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ORIGIN, TREATMENT AND PREVENTION OF GOUT DISEASE

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Annotation: Gout is a common and complex form of arthritis that can affect anyone. It's characterized by sudden, severe attacks of pain, swelling, redness and tenderness in one or more joints, most often in the big toe. An attack of gout can occur suddenly, often waking you up in the middle of the night with the sensation that your big toe is on fire. The affected joint is hot, swollen and so tender that even the weight of the bedsheet on it may seem intolerable.

Key words: Gout, chondrocalcinosis, metabolic disease.

Gout, metabolic disorder characterized by recurrent acute attacks of severe inflammation in one or more of the joints of the extremities. Gout results from the deposition, in and around the joints, of uric acid salts, which are excessive throughout the body in persons with the disorder. Uric acid is a product of the breakdown of purines, compounds that are essential components of DNA and RNA and of many biosynthetic reactions and that are normally steadily excreted into the urine. Gout accounts for at least 5 percent of all cases of arthritis. However, it is uncommon in women; the male-female ratio is 20:1. Pseudogout (chondrocalcinosis) is a similar condition caused by deposits of calcium pyrophospate crystals in the joints.

Although gout is suspected to be an inborn disorder, the initial attack of acute joint inflammation, or gouty arthritis, usually does not appear until middle age. Any peripheral joint may be affected, but the joint at the base of the big toe is especially susceptible. Symptoms include redness of the skin and extreme tenderness, warmth, and pain of the affected joints. An attack, even when untreated, may subside in a week or two. Attacks may come and go without apparent reason, but there are a number of precipitating factors, including acute infection, emotional upset, excessive alcohol consumption, poor diet, obesity, diuresis, surgery, trauma, and the administration of certain medications. Precipitation of uric acid in the joint cartilage precedes the first attack. In some cases, continued deposition of uric acid salts may cause knobby deformities (tophi) and may also occur in cartilage that is not associated with the joints, such as the rim of the ear.

Many people who are affected by gout have family members who also have been affected; however, the pattern of inheritance of the disorder is unknown. Several genetic variations have been identified in association with abnormal uric acid metabolism. The best characterized of these variations occurs in a gene known as SLC2A9 (solute carrier family 2, member 9), which normally encodes a protein involved in maintaining uric acid homeostasis. Although the precise mechanisms by which variants of SLC2A9 increase susceptibility to gout is not known with certainty, scientists suspect that the variants produce abnormal proteins capable of disrupting uric acid transport and uptake into cells. Understanding the genetic mechanisms that give rise to gout may facilitate the identification of methods for prevention and the development of drugs for treatment of the disorder.

Treatment for an acute attack of gout includes the administration of nonsteroidal anti-inflammatory drugs (NSAIDs), such as indomethacin and naproxen. Corticosteroids may also be injected into the affected joint to reduce inflammation. A medication called colchicine may be

administered if NSAIDs and corticosteroids are not effective. Medications such as allopurinol, which reduces urate formation, and probenecid, which promotes urinary excretion of uric acid, are used to treat recurrent acute attacks. In addition, the frequency and severity of recurrent attacks may be reduced by supplementation with vitamin C, which increases excretion of uric acid by the kidneys, thereby decreasing the amount of uric acid circulating in the body.

Metabolic disease, any of the diseases or disorders that disrupt normal metabolism, the process of converting food to energy on a cellular level. Thousands of enzymes participating in numerous interdependent metabolic pathways carry out this process. Metabolic diseases affect the ability of the cell to perform critical biochemical reactions that involve the processing or transport of proteins (amino acids), carbohydrates (sugars and starches), or lipids (fatty acids).

Metabolic diseases are typically hereditary, yet most persons affected by them may appear healthy for days, months, or even years. The onset of symptoms usually occurs when the body's metabolism comes under stress—for example, after prolonged fasting or during a febrile illness. For some metabolic disorders, it is possible to obtain prenatal diagnostic screening. Such analysis usually is offered to families who have previously had a child with a metabolic disease or who are in a defined ethnic group. For example, testing for Tay-Sachs disease is relatively common in the Ashkenazi Jewish population. Countries that perform screening for metabolic diseases at birth typically test for up to 10 different conditions. Tandem mass-spectrometry is a new technology that allows for the detection of multiple abnormal metabolites almost simultaneously, making it possible to add approximately 30 disorders to the list of conditions for which newborns may be tested. If an infant is known to have a metabolic disorder soon after birth, appropriate therapy can be started early, which may result in a better prognosis. Some metabolic disorders respond very well if treatment is introduced at an early age. However, others have no effective therapy and cause severe problems, despite early diagnosis. In the future, gene therapy may prove successful in the treatment of some of these diseases.

Metabolic diseases are quite rare individually, but they are relatively common when considered as a group. Specific metabolic disorders have incidences ranging from approximately 1 in 500 (or even higher in isolated populations) to fewer than 1 in 1,000,000. As a group, it has been estimated that metabolic disorders affect approximately 1 in 1,000 individuals.

