms for some people might not for you. In general, anything that increases your stress can trigger a flare-up, including:

* Emotional stress caused by your job, financial situation or social life.
* Changes in your daily routine.
* Changes in your diet or not getting enough nutrition.
* Hormone changes.
* Not getting enough sleep or changing when you sleep.
* Weather or temperature changes.
* Getting sick.
* Starting new medication or treatments, or changing something in your usual fibromyalgia treatment routine.

## Diagnosis and Tests

### **How is fibromyalgia diagnosed?**

A healthcare provider will diagnose fibromyalgia with a physical exam and discussion of your health history. They’ll ask about your symptoms and when you first noticed them.

There’s no test that can diagnose fibromyalgia. Usually, diagnosing it is part of a differential diagnosis — a medical process of elimination. Your provider will make a diagnosis by comparing several conditions with related symptoms. This process leads to your final diagnosis.

Your provider might use blood tests to rule out other common causes of fatigue like anemia or issues with your thyroid gland.

## Management and Treatment

### **How is fibromyalgia treated?**

There isn’t a single treatment that works for every person with fibromyalgia. Your provider will work with you to find a combination of treatments that relieve your symptoms. Tell your provider which symptoms you’re experiencing and when they change (including when they’re improving or getting worse).

Treatments you might need include:

* Over-the-counter (OTC) or prescription medicine to relieve pain.
* Exercises like stretches or strength training.
* Sleep therapy.
* Cognitive behavioral therapy.
* Stress management therapy.
* Antidepressants.

#### **What are the four stages of fibromyalgia?**

Fibromyalgia is a dynamic condition. This means you won’t experience symptoms in any specific order — there’s no roadmap to know when or how fibromyalgia symptoms will affect you.

Your provider might treat your fibromyalgia in stages based on how you feel. These stages aren’t a step-by-step treatment plan. Every person is different, and how fibromyalgia affects your body will be unique. The stages are more like loose categories that can help you understand which treatments you’ll need to manage your symptoms. The four stages of treating fibromyalgia include:

* Non-pharmacological treatments: Your provider or a physical therapist will give you stretches and exercises to loosen, relax and strengthen your muscles and joints.
* Psychological treatments: A mental health professional will help you identify ways to maintain a healthy self-image. They’ll suggest strategies to manage symptoms that affect your mental and emotional health.
* Pharmacological treatment: Taking medicine to manage your symptoms.
* Daily functioning: An occupational therapist can help you navigate your daily routine if you’re experiencing severe symptoms that make it hard to participate in your regular activities.

## Outlook / Prognosis

### **What can I expect if I have fibromyalgia?**

You should expect to manage fibromyalgia symptoms for a long time — maybe for the rest of your life. Some people with fibromyalgia experience fewer flare-ups with milder symptoms after they find treatments that work for them. Ask your provider how often you need follow-up appointments to adjust your treatments or to adjust any medications you’re taking.

Fibromyalgia is a real condition that has a real impact on your life. Some days it might feel like “it’s all in your head,” but it’s not. Talk to your provider or a mental health professional if you need help managing stress and other emotional symptoms.

### **What are the complications of fibromyalgia?**

People with fibromyalgia are more likely to be hospitalized because of pain, fatigue or mental health symptoms. You’re also more likely to experience memory problems and have trouble concentrating.

Talk to your provider as soon as you notice any changes in your symptoms, especially if you feel like they’re affecting your memory or mental health.

## Prevention

### **How can I prevent fibromyalgia?**

Because experts don’t know what causes fibromyalgia, you can’t prevent it.

Maintaining your overall health can help reduce the severity of fibromyalgia symptoms:

* Manage stress as well as you can.
* Follow a diet and exercise plan that’s healthy for you.
* Get enough sleep and practice good sleep hygiene.

## Living With

### **When should I see my healthcare provider?**

Visit a healthcare provider if you’re experiencing new symptoms like pain, fatigue or changes in your mental health, including:

* Depression or suicidal thoughts.
* Headaches or migraines.
* Memory problems or you feel like your brain is “foggy.”
* Sleep problems.

### **What questions should I ask my doctor?**

* Do I have fibromyalgia or another condition?
* Which tests will I need?
* Which treatments will work best for me?
* How often will I need follow-up appointments to adjust my treatments?
* Should I work with a mental health professional?
* Does this mean my family members are more likely to develop fibromyalgia?

### **A note from Cleveland Clinic**

Fibromyalgia causes pain all throughout your body. It can also make you feel fatigued and like your mind is clouded by a fog. There’s no cure for fibromyalgia, but your healthcare provider will help you find a combination of treatments that relieve your symptoms.

Even though experts don’t know what causes fibromyalgia, it’s real — and so are your symptoms. They might come and go or be hard to describe, but how you feel is valid and important. Living with a chronic condition like fibromyalgia can be a challenge, but you don’t have to do it alone. Talk to your provider or a mental health professional about managing stress and maintaining a positive self-image.

# Epilepsy

Epilepsy is a brain disease where nerve cells don’t signal properly, which causes seizures. Seizures are uncontrolled bursts of electrical activity that change sensations, behaviors, awareness, and muscle movements. Although epilepsy can’t be cured, many treatment options are available. Up to 70% of people with epilepsy can manage the disease with medications.

## What is epilepsy?

Epilepsy is a long-term (chronic) disease that causes repeated seizures due to abnormal electrical signals produced by damaged brain cells. A burst of uncontrolled electrical activity within brain cells causes a seizure. Seizures can include changes to your awareness, muscle control (your muscles may twitch or jerk), sensations, emotions and behavior.

Epilepsy is also called a seizure disorder.

### **Who does epilepsy affect?**

Anyone, of any age, race or sex, can develop epilepsy.

### **How common is epilepsy?**

In the U.S., about 3.4 million people have epilepsy. Of this number, 3 million are adults and 470,000 are children. There are 150,000 new cases of epilepsy in the U.S. each year. Worldwide, about 65 million people have epilepsy.

### **What happens in your brain when you have epilepsy?**

The cells in your brain send messages to and receive messages from all areas of your body. These messages are transmitted via a continuous electrical impulse that travels from cell to cell. Epilepsy disrupts this rhythmic electrical impulse pattern. Instead, there are bursts of electrical energy — like an unpredictable lightning storm — between cells in one or more areas of your brain. This electrical disruption causes changes in your awareness (including loss of consciousness), sensations, emotions and muscle movements.

### **What are the types of epilepsies and their seizure symptoms?**

Healthcare providers classify epilepsies by their seizure type. Seizure categories are based on where they start in your brain, your level of awareness during a seizure and by presence or absence of muscle movements.

There are two major seizure groups:

#### **Focal onset seizures**

Focal onset seizures start in one area, or network of cells, on one side of your brain. This seizure used to be called partial onset seizure. There are two types of focal seizures:

* Focal onset aware seizure means you’re awake and aware during the seizure. Healthcare providers once called this a simple partial seizure. Symptoms may include:
  + Changes in your senses — how things taste, smell or sound.
  + Changes in your emotions.
  + Uncontrolled muscle jerking, usually in arms or legs.
  + Seeing flashing lights, feeling dizzy, having a tingling sensation.
* Focal onset impaired awareness seizure means you’re confused or have lost awareness or consciousness during the seizure. This seizure type used to be called complex partial seizure. Symptoms may include:
  + Blank stare or a “staring into space.”
  + Repetitive movements like eye blinking, lip-smacking or chewing motion, hand rubbing or finger motions.

#### **Generalized onset seizures**

General onset seizures affect a widespread network of cells on both sides of your brain at the same time. There are six types of generalized seizures.

* Absence seizures: This seizure type causes a blank stare or “staring into space” (a brief loss of awareness). There may be minor muscle movements, including eye blinking, lip-smacking or chewing motions, hand motions or rubbing fingers. Absence seizures are more common in children, last for only seconds (usually less than 10 seconds) and are commonly mistaken for daydreaming. This seizure type used to be called petit mal seizures.
* Atonic seizures: Atonic means “without tone.” An atonic seizure means you’ve lost muscle control or your muscles are weak during your seizure. Parts of your body may droop or drop such as your eyelids or head, or you may fall to the ground during this short seizure (usually less than 15 seconds). This seizure type is sometimes called “drop seizure” or “drop attack.”
* Tonic seizures: Tonic means “with tone.” A tonic seizure means your muscle tone has greatly increased. Your arms, legs, back or whole body may be tense or stiff, causing you to fall. You may be aware or have a small change in awareness during this short seizure (usually less than 20 seconds).
* Clonic seizures: “Clonus” means fast, repeating stiffening and relaxing of a muscle (“jerking”). A clonic seizure happens when muscles continuously jerk for seconds to a minute or muscles stiffen followed by jerking for seconds up to two minutes.
* Tonic-clonic seizures: This seizure type is a combination of muscle stiffness (tonic) and repeated, rhythmic muscle jerking (clonic). Healthcare providers may call this seizure a convulsion, and once called it a grand mal seizure. Tonic-clonic seizures are what most people think of when they hear the word “seizure.” You lose consciousness, fall to the ground, your muscles stiffen and jerk for one to five minutes. You may bite your tongue, drool and lose muscle control of bowels or bladder, making you poop or pee.
* Myoclonic seizures: This seizure type causes brief, shock-like muscle jerks or twitches (“myo” means muscle, “clonus” means muscle jerking). Myoclonic seizures usually last only a couple of seconds.

As your healthcare provider learns more, your seizure type may change to focal or generalized onset seizure.

### **What are seizure triggers?**

Seizure triggers are events or something that happens before the start of your seizure.

Commonly reported seizure triggers include:

* Stress.
* Sleep issues such as not sleeping well, not getting enough sleep, being overtired, disrupted sleep and sleep disorders like sleep apnea.
* Alcohol use, alcohol withdrawal, recreational drug use.
* Hormonal changes or menstrual hormonal changes.
* Illness, fever.
* Flashing lights or patterns.
* Not eating healthy, balanced meals or drinking enough fluids; vitamin and mineral deficiencies, skipping meals.
* Physical overexertion.
* Specific foods (caffeine is a common trigger).
* Dehydration.
* Certain times of the day or night.
* Use of certain medications. Diphenhydramine, an ingredient in cold, allergy and sleep over-the-counter products, is a reported trigger.
* Missed anti-seizure medication doses.

### **How can I figure out my seizure triggers?**

Some people discover that their seizures occur consistently during certain times of the day or around certain events or other factors. You may want to track your seizures — and the events around your seizures — to see if there’s a pattern.

In your seizure diary, note the time of day each seizure happened, the events or special circumstances happening around the time of the seizure and how you felt. If you suspect you’ve identified a trigger, track that trigger to find out if it’s really a trigger. For example, if you think caffeine is a seizure trigger, do you have a seizure after consuming every caffeinated food or beverage, after “x” number of caffeinated foods/beverages or at certain times of day after consuming caffeine? Caffeine may or may not be the trigger when thoroughly reviewed.

## Symptoms and Causes

### **What are the signs and symptoms of epileptic seizures?**

The main symptom of epilepsy is recurring seizures. Your symptoms, however, vary depending on the type of seizure you have.

Seizure signs and symptoms include:

* Temporary loss of awareness or consciousness.
* Uncontrolled muscle movements, muscle jerking, loss of muscle tone.
* Blank stare or “staring into space” look.
* Temporary confusion, slowed thinking, problems with talking and understanding.
* Changes in hearing, vision, taste, smell, feelings of numbness or tingling.
* Problems talking or understanding.
* Upset stomach, waves of heat or cold, goosebumps.
* Lip-smacking, chewing motion, rubbing hands, finger motions.
* Psychic symptoms, including fear, dread, anxiety or déjà vu.
* Faster heart rate and/or breathing.

