[Template:Redirect](/wiki/Template:Redirect" \o "Template:Redirect) [Template:Pp-semi](/wiki/Template:Pp-semi) [Template:Infobox medical condition (new)](/wiki/Template:Infobox_medical_condition_(new)) **Gout** is usually characterized by recurrent attacks of [inflammatory arthritis](/wiki/Inflammatory_arthritis)—a red, tender, hot, and [swollen joint](/wiki/Joint_effusion).<ref name=Review08>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Pain typically comes on rapidly in less than twelve hours.<ref name=Lancet2010/> The [joint at the base of the big toe](/wiki/Metatarsophalangeal_articulations) is affected in about half of cases.<ref name=PM2010>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> It may also result in [tophi](/wiki/Tophus), [kidney stones](/wiki/Kidney_stone), or [urate nephropathy](/wiki/Urate_nephropathy).<ref name=Lancet2010/>

The cause is a combination of diet and [genetic](/wiki/Heredity) factors. It occurs more commonly in those who eat a lot of meat, drink a lot of beer, or are [overweight](/wiki/Overweight). The underlying mechanism involves elevated levels of [uric acid](/wiki/Uric_acid) in the [blood](/wiki/Blood). At high levels, the uric acid crystallizes and the [crystals](/wiki/Crystal) deposit in joints, [tendons](/wiki/Tendon) and surrounding [tissues](/wiki/Tissue_(biology)), an attack of gout occurs. Diagnosis may be confirmed by seeing the crystals in joint fluid or tophus. Blood uric acid levels may be normal during an attack.<ref name=Lancet2010/>

Treatment with [nonsteroidal anti-inflammatory drugs](/wiki/Nonsteroidal_anti-inflammatory_drugs) (NSAIDs), [steroids](/wiki/Steroid), or [colchicine](/wiki/Colchicine) improves symptoms. Once the acute attack subsides, levels of uric acid can be lowered via lifestyle changes and in those with frequent attacks, [allopurinol](/wiki/Allopurinol) or [probenecid](/wiki/Probenecid) provides long-term prevention.<ref name=Lancet2010/> Taking [vitamin C](/wiki/Vitamin_C) and eating a diet high in low fat dairy products may be preventive.[[1]](#cite_note-1) Gout affects about 1 to 2% of the [Western](/wiki/Western_world) population at some point in their lives. It has become more common in recent decades. This is believed to be due to increasing risk factors in the population, such as [metabolic syndrome](/wiki/Metabolic_syndrome), longer [life expectancy](/wiki/Life_expectancy) and changes in diet. Older males are most commonly affected.<ref name=Lancet2010/> Gout was historically known as "the disease of kings" or "rich man's disease".<ref name=Lancet2010>[Template:Cite journal](/wiki/Template:Cite_journal)</ref><ref name=Dic>[Template:Cite web](/wiki/Template:Cite_web)</ref> It has been recognized at least since the time of the [ancient Egyptians](/wiki/Ancient_Egyptians).<ref name=Lancet2010/>

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## Signs and symptoms[[edit](/index.php?title=(none)&action=edit&section=1)]

[thumb|upright=1.4|alt=side view of a foot showing a red patch of skin over the joint at the base of the big toe|Gout presenting in the metatarsal-phalangeal joint of the big toe: Note the slight redness of the skin overlying the joint.](/wiki/Image:Gout2010.JPG) Gout can present in multiple ways, although the most usual is a recurrent attack of acute [inflammatory arthritis](/wiki/Inflammatory_arthritis) (a red, tender, hot, swollen joint).<ref name=Review08/> The [metatarsal-phalangeal joint](/wiki/Metatarsophalangeal_articulations) at the base of the [big toe](/wiki/Hallux) is affected most often, accounting for half of cases.<ref name=PM2010/> Other joints, such as the heels, knees, wrists and fingers, may also be affected.<ref name=PM2010/> Joint pain usually begins over 2–4 hours and during the night.<ref name=PM2010/> This is mainly due to lower body temperature.<ref name=Egg2007>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Other symptoms may rarely occur along with the joint pain, including [fatigue](/wiki/Fatigue_(medical)) and a high [fever](/wiki/Fever).<ref name=Egg2007/><ref name=PM2010/>

