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UNDERSTANDING GOUT: A REVIEW OF PATHOPHYSIOLOGY, DIAGNOSIS AND MANAGEMENT

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ABSTRACT

Background: Gout is a chronic metabolic disease caused by persistent hyperuricemia and strongly associated with cardiometabolic comorbidities such as obesity, diabetes, renal impairment, and cardiovascular disease. Recent epidemiological data show a continuous global increase in gout prevalence, reaching 1–6% of adults, with rising healthcare costs and disability-adjusted life years (DALYs). Despite the availability of effective urate-lowering agents, fewer than half of patients achieve target serum urate levels in routine practice. This reflects significant gaps in disease awareness, early diagnosis, and adherence to long-term management. Rapid progress in understanding inflammasome-driven inflammation and the development of novel diagnostic and therapeutic modalities require a comprehensive reassessment of current evidence.

Aim: This review summarizes and critically analyzes contemporary data on the pathophysiology, diagnosis, and management of gout, integrating pharmacological and non-pharmacological approaches and identifying key areas of controversy and unmet clinical needs.

Materials and Methods: A narrative evidence-based review was conducted through PubMed and Google Scholar for publications issued between January 2005 and June 2025. Search terms included "gout", "hyperuricemia", "pathogenesis", "diagnosis", "urate-lowering therapy", and "lifestyle modification". Peer-reviewed studies, clinical trials, meta-analyses, and international guidelines were selected based on methodological quality and relevance. Only English-language papers were included.

Results: Gout develops due to serum uric acid levels exceeding 6.8 mg/dL, leading to monosodium urate crystal deposition, activation of the NLRP3 inflammasome, and recurrent inflammation. Advances in imaging techniques, particularly ultrasonography and dual-energy computed tomography, have improved diagnostic accuracy and early detection. Updated international guidelines highlight early anti-inflammatory therapy and individualized urate-lowering strategies, while emerging data emphasize the importance of weight reduction, dietary modification, and metabolic control

in preventing recurrent flares and improving long-term outcomes.

Conclusions: Effective gout management requires an integrated, multidisciplinary approach combining pharmacologic therapy, lifestyle modification, and preventive measures. Early recognition and personalized treatment reduce flare frequency, prevent joint destruction, and mitigate systemic complications. Sustained metabolic control and patient education are essential to improving adherence and reducing the overall societal and economic burden of this increasingly prevalent disease.

Keywords: gout, hyperuricemia, urate-lowering therapy, inflammation, lifestyle modification, comorbidities, NLRP3 inflammasome

INTRODUCTION

Gout affects approximately 1–6% of the adult population worldwide, with higher prevalence observed in men and older adults. In Europe, the disease affects 1–4% of adults, whereas in the United States its prevalence reaches nearly 4% [2,4]. The disease is characterized by the deposition of monosodium urate (MSU) crystals in tissues, especially in and around joints, which induces episodes of acute inflammation [1]. Once perceived as a condition associated with affluence and excessive nutrition, gout has now emerged as a major global health issue affecting diverse populations across demographic and socioeconomic groups. The rising incidence of gout worldwide reflects a complex interaction of metabolic, genetic, and environmental determinants, including aging, dietary habits, obesity, and comorbidities such as diabetes, renal dysfunction, and cardiovascular disease [1,2,3].

Despite extensive clinical experience, several aspects of gout pathogenesis and management remain insufficiently clarified. These include the role of inflammasome activation in chronic inflammation, the optimal integration of urate-lowering and anti-inflammatory therapy, and the impact of non-pharmacological interventions such as diet and weight reduction on long-term disease control. Furthermore, diagnostic strategies continue to evolve with the use of advanced imaging modalities such as ultrasound and dual-energy computed tomography, which enable earlier and more accurate detection of urate deposits. The rapidly expanding body of evidence requires periodic reassessment and synthesis to guide clinical practice.

OBJECTIVES

The aim of this review is to summarize and critically analyze current evidence on the pathophysiology, diagnostic criteria, and therapeutic approaches to gout, with an emphasis on integrating pharmacologic and lifestyle-based management. The specific objectives are:

1. to outline recent advances in understanding the mechanisms of urate crystal formation and inflammation;
2. to present updated diagnostic standards and imaging criteria;
3. to evaluate modern pharmacological and non-pharmacological treatment options based on recent guidelines and trials;
4. to highlight the clinical and public health implications of effective long-term disease control.

This synthesis is intended to provide clinicians and researchers with an updated framework for evidence-based management of gout, emphasizing early diagnosis, comprehensive therapy, and prevention of comorbid complications.

MATERIALS AND METHODS

This narrative evidence-based review was conducted in accordance with the principles of transparent and reproducible literature synthesis. A comprehensive search was performed in PubMed and Google Scholar databases for publications issued between January 2005 and June 2025. The search strategy combined Medical Subject Headings (MeSH) and free-text terms related to gout, including “gout”, “hyperuricemia”, “pathogenesis of gout”, “clinical manifestations of gout”, “diagnosis of gout”, “urate-lowering therapy”, “gout treatment”, “lifestyle modification”, and “gout prevention”.

Inclusion criteria comprised peer-reviewed original studies, clinical trials, meta-analyses, systematic and narrative reviews, and official clinical guidelines addressing the pathophysiology, diagnosis, or management of gout in adult human populations. Publications in English and other languages were considered when relevant and of verifiable scientific quality, including national Polish epidemiological or clinical reports that contribute to understanding local disease prevalence and management patterns.

Exclusion criteria included non-reviewed materials, conference abstracts, isolated case reports without analytical content, and publications not directly related to gout.