Most people with epilepsy tend to have the same type of seizure, so have similar symptoms with each seizure.

### **What causes epilepsy?**

Most of the time (in up to 70% of cases), the cause of seizures is not known. Known causes include:

* Genetics. Some types of epilepsy (like juvenile myoclonic epilepsy and childhood absence epilepsy) are more likely to run in families (inherited). Researchers believe that although there’s some evidence that specific genes are involved, the genes only increase the risk of epilepsy, and other factors may be involved. There are certain epilepsies that result from abnormalities that affect how brain cells can communicate with each other and can lead to abnormal brain signals and seizures.
* Mesial temporal sclerosis. This is a scar that forms in the inner part of your temporal lobe (part of your brain near your ear) that can give rise to focal seizures.
* Head injuries. Head injuries can result from vehicular accidents, falls or any blow to the head.
* Brain infections. Infections can include brain abscess, meningitis, encephalitis and neurocysticercosis.
* Immune disorders. Conditions that cause your immune system to attack brain cells (also called autoimmune diseases) can lead to epilepsy.
* Developmental disorders. Birth abnormalities affecting the brain are a frequent cause of epilepsy, particularly in people whose seizures aren’t controlled with anti-seizure medications. Some birth abnormalities known to cause epilepsy include focal cortical dysplasia, polymicrogyria and tuberous sclerosis. There’s a wide range of other brain malformations known to cause epilepsy.
* Metabolic disorders. People with a metabolic condition (how your body obtains energy for normal functions) can have epilepsy. Your healthcare provider can detect many of these disorders through genetic tests.
* Brain conditions and brain vessel abnormalities. Brain health issues that can cause epilepsy include brain tumors, strokes, dementia and abnormal blood vessels, such as arteriovenous malformations.

## Diagnosis and Tests

### **How is epilepsy diagnosed?**

Technically, if you experience two or more seizures that weren’t caused by a known medical condition — for example, from alcohol withdrawal or low blood sugar — you’re considered to have epilepsy. Before making a diagnosis, your healthcare provider (or epilepsy specialist) will perform a physical exam, take your medical history and may order blood work (to rule out other causes). They may ask about your symptoms during the seizure and conduct other tests, as well.

Your healthcare provider will ask you or your family member (who’s witnessed your seizure) if you experienced any of the following during a seizure:

* Muscle jerks.
* Muscle stiffness.
* Loss of bowel or bladder control (you peed or pooped during the seizure).
* Change in breathing.
* Skin color turned pale.
* Had a blank stare.
* Lost consciousness.
* Had problems talking or understanding what was said to you.

### **What tests will be done to diagnose this condition?**

Tests include:

* Electroencephalography (EEG): This test measures the electrical activity in your brain. Certain abnormal electrical patterns are related to seizures.
* Brain scans: Magnetic resonance imaging (MRI) to look for such things as tumors, infections or blood vessel abnormalities.

## Management and Treatment

### **How is epilepsy treated?**

Treatments to control epilepsy include anti-seizure medications, special diets (usually in addition to anti-seizure medications) and surgery.

#### **Anti-seizure medications**

Anti-seizure medications can control seizures in about 60% to 70% of people with epilepsy. Anti-seizure medication treatment is individualized. The U.S. Food and Drug Administration (FDA) has approved more than 20 anti-seizure medications for treating epilepsy. Your healthcare provider may try one or more medications, doses of medications or a combination of medications to find what works best to control your seizures.

Choice of an anti-seizure medication depends on:

* Seizure type.
* Your prior response to anti-seizure medications.
* Other medical conditions you have.
* The potential for interaction with other medications you take.
* Side effects of the anti-seizure drug (if any).
* Your age
* General health.
* Cost.

Because some anti-seizure medications are linked to birth defects, let your healthcare provider know if you’re pregnant or planning to become pregnant.

If anti-seizure medications don’t control your seizures, your healthcare provider will discuss other treatment options, including special diets, medical devices or surgery.

#### **Diet therapy**

The ketogenic diet and the modified Atkins diet — diets high in fat, moderate in protein and low in carbohydrates — are the two most common diets sometimes recommended for people with epilepsy. Diets are mostly recommended for children where medication was not effective and who aren’t candidates for surgery. Low glycemic index diets may also reduce seizures in some people with epilepsy.

#### **Surgery and devices**

Your healthcare provider will consider surgery if anti-seizure medications don’t control your seizures, and if your seizures are severe and debilitating. Epilepsy surgery can be a safe and effective treatment option when more than two anti-seizure medication trials fail to control your seizures. It’s important to be evaluated at an epilepsy center to see if you’re a candidate for epilepsy surgery if anti-seizure medications don’t control your seizures.

Surgery options include surgical resection (removal of abnormal tissue), disconnection (cutting fiber bundles that connect areas of your brain), stereotactic radiosurgery (targeted destruction of abnormal brain tissue) or implantation of neuromodulation devices. These devices send electrical impulses to your brain to reduce seizures over time.

## Outlook / Prognosis

### **Is there a cure for epilepsy?**

There’s no cure for epilepsy. But there are many options to treat epilepsy.

### **Will I always have seizures?**

About 70% of people become seizure-free with proper treatment within a few years. The remaining 30% are considered to have drug-resistant epilepsy. These people should go to an epilepsy center to determine if they’re candidates for epilepsy surgery.

### **How long will I have to take anti-epileptic medications?**

It depends on the type of epilepsy you have and your response to medication. Some people who remain seizure-free for several years may be able to stop their medication. Your healthcare provider makes this decision. They’ll consider a variety of factors when making this decision, including an absence of brain lesions on your MRI, EEG findings and your medical history. Some people may require life-long medication.

## Prevention

### **Can epilepsy be prevented?**

Although many causes of epilepsy are out of your control and unpreventable, you can reduce your chance of developing a few conditions that might lead to epilepsy, such as:

* To lower your risk of traumatic brain injury (from blows to your head), always wear your seatbelt when driving and drive “defensively”; wear a helmet when biking; clear your floors of clutter and power cords to prevent falls; and stay off ladders.
* To lower your risk of stroke, eat a healthy diet (such as the Mediterranean diet), maintain a healthy weight and exercise regularly.
* Seek therapy for substance abuse. Alcohol and other illegal drugs can damage your brain, which can then lead to epilepsy.

## Living With

### **When should I see my doctor? When should I go to the emergency room?**

See your primary healthcare provider if you’ve never had a seizure before and think you’ve had one — or the people around you tell you you’ve “zoned out” or lost awareness. You may be referred to a neurologist for additional follow-up and testing.

Call 911 (or have a friend or bystander call 911) if you’ve had a seizure that lasts longer than five minutes or a series of seizures in a row without recovery.

### **How can I manage my seizures?**

To help manage your seizures:

* Take your medications exactly as prescribed by your healthcare provider. If you miss a dose, call your healthcare provider right away.
* Get an adequate amount of sleep (typically seven to nine hours a night).
* Manage your stress. Stress causes the release of certain chemicals in the areas of your brain more prone to seizures. To reduce your stress, try yoga, meditation, deep breathing exercises, biofeedback or other relaxation methods.
* Exercise regularly (about 30 minutes a day, five days a week).
* Avoid excessive alcohol use.
* Tell all your healthcare providers you have epilepsy. Check with your healthcare provider who manages your epilepsy if another doctor prescribes additional medications (to treat other health issues). Some medications, including antidepressants, antihistamines and stimulants, can interfere with the effectiveness of your anti-seizure drugs or cause side effects.
* Always tell your healthcare provider who’s managing your epilepsy about all the products you take, including over-the-counter medications, vitamins and supplements, and herbal products.
* Identify and avoid your seizure triggers.
* Eat a healthy diet.

### **Can I drive if I’ve been diagnosed with epilepsy?**

In the U.S., each state has its own driving rules. People with epilepsy are required to report their condition to the Department of Motor Vehicles (DMV). However, states differ about the identity of the person who has to report. Some states require the healthcare provider report the person. Other states ask the person with epilepsy or seizures to sign a simple form at the time of application for a license or license renewal. On the form, the person states that they’ll notify the DMV of changes in their health status or driving ability.

Ask your healthcare provider if you can drive. Generally, you shouldn’t drive until your seizures are under control.

### **What are the life-threatening complications of epilepsy?**

Seizures can lead to serious physical injuries. In addition, life-threatening conditions associated with epilepsy include status epilepticus and sudden unexplained death in epilepsy (SUDEP).

#### **Status epilepticus**

Status epilepticus is a long-lasting (five to 30 minutes) seizure or seizures that occur close together without time to recover between them. It’s considered a medical emergency.

Emergency treatment at a hospital may include:

* Medications, oxygen and intravenous fluids.
* Placement (with anesthetics) into a coma to stop the seizures.
* EEG monitoring to determine response to treatment.
* Tests to discover the cause of the seizure.

#### **Sudden unexplained death in epilepsy (SUDEP)**

Sudden unexplained death in epilepsy (SUDEP) is a rare condition in which an otherwise healthy young-to-middle-aged person with epilepsy dies without a clear cause. The person often dies at night or during sleep without witnesses. Researchers believe some of the causes might include:

* Irregular heart rhythm. Seizures may cause a serious heart rhythm problem or cardiac arrest.
* Breathing difficulty. If breathing stops (for example, due to [sleep apnea](https://my.clevelandclinic.org/health/diseases/8718-sleep-apnea)), lack of oxygen to your heart and brain can be life-threatening. Also, sometimes airways can get blocked during a convulsive seizure, which could cause suffocation.
* Inhaling vomit. Inhaling vomit during or after a seizure can block your airway.
* Brain function interference. A seizure might interfere with areas of your brain that control breathing and heart rate.

About 1 in 1,000 people with epilepsy die from SUDEP each year. It’s the leading cause of death in people with uncontrolled seizures. Ways to reduce your risk of SUDEP include knowing and avoiding your seizure triggers, taking your medications as directed by your healthcare provider and following general healthy living practices (be well-rested, exercise, eat healthy foods, avoid smoking and avoid drinking too much or using recreational drugs).

## Additional Common Questions

### **What’s the difference between convulsions, seizures and epilepsy?**

A convulsion involves uncontrolled, jerky muscle movements and altered consciousness. But people often use the terms convulsion and seizure interchangeably. People also tend to use the word convulsion to refer to a tonic-clonic seizure.

Seizures result from abnormal electrical activity from cells in your brain. You can have a seizure without having any symptoms. Healthcare providers refer to this as an EEG seizure (picked up during EEG tests). Most of the time, seizures present with a variety of different symptoms that are described above. Seizures are a symptom of epilepsy, but not all seizures are caused by epilepsy.

Epilepsy is a neurological disease defined by having multiple, ongoing seizures. Epilepsy can be a life-long condition.

# Stroke

Strokes happen when a blood clot or broken vessel prevents blood from getting to your brain. They can be fatal and need immediate treatment. Call 911 or your local emergency services number right away if you think you or someone you’re with is having a stroke. The BE FAST acronym can help you spot symptoms.