Long-standing elevated [uric acid](/wiki/Uric_acid) levels ([hyperuricemia](/wiki/Hyperuricemia)) may result in other symptoms, including hard, painless deposits of uric acid crystals known as [tophi](/wiki/Tophi). Extensive tophi may lead to chronic [arthritis](/wiki/Arthritis) due to bone erosion.<ref name=Nature2009/> Elevated levels of uric acid may also lead to crystals precipitating in the [kidneys](/wiki/Kidney), resulting in [stone](/wiki/Kidney_stone) formation and subsequent [urate nephropathy](/wiki/Acute_uric_acid_nephropathy).<ref name=German09/>

## Cause[[edit](/index.php?title=(none)&action=edit&section=2)]

The [crystallization](/wiki/Crystallization) of [uric acid](/wiki/Uric_acid), often related to relatively high levels in the blood, is the underlying cause of gout. This can occur because diet, genetic predisposition, or underexcretion of [urate](/wiki/Uric_acid#Solubility_of_uric_acid_and_its_salts), the salts of uric acid.<ref name=Review08/> Underexcretion of uric acid by the kidney is the primary cause of hyperuricemia in about 90% of cases, while overproduction is the cause in less than 10%.<ref name=Lancet2010/> About 10% of people with [hyperuricemia](/wiki/Hyperuricemia) develop gout at some point in their lifetimes.[[2]](#cite_note-2) The risk, however, varies depending on the degree of hyperuricemia. When levels are between 415 and 530 μmol/l (7 and 8.9 mg/dl), the risk is 0.5% per year, while in those with a level greater than 535 μmol/l (9 mg/dL), the risk is 4.5% per year.<ref name=Egg2007/>

### Lifestyle[[edit](/index.php?title=(none)&action=edit&section=3)]

Dietary causes account for about 12% of gout,<ref name=Review08/> and include a strong association with the consumption of alcohol, [fructose](/wiki/Fructose)-sweetened drinks, meat and seafood.<ref name=Nature2009/>[[3]](#cite_note-3) Other triggers include [physical trauma](/wiki/Physical_trauma) and surgery.<ref name=Lancet2010/>

Studies in the early 2000s found that other dietary factors are not relevant.<ref name=Choi2004>[Template:Cite journal](/wiki/Template:Cite_journal)</ref><ref name=Epi2008/> Specifically, moderate consumption of [purine](/wiki/Purine)-rich vegetables (e.g. beans, peas, lentils and spinach) are not associated with gout.<ref name=Singh2011>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Neither is [total consumption of protein](/wiki/Protein_toxicity).<ref name=Choi2004/><ref name=Singh2011/> Alcohol consumption is strongly associated with an increased risk, with wine presenting somewhat less of a risk than beer and spirits.[[4]](#cite_note-4)[[5]](#cite_note-5) The consumption of [coffee](/wiki/Coffee), [vitamin C](/wiki/Vitamin_C) and [dairy products](/wiki/Dairy_products), as well as [physical fitness](/wiki/Physical_fitness), appear to decrease the risk.[[6]](#cite_note-6)[[7]](#cite_note-7)<ref name=Life2010>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> This is believed to be partly due to their effect in reducing [insulin resistance](/wiki/Insulin_resistance).<ref name=Life2010/>

### Genetics[[edit](/index.php?title=(none)&action=edit&section=4)]

Gout is partly genetic, contributing to about 60% of [variability](/wiki/Genetic_variability) in uric acid level.<ref name=Lancet2010/> The [*SLC2A9*](/wiki/SLC2A9), [*SLC22A12*](/wiki/SLC22A12) and [*ABCG2*](/wiki/ABCG2) genes have been found to be commonly associated with gout and variations in them can approximately double the risk.[[8]](#cite_note-8)[[9]](#cite_note-9) [Loss-of-function mutations](/wiki/Loss-of-function_mutation) in *SLC2A9* and *SLC22A12* cause hereditary hypouricaemia by reducing urate absorption and unopposed urate secretion.<ref name=Reginato2012/> The rare genetic disorders [familial juvenile hyperuricemic nephropathy](/wiki/Tamm-Horsfall_protein), [medullary cystic kidney disease](/wiki/Medullary_cystic_kidney_disease), [phosphoribosylpyrophosphate synthetase](/wiki/PRPSAP1) superactivity and [hypoxanthine-guanine phosphoribosyltransferase](/wiki/Hypoxanthine-guanine_phosphoribosyltransferase) deficiency as seen in [Lesch-Nyhan syndrome](/wiki/Lesch-Nyhan_syndrome), are complicated by gout.<ref name=Lancet2010/>

