

Recognizing
The National
Bone and Joint Decade
2002–2011

Questions & Answers

about . . .

Gout

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
National Institutes of Health
Public Health Service • U.S. Department of Health and Human Services

For Your Information

This publication contains information about medications used to treat the health condition discussed here. When this publication was printed, we included the most up-to-date (accurate) information available. Occasionally, new information on medications is released.

For updates and for any questions about any medications you are taking, please contact the U.S. Food and Drug Administration at 1-888-INFO-FDA (1-888-463-6322, a toll-free call) or visit their Web site at www.fda.gov.

This booklet is not copyrighted. Readers are encouraged to duplicate and distribute as many copies as needed.

Additional copies of this booklet are available from:

National Institute of Arthritis and Musculoskeletal
and Skin Diseases
NIAMS/National Institutes of Health
1 AMS Circle
Bethesda, MD 20892-3675

You can also find this booklet on the NIAMS Web site at www.niams.nih.gov.

Table of Contents

What Is Gout?	1
What Is Uric Acid?	1
What Are the Four Stages of Gout?	2
What Causes Gout?	4
Who Is Likely to Develop Gout?	6
How Is Gout Diagnosed?	6
How Is Gout Treated?	7
What Can People With Gout Do to Stay Healthy?	9
What Research Is Being Conducted to Help People With Gout?	11
Where Can People Find More Information About Gout?	13
Key Words	15

Information Boxes

When It's Not Gout, It May Be Pseudogout	3
Signs and Symptoms of Gout	7
High-Purine Foods	10

This booklet contains general information about gout. It describes what gout is and how it develops. It also explains how gout is diagnosed and treated. If you have further questions after reading this booklet, you may wish to discuss them with your doctor.

What Is Gout?

Gout is a painful condition that occurs when the bodily waste product uric acid is deposited as needle-like crystals in the joints and/or soft tissues. In the joints, these uric acid crystals cause inflammatory arthritis, which in turn leads to intermittent swelling, redness, heat, pain, and stiffness in the joints.

In many people, gout initially affects the joints of the big toe (a condition called podagra). But many other joints and areas around the joints can be affected in addition to or instead of the big toe. These include the insteps, ankles, heels, knees, wrists, fingers, and elbows. Chalky deposits of uric acid, also known as tophi, can appear as lumps under the skin that surrounds the joints and covers the rim of the ear. Uric acid crystals can also collect in the kidneys and cause kidney stones.

What Is Uric Acid?

Uric acid is a substance that results from the breakdown of purines. A normal part of all human tissue, purines are found in many foods. Normally, uric acid is dissolved in the blood and passed through the kidneys into the urine, where it is eliminated.

If there is an increase in the production of uric acid or if the kidneys do not eliminate enough uric acid from the body, levels of it build up in the blood (a condition called hyperuricemia). Hyperuricemia also may result when a person eats too many high-purine foods, such as liver, dried beans and peas, anchovies, and gravies. Hyperuricemia is not a disease, and by itself it is not dangerous. However, if excess uric acid crystals form as a result of hyperuricemia, gout can develop. The crystals form and accumulate in the joint, causing inflammation.

What Are the Four Stages of Gout?

Literally translated, arthritis means “joint inflammation.” It refers to more than 100 different diseases that affect the joints. Gout accounts for approximately 5 percent of all cases of arthritis. The disease can progress through four stages:

1. **Asymptomatic (without symptoms) hyperuricemia** – In this stage, a person has elevated levels of uric acid in the blood (hyperuricemia), but no other symptoms. Treatment is usually not required.
2. **Acute gout, or acute gouty arthritis** – In this stage, hyperuricemia has caused the deposit of uric acid crystals in joint spaces. This leads to a sudden onset of intense pain and swelling in the joints, which also may be warm and very tender. An acute attack commonly occurs at night and can be triggered by stressful events, alcohol or drugs, or the presence of another illness.