### **What is a stroke?**

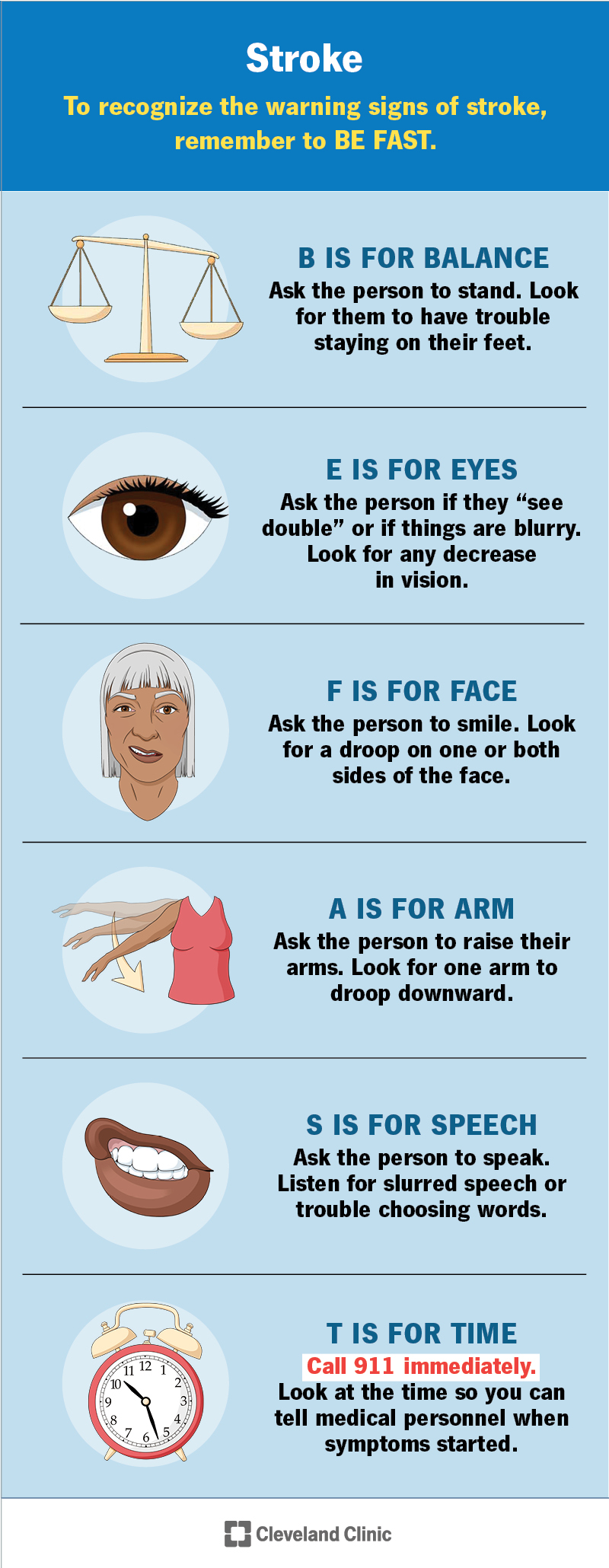
A stroke is a medical emergency that happens when something prevents your brain from getting enough blood flow. A blocked blood vessel or bleeding in your brain can cause strokes.

Healthcare providers sometimes refer to strokes as cerebrovascular accidents (CVAs) or brain attacks.

Strokes are the second leading cause of death worldwide and the fifth most common in the U.S.

If you think you or someone you’re with is having a stroke, immediately call 911 or your local emergency services number. Strokes are life-threatening and can be fatal. The sooner someone is diagnosed and treated, the more likely it is they’ll survive a stroke. Every second counts.

## Symptoms and Causes

****Remember the phrase BE FAST to help spot stroke symptoms.

### **What are stroke symptoms?**

A stroke can cause different symptoms depending on which area of your brain it affects. Some of the most common symptoms include:

* Aphasia (trouble speaking or a complete loss of speech)
* Blurry vision or double vision (diplopia)
* Confusion or agitation
* Coma
* Dizziness or vertigo
* Headaches (usually sudden and severe)
* Loss of muscle control on one side of your face
* Loss of coordination or clumsiness (ataxia)
* Memory loss (amnesia)
* Mood swings or sudden personality changes
* Nausea and vomiting
* Neck stiffness
* Passing out or fainting
* Seizures
* Slurred or garbled speaking (dysarthria)
* Sudden worsening or loss of your senses (including vision, hearing, smell, taste and touch)
* Weakness or paralysis on one side of your face and body

#### **How long does a stroke last?**

A stroke lasts as long as your brain isn’t getting the right amount of blood flow. Your brain cells die if they go too long without oxygen from fresh blood. If enough brain cells in an area die, the damage becomes permanent. This can cause permanent disabilities and other changes in how you can use your body.

Restoring your normal blood flow may prevent that permanent damage or reduce its severity. That’s why time is critical in treating a stroke.

Even after you receive treatment, it’s common for the effects to linger. Symptoms and after-effects can continue for a year or longer.

### **What are the warning signs of a stroke?**

Strokes can cause lots of different symptoms. To recognize the warning signs of a stroke in yourself or a loved one, remember the acronym BE FAST:

* Balance. Watch for a sudden loss of balance.
* Eyes. Look out for sudden vision loss or changes in one or both eyes.
* Face. Smile. Look for a droop on one or both sides of the face.
* Arms. Raise both arms. If you or someone is having a stroke, one arm will sag or drop in a way that it usually doesn’t.
* Speech. You or someone might slur your or their speech or have trouble choosing the right words.
* Time. Time is critical — call for help immediately. If possible, look at your watch, phone or a clock to track when symptoms start. Telling a healthcare provider when symptoms began can help them know which treatment options are best.

### **What causes strokes?**

There are two types of strokes.

Ischemic strokes usually happen because a blood clot blocks a blood vessel connected to your brain. Issues that can cause these kinds of clots include:

* Atherosclerosis (hardened arteries)
* Atrial fibrillation (especially when sleep apnea causes it)
* Clotting disorders
* Heart defects (including atrial septal defect and ventricular septal defect)
* Microvascular ischemic disease

Hemorrhagic strokes happen when a blood vessel in your brain breaks or tears (ruptures). Causes can include:

* Brain aneurysms
* Brain tumors
* High blood pressure (especially if it’s very high or you have it for a long time)
* Moyamoya disease (and any other condition that weakens blood vessels in your brain)

#### **Transient ischemic attack**

A transient ischemic attack (TIA) — sometimes called a “mini-stroke” — is like a stroke, but the effects are temporary. These are often warning signs that a person has a very high risk of having a true stroke soon. A person who has a TIA needs emergency medical care as soon as possible.

#### **Stroke risk factors**

Anybody can have a stroke, but some groups have a higher risk, including people who:

* Are older than 65
* Smoke or use other forms of tobacco or nicotine (like vaping)
* Use recreational or nonprescription drugs

Having certain health conditions can increase your stroke risk, including:

* Alcohol use disorder
* COVID-19
* Frequent migraine headaches
* High blood pressure (hypertension)
* High cholesterol (hyperlipidemia)
* Type 2 diabetes

## Diagnosis and Tests

### **How are strokes diagnosed?**

A healthcare provider will diagnose a stroke using a combination of a neurological exam and tests. Providers in the emergency room may diagnose a stroke if emergency services transport you to the ER.

Your provider will use some of the following tests to confirm that you’ve had a stroke:

* Blood tests
* CT scan
* Electroencephalogram (EEG)
* Electrocardiogram (EKG)
* MRI

## Management and Treatment

### **What are stroke treatments?**

The treatments you’ll need will depend on a few factors, including:

* How much the stroke damaged your brain
* Which area of your brain is affected
* Which type you have

Your providers will restore normal blood flow to your brain as fast as possible to limit the risk of permanent brain damage.

If you experience an ischemic stroke, your providers will break up or remove the blood clot that caused it. You’ll need thrombolytic medications and/or surgery (usually a mechanical thrombectomy). Your providers may also give you medications to manage your blood pressure.

If you have a hemorrhagic stroke, your providers will control the bleeding that caused it. You’ll need medications to stop the bleeding in your brain and manage your blood pressure. You may need surgery to reduce the increased intracranial pressure around your brain.

Your healthcare providers or surgeon will tell you exactly which treatments are best for you, what to expect and how long it will take to recover.

#### **Stroke rehabilitation**

Stroke rehab is an important part of stroke treatment. You’ll need rehab to help you adjust to changes in your brain and body after a stroke. You may need to regain abilities you had before or adjust to new or different disabilities. You might need a combination of:

* Cognitive rehab to help improve your memory, concentration and other mental abilities
* Occupational therapy to help you safely complete your daily tasks, especially chores or activities that need precise body movements
* Physical therapy to strengthen your muscles, improve your balance and regain use of your arms and legs
* Speech therapy to regain or improve your language and speaking abilities and control the muscles that help you talk, breathe, eat and swallow

## Outlook / Prognosis

### **What is the stroke survival rate?**

It’s hard for experts to estimate a stroke survival rate that applies to everyone. Strokes can be fatal, and they can cause permanent disabilities. But there’s no one set recovery timeline or outlook that’s accurate for everyone.

Ischemic strokes usually have better outcomes than hemorrhagic strokes, but that doesn’t mean your recovery will be easier, faster or better if you have one type or the other.

#### **Stroke recovery time**

Everyone’s body responds differently to a stroke. What you can expect (the prognosis) after a stroke depends on a few factors, including:

* How quickly it was treated
* Which areas of your brain it affected
* Which type of stroke you had
* Your overall health

Most people take a few months to recover after a stroke. Your provider will tell you what to expect. They’ll help you set recovery goals and expectations that fit your unique health and situation.

## Prevention

### **How can you prevent a stroke?**

Maintaining your overall health is the best way to reduce your stroke risk. Try to:

* Eat plenty of healthy foods and maintain a weight that’s healthy for you.
* Get regular physical activity.
* Manage your blood pressure, cholesterol and any health conditions you have.
* Quit smoking.

Visit a healthcare provider for a check-up every year (or as often as they suggest). Many of the health conditions and issues that can cause stroke develop and build up over time, and may not cause symptoms you can notice. Many people with high blood pressure never feel or sense anything wrong. Your provider will help you catch and manage any warning signs before they increase your risk of a stroke later on.

## Living With

### **How do I take care of myself after a stroke?**

Recovering and rehabbing after a stroke is hard work. Once you and your provider finalize your treatment plan, follow it as closely as possible. In general, you should:

* Go to your rehab and other therapy appointments. Tell your therapists if anything makes you feel unsafe or uncomfortable. Rehab is hard work, but you shouldn’t be in constant pain or discomfort.
* Remember your mental health. Depression and anxiety are extremely common after a stroke. You’re not weak or a quitter for feeling sad or upset. Your emotional health can be just as important as how your physical body is doing. Talk to your provider or a mental health professional if you feel like you need help processing anything during your recovery.
* Take your medications. Taking your medicine as your provider directs will help your body heal.

### **When should I go to the ER?**

Call 911 (or your local emergency services number) if you think you’re experiencing stroke symptoms again. Another stroke has an even higher risk of causing severe complications and being fatal. Don’t wait to call for help or go to the emergency room.

People who’ve had a stroke have an increased risk of other potentially serious complications, including:

* Deep vein thrombosis (DVT)
* Heart attack
* Pneumonia
* Pulmonary embolism
* Seizures

Call emergency services or go to the ER if you think you’re experiencing any symptoms of these complications.

### **Which questions should I ask my doctor?**

You might want to ask your provider a few questions, including:

* Which type of stroke did I have?
* Will I have any long-term effects from the stroke?
* Which kinds of therapy and rehab will I need?
* What warning signs of another stroke should I watch out for?