### Medical conditions[[edit](/index.php?title=(none)&action=edit&section=5)]

Gout frequently occurs in combination with other medical problems. [Metabolic syndrome](/wiki/Metabolic_syndrome), a combination of [abdominal obesity](/wiki/Abdominal_obesity), [hypertension](/wiki/Hypertension), [insulin resistance](/wiki/Insulin_resistance) and [abnormal lipid levels](/wiki/Dyslipidemia), occurs in nearly 75% of cases.<ref name=PM2010/> Other conditions commonly complicated by gout include: [polycythemia](/wiki/Polycythemia), [lead poisoning](/wiki/Lead_poisoning), [kidney failure](/wiki/Kidney_failure), [hemolytic anemia](/wiki/Hemolytic_anemia), [psoriasis](/wiki/Psoriasis) and [solid organ transplants](/wiki/Organ_transplant).[[10]](#cite_note-10) A [body mass index](/wiki/Body_mass_index) greater than or equal to 35 increases male risk of gout threefold.<ref name=Epi2008/> Chronic lead exposure and lead-contaminated alcohol are risk factors for gout due to the harmful effect of lead on kidney function.[[11]](#cite_note-11) [Lesch-Nyhan syndrome](/wiki/Lesch-Nyhan_syndrome) is often associated with gouty arthritis.

### Medication[[edit](/index.php?title=(none)&action=edit&section=6)]

[Diuretics](/wiki/Diuretic) have been associated with attacks of gout. However, a low dose of [hydrochlorothiazide](/wiki/Hydrochlorothiazide) does not seem to increase risk.<ref name=CFP09/> Other medicines that do increase the risk include [niacin](/wiki/Niacin) and [aspirin](/wiki/Aspirin) (acetylsalicylic acid).<ref name=Nature2009/> The [immunosuppressive drugs](/wiki/Immunosuppressive_drug) [ciclosporin](/wiki/Ciclosporin) and [tacrolimus](/wiki/Tacrolimus) are associated with gout,<ref name=Lancet2010/> the former more so when used in combination with hydrochlorothiazide.[[12]](#cite_note-12)

## Pathophysiology[[edit](/index.php?title=(none)&action=edit&section=7)]

[thumb|upright=1.4|alt=structure of organic compound: 7,9-dihydro-1H-purine-2,6,8(3H)-trione|](/wiki/Image:Harnsäure_Ketoform.svg)[Uric acid](/wiki/Uric_acid) Gout is a disorder of [purine metabolism](/wiki/Purine_metabolism),<ref name=Lancet2010/> and occurs when its final metabolite, [uric acid](/wiki/Uric_acid), crystallizes in the form of monosodium urate, [precipitating](/wiki/Precipitation_(chemistry)) and forming deposits (tophi) in joints, on tendons and in the surrounding tissues.<ref name=Nature2009/> Microscopic tophi may be walled off by a ring of proteins, which blocks interaction of the crystals with cells and therefore avoids inflammation.<ref name=LB&R>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Naked crystals may break out of walled-off tophi due to minor physical trauma to the joint, medical or surgical stress, or rapid changes in uric acid levels.<ref name=LB&R/> When they breach the tophi, they trigger a local [immune](/wiki/Immune)-mediated [inflammatory](/wiki/Inflammation) reaction,<ref name=Nature2009/><ref name=LB&R/> with one of the key proteins in the inflammatory cascade being [interleukin 1β](/wiki/Interleukin-1_beta).<ref name=Lancet2010/> An evolutionary loss of [urate oxidase](/wiki/Urate_oxidase) (uricase), which breaks down uric acid, in humans and higher [primates](/wiki/Primate) has made this condition common.<ref name=Lancet2010/>