Attacks usually subside within 3 to 10 days, even without treatment, and the next attack may not occur for months or even years. Over time, however, attacks can last longer and occur more frequently.

3. **Interval or intercritical gout** – This is the period between acute attacks. In this stage, a person does not have any symptoms
4. **Chronic tophaceous gout** – This is the most disabling stage of gout. It usually develops over a long period, such as 10 years. In this stage, the disease may have caused permanent damage to the affected joints and sometimes to the kidneys. With proper treatment, most people with gout do not progress to this advanced stage.

When It's Not Gout, It May Be Pseudogout

Gout is sometimes confused with other forms of arthritis because the symptoms – acute and episodic attacks of joint warmth, pain, swelling, and stiffness – can be similar. One form of arthritis often confused with gout is called pseudogout. The pain, swelling, and redness of pseudogout can also come on suddenly and may be severe, closely resembling the symptoms of gout. However, the crystals that irritate the joint are calcium phosphate crystals, not uric acid. Therefore, pseudogout is treated somewhat differently and is not reviewed in this booklet.

What Causes Gout?

A number of risk factors are associated with hyperuricemia and gout. They include:

- **genetics.** Twenty percent of people with gout have a family history of the disease.
- **gender and age.** It is more common in men than in women and more common in adults than in children.
- **weight.** Being overweight increases the risk of developing hyperuricemia and gout because there is more tissue available for turnover or breakdown, which leads to excess uric acid production.
- **alcohol consumption.** Drinking too much alcohol can lead to hyperuricemia, because alcohol interferes with the removal of uric acid from the body.
- **diet.** Eating too many foods that are rich in purines can cause or aggravate gout in some people.
- **lead exposure.** In some cases, exposure to lead in the environment can cause gout.
- **other health problems.** Renal insufficiency, or the inability of the kidneys to eliminate waste products, is a common cause of gout in older people. Other medical problems that contribute to high blood levels of uric acid include:
 - high blood pressure
 - hypothyroidism (underactive thyroid gland)

- conditions that cause an excessively rapid turnover of cells, such as psoriasis, hemolytic anemia, or some cancers
- Kelley-Seegmiller syndrome or Lesch-Nyhan syndrome, two rare conditions in which the enzyme that helps control uric acid levels either is not present or is found in insufficient quantities.
- **medications.** A number of medications may put people at risk for developing hyperuricemia and gout. They include:
 - **diuretics**, such as furosemide (Lasix*), hydrochlorothiazide (Esidrix, Hydro-chlor), and metolazone (Diulo, Zaroxolyn), which are taken to eliminate excess fluid from the body in conditions like hypertension, edema, and heart disease, and which decrease the amount of uric acid passed in the urine
 - **salicylate-containing drugs**, such as aspirin
 - **niacin**, a vitamin also known as nicotinic acid
 - **cyclosporine (Sandimmune, Neoral)**, a medication that suppresses the body's immune system (the system that protects the body from infection and disease). This medication is used in the treatment of some autoimmune diseases, and to prevent the body's rejection of transplanted organs.

* Brand names included in this booklet are provided as examples only, and their inclusion does not mean that these products are endorsed by the National Institutes of Health or any other Government agency. Also, if a particular brand name is not mentioned, this does not mean or imply that the product is unsatisfactory.

- **levodopa (Larodopa)**, a medicine used to support communication along nerve pathways in the treatment of Parkinson’s disease.

Who Is Likely to Develop Gout?

Gout occurs in 8.4 of every 1,000 people. It is rare in children and young adults. Men, particularly those between the ages of 40 and 50, are more likely to develop gout than women, who rarely develop the disorder before menopause. People who have had an organ transplant are more susceptible to gout.

How Is Gout Diagnosed?

Gout may be difficult for doctors to diagnose because the symptoms can be vague, and gout often mimics other conditions. Although most people with gout have hyperuricemia at some time during the course of their disease, it may not be present during an acute attack. In addition, having hyperuricemia alone does not mean that a person will get gout. In fact, most people with hyperuricemia do not develop the disease.