The signs and symptoms of gout almost always occur suddenly, and often at night. They include:

- Intense joint pain. Gout usually affects the big toe, but it can occur in any joint. Other commonly affected joints include the ankles, knees, elbows, wrists and fingers. The pain is likely to be most severe within the first four to 12 hours after it begins.
- Lingering discomfort. After the most severe pain subsides, some joint discomfort may last from a few days to a few weeks. Later attacks are likely to last longer and affect more joints.
- Inflammation and redness. The affected joint or joints become swollen, tender, warm and red.
- Limited range of motion. As gout progresses, you may not be able to move your joints normally.

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Picteru 1. Gout causes intense pain and swelling around one or more joints. Gout most commonly affects the joint at the base of the big toe.

Gout occurs when urate crystals accumulate in your joint, causing the inflammation and intense pain of a gout attack. Urate crystals can form when you have high levels of uric acid in your blood. Your body produces uric acid when it breaks down purines — substances that are found naturally in your body.

Purines are also found in certain foods, including red meat and organ meats, such as liver. Purine-rich seafood includes anchovies, sardines, mussels, scallops, trout and tuna. Alcoholic beverages, especially beer, and drinks sweetened with fruit sugar (fructose) promote higher levels of uric acid.

Normally, uric acid dissolves in your blood and passes through your kidneys into your urine. But sometimes either your body produces too much uric acid or your kidneys excrete too little uric acid. When this happens, uric acid can build up, forming sharp, needlelike urate crystals in a joint or surrounding tissue that cause pain, inflammation and swelling.

You're more likely to develop gout if you have high levels of uric acid in your body. Factors that increase the uric acid level in your body include:

- Diet. Eating a diet rich in red meat and shellfish and drinking beverages sweetened with fruit sugar (fructose) increase levels of uric acid, which increase your risk of gout. Alcohol consumption, especially of beer, also increases the risk of gout.
- Weight. If you're overweight, your body produces more uric acid and your kidneys have a more difficult time eliminating uric acid.
- Medical conditions. Certain diseases and conditions increase your risk of gout. These include untreated high blood pressure and chronic conditions such as diabetes, obesity, metabolic syndrome, and heart and kidney diseases.
- Certain medications. Low-dose aspirin and some medications used to control hypertension — including thiazide diuretics, angiotensin-converting enzyme (ACE)

inhibitors and beta blockers — also can increase uric acid levels. So can the use of anti-rejection drugs prescribed for people who have undergone an organ transplant.

- Family history of gout. If other members of your family have had gout, you're more likely to develop the disease.
- Age and sex. Gout occurs more often in men, primarily because women tend to have lower uric acid levels. After menopause, however, women's uric acid levels approach those of men. Men are also more likely to develop gout earlier — usually between the ages of 30 and 50 — whereas women generally develop signs and symptoms after menopause.
- Recent surgery or trauma. Experiencing recent surgery or trauma can sometimes trigger a gout attack. In some people, receiving a vaccination can trigger a gout flare.

Gout medications are available in two types and focus on two different problems. The first type helps reduce the inflammation and pain associated with gout attacks. The second type works to prevent gout complications by lowering the amount of uric acid in your blood.

Which type of medication is right for you depends on the frequency and severity of your symptoms, along with any other health problems you may have.

Medications to treat gout attacks

Drugs used to treat gout flares and prevent future attacks include:

- Nonsteroidal anti-inflammatory drugs (NSAIDs). NSAIDs include over-the-counter options such as ibuprofen (Advil, Motrin IB, others) and naproxen sodium (Aleve), as well as more-powerful prescription NSAIDs such as indomethacin (Indocin, Tivorbex) or celecoxib (Celebrex). NSAIDs carry risks of stomach pain, bleeding and ulcers.
- Colchicine. Your doctor may recommend colchicine (Colcrys, Gloperba, Mitigare), an anti-inflammatory drug that effectively reduces gout pain. The drug's effectiveness may be offset, however, by side effects such as nausea, vomiting and diarrhea.
- Corticosteroids. Corticosteroid medications, such as prednisone, may control gout inflammation and pain. Corticosteroids may be in pill form, or they can be injected into your joint. Side effects of corticosteroids may include mood changes, increased blood sugar levels and elevated blood pressure.

Medications to prevent gout complications

If you experience several gout attacks each year, or if your gout attacks are less frequent but particularly painful, your doctor may recommend medication to reduce your risk of gout-related complications. If you already have evidence of damage from gout on joint X-rays, or you have tophi, chronic kidney disease or kidney stones, medications to lower your body's level of uric acid may be recommended.

- Medications that block uric acid production. Drugs such as allopurinol (Aloprim, Lopurin, Zyloprim) and febuxostat (Uloric) help limit the amount of uric acid your body makes. Side effects of allopurinol include fever, rash, hepatitis and kidney problems. Febuxostat

side effects include rash, nausea and reduced liver function. Febuxostat also may increase the risk of heart-related death.

- Medications that improve uric acid removal. Drugs such as probenecid (Probalan) help improve your kidneys' ability to remove uric acid from your body. Side effects include a rash, stomach pain and kidney stones.

Make an appointment with your doctor if you have symptoms that are common to gout. After an initial examination, your doctor may refer you to a specialist in the diagnosis and treatment of arthritis and other inflammatory joint conditions (rheumatologist).

Here's some information to help you get ready for your appointment, and what to expect from your doctor.

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