The triggers for precipitation of uric acid are not well understood. While it may crystallize at normal levels, it is more likely to do so as levels increase.[[13]](#cite_note-13) Other triggers believed to be important in acute episodes of arthritis include cool temperatures, rapid changes in uric acid levels, [acidosis](/wiki/Acidosis),[[14]](#cite_note-14)[[15]](#cite_note-15) articular hydration and [extracellular matrix](/wiki/Extracellular_matrix) proteins, such as [proteoglycans](/wiki/Proteoglycan), [collagens](/wiki/Collagen) and [chondroitin sulfate](/wiki/Chondroitin_sulfate).[[16]](#cite_note-16) The increased precipitation at low temperatures partly explains why the joints in the feet are most commonly affected.[[17]](#cite_note-17) Rapid changes in uric acid may occur due to factors including trauma, surgery, [chemotherapy](/wiki/Chemotherapy), diuretics and stopping or starting [allopurinol](/wiki/Allopurinol).[[18]](#cite_note-18) [Calcium channel blockers](/wiki/Calcium_channel_blocker) and [losartan](/wiki/Losartan) are associated with a lower risk of gout compared to other medications for [hypertension](/wiki/Hypertension).[[19]](#cite_note-19)

## Diagnosis[[edit](/index.php?title=(none)&action=edit&section=8)]

[thumb|upright=1.4|Gout on](/wiki/File:Gichtfuss_im_Roentgenbild_002.png) [X-rays](/wiki/X-rays) of a left foot. The typical location is the big toe joint. Note also the soft tissue swelling at the lateral border of the foot. [thumb|upright=1.4|alt=numerous multi-colored needle-shaped crystals against a purple background|Spiked rods of uric acid crystals from a](/wiki/File:Fluorescent_uric_acid.JPG) [synovial fluid](/wiki/Synovial_fluid) sample photographed under a microscope with [polarized light](/wiki/Polarization_(waves)). Formation of uric acid crystals in the joints is associated with gout.

Gout may be diagnosed and treated without further investigations in someone with hyperuricemia and the classic acute arthritis of the base of the great toe (known as podagra). Synovial fluid analysis should be done, however, if the diagnosis is in doubt.<ref name=Egg2007/> [X-rays](/wiki/X-rays), while useful for identifying chronic gout, have little utility in acute attacks.<ref name=Lancet2010/>

### Synovial fluid[[edit](/index.php?title=(none)&action=edit&section=9)]

A definitive diagnosis of gout is based upon the identification of [monosodium urate crystals](/wiki/Urate) in [synovial fluid](/wiki/Synovial_fluid) or a [tophus](/wiki/Tophus).<ref name=PM2010/> All synovial fluid samples obtained from undiagnosed inflamed joints by [arthrocentesis](/wiki/Arthrocentesis) should be examined for these crystals.<ref name=Lancet2010/> Under [polarized light](/wiki/Polarized_light) microscopy, they have a needle-like morphology and strong negative [birefringence](/wiki/Birefringence). This test is difficult to perform and requires a trained observer.[[20]](#cite_note-20) The fluid must be examined relatively soon after aspiration, as temperature and pH affect solubility.<ref name=Lancet2010/>

### Blood tests[[edit](/index.php?title=(none)&action=edit&section=10)]

[Hyperuricemia](/wiki/Hyperuricemia) is a classic feature of gout, but it occurs nearly half of the time without hyperuricemia and most people with raised uric acid levels never develop gout.<ref name=PM2010/>[[21]](#cite_note-21) Thus, the diagnostic utility of measuring uric acid level is limited.<ref name=PM2010/> Hyperuricemia is defined as a [plasma](/wiki/Blood_plasma) urate level greater than 420 μmol/l (7.0 mg/dl) in males and 360 μmol/l (6.0 mg/dl) in females.[[22]](#cite_note-22) Other blood tests commonly performed are [white blood cell count](/wiki/White_blood_cell_count), [electrolytes](/wiki/Electrolyte), [kidney function](/wiki/Kidney_function) and [erythrocyte sedimentation rate](/wiki/Erythrocyte_sedimentation_rate) (ESR). However, both the white blood cells and ESR may be elevated due to gout in the absence of infection.[[23]](#cite_note-23)[[24]](#cite_note-24) A white blood cell count as high as 40.0×109/l (40,000/mm3) has been documented.<ref name=Egg2007/>