To confirm a diagnosis of gout, a doctor may insert a needle into an inflamed joint and draw a sample of synovial fluid, the substance that lubricates a joint. The joint fluid is placed on a slide and examined under a microscope for uric acid crystals. Their absence, however, does not completely rule out the diagnosis.

Signs and Symptoms of Gout

- hyperuricemia
- presence of uric acid crystals in joint fluid
- more than one attack of acute arthritis
- arthritis that develops in a day, producing a swollen, red, and warm joint
- attack of arthritis in only one joint, often the toe, ankle, or knee

The doctor also may find it helpful to look for uric acid crystals around joints to diagnose gout. Gout attacks may mimic joint infections, and a doctor who suspects a joint infection (rather than gout) may also culture the joint fluid to see whether bacteria are present.

How Is Gout Treated?

With proper treatment, most people who have gout are able to control their symptoms and live productive lives. Gout can be treated with one or a combination of therapies. The goals of treatment are to ease the pain associated with acute attacks, to prevent future attacks, and to avoid the formation of tophi and kidney stones. Successful treatment can reduce discomfort caused by the symptoms of gout, as well as long-term damage to the affected joints. Treatment will help to prevent disability due to gout.

The most common treatments for an acute attack of gout are nonsteroidal anti-inflammatory drugs (NSAIDs) taken orally (by mouth), or corticosteroids, which are taken orally or injected into the affected joint. NSAIDs reduce the inflammation caused by deposits of uric acid crystals, but have no effect on the amount of uric acid in the body. The NSAIDs most commonly prescribed for gout are indomethacin (Indocin) and naproxen (Anaprox, Naprosyn), which are taken orally every day. Corticosteroids are strong anti-inflammatory hormones. The most commonly prescribed corticosteroid is prednisone. Patients often begin to improve within a few hours of treatment with a corticosteroid, and the attack usually goes away completely within a week or so.

When NSAIDs or corticosteroids do not control symptoms, the doctor may consider using colchicine. This drug is most effective when taken within the first 12 hours of an acute attack. Doctors may ask patients to take oral colchicine as often as every hour until joint symptoms begin to improve or side effects such as nausea, vomiting, abdominal cramps, or diarrhea make it uncomfortable to continue the drug.

For some patients, the doctor may prescribe either NSAIDs or oral colchicine in small daily doses to prevent future attacks. The doctor also may consider prescribing medicine such as allopurinol (Zyloprim) or probenecid (Benemid) to treat hyperuricemia and reduce the frequency of sudden attacks and the development of tophi.

People who have other medical problems, such as high blood pressure or high blood triglycerides (fats), may find that the drugs they take for those conditions can also be useful for gout. Both losartan (Cozaar), a blood pressure medication, and fenofibrate (Tricor), a triglyceride-lowering drug, also help reduce blood levels of uric acid.

The doctor may also recommend losing weight, for those who are overweight; limiting alcohol consumption; and avoiding or limiting high-purine foods (see box on page 10), which can increase uric acid levels.

What Can People With Gout Do to Stay Healthy?

Fortunately, gout can be controlled. People with gout can decrease the severity of attacks and reduce their risk of future attacks by taking their medications as prescribed. Acute gout is best controlled if medications are taken at the first sign of pain or inflammation. Other steps you can take to stay healthy and minimize gout's effect on your life include the following:

- Tell your doctor about all the medicines and vitamins you take. He or she can tell you if any of them increase your risk of hyperuricemia.
- Plan followup visits with your doctor to evaluate your progress.

- Drink plenty of nonalcoholic fluids, especially water. Nonalcoholic fluids help remove uric acid from the body. Alcohol, on the other hand, can raise the levels of uric acid in your blood.
- Exercise regularly and maintain a healthy body weight. Lose weight if you are overweight, but avoid low-carbohydrate diets that are designed for quick weight loss. When carbohydrate intake is insufficient, your body can't completely burn its own fat. As a consequence, substances called ketones form and are released into the bloodstream, resulting in a condition called ketosis. After a short time, ketosis can increase the level of uric acid in your blood.
- Avoid foods that are high in purines.