# Parkinson’s Disease

Parkinson’s disease is an age-related degenerative brain condition, meaning it causes parts of your brain to deteriorate. It’s best known for causing slowed movements, tremors, balance problems and more. Most cases happen for unknown reasons, but some are inherited. The condition isn’t curable, but there are many different treatment options.

### **What is Parkinson’s disease?**

Parkinson’s disease is a condition where a part of your brain deteriorates, causing more severe symptoms over time. While this condition is best known for how it affects muscle control, balance and movement, it can also cause a wide range of other effects on your senses, thinking ability, mental health and more.

### **Who does it affect?**

The risk of developing Parkinson’s disease naturally increases with age, and the average age at which it starts is 60 years old. It’s slightly more common in males.

While Parkinson’s disease is usually age-related, it can happen in adults as young as 20 (though this is extremely rare, and often people have a parent, full sibling or child with the same condition).

### **How common is this condition?**

Parkinson’s disease is very common overall, ranking second among age-related degenerative brain diseases. It’s also the most common motor (movement-related) brain disease. Experts estimate that it affects at least 1% of people over age 60 worldwide.

### **How does this condition affect my body?**

Parkinson’s disease causes a specific area of your brain, the basal ganglia, to deteriorate. As this area deteriorates, you lose the abilities those areas once controlled. Researchers have uncovered that Parkinson’s disease causes a major shift in your brain chemistry.

Under normal circumstances, your brain uses chemicals known as neurotransmitters to control how your brain cells (neurons) communicate with each other. When you have Parkinson’s disease, you don’t have enough dopamine, one of the most important neurotransmitters.

When your brain sends activation signals that tell your muscles to move, it fine-tunes your movements using cells that require dopamine. That’s why lack of dopamine causes the slowed movements and tremors symptoms of Parkinson’s disease.

As Parkinson’s disease progresses, the symptoms expand and intensify. Later stages of the disease often affect how your brain functions, causing dementia-like symptoms and depression.

### **What is the difference between Parkinson’s disease vs. parkinsonism?**

“Parkinsonism” is an umbrella term that describes Parkinson’s disease and conditions with similar symptoms. It can refer not only to Parkinson’s disease but also to other conditions like multiple system atrophy or corticobasal degeneration.

## Symptoms and Causes

### **What are the symptoms?**

The best-known symptoms of Parkinson’s disease involve loss of muscle control. However, experts now know that muscle control-related issues aren’t the only possible symptoms of Parkinson’s disease.

#### **Motor-related symptoms**

Motor symptoms — which means movement-related symptoms — of Parkinson’s disease include the following:

* Slowed movements (bradykinesia). A Parkinson’s disease diagnosis requires that you have this symptom. People who have this describe it as muscle weakness, but it happens because of muscle control problems, and there’s no actual loss of strength.
* Tremor while muscles are at rest. This is a rhythmic shaking of muscles even when you’re not using them and happens in about 80% of Parkinson’s disease cases. Resting tremors are different from essential tremors, which don’t usually happen when muscles are at rest.
* Rigidity or stiffness. Lead-pipe rigidity and cogwheel stiffness are common symptoms of Parkinson’s disease. Lead-pipe rigidity is a constant, unchanging stiffness when moving a body part. Cogwheel stiffness happens when you combine tremor and lead-pipe rigidity. It gets its name because of the jerky, stop-and-go appearance of the movements (think of it as the second hand on a mechanical clock).
* Unstable posture or walking gait. The slowed movements and stiffness of Parkinson’s disease cause a hunched over or stooped stance. This usually appears as the disease gets worse. It’s visible when a person walks because they’ll use shorter, shuffling strides and move their arms less. Turning while walking may take several steps.

Additional motor symptoms can include:

* Blinking less often than usual. This is also a symptom of reduced control of facial muscles.
* Cramped or small handwriting. Known as micrographia, this happens because of muscle control problems.
* Drooling. Another symptom that happens because of loss of facial muscle control.
* Mask-like facial expression. Known as hypomimia, this means facial expressions change very little or not at all.
* Trouble swallowing (dysphagia). This happens with reduced throat muscle control. It increases the risk of problems like pneumonia or choking.
* Unusually soft speaking voice (hypophonia). This happens because of reduced muscle control in the throat and chest.

#### **Non-motor symptoms**

Several symptoms are possible that aren’t connected to movement and muscle control. In years past, experts believed non-motor symptoms were risk factors for this disease when seen before motor symptoms. However, there’s a growing amount of evidence that these symptoms can appear in the earliest stages of the disease. That means these symptoms might be warning signs that start years or even decades before motor symptoms.

Non-motor symptoms (with the potential early warning symptoms in bold) include:

* Autonomic nervous system symptoms. These include orthostatic hypotension (low blood pressure when standing up), constipation and gastrointestinal problems, urinary incontinence and sexual dysfunctions.
* Depression.
* Loss of sense of smell (anosmia).
* Sleep problems such as periodic limb movement disorder (PLMD), rapid eye movement (REM) behavior disorder and restless legs syndrome.
* Trouble thinking and focusing (Parkinson’s-related dementia).

#### **Stages of Parkinson’s disease**

Parkinson’s disease can take years or even decades to cause severe effects. In 1967, two experts, Margaret Hoehn and Melvin Yahr, created the staging system for Parkinson’s disease. That staging system is no longer in widespread use because staging this condition is less helpful than determining how it affects each person’s life individually and then treating them accordingly.

Today, the Movement Disorder Society-Unified Parkinson’s Disease Rating Scale (MDS-UPDRS) is healthcare providers’ main tool to classify this disease. The MDS-UPDRS examines four different areas of how Parkinson’s disease affects you:

* Part 1: Non-motor aspects of experiences of daily living. This section deals with non-motor (non-movement) symptoms like dementia, depression, anxiety and other mental ability- and mental health-related issues. It also asks questions about pain, constipation, incontinence, fatigue, etc.
* Part 2: Motor aspects of experiences of daily living. This section covers the effects on movement-related tasks and abilities. It includes your ability to speak, eat, chew and swallow, dress and bathe yourself if you have tremors, and more.
* Part 3: Motor examination. A healthcare provider uses this section to determine the movement-related effects of Parkinson’s disease. The criteria measure effects based on how you speak, facial expressions, stiffness and rigidity, walking gait and speed, balance, movement speed, tremors, etc.
* Part 4: Motor complications. This section involves a provider determining how much of an impact the symptoms of Parkinson’s disease are affecting your life. That includes both the amount of time you have certain symptoms each day, and whether or not those symptoms affect how you spend your time.

### **What causes the condition?**

Although there are several recognized risk factors for Parkinson’s disease, such as exposure to pesticides, for now, the only confirmed causes of Parkinson’s disease are genetic. When Parkinson’s disease isn’t genetic, experts classify it as “idiopathic” (this term comes from Greek and means “a disease of its own”). That means they don’t know exactly why it happens.

Many conditions look like Parkinson’s disease but are instead parkinsonism (which refers to Parkinson’s disease-like conditions) from a specific cause like some psychiatric medications.

#### **Familial Parkinson’s disease**

Parkinson’s disease can have a familial cause, which means you can inherit it from one or both of your parents. However, this only makes up about 10% of all cases.

Experts have linked at least seven different genes to Parkinson’s disease. They’ve linked three of those to early onset of the condition (meaning at a younger-than-usual age). Some genetic mutations also cause unique, distinguishing features.

#### **Idiopathic Parkinson’s disease**

Experts believe idiopathic Parkinson’s disease happens because of problems with how your body uses a protein called α-synuclein (alpha sy-nu-clee-in). Proteins are chemical molecules that have a very specific shape. When some proteins don’t have the correct shape — a problem known as protein misfolding — your body can’t use them and can’t break them down.

With nowhere to go, the proteins build up in various places or in certain cells (tangles or clumps of these proteins are called Lewy bodies). The buildup of these Lewy bodies (which doesn’t happen with some of the genetic problems that cause Parkinson’s disease) causes toxic effects and cell damage.

Protein misfolding is common in many other disorders, such as Alzheimer’s disease, Huntington’s disease, multiple forms of amyloidosis and more.

#### **Induced parkinsonism**

There are conditions or circumstances experts have linked to parkinsonism. While these aren’t true Parkinson’s disease, they have similar features, and healthcare providers may consider these causes while diagnosing Parkinson’s disease.

The possible causes are:

* Medications. Several medications can cause a parkinsonism-like effect. The Parkinson's-like effects are often temporary if you stop taking the medication that caused them before the effects become permanent. However, the effects can linger for weeks or even months after you stop taking the medication.
* Encephalitis. Inflammation of your brain, known as encephalitis, can sometimes cause parkinsonism.
* Toxins and poisons. Exposure to several substances, such as manganese dust, carbon monoxide, fumes from welding or certain pesticides, can lead to parkinsonism.
* Damage from injuries. Repeated head injuries, such as those from high-impact or contact sports like boxing, football, hockey, etc., can cause brain damage. The term for this is “post-traumatic parkinsonism.”

### **Is it contagious?**

Parkinson’s disease isn’t contagious, and you can’t contract it from another person.

## Diagnosis and Tests

### **How is it diagnosed?**

Diagnosing Parkinson’s disease is mostly a clinical process, meaning it relies heavily on a healthcare provider examining your symptoms, asking questions and reviewing your medical history. Some diagnostic and lab tests are possible, but these are usually needed to rule out other conditions or certain causes.

But most lab tests aren’t necessary unless you don’t respond to treatment for Parkinson’s disease, which can indicate you have another condition.

### **What tests will be done to diagnose this condition?**

When healthcare providers suspect Parkinson’s disease or need to rule out other conditions, various imaging and diagnostic tests are possible. These include:

* Blood tests (these can help rule out other forms of parkinsonism).
* Computed tomography (CT) scan.
* Genetic testing.
* Magnetic resonance imaging (MRI).
* Positron emission tomography (PET) scan.

#### **New lab tests are possible**

Researchers have found possible ways to test for possible indicators of Parkinson’s disease. Both of these new tests involve the alpha-synuclein protein but test for it in new, unusual ways. While these tests can’t tell you what conditions you have because of misfolded alpha-synuclein proteins, that information can still help your provider make a diagnosis.

The two tests use the following methods.

* Spinal tap. One of these tests looks for misfolded alpha-synuclein proteins in cerebrospinal fluid, which is the fluid that surrounds your brain and spinal cord. This test involves a spinal tap (lumbar puncture), where a healthcare provider inserts a needle into your spinal canal to collect some cerebrospinal fluid for testing.
* Skin biopsy. Another possible test involves a biopsy of surface nerve tissue. A biopsy includes collecting a small sample of your skin, including the nerves in the skin. The samples come from a spot on your back and two spots on your leg. Analyzing the samples can help determine if your alpha-synuclein has a certain kind of malfunction that could increase the risk of developing Parkinson’s disease.

## Management and Treatment

### **How is it treated, and is there a cure?**

For now, Parkinson’s disease isn’t curable, but there are multiple ways to manage its symptoms. The treatments can also vary from person to person, depending on their specific symptoms and how well certain treatments work. Medications are the primary way to treat this condition.

A secondary treatment option is surgery to implant a device that will deliver a mild electrical current to part of your brain (this is known as deep brain stimulation). There are also some experimental options, such as stem cell-based treatments, but their availability often varies, and many aren’t an option for people with Parkinson’s disease.

### **What medications and treatments are used?**

Medication treatments for Parkinson’s disease fall into two categories: Direct treatments and symptom treatments. Direct treatments target Parkinson’s itself. Symptom treatments only treat certain effects of the disease.