### Differential diagnosis[[edit](/index.php?title=(none)&action=edit&section=11)]

The most important [differential diagnosis](/wiki/Differential_diagnosis) in gout is [septic arthritis](/wiki/Septic_arthritis).<ref name=Lancet2010/><ref name=PM2010/> This should be considered in those with signs of infection or those who do not improve with treatment.<ref name=PM2010/> To help with diagnosis, a synovial fluid [Gram stain](/wiki/Gram_stain) and culture may be performed.<ref name=PM2010/> Other conditions that look similar include [pseudogout](/wiki/Pseudogout) and [rheumatoid arthritis](/wiki/Rheumatoid_arthritis).<ref name=PM2010/> Gouty tophi, in particular when not located in a joint, can be mistaken for [basal cell carcinoma](/wiki/Basal_cell_carcinoma)[[25]](#cite_note-25) or other [neoplasms](/wiki/Neoplasm).[[26]](#cite_note-26)

## Prevention[[edit](/index.php?title=(none)&action=edit&section=12)]

Both lifestyle changes and medications can decrease uric acid levels. Dietary and lifestyle choices that are effective include reducing intake of food such as meat and seafood, consuming adequate [vitamin C](/wiki/Vitamin_C), limiting [alcohol](/wiki/Alcohol) and [fructose](/wiki/Fructose) consumption and avoiding [obesity](/wiki/Obesity).<ref name=Review08/> A [low-calorie diet](/wiki/Low-calorie_diet) in obese men decreased uric acid levels by 100 µmol/l (1.7 mg/dl).<ref name=CFP09/> Vitamin C intake of 1,500 mg per day decreases the risk of gout by 45%.[[27]](#cite_note-27) Coffee, but not tea, consumption is associated with a lower risk of gout.[[28]](#cite_note-28) Gout may be secondary to [sleep apnea](/wiki/Sleep_apnea) via the release of [purines](/wiki/Purine) from oxygen-starved cells. Treatment of apnea can lessen the occurrence of attacks.[[29]](#cite_note-29)

## Treatment[[edit](/index.php?title=(none)&action=edit&section=13)]

The initial aim of treatment is to settle the symptoms of an acute attack.[[30]](#cite_note-30) Repeated attacks can be prevented by medications that reduce serum uric acid levels.[[30]](#cite_note-30) Tentative evidence supports the application of ice for 20 to 30 minutes several times a day to decrease pain.<ref name=Moi2013>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Options for acute treatment include [nonsteroidal anti-inflammatory drugs](/wiki/Nonsteroidal_anti-inflammatory_drug) (NSAIDs), [colchicine](/wiki/Colchicine) and [steroids](/wiki/Steroids),<ref name=Review08/> while options for prevention include [allopurinol](/wiki/Allopurinol), [febuxostat](/wiki/Febuxostat) and [probenecid](/wiki/Probenecid). Lowering uric acid levels can cure the disease.<ref name=Lancet2010/> Treatment of [associated health problems](/wiki/Comorbidity) is also important.<ref name=Lancet2010/> Lifestyle interventions have been poorly studied.<ref name=Moi2013/> It is unclear whether dietary supplements have an effect in people with gout.[[31]](#cite_note-31)

### NSAIDs[[edit](/index.php?title=(none)&action=edit&section=14)]

NSAIDs are the usual first-line treatment for gout. No specific agent is significantly more or less effective than any other.<ref name=Review08/> Improvement may be seen within four hours and treatment is recommended for one to two weeks.<ref name=Review08/><ref name=Lancet2010/> They are not recommended, however, in those with certain other health problems, such as [gastrointestinal bleeding](/wiki/Gastrointestinal_bleeding), [kidney failure](/wiki/Kidney_failure), or [heart failure](/wiki/Heart_failure).<ref name=JFP09/> While [indometacin](/wiki/Indometacin) has historically been the most commonly used NSAID, an alternative, such as [ibuprofen](/wiki/Ibuprofen), may be preferred due to its better side effect profile in the absence of superior effectiveness.<ref name=CFP09>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> For those at risk of gastric side effects from NSAIDs, an additional [proton pump inhibitor](/wiki/Proton_pump_inhibitor) may be given.[[32]](#cite_note-32) There is some evidence that [COX-2 inhibitors](/wiki/COX-2_inhibitor) may work as well as nonselective NSAIDs for acute gout attack with fewer side effects.[[33]](#cite_note-33)[[34]](#cite_note-34)