High-Purine Foods

- | | |
|------------------------|---------------|
| ▪ anchovies | ▪ herring |
| ▪ asparagus | ▪ liver |
| ▪ beef kidneys | ▪ mackerel |
| ▪ brains | ▪ mushrooms |
| ▪ dried beans and peas | ▪ sardines |
| ▪ game meats | ▪ scallops |
| ▪ gravy | ▪ sweetbreads |

What Research Is Being Conducted to Help People with Gout?

Because uric acid's role in gout is well understood and medications to ease attacks and reduce the risk or severity of future attacks are widely available, gout is one of the most – if not the most – controllable forms of arthritis. But researchers continue to make advances that help people live with gout. Perhaps someday these advances will prevent this extremely painful disease.

Some current areas of gout research include the following:

- **refining current treatments.** While many medications are available to treat gout, doctors are trying to determine which of the treatments are most effective and at which dosages. Recent studies have compared the effectiveness of different NSAIDs in treating the pain and inflammation of gout and have looked at the optimal dosages of colchicine and allopurinol (a uric-acid-lowering drug) to control and/or prevent painful attacks.
- **evaluating new therapies.** A number of new therapies have shown promise in recent studies. They include infliximab (Remicade) and other biologic agents that block a chemical called tumor necrosis factor. This chemical is believed to play a role in the inflammation of gout. Another new drug therapy is febuxostat, which works by blocking an enzyme involved in the production of uric acid.

- **discovering the role of foods.** Gout is the one form of arthritis for which there is proof that specific foods worsen the symptoms. Now research is suggesting that certain foods may also prevent gout. In a study published in the *New England Journal of Medicine*, scientists found that a high intake of low-fat dairy products reduces the risk of gout in men by half. The reason for this protective effect is not yet known. Another study examining the effects of vitamin C on uric acid suggests that it may be beneficial in the prevention and management of gout and other diseases that are associated with uric acid production.
- **searching for new treatment approaches.** Scientists are also studying the contributions of different types of cells that participate in both the acute and chronic joint manifestations of gout. The specific goals of this research are to better understand how urate crystals activate white blood cells called neutrophils, leading to acute gout attacks; how urate crystals affect the immune system, leading to chronic gout; and how urate crystals interact with bone cells in a way that causes debilitating bone lesions among people with chronic gout. The hope is that a better understanding of the various inflammatory reactions that occur in gout will provide innovative clues for treatment.

- **examining how genetics and environmental factors can affect hyperuricemia.** Researchers are studying different populations in which gout is prevalent to determine how certain genes and environmental factors may affect blood levels of uric acid, which can leak out and crystallize in the joint, leading to gout.

Where Can People Find More Information About Gout?

- **National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)**

National Institutes of Health

1 AMS Circle

Bethesda, MD 20892-3675

Phone: 301-495-4484 or

877-22-NIAMS (226-4267) (free of charge)

TTY: 301-565-2966

Fax: 301-718-6366

E-mail: NIAMSInfo@mail.nih.gov

www.niams.nih.gov

NIAMS provides information about various forms of arthritis and other rheumatic diseases, as well as other bone, muscle, joint, and skin diseases. It distributes patient and professional education materials and refers people to other sources of information. Additional information and updates can also be found on the NIAMS Web site.

- **American College of Rheumatology/Association of Rheumatology Health Professionals**

1800 Century Place, Suite 250

Atlanta, GA 30345-4300

Phone: 404-633-3777

Fax: 404-633-1870

www.rheumatology.org

This association provides referrals to rheumatologists. The organization also provides educational materials and guidelines about many different rheumatic diseases.