#### **Medications**

Medications that treat Parkinson’s disease do so in multiple ways. Because of that, drugs that do one or more of the following are most likely:

* Adding dopamine. Medications like levodopa can increase the available levels of dopamine in your brain. This medication is almost always effective, and when it doesn’t work, that’s usually a sign of some other form of parkinsonism rather than Parkinson’s disease. Long-term use of levodopa eventually leads to side effects that make it less effective.
* Simulating dopamine. Dopamine agonists are medications that have a dopamine-like effect. Dopamine is a neurotransmitter, causing cells to act in a certain way when a dopamine molecule latches onto them. Dopamine agonists can latch on and cause cells to behave the same way. These are more common in younger patients to delay starting levodopa.
* Dopamine metabolism blockers. Your body has natural processes to break down neurotransmitters like dopamine. Medications that block your body from breaking down dopamine allow more dopamine to remain available to your brain. They're especially useful early on and can also help when combined with levodopa in later stages of Parkinson's disease.
* Levodopa metabolism inhibitors. These medications slow down how your body processes levodopa, helping it last longer. These medications may need careful use because they can have toxic effects and damage your liver. They’re most often used to help as levodopa becomes less effective.
* Adenosine blockers. Medications that block how certain cells use adenosine (a molecule used in various forms throughout your body) can have a supportive effect when used alongside levodopa.

Several medications treat specific symptoms of Parkinson’s disease. Symptoms treated often include the following:

* Erectile and sexual dysfunction.
* Fatigue or sleepiness.
* Constipation.
* Sleep problems.
* Depression.
* Dementia.
* Anxiety.
* Hallucinations and other psychosis symptoms.

#### **Deep brain stimulation**

In years past, surgery was an option to intentionally damage and scar a part of your brain that was malfunctioning because of Parkinson’s disease. Today, that same effect is possible using deep-brain stimulation, which uses an implanted device to deliver a mild electrical current to those same areas.

The major advantage is that deep-brain stimulation is reversible, while intentional scarring damage is not. This treatment approach is almost always an option in later stages of Parkinson’s disease when levodopa therapy becomes less effective, and in people who have tremor that doesn’t seem to respond to the usual medications.

#### **Experimental treatments**

Researchers are exploring other possible treatments that could help with Parkinson’s disease. While these aren’t widely available, they do offer hope to people with this condition. Some of the experimental treatment approaches include:

* Stem cell transplants. These add new dopamine-using neurons into your brain to take over for damaged ones.
* Neuron-repair treatments. These treatments try to repair damaged neurons and encourage new neurons to form.
* Gene therapies and gene-targeted treatments. These treatments target specific mutations that cause Parkinson’s disease. Some also boost the effectiveness of levodopa or other treatments.

#### **Complications or side effects possible with treatments**

The complications and side effects that happen with Parkinson’s disease treatments depend on the treatments themselves, the severity of the condition, any other health issues you have, and more. Your healthcare provider is the best person to tell you more about the likely side effects and complications that you might experience. They can also tell you what you can do to minimize how those side effects or complications affect your life.

More about levodopa

The most common and effective treatment for Parkinson’s disease is levodopa. While this medication has greatly improved the treatment of Parkinson’s disease, providers use it cautiously because of how it works. They also commonly prescribe other medications that make levodopa more effective or help with side effects and certain symptoms.

Levodopa is often combined with other medications to keep your body from processing it before it enters your brain. That helps avoid other side effects of dopamine, especially nausea, vomiting and low blood pressure when you stand up (orthostatic hypotension).

Over time, the way your body uses levodopa changes, and levodopa can also lose its effectiveness. Increasing your dose can help with that, but that increases the chance and severity of side effects, and the dose can only go so high before it reaches toxic levels.

### **How can I take care of myself or manage the symptoms?**

Parkinson’s disease isn’t a condition you can self-diagnose, and you shouldn’t try to manage the symptoms without first talking to a healthcare provider.

### **How soon after treatment will I feel better, and how long will it take to recover?**

The time it takes to recover and see the effects of Parkinson’s disease treatments depends strongly on the type of treatments, the severity of the condition and other factors. Your healthcare provider is the best person to offer more information about what you can expect from treatment. The information they give you can consider any unique factors that might affect what you experience.

## Outlook / Prognosis

### **What can I expect if I have this condition?**

Parkinson’s disease is a degenerative condition, meaning the effects on your brain get worse over time. However, this condition usually takes time to get worse. Most people have a normal life span with this condition.

You’ll need little to no help in the earlier stages and can keep living independently. As the effects worsen, you’ll need medication to limit how the symptoms affect you. Most medications, especially levodopa, are moderately or even very effective once your provider finds the minimum dose you need to treat your symptoms.

Most of the effects and symptoms are manageable with treatment, but the treatments become less effective and more complicated over time. Living independently will also become more and more difficult as the disease worsens.

#### **How long does Parkinson’s disease last?**

Parkinson’s disease isn’t curable, which means it’s a permanent, lifelong condition.

#### **What’s the outlook for Parkinson’s disease?**

Parkinson’s disease isn’t fatal, but the symptoms and effects are often contributing factors to death. The average life expectancy for Parkinson’s disease in 1967 was a little under 10 years.

Since then, the average life expectancy has increased by about 55%, rising to more than 14.5 years. That, combined with the fact that Parkinson’s diagnosis is much more likely after age 60, means this condition doesn’t often affect your life expectancy by more than a few years (depending on the life expectancy in your country).

## Prevention

### **How can I reduce my risk or prevent this condition?**

Parkinson’s disease happens for either genetic reasons or unpredictably. Neither is preventable, and you can’t reduce your risk of developing it. There are certain high-risk occupations such as farming and welding, but not everyone in these professions develops parkinsonism.

## Living With

### **How do I take care of myself?**

If you have Parkinson’s disease, the best thing you can do is follow the guidance of your healthcare provider on how to take care of yourself.

* Take your medication as prescribed. Taking your medications can make a huge difference in the symptoms of Parkinson’s disease. You should take your medications as prescribed and talk to your provider if you notice side effects or start to feel like your medications aren't as effective.
* See your provider as recommended. Your healthcare provider will set up a schedule for you to see them. These visits are especially important to help with managing your conditions and finding the right medications and dosages.
* Don’t ignore or avoid symptoms. Parkinson’s disease can cause a wide range of symptoms, many of which are treatable by treating the condition or the symptoms themselves. Treatment can make a major difference in keeping symptoms from having worse effects.

### **When should I see my healthcare provider or when should I seek care?**

You should see your healthcare provider as recommended, or if you notice changes in your symptoms or the effectiveness of your medication. Adjustments to medications and dosages can make a huge difference in how Parkinson’s affects your life.

#### **When should I go to the ER?**

Your healthcare provider can give you guidance and information on signs or symptoms that mean you should go to the hospital or seek medical care. In general, you should seek care if you fall, especially when you lose consciousness or might have an injury to your head, neck, chest, back or abdomen.

## Additional Common Questions

### **How does a person get Parkinson’s disease?**

Experts don’t know how most cases of Parkinson’s disease happen. About 10% of cases are genetic, meaning you inherit them from one or both parents. However, the remaining 90% or so are idiopathic, which means they happen for reasons that are still unknown.

### **What are the early warning signs of Parkinson’s disease?**

Parkinson’s warning signs can be motor (movement-related) symptoms like slow movements, tremors or stiffness. However, they can also be non-motor symptoms. Many of the possible non-motor symptoms can appear years or even decades ahead of motor symptoms. But non-motor symptoms can also be vague, making it difficult to connect them to Parkinson’s disease.

Non-motor symptoms that might be early warning signs include:

* Autonomic nervous system symptoms. These include lightheadedness on standing up (orthostatic hypotension) and constipation.
* Loss of sense of smell (anosmia).
* Sleep problems such as periodic limb movement disorder (PLMD), rapid eye movement (REM) behavior disorder and restless legs syndrome.

### **Is Parkinson’s disease fatal?**

No, Parkinson’s disease isn’t fatal on its own. But it can contribute to other conditions or problems that are sometimes fatal.

### **Can Parkinson’s disease be cured?**

No, Parkinson’s disease isn’t curable. However, it is treatable, and many treatments are highly effective. It might also be possible to delay the progress and more severe symptoms of the disease.

### **A note from Cleveland Clinic**

Parkinson’s disease is a very common condition, and it’s more likely to happen to people as they get older. While Parkinson’s isn't curable, there are many ways to treat this condition. They include several different classes of medications, surgery to implant brain-stimulation devices and more. Thanks to advances in treatment and care, people can live for years or even decades with this condition and can adapt to or receive treatment for the effects and symptoms.

# Multiple Sclerosis (MS)

Multiple sclerosis (MS) damages the protective cover around nerves called myelin in your central nervous system. It can cause muscle weakness, vision changes, numbness and memory issues. While there isn’t a cure, treatment options can help you manage symptoms and slow disease progression.

### **What is multiple sclerosis?**

Multiple sclerosis (MS) is an autoimmune condition that affects your brain and spinal cord (central nervous system).

With MS, your immune system mistakenly attacks myelin cells. These are the protective covers (sheaths) that surround your brain and spinal cord nerves. Myelin sheath damage interrupts messages (signals) that your nerves send throughout your body to perform functions like vision, sensation and movement.

Myelin damage can occur in your brain, spinal cord and nerves that supply your eyes. There’s no cure for MS, but treatment is available to help minimize ongoing damage and help you manage symptoms.

#### **What are the types of multiple sclerosis?**

There are four types of multiple sclerosis. You can think of the types as a way for your provider to describe your symptoms, instead of being four different conditions:

* Clinically isolated syndrome (CIS). This is when you have the first episode of symptoms suggestive of MS, but don’t meet the criteria for having MS, healthcare providers often categorize it as CIS. Inflammation and myelin damage cause your symptoms. CIS may develop into multiple sclerosis.
* Relapsing-remitting multiple sclerosis (RRMS). This is the most common way that multiple sclerosis begins — an estimated 85% of people diagnosed with MS have this type. MS causes flare-ups (relapses or attacks) of new or old symptoms. Periods of remission follow (when symptoms stabilize or go away).
* Secondary progressive multiple sclerosis (SPMS). In many cases, RRMS eventually progresses to SPMS. In the secondary progressive stage of multiple sclerosis, nerve damage accumulates and symptoms gradually worsen. You may still experience some relapses or flares, but periods of remission (when symptoms stabilize or go away) are less likely to happen.
* Primary progressive multiple sclerosis (PPMS). In some cases, MS symptoms may start off slowly and gradually worsen over time from the very beginning, without any periods of clear relapses or remission.