### Colchicine[[edit](/index.php?title=(none)&action=edit&section=15)]

[Colchicine](/wiki/Colchicine) is an alternative for those unable to tolerate NSAIDs.<ref name=Review08/> At high doses, side effects (primarily gastrointestinal upset) limit its usage.[[35]](#cite_note-35) At lower doses, which are still effective, it is well tolerated.<ref name=CFP09/>[[36]](#cite_note-36) Colchicine may interact with other commonly prescribed drugs, such as [atorvastatin](/wiki/Atorvastatin) and [erythromycin](/wiki/Erythromycin), among others.[[35]](#cite_note-35)

### Steroids[[edit](/index.php?title=(none)&action=edit&section=16)]

[Glucocorticoids](/wiki/Glucocorticoid) have been found to be as effective as NSAIDs[[37]](#cite_note-37)[[38]](#cite_note-38) and may be used if contraindications exist for NSAIDs. They also lead to improvement when [injected into the joint](/wiki/Joint_injection). A [joint infection](/wiki/Septic_arthritis) must be excluded, however, as steroids worsen this condition.<ref name=Review08/>

### Pegloticase[[edit](/index.php?title=(none)&action=edit&section=17)]

[Pegloticase](/wiki/Pegloticase) was approved in the USA to treat gout in 2010.<ref name=FDA2010>[Template:Cite web](/wiki/Template:Cite_web)</ref> It is an option for the 3% of people who are intolerant to other medications.<ref name=FDA2010/> Pegloticase is administered as an intravenous infusion every two weeks,<ref name=FDA2010/> and reduces uric acid levels.[[39]](#cite_note-39) It is likely useful for tophi but has a high rate of side effects.[[40]](#cite_note-40)

### Prophylaxis[[edit](/index.php?title=(none)&action=edit&section=18)]

A number of medications are useful for preventing further episodes of gout, including [xanthine oxidase inhibitors](/wiki/Xanthine_oxidase_inhibitor) (including [allopurinol](/wiki/Allopurinol) and [febuxostat](/wiki/Febuxostat)) and [uricosurics](/wiki/Uricosuric) (including [probenecid](/wiki/Probenecid) and [sulfinpyrazone](/wiki/Sulfinpyrazone)). They are not usually started until one to two weeks after an acute flare has resolved, due to theoretical concerns of worsening the attack.<ref name=Review08/> They are often used in combination with either an NSAID or colchicine for the first three to six months.<ref name=Lancet2010/> They are not recommended until a person has had two attacks of gout,<ref name=Review08/> unless destructive joint changes, tophi, or [urate nephropathy](/wiki/Acute_uric_acid_nephropathy) exist,<ref name=German09>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> because the medications have not been found to be cost-effective.<ref name=Review08/> Urate-lowering measures should be increased until serum uric acid levels are below 300–360 µmol/l (5.0–6.0 mg/dl) and continue indefinitely.<ref name=Review08/><ref name=Lancet2010/> If these medications are in chronic use at the time of an attack, discontinuation is recommended.<ref name=PM2010/> Levels that cannot be brought below 6.0 mg/dl while attacks continue indicates treatment failure or refractory gout.[[41]](#cite_note-41) Overall, probenecid appears to be less effective than allopurinol.<ref name=Review08/>

[Uricosuric](/wiki/Uricosuric) medications are typically preferred if undersecretion of uric acid, as indicated by a 24-hour collection of urine results in a uric acid amount of less than 800 mg, is found.<ref name=agabegi2nd251>[Template:Cite book](/wiki/Template:Cite_book)</ref> They are, however, not recommended if a person has a history of [kidney stones](/wiki/Kidney_stone).<ref name=agabegi2nd251/> A 24-hour urine excretion of more than 800 mg, which indicates overproduction, is an indication for a xanthine oxidase inhibitor.<ref name=agabegi2nd251/>

Xanthine oxidase inhibitors block uric acid production. Long-term therapy is safe and well tolerated and can be used in people with decreased kidney function or urate stones, although allopurinol has caused [hypersensitivity](/wiki/Hypersensitivity) in a small number of individuals.<ref name=Review08/> In such cases febuxostat is recommended.[[42]](#cite_note-42)