- **Arthritis Foundation**

P.O. Box 7669

Atlanta, GA 30357-0669

Phone: 404-872-7100 or

800-568-4045 (free of charge) or call your local chapter listed in the phone directory

www.arthritis.org

This is the main voluntary organization devoted to arthritis. The foundation publishes free pamphlets on many types of arthritis and *Arthritis Today*, a bimonthly magazine that provides up-to-date information on arthritis. The foundation also provides clinic referrals.

Key Words

Corticosteroids – powerful anti-inflammatory hormones made naturally in the body or manmade for use as medicine. Injections of corticosteroid drugs are sometimes used to treat inflammation in the shoulder, knee, and other joints.

Diuretics – a type of medication that promotes the formation and output of urine. Diuretics are prescribed to treat the accumulation of excess fluid in bodily tissues that can result from diseases of the kidneys, liver, lungs, or heart. They may also be used to treat high blood pressure or glaucoma, a condition in which pressure builds up inside the eye.

Hemolytic anemia – a form of anemia (deficiency of red blood cells) caused by the destruction of the cells rather than the body's inability to produce them in adequate numbers.

Hyperuricemia – the presence of elevated levels of uric acid in the blood.

Hypothyroidism – a condition in which the thyroid gland (the gland that makes and stores hormones that regulate heart rate, blood pressure, body temperature, and the rate at which food is converted to energy) is underactive. Without treatment, this condition can result in fatigue, weight gain, death, and, if not treated, other serious medical problems.

NSAIDs – a class of medications, available over the counter or with a prescription, that ease pain and inflammation. Commonly used NSAIDs include ibuprofen (Advil, Motrin), naproxen sodium (Aleve), and ketoprofen (Actron, Orudis KT).

Podagra – gout in the big toe.

Pseudogout – a condition often mistaken for gout that results from the deposit of calcium phosphate crystals (not uric acid crystals as in gout) in the joints and other tissues. This condition is also called chondrocalcinosis.

Psoriasis – an autoimmune disease characterized by a red scaly rash that is often located over the surfaces of the elbows, knees, and scalp, and around or in the ears, navel, genitals, or buttocks. Approximately 10 to 15 percent of people with psoriasis develop an associated arthritis referred to as psoriatic arthritis.

Purines – found in the DNA and RNA within the nuclei of cells, purines are part of all human tissue and are found in many foods, especially those high in protein.

Synovial fluid – the slippery fluid produced by the synovium (joint lining) to lubricate the joints.

Tophi – nodular masses of uric acid crystals that sometimes form in the soft tissue of people with chronic gout. Although tophi are most common around the fingers, elbows, and big toe, they can occur in virtually any part of the body. (The singular is tophus.)

Uric acid – a substance that results from the breakdown of purines, which are part of all human tissue and are found in many foods.

Acknowledgments

The NIAMS gratefully acknowledges the assistance of Barbara Mittleman, M.D., and Bernadette Tyree, Ph.D., NIAMS, NIH; John H. Klippel, M.D., Arthritis Foundation, Atlanta; Roland W. Moskowitz, M.D., University Hospitals of Cleveland, OH; and Lawrence Ryan, M.D., Medical College of Wisconsin in Milwaukee; in the preparation and review of this publication.



The mission of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), a part of the Department of Health and Human Services' National Institutes of Health (NIH), is to support research into the causes, treatment, and prevention of arthritis and musculoskeletal and skin diseases; the training of basic and clinical scientists to carry out this research; and the dissemination of information on research progress in these diseases. The National Institute of Arthritis and Musculoskeletal and Skin Diseases Information Clearinghouse is a public service sponsored by the NIAMS that provides health information and information sources. Additional information can be found on the NIAMS Web site at www.niams.nih.gov.



U.S. Department of Health and Human Services
Public Health Service
National Institutes of Health
National Institute of Arthritis and
Musculoskeletal and Skin Diseases

NIH Publication No. 07-5027
March 2002
Revised December 2006