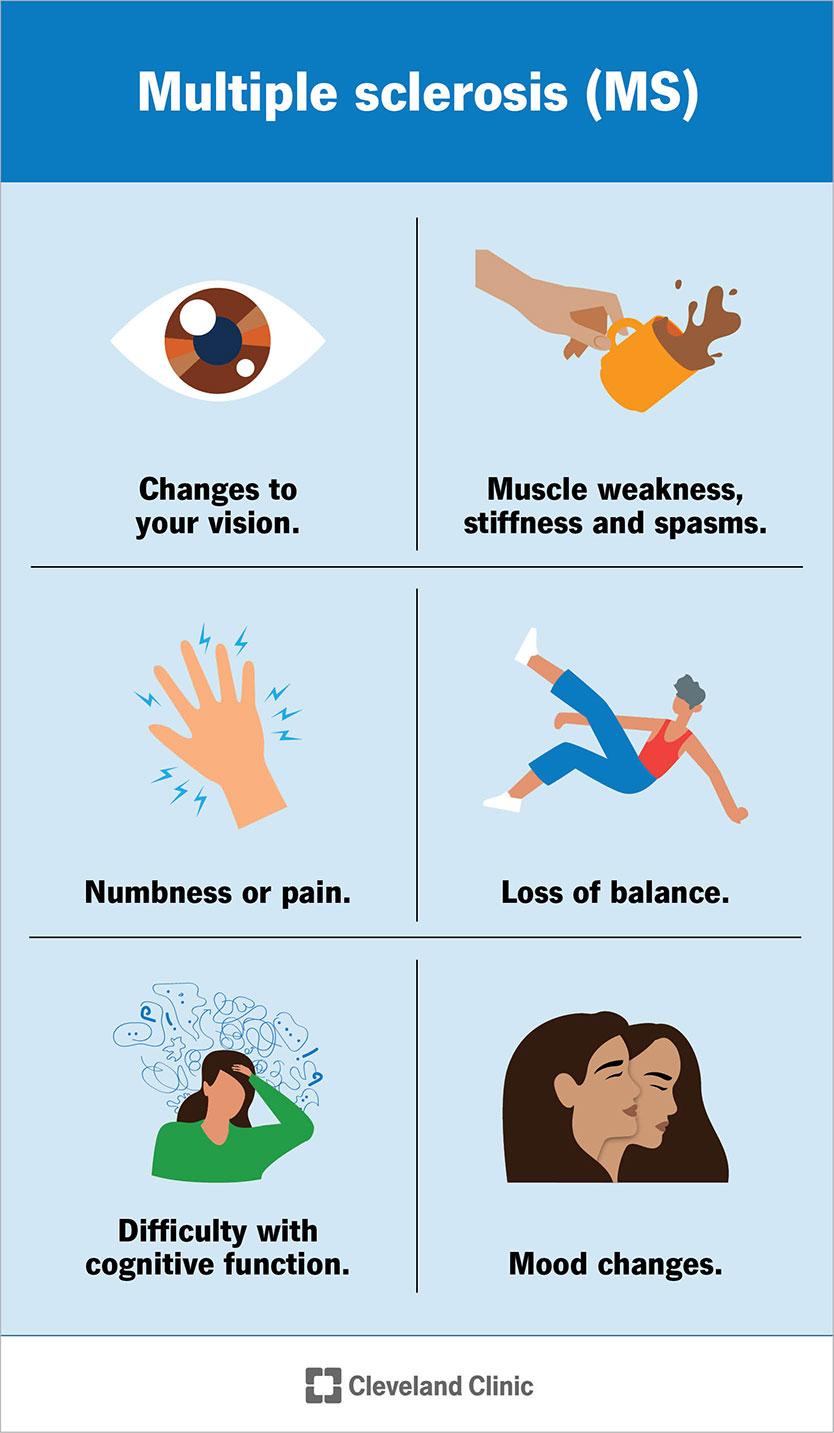
Three rare MS variants include:

* Tumefactive multiple sclerosis. A characterization of this variant of MS is the formation of large areas of demyelination in your brain, which may appear similar to tumors. Often, a sample of brain tissue is needed to differentiate this from other issues, like brain cancers.
* Balo’s concentric sclerosis. A characteristic of this variant of MS is lesions with the appearance of concentric rings (in the shape of a target) of myelin damage appearing on an MRI, which gives this condition its name.
* Marburg variant multiple sclerosis. This is a very rare and aggressive form of MS characterized by rapid progression, which may result in death when left untreated.

#### **How common is multiple sclerosis?**

Studies show that there are almost 1 million adults in the U.S. living with multiple sclerosis.

## Symptoms and Causes

****Multiple sclerosis symptoms affect your brain, spinal cord and eyes.

### **What are the early symptoms of multiple sclerosis?**

Early signs and symptoms of MS include:

* Changes to your vision (optic neuritis, double vision, vision loss)
* Muscle weakness (usually affecting one side of your face or body, or below your waist)
* Numbness or abnormal sensations (usually affecting one side of your face or body, or below your waist)

### **What are the symptoms of multiple sclerosis?**

Common symptoms of MS include:

* Fatigue
* Clumsiness
* Dizziness
* Difficulty with bladder regulation
* Loss of balance and coordination
* Difficulty with cognitive function (thinking, memory, concentration, learning and judgment)
* Mood changes
* Muscle stiffness and muscle spasms (tremors)

These symptoms vary from person to person and may fluctuate in severity from one day to the next. You may have a few of these symptoms, but it’s unlikely you’ll experience all of them at once.

#### **Do you ever feel normal with MS?**

This can be challenging to predict because everyone perceives “normal” in their own way. With MS, you may have periods of remission where your symptoms go away, and you feel more like yourself. You might even forget you have MS until symptoms flare up (return) again. This feeling of normalcy, and the degree of normalcy, can vary by type and stage.

### **What causes MS?**

Demyelination, or the destruction of myelin, causes multiple sclerosis. Myelin is a protective cover (sheath) around nerve cells (neurons) in your brain and spinal cord. It moves messages (signals) between your brain and the rest of your body to control functions like vision, sensation and movement.

Your immune system’s job is to protect your body from things that can harm it, like bacteria or viruses. With MS, your immune system becomes overactive and mistakes healthy myelin (and sometimes, the nerve cells below the myelin) as a threat to your body. Your immune system’s attack on the healthy myelin damages it. This is demyelination.

On an imaging test (an MRI), your provider can find evidence of myelin damage. They may refer to it as a scar, lesion or plaque. Messages don’t pass between nerve cells easily where there is myelin damage, which leads to the development of MS symptoms.

Experts aren’t sure why some people develop MS. Research suggests the following may contribute to an elevated risk of developing MS:

* Smoking
* Toxin exposure, like secondhand smoke and pesticides
* Low levels of vitamin D
* Exposure to a virus (Epstein-Barr virus or mononucleosis)
* Obesity during childhood
* Genetic predisposition (someone in your biological family has the condition or carries genes, which can lead to you being more susceptible to developing the disease)

#### **What are the risk factors for multiple sclerosis?**

You may be more at risk of MS if you:

* Are between the ages 20 and 40
* Are of Northern European descent
* Are female

MS can affect anyone. Rarer cases can affect children.

### **What are the complications of multiple sclerosis?**

Worsening or progressive symptoms of MS may lead to complications such as:

* Difficulty walking without assistance
* Loss of bowel or bladder control
* Memory loss
* Sexual dysfunction
* Depression and anxiety

## Diagnosis and Tests

### **How is multiple sclerosis diagnosed?**

There isn’t a single diagnostic tool available to pinpoint the condition. Instead, a provider will diagnose MS after a physical exam, a neurological exam and testing.

During an exam, your provider will learn more about your symptoms and medical history. Testing may include blood work, MRIs of your brain and spinal cord, and an analysis of your spinal fluid.

It can take time before you receive an official MS diagnosis. You may need to make several trips to see your provider before you know for sure. This happens because MS symptoms can look like or happen with several other common conditions. While the delay in an official diagnosis can be frustrating, getting the right diagnosis helps your provider accurately treat your symptoms.

#### **What tests diagnose multiple sclerosis?**

Diagnostic testing helps your provider rule out conditions with similar symptoms to MS. Testing may include:

* Blood tests and urine tests
* Magnetic resonance imaging test (MRI)
* Optical coherence tomography (OCT) test
* Lumbar puncture
* Evoked potential (EP) test

#### **Who diagnoses MS?**

If your primary care provider suspects you may have MS, they may refer you to see a neurologist. A neurologist is a doctor who specializes in treating conditions that affect the nervous system, which includes your brain and spinal cord.

## Management and Treatment

### **Is there a cure for multiple sclerosis?**

There isn’t currently a cure for MS.

### **How is multiple sclerosis treated?**

Multiple sclerosis treatment focuses on minimizing further damage, managing symptoms and preventing complications. Your treatment plan may include:

* Medications
* Physical, occupational or speech therapy
* Mental health counseling

Other types of symptom management vary based on how the condition affects you. Management may include:

* Wearing glasses or taking medications for vision symptoms
* Deep brain stimulation for muscle spasms (tremors)
* Using assistive mobility devices like a cane, walker or wheelchair
* Antiseizure medications or antispasmodic medications (gabapentin or nortriptyline) for pain
* Medications like donepezil for cognitive symptoms
* Alternative therapies like acupuncture and yoga

Your healthcare provider may recommend plasma exchange (plasmapheresis) if your body doesn’t respond well to certain medications during an MS attack. This is more effective in minimizing damage from an ongoing attack as opposed to preventing additional attacks in the long term.

Your provider can also discuss if any clinical trials are available to participate in. Clinical trials are tests of new medications or uses of existing medications on humans to find new treatment options for MS and other conditions.

#### **Multiple sclerosis medications**

Medications for multiple sclerosis can reduce relapses (periods when symptoms worsen or new symptoms develop) and the development of new lesions/scars, and slow the disease’s progression. Common types of medications for MS include:

* Disease-modifying therapies (DMTs). DMTs reduce how often you have relapses, slow down MS progression, and prevent new lesions from forming on your brain and spinal cord. Several medications have U.S. Food and Drug Administration (FDA) approval for long-term MS treatment.
* Relapse management medications. For severe symptom attacks, corticosteroids (like methylprednisolone) quickly reduce inflammation by suppressing your immune system. These medications can speed up your recovery time after an attack. They also slow damage to the myelin sheath surrounding your nerve cells. Your provider may give you this medication into a vein in your arm through an IV (intravenously). Other short-term treatments for severe attacks include IV immunoglobulin therapy or plasma exchange.

DMTs for MS

Common disease-modifying therapies (DMTs) for MS and their administration types include:

* Injections into your skin: Beta interferon, glatiramer acetate or ofatumumab
* Infusions into a vein (IV): Alemtuzumab, natalizumab, rituximab, ocrelizumab or ublituximab
* Oral medications (taken by mouth): Cladribine, dimethyl fumarate, diroximel fumarate, monomethyl fumarate, fingolimod, siponimod, ponesimod, ozanimod or teriflunomide
* Stem cell transplant

## Outlook / Prognosis

### **What’s the outlook for multiple sclerosis?**

Multiple sclerosis is a lifelong condition without a cure. However, available treatment options are very effective in helping manage symptoms and minimizing the frequency of flare-ups. Regardless of treatment, MS can lead to disability and make it difficult to do routine things without assistance over time. Your care team is available to help you throughout your MS journey, to take steps to prevent complications and improve your quality of life.

### **Does multiple sclerosis affect your life expectancy?**

You can expect to have a normal life expectancy with MS. Older studies have shown that MS can take up to 10 years off of your life expectancy, but advances in treatment options have significantly improved this outlook. Only in very rare cases is MS fatal.

## Prevention

### **Can multiple sclerosis be prevented?**

There isn’t a known way to prevent MS.

#### **How can I lower my risk of multiple sclerosis symptom flare-ups?**

Disease-modifying therapies are the most effective way to reduce the number of flare-ups (also called relapses or attacks) you experience.

Leading a healthy lifestyle is also important. The choices you make can help slow disease progression. Your provider may recommend the following to stay healthy:

* Eating nutritious meals
* Getting enough sleep
* Participating in physical activities regularly
* Not using tobacco products

Coping with a chronic condition can be emotionally challenging. MS can sometimes affect your mood and memory. Working with a neuropsychologist or a mental health provider is an essential part of managing the condition long term.