## Prognosis[[edit](/index.php?title=(none)&action=edit&section=19)]

Without treatment, an acute attack of gout usually resolves in five to seven days; however, 60% of people have a second attack within one year.<ref name=Egg2007/> Those with gout are at increased risk of [hypertension](/wiki/Hypertension), [diabetes mellitus](/wiki/Diabetes_mellitus), [metabolic syndrome](/wiki/Metabolic_syndrome) and kidney and [cardiovascular disease](/wiki/Cardiovascular_disease) and thus are at increased risk of death.<ref name=Lancet2010/><ref name=Rh2008>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> This may be partly due to its association with [insulin resistance](/wiki/Insulin_resistance) and [obesity](/wiki/Obesity), but some of the increased risk appears to be independent.<ref name=Rh2008/>

Without treatment, episodes of acute gout may develop into chronic gout with destruction of joint surfaces, joint deformity and painless tophi.<ref name=Lancet2010/> These tophi occur in 30% of those who are untreated for five years, often in the [helix](/wiki/Helix_(ear)) of the ear, over the [olecranon](/wiki/Olecranon) processes, or on the [Achilles tendons](/wiki/Achilles_tendons).<ref name=Lancet2010/> With aggressive treatment, they may dissolve. [Kidney stones](/wiki/Kidney_stones) also frequently complicate gout, affecting between 10 and 40% of people and occur due to low urine pH promoting the precipitation of uric acid.<ref name=Lancet2010/> Other forms of [chronic kidney dysfunction](/wiki/Kidney_failure) may occur.<ref name=Lancet2010/>

<gallery> File:Case 30-top.jpg|Nodules of the finger and helix of the ear representing gouty [tophi](/wiki/Tophus) Image:ChronicGout.jpg|Tophus of the knee Image:Case 30-bottom.jpg|Tophus of the toe, and over the external malleolus Image:Tophigout.JPG|Gout complicated by ruptured tophi (exudate tested positive for uric acid crystals) Image:GoutCropped2016.jpg|Gout of the right MP joint of the big toe </gallery>

## Epidemiology[[edit](/index.php?title=(none)&action=edit&section=20)]

Gout affects around 1–2% of the Western population at some point in their lifetimes and is becoming more common.<ref name=Review08/><ref name=Lancet2010/> Some 5.8 million people were affected in 2013.<ref name=GBD2015>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Rates of gout approximately doubled between 1990 and 2010.<ref name=Nature2009>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> This rise is believed to be due to increasing life expectancy, changes in diet and an increase in diseases associated with gout, such as metabolic syndrome and [high blood pressure](/wiki/High_blood_pressure).<ref name=Epi2008>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Factors that influence rates of gout, include age, race and the season of the year. In men over 30 and women over 50, rates are 2%.<ref name=JFP09>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

In the United States, gout is twice as likely in males of African descent than those of European descent.[[43]](#cite_note-43) Rates are high among Pacific Islanders and the [Māori](/wiki/Māori_people), but rare in [aboriginal Australians](/wiki/Aboriginal_Australians), despite a higher mean uric acid serum concentration in the latter group.[[44]](#cite_note-44) It has become common in China, Polynesia and urban sub-Saharan Africa.<ref name=Lancet2010/> Some studies found that attacks of gout occur more frequently in the spring. This has been attributed to seasonal changes in diet, alcohol consumption, physical activity and temperature.[[45]](#cite_note-45)

## History[[edit](/index.php?title=(none)&action=edit&section=21)]

[thumb|upright=1.4|alt=A man wearing a long, curly wig and a full robe is sitting, looking out. His left arm rests on a small table, with his left hand holding a box. Behind him is a globe.|](/wiki/File:Anthonie_van_Leeuwenhoek_(1632-1723)._Natuurkundige_te_Delft_Rijksmuseum_SK-A-957.jpeg)[Antonie van Leeuwenhoek](/wiki/Antonie_van_Leeuwenhoek) described the microscopic appearance of uric acid crystals in 1679.[[46]](#cite_note-46)

The term "gout" was initially used by Randolphus of Bocking, around 1200 AD. It is derived from the [Latin](/wiki/Latin) word *gutta*, meaning "a drop" (of liquid).[[46]](#cite_note-46) According to the [Oxford English Dictionary](/wiki/Oxford_English_Dictionary), this is derived from [humorism](/wiki/Humorism) and "the notion of the 'dropping' of a morbid material from the blood in and around the joints".[[47]](#cite_note-47) Gout has been known since antiquity. Historically, it was referred to as "the king of diseases and the disease of kings"<ref name=Lancet2010/>[[48]](#cite_note-48) or "rich man's disease".<ref name=Dic/> The first documentation of the disease is from Egypt in 2,600 BC in a description of arthritis of the big toe. [Greek](/wiki/Ancient_Greece) physician [Hippocrates](/wiki/Hippocrates) around 400 BC commented on it in his [*Aphorisms*](/wiki/Aphorisms), noting its absence in [eunuchs](/wiki/Eunuchs) and [premenopausal](/wiki/Premenopausal) women.[[46]](#cite_note-46)[[49]](#cite_note-49) [Aulus Cornelius Celsus](/wiki/Aulus_Cornelius_Celsus) (30 AD) described the linkage with alcohol, later onset in women and associated kidney problems:

Again thick urine, the sediment from which is white, indicates that pain and disease are to be apprehended in the region of joints or viscera... Joint troubles in the hands and feet are very frequent and persistent, such as occur in cases of podagra and cheiragra. These seldom attack eunuchs or boys before coition with a woman, or women except those in whom the menses have become suppressed... some have obtained lifelong security by refraining from wine, mead and [venery](/wiki/Sexual_intercourse).[[50]](#cite_note-50)

In 1683, [Thomas Sydenham](/wiki/Thomas_Sydenham), an English physician, described its occurrence in the early hours of the morning and its predilection for older males:

Gouty patients are, generally, either old men, or men who have so worn themselves out in youth as to have brought on a premature old age—of such dissolute habits none being more common than the premature and excessive indulgence in venery and the like exhausting passions. The victim goes to bed and sleeps in good health. About two o'clock in the morning he is awakened by a severe pain in the great toe; more rarely in the heel, ankle or instep. The pain is like that of a dislocation and yet parts feel as if cold water were poured over them. Then follows chills and shivers and a little fever... The night is passed in torture, sleeplessness, turning the part affected and perpetual change of posture; the tossing about of body being as incessant as the pain of the tortured joint and being worse as the fit comes on.[[51]](#cite_note-51)

The Dutch scientist [Antonie van Leeuwenhoek](/wiki/Antonie_van_Leeuwenhoek) first described the microscopic appearance of urate crystals in 1679.[[46]](#cite_note-46) In 1848, English physician [Alfred Baring Garrod](/wiki/Alfred_Baring_Garrod) identified excess uric acid in the blood as the cause of gout.[[52]](#cite_note-52)

## Other animals[[edit](/index.php?title=(none)&action=edit&section=22)]

Gout is rare in most other animals due to their ability to produce [uricase](/wiki/Uricase), which breaks down uric acid.<ref name=Animals01>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Humans and other [great apes](/wiki/Great_apes) do not have this ability, thus gout is common.<ref name=Egg2007/><ref name=Animals01/> Other animals with uricase include fish, amphibians and most non primate mammals.<ref name=Choi2005>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> The [*Tyrannosaurus rex*](/wiki/Tyrannosaurus_rex) specimen known as "[Sue](/wiki/Sue_(dinosaur))", however, is believed to have suffered from gout.[[53]](#cite_note-53)

## Research[[edit](/index.php?title=(none)&action=edit&section=23)]

A number of new medications are under study for treating gout, including [anakinra](/wiki/Anakinra), [canakinumab](/wiki/Canakinumab) and [rilonacept](/wiki/Rilonacept).[[54]](#cite_note-54) Canakinumab may result in better outcomes than a low dose of a steroid but costs five thousand times more.[[55]](#cite_note-55) A [recombinant](/wiki/Recombinant_DNA) [uricase](/wiki/Uricase) enzyme ([rasburicase](/wiki/Rasburicase)) is available; its use, however, is limited, as it triggers an [autoimmune](/wiki/Autoimmune) response. Less [antigenic](/wiki/Antigenic) versions are in development.<ref name=Egg2007/>

## References[[edit](/index.php?title=(none)&action=edit&section=24)]

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## External links[[edit](/index.php?title=(none)&action=edit&section=25)]

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