## Living With

### **Can a person with MS live a normal life?**

Yes. MS can be a challenging condition to diagnose and manage, but your care team will help you every step of the way. Despite having a condition without a cure, you can still lead a fulfilling and active life with MS. Support is available to help you maximize your function both physically and mentally, from medications to therapy. There are even support groups you can join to help you connect with people who share a similar experience.

### **When should I see a healthcare provider?**

You should contact a healthcare provider if you experience the following:

* Feeling overly sensitive to heat
* Feeling unsteady or off balance
* Difficulty remembering things
* Numbness or tingling, especially in your arms or legs
* Sudden vision changes
* Weakness in your arms or legs

Let your healthcare provider know if you have MS and experience new or worsening symptoms.

### **What questions should I ask my healthcare provider?**

You may want to ask your healthcare provider:

* What kind of treatment do you recommend?
* How often should I participate in physical therapy?
* Are there side effects of the medications you prescribed?
* When and how often should I take medications?
* What symptoms should I look out for?
* Can you offer advice on how to maintain good health?
* Can you recommend any support groups?

# Dementia

Dementia is a general term that represents a group of diseases and illnesses that affect your thinking, memory, reasoning, personality, mood and behavior. The decline in mental function interferes with your daily life and activities. It’s estimated that about 50% of people age 85 and older have dementia. Current medications may help slow the mental decline.

## What is Dementia?

Learn more about living with Alzheimer's disease.

Dementia is a description of the state of a person’s mental function and not a specific disease.

Dementia entails a decline in mental function from a previously higher level that’s severe enough to interfere with daily living. A person with dementia has two or more of these specific difficulties, including a decline in:

* Memory.
* Reasoning.
* Language.
* Coordination.
* Mood.
* Behavior.

Dementia develops when the parts of your brain involved with learning, memory, decision-making or language are affected by infections or diseases. The most common cause of dementia is Alzheimer’s disease.

But other known causes of dementia include:

* Vascular dementia.
* Dementia with Lewy bodies.
* Frontotemporal dementia.
* Mixed dementia.
* Dementia due to Parkinson’s disease.
* Dementia-like conditions due to reversible causes, such as medication side effects or thyroid problems.

### **What’s the difference between dementia and Alzheimer’s disease?**

Dementia is a description of the state of a person’s mental function and not a specific disease. Dementia is an “umbrella category” describing mental decline that’s severe enough to interfere with daily living.

There are many underlying causes of dementia, including Alzheimer’s disease and Parkinson’s disease. Alzheimer’s disease is the most common underlying cause of dementia.

### **Who gets dementia?**

Dementia is considered a late-life disease because it tends to develop mostly in people who are older.

About 5% to 8% of all people over the age of 65 have some form of dementia, and this number doubles every five years above that age. It’s estimated that as many as half of people 85 years of age and older have dementia.

The number of people age 65 and older who have Alzheimer’s disease and related dementias by race is:

* Blacks: 14%
* Hispanics: 12%
* Non-Hispanic whites: 10%
* American Indian and Alaska Natives: 9%
* Asian and Pacific Islanders: 8%

### **How common is dementia?**

The U.S. Centers for Disease Control and Prevention (CDC) estimate that 5 million U.S. adults age 65 or older have Alzheimer’s and related dementia. By 2060, the CDC projects that about 14 million people will have dementia, which is about 3.3% of the population.

Alzheimer’s disease is the sixth leading cause of death in the U.S. and the fifth leading cause of death in Americans age 65 and older.

### **Does memory loss mean dementia is starting?**

One common misbelief about memory loss is that it always means you or a loved one has dementia. There are many causes of memory loss. Memory loss alone doesn’t necessarily confirm a diagnosis of dementia.

It’s also true that some memory changes are normal as a person ages (some neurons in your brain naturally die as we age). However, this type of memory loss isn’t functionally disabling; meaning, it doesn’t interfere with daily life.

Dementia interferes with your ability to function. Dementia isn’t forgetting where you left your keys. A person with dementia can have situations like forgetting what keys are used for. Dementia isn’t a normal part of aging.

### **Are there different types of dementia?**

Dementias can be divided into three groups:

* Primary (diseases and conditions in which dementia is the main illness).
* Secondary (dementia due to another disease or condition).
* Reversible dementia-like symptoms caused by other illnesses or causes.

#### **Primary dementia**

Types of primary dementia include:

* Alzheimer’s disease: This is the most common type of dementia. Two abnormal proteins build up in your brain: tau and amyloid proteins. These proteins disrupt communication between nerve cells in your brain. Nerve cells die, starting in one area and spreading as more nerve cells die in other areas. Symptoms include short-term memory loss, confusion, personality and behavior changes. Trouble talking, remembering distant memories and issues with walking happen later in the disease. Alzheimer’s disease mainly affects adults who are older — up to 10% of those over age 65 and about 50% of people older than 85 have the disease. Family history is an important risk factor. Approximately 60% to 80% of people with dementia have this type.
* Vascular dementia: This is the second most common type of dementia. It’s caused by conditions such as strokes or atherosclerosis, which block and damage blood vessels in your brain. Symptoms include memory problems, confusion and trouble concentrating and completing tasks. The decline may appear suddenly (following a major stroke) or in steps (following a series of mini strokes). Risk factors include high blood pressure, diabetes, and high cholesterol levels. About 15% to 25% of people with dementia have vascular dementia.
* Lewy body dementia: This condition involves the buildup of clumps of proteins — called Lewy bodies — in your brain’s nerve cells. Lewy bodies damage nerve cells. Symptoms include movement and balance problems, changes in sleep patterns, memory loss, planning and problem-solving difficulties, and visual hallucinations and delusions. About 5% to 10% of dementias are Lewy Body dementia.
* Frontotemporal dementia (FTD): This dementia results from damage to the frontal and temporal lobes of your brain. The damage is caused by the buildup of abnormal proteins in these areas. It causes changes in social behavior, personality, and/or loss of language skills (speaking, understanding or forgetting the meaning of common words) or motor coordination. FTD is a common cause of early dementia, often occurring in people between the ages of 45 and 64. Between 5% and 6% of all dementias are FTD.
* Mixed dementia: This is a combination of two or more types of dementia. The most common combination is Alzheimer’s disease with vascular dementia. It’s most common in people 80 years of age and over. It’s often hard to diagnose because symptoms of one dementia may be more obvious and/or many symptoms of each type overlap. The decline is faster in people who have mixed dementia compared with those who only have one type.

#### **Dementia due to other diseases and conditions**

Other causes of dementia include:

* Huntington’s disease: A single defective gene causes this brain disorder. The disease causes a breakdown in your brain’s nerve cells, which causes body movement control problems, as well as thinking, decision-making, and memory trouble, and personality changes.
* Parkinson’s disease: Many people in the later stages of Parkinson’s disease develop dementia. Symptoms include trouble with thinking and memory, hallucinations and delusions, depression and trouble with speech.
* Creutzfeldt-Jakob disease: This rare infective brain disease affects about only 1 in 1 million people. An abnormal protein in your brain called prions causes the disease. These prions clump together and cause nerve cell death in your brain. Symptoms include problems with thinking, memory, communication, planning and/or judgment, confusion, behavior changes, agitation and depression.
* Wernicke-Korsakoff syndrome: This brain disorder is caused by a severe thiamine (vitamin B1) deficiency. This can result in bleeding in key areas related to memory in your brain. It’s most commonly caused by alcohol use disorder but can also be due to malnutrition and chronic infection. Symptoms include double vision, loss of muscle coordination, and difficulty processing information, learning new skills and remembering things.
* Traumatic brain injury: Repeated blows to your head can cause this injury. It’s most often seen in football players, boxers, soldiers and people who’ve had a vehicle accident. Dementia symptoms, which appear years later, include memory loss, behavior or mood changes, slurred speech and headaches.

#### **Dementias due to reversible causes**

Some conditions can cause dementia-like symptoms that can be reversed with treatment, including:

* Normal pressure hydrocephalus (NPH): This condition happens when cerebrospinal fluid (CSF) builds up in your brain’s spaces (ventricles). The excess buildup harms your brain. NPH can be caused by a brain infection, brain injury, brain bleed or previous brain surgery. Symptoms include poor balance, forgetfulness, trouble paying attention, mood swings, frequent falls and loss of bladder control. Your healthcare provider can drain excess fluid through the surgical placement of a shunt (tube).
* Vitamin deficiency: Not getting enough vitamin B1, B6, B12 cooper and vitamin E in your diet can cause dementia-like symptoms.
* Infections: Infections that can cause dementia-like symptoms include HIV infection, syphilis and Lyme disease. Symptoms reported with COVID-19 infection include “brain fog” and acute delirium. Because of the inflammation and stroke risk seen with COVID-19 infection, both short- and long-term cognitive effects are being investigated. Urinary tract infections (UTIs) and infections in your lungs in the elderly can also result in dementia-like symptoms. Other central nervous system infections and brain infections caused by fungi, bacteria and parasites can also cause cognitive symptoms.
* Metabolic and endocrine conditions: Conditions that can mimic dementia include Addison’s disease, Cushing’s disease, low blood sugar (hypoglycemia) exposure to heavy metals (like arsenic or mercury), high calcium levels (hypercalcemia, often due to hyperparathyroidism), liver cirrhosis and thyroid problems.
* Medication side effects: Some medications, in some people, can mimic dementia symptoms. These include sleeping pills, anti-anxiety drugs, antidepressants, anti-seizure drugs, antiparkinson drugs, nonbenzodiazepine sedatives, narcotic pain relievers, statins and others. Ask your healthcare provider to review your medications if you have any dementia-like symptoms.
* Other causes: Other causes of dementia-like symptoms include brain tumors and subdural hematomas (brain bleeds between your brain’s surface and the covering over your brain).

## Symptoms and Causes

### **What are the symptoms of dementia?**

Early symptoms of dementia include:

* Forgetting recent events or information.
* Repeating comments or questions over a very short period.
* Misplacing commonly used items or placing them in unusual spots.
* Not knowing the season, year or month.
* Having difficulty coming up with the right words.
* Experiencing a change in mood, behavior or interests.

Signs that dementia is getting worse include:

* Your ability to remember and make decisions further declines.
* Talking and finding the right words becomes more difficult.
* Daily complex tasks, such as brushing your teeth, making a cup of coffee, working a TV remote, cooking and paying bills become more challenging.
* Lessening of rational thinking and behavior and your ability to problem-solve.
* Sleeping pattern changes.
* Increases or worsening of anxiety, frustration, confusion, agitation, suspiciousness, sadness and/or depression.
* Needing more help with activities of daily living, such as grooming, toileting, bathing and eating.
* Experiencing hallucinations (seeing people or objects that aren’t there).

These symptoms are general symptoms of dementia. Each person diagnosed with dementia has different symptoms, depending on what area of their brain is damaged. Additional symptoms and/or unique symptoms occur with specific types of dementia.

### **What are the causes of dementia?**

Dementia is caused by damage to your brain. Dementia affects your brain’s nerve cells, which destroys your brain’s ability to communicate with its various areas. Dementia can also result from blocked blood flow to your brain, depriving it of needed oxygen and nutrients. Without oxygen and nutrients, brain tissue dies.

Damage to your brain results in different symptoms, depending on the area of your brain affected. Some dementias aren’t reversible and will worsen over time. Other dementias are due to other medical conditions that also affect your brain. Another group of health issues can result in dementia-like symptoms. Many of these conditions are treatable, and the dementia symptoms are reversible.

All of the possible causes of dementia are discussed in the question, “Are there different types of dementia?”

## Diagnosis and Tests

### **How is dementia diagnosed?**

Confirming a diagnosis of dementia can be difficult. Many diseases and conditions can cause or lead to dementia. In addition, many of its symptoms are common to many other illnesses.

Your healthcare provider will:

* Ask about the course of your symptoms.
* Ask about your medical history.
* Review your current medications.
* Ask about your family history of disease including dementia.

They may also order tests, including laboratory tests, imaging tests and neurocognitive tests (thinking tests).

Neurologists and geriatricians may assist in making the diagnosis of dementia.

#### **Laboratory tests**

Laboratory tests rule out other diseases and conditions as the cause of dementia, such as infection, inflammation, underactive thyroid and vitamin deficiency (especially B12).

Sometimes, healthcare providers order cerebrospinal fluid tests to evaluate autoimmune conditions and neurodegenerative diseases, if warranted.

#### **Imaging tests**

Your healthcare provider may order the following imaging tests of your brain:

* Computed tomography (CT) and magnetic resonance imaging (MRI): CT uses X-rays and a computer to show detailed images of your brain. MRI uses magnets, radio frequencies and a computer to create detailed images of your brain. These imaging tests look for evidence of stroke, bleeding, tumors and fluid on your brain.
* FDG-PET scan: This is a special type of brain scan that aids in determining brain function and cognitive decline by the pattern of how a type of glucose is absorbed by brain tissue, and is sometimes needed in specific diagnoses.

#### **Neurocognitive testing**

During neurocognitive testing, your healthcare provider uses written and computerized tests to evaluate your mental abilities, including:

* Problem solving.
* Learning.
* Judgment.
* Memory.
* Planning.
* Reasoning.
* Language.

#### **Psychiatric evaluation**

A mental health professional may check for signs of depression, mood changes or other mental health issues that might cause memory loss.

## Management and Treatment

### **Is dementia treatable?**

First, it’s important to understand the terms “treatable,” “reversible” and “curable.” All or almost all forms of dementia are treatable, in that medication and other measures can help manage your symptoms. However, most types of dementia can’t be cured or reversed, and treatments provide only modest benefits.

Fortunately, some types of dementia, like those brought on by treatable causes, may be successfully reversed. These dementia-like symptoms are caused by:

* Side effects of medications, illicit drugs or alcohol.
* Tumors that can be removed.
* Subdural hematoma (a buildup of blood beneath the outer covering of your brain that’s caused by a head injury).
* Normal pressure hydrocephalus (a buildup of cerebrospinal fluid in your brain).
* Metabolic disorders, such as a vitamin B12 deficiency.
* Hypothyroidism, a condition that results from low levels of thyroid hormones.
* Hypoglycemia (low blood sugar).
* Depression.

Dementias that aren’t reversible may still partially respond to medications that treat memory loss or behavior problems. These dementias include:

* Alzheimer's disease.
* Multi-infarct (vascular) dementia.
* Dementias associated with Parkinson's disease and similar disorders.
* AIDS dementia complex.
* Creutzfeldt-Jakob disease.

### **What medications are available to manage dementia?**

Drugs approved for the most common form of dementia, Alzheimer’s disease, include:

* Cholinesterase inhibitors, including donepezil (Aricept®), rivastigmine (Exelon®) and galantamine (Razadyne®).
* NMDA receptor antagonist memantine (Namenda®).
* Anti-amyloid antibody aducanumab (Aduhelm®).

Healthcare providers use these drugs to treat people with some of the other forms of dementia.

Cholinesterase inhibitors and the NMDA receptor antagonist affect different chemical processes in your brain. Both drug classes have been shown to provide some benefit in improving or stabilizing memory function in some people with dementia.

Cholinesterase inhibitors manage the chemicals in your brain that allow messages to be sent between brain cells, which is needed for proper brain function. (Connections are lost as brain cells die when dementia worsens.) Memantine works similarly to cholinesterase inhibitors except it works on a different chemical messenger and helps the nerve cells survive longer.

Aducanumab targets amyloid proteins, which build up into the plaques seen in the brains of people with Alzheimer’s disease.

Although none of these drugs appear to stop the progression of the underlying disease, they may slow it down.

If other medical conditions are causing dementia or co-exist with dementia, healthcare providers prescribe the appropriate drugs used to treat those specific conditions. These other conditions include sleeping problems, depression, hallucinations and agitation.

## Outlook / Prognosis

### **Is there a cure for dementia?**

Unfortunately, there isn’t a cure for the most common types of dementia. Currently, approved medications can, at best, slow the decline.

### **What are the possible complications of dementia?**

Your brain controls all of your body’s functions. When your brain functions decline, your overall health is eventually at risk. Many illnesses and conditions can happen as a result of having dementia.

Possible complications of dementia include:

* Dehydration and malnutrition.
* Bedsores (pressure ulcers).
* Injuries and bone fractures from falls.
* Strokes.
* Heart attacks.
* Kidney failure.
* Pneumonia and aspiration pneumonia (food particles are inhaled into your lung and cause infection).
* Sepsis (infection).

### **What can I expect if I have dementia?**

Getting a diagnosis of dementia is certainly difficult to hear. Several types of dementia aren’t reversible. Others are a side effect of other serious diseases. Some dementia-like symptoms are due to conditions that can be treated and reversed.

Your healthcare team, which will probably include a neurologist and/or a geriatric-psychiatrist or a geriatrician, will order the needed tests to make the correct diagnosis. The medications available today focus on slowing the decline.

The goal is to maintain your or your loved one’s quality of life. Some people with Alzheimer’s dementia can live up to two decades, but each person has their own unique course. Researchers continue learning about the mechanisms that cause dementia and testing different methods to slow, and someday, hopefully, cure this disease.

## Prevention

### **Can dementia be prevented?**

Although dementia can’t be prevented, living a health-focused life might reduce risk factors for certain types of dementia.

Keeping blood vessels clear of cholesterol buildup, maintaining normal blood pressure, maintaining healthy blood sugar levels, staying at a healthy weight — basically, staying as healthy as you can — can keep your brain fueled with the oxygen and nutrients it needs to function at its highest possible level. Specific healthful steps you can take include:

* Stop smoking.
* Follow a Mediterranean diet, which is one filled with whole grains, vegetables, fruits, fish and shellfish, nuts, beans, olive oil and only limited amounts of red meats.
* Exercise. Get at least 30 minutes of exercise most days of the week.
* Keep your brain engaged. Solve puzzles, play word games and try other mentally stimulating activities. These activities may delay the start of dementia.
* Stay socially active. Interact with people, discuss current events, and keep your mind, heart and soul engaged.

### **What are the risk factors for dementia?**

Risk factors for dementia include:

* Age: This is the strongest risk factor. Your chance of dementia increases as you age. Most cases affect people over the age of 65.
* Family history: If you have biological parents or siblings with dementia, you’re more likely to develop dementia.
* Down syndrome: If you have Down syndrome, you’re at risk of developing early-onset Alzheimer’s disease by middle age.
* Poor heart health: If you have high cholesterol levels, high blood pressure, atherosclerosis or smoke, you increase your risk of dementia. These health problems, as well as diabetes, affect your blood vessels. Damaged blood vessels can lead to reduced blood flow and strokes.
* Race and ethnicity: If you’re a Black person, you have twice the risk as a white person for developing dementia. If you’re a Hispanic person, you’re 1.5 times more likely than a white person to develop dementia.
* Brain injury: If you’ve had a severe brain injury, you’re at a higher risk for dementia.

## Living With

### **When should I see my doctor about dementia?**

Make an appointment with your healthcare provider if you or your friends and family see changes in:

* Your memory.
* Your mental functioning.
* Your ability to perform everyday tasks.
* Your behavior.
* Your personality.

### **What happens to a person’s brain and body as dementia gets worse?**

Unfortunately, many types of dementia are conditions that worsen over time. When your brain doesn’t get the nutrients and oxygen it needs, or “junk” (abnormal proteins) blocks needed communication between the nerve cells of the brain, your brain tissue begins to die.

Alzheimer’s disease and other types of dementia usually begin with memory loss or lapses in judgment — things that can be lived with for a while. As you lose more and more brain function, functions vital to life begin to be affected. Vital functions include breathing, digestion, heart rate and sleep.

In the late stages of dementia, people can’t perform the tasks needed to keep their bodies alive. Brain damage and muscle weakness no longer allow even simple, needed movements. You can’t communicate, walk, talk, control your bladder or bowels, feed yourself, or chew or swallow food without help.

When you can’t care for yourself, move about, eat or drink enough to keep yourself hydrated and nourished, plus have mental decline, you leave yourself vulnerable to other illnesses. Pneumonia is one of these commonly seen illnesses in people with dementia. With a now frail body, a person may not be able to fight infections or even benefit from medication. The person’s pain and discomfort may outweigh treatment options that can only offer a short-term benefit.

At this point, many families choose hospice for end-of-life care. Hospice provides comfort care, with a focus on your quality of life over life-extending measures. Many people who pass away from a dementia-related condition don’t have that listed on their death certificate. This is because the complication from which they die — pneumonia, for example — is listed instead. Another reason may be that many people were never officially diagnosed with a dementia condition before they passed away.

### **What's the life expectancy of a person with dementia?**

There’s no easy way to answer this question. Dementia is an “umbrella” term that covers the many different types of underlying neurodegenerative diseases.

Each type of neurodegenerative disease has its own unique pattern and development in each person. Also, each person has a unique health profile. Some people may be relatively healthy and others may have several co-existing health issues. All of these factors play a role in the pace of decline in a person with dementia.

To answer more broadly, Alzheimer’s is the most common type of dementia. The average lifespan after the earliest symptoms is eight years. However, some people have lived as long as 20 years after an Alzheimer’s disease diagnosis.

## Additional Common Questions

### **Are there stages of dementia?**

No national dementia-related organizations define dementia by numerical stages. The Alzheimer’s Association does, however, define three stages of Alzheimer’s disease. Alzheimer’s disease dementia is the most common type of dementia. Some of the symptoms in these three stages are the same as symptoms for many of the forms of dementia.

#### **Early-stage Alzheimer’s disease (mild)**

People in the mild stage of Alzheimer’s disease are still able to function on their own. They may still drive, go to work and socialize. Some changes are happening that may or may not be noticed by the person with Alzheimer’s disease, but may be noticeable by close friends and family members.

Difficulties may include:

* Trouble remembering a person’s name after being introduced.
* Losing or misplacing multiple objects.
* Having a hard time coming up with the right word consistently.
* Trouble planning, organizing, managing or completing tasks.
* Consistently forgetting what you just read.

#### **Middle-stage Alzheimer’s disease (moderate)**

People in the middle stage of Alzheimer’s disease can be in this stage for many years. They can take part in everyday activities with help. Symptoms are more obvious.

Difficulties may include:

* Confusion about what year/season it is or where you are.
* Forgetting events and being unable to recall personal history (phone number, address, the college you attended, etc.).
* Changes in personality, mood and behavior, such as becoming suspicious, delusional and performing compulsive, repetitive actions.
* Changes in day/night sleeping patterns.
* Controlling your bladder and/or bowels.
* Wearing clothes for the wrong season or occasion.
* Wandering and becoming lost.

#### **Late-stage Alzheimer’s disease (severe)**

People in the late stage of Alzheimer’s disease can’t carry on conversations, lose awareness of what’s going on around them and can’t control their movement.

Difficulties may include:

* Trouble communicating, which may include only being able to say a few words or phrases.
* Trouble walking.
* Trouble swallowing.
* Being more prone to infections, especially pneumonia.
* Requiring 24-hour assistance with care.