Titles and abstracts were independently screened for relevance, and the full texts of potentially eligible studies were evaluated for methodological quality and contribution to the subject. Reference lists of key publications were manually reviewed to identify additional relevant works.

QUANTITATIVE SUMMARY OF THE LITERATURE SEARCH:

A total of 260 records were initially identified. After removal of duplicates, 180 remained. Based on title and abstract screening, 85 were excluded for lack of clinical or methodological relevance. Ninty-five full-text articles were reviewed in

detail, and 51 studies met the inclusion criteria and were retained for qualitative synthesis. Additional relevant publications were identified through manual reference screening.

To enhance the regional relevance of this analysis, inclusion of national epidemiological and clinical data from Poland is recommended in future updates, which would provide a more comprehensive representation of local disease trends.

This approach ensured broad coverage of both pharmacological and non-pharmacological management strategies and integrated the latest recommendations of major rheumatology societies (ACR, EULAR) with recent clinical and translational research findings.

GOUT IN THE CURRENT STATE OF KNOWLEDGE

EPIDEMIOLOGY AND RISK FACTORS

The prevalence of gout varies globally, ranging from 1% to 6.8%. In Europe, the disease affects approximately 1% to 4% of the population, while in the United States the figure reaches about 3.9%[2]. According to the 2008 U.S. National Health and Nutrition Examination Survey, nearly 4.7 million older adults were living with gout [4]. Furthermore, about 31.9% of new diagnoses occur in individuals aged 65 years and older, confirming the strong association between gout and advancing age [5]. Age-related reductions in renal uric acid excretion and accumulation of comorbidities are likely contributing factors [6]. Sex is another major determinant of disease prevalence. Men are nearly twice as likely to be affected as women, due in part to higher baseline serum uric acid levels and sex-specific differences in metabolism. Estrogen enhances renal uric acid excretion, providing premenopausal women with a degree of protection. After menopause, this hormonal advantage diminishes, and gout risk in women rises significantly [3]. Environmental and seasonal influences have also been implicated. Lower ambient temperatures in winter may facilitate the crystallization of MSU, while summer conditions, through dehydration and dietary changes, can lead to elevated serum uric acid levels, both promoting acute attacks [7]. Lifestyle and dietary habits are critical modifiable risk factors. Men are more likely to consume purine-rich foods, such as red meat and seafood, and alcohol, both of which are strongly associated with gout exacerbations [3]. Certain pharmacological agents contribute to hyperuricemia. Diuretics inhibit urate excretion via the OAT1 and OAT3 transporters, while cyclosporine impairs ABCG2 function. Additionally, obesity and insulin resistance enhance urate retention through upregulation of the URAT1 transporter, further elevating gout risk [3]. Socioeconomic conditions, captured by the Socio-demographic Index (SDI), also play a role. Regions with high SDI scores, reflecting higher education, income, and health infrastructure, report greater gout prevalence, potentially due to sedentary lifestyles and diets rich in purines and calories. Interestingly, the lowest prevalence is observed in middle-SDI regions, while underdiagnosis may occur in low-SDI areas due to limited access to care [8].

COMORBIDITIES ASSOCIATED WITH GOUT

Gormin and sodium-glucose cotransporter-2 inhibitors (SGLT-2i) appear to carry compaut rarely occurs in isolation. It is frequently accompanied by cardiometabolic comorbidities that increase disease severity, complicate management, and contribute to functional decline. Obesity, insulin resistance, and type 2 diabetes are among the most common metabolic disorders associated with gout. In addition, renal impairment, particularly a glomerular filtration rate below 60 mL/min/1.73 m², reduces urate clearance and intensifies hyperuricemia [3]. Patients with gout are also at elevated risk for cardiovascular disease, even when uric acid levels are within the normal range. Conversely, in individuals without gout, higher serum urate concentrations positively correlate with cardiovascular risk. These findings underscore the importance of lifestyle interventions to mitigate cardiovascular risk in both populations, regardless of urate levels [9]. In the context of diabetes treatment, recent studies have evaluated the effect of antidiabetic therapies on gout risk. Metforable gout risk, although SGLT-2 inhibitors are more effective in lowering serum uric acid [10]. A newly described clinical entity, urate-lowering therapy–resistant gout (UALT-RG), affects an estimated 9.08% of gout patients in the U.S. population. This subgroup is more likely to present with obesity, diabetes, and chronic kidney disease. Importantly, elevated Body Roundness Index (BRI) and reduced eGFR have been proposed as independent predictors and potential screening markers for UALT-RG[11].

PATHOGENESIS

The pathogenesis of gout is a strong inflammatory response triggered by monosodium urate (MSU) crystals, which form in presence of increased urate concentrations [12]. Urate is the salt of uric acid, a product of purine metabolism. Most studies state that the main mechanism of hyperuricemia is underexcretion of urate regulated by a group of urate transporters in proximal tubules of kidney and intestine. In the kidney 90 percent of filtered by renal glomeruli urate is reabsorbed in the proximal tubule. Genetic variation in urate transporter genes corresponds with variance in serum urate levels [1,13]. The main genes associated with this changes are SLC2A9 which encode Glucose transporter 9(GLUT9), SLC22A12 encoding urate transporter 1(URAT1) and ABCG2 which encode Adenosine triphosphate (ATP)-binding cassette super-family G member 2(ABCG2). We can divide them into two groups, GLUT9 on basolateral membrane, URAT1 on apical membrane in the proximal tubule of kidney which are responsible for urate reabsorption and ABCG2 which plays a major role in renal and intestinal excretion [13]. High concentration of sodium in the extracellular compartment leads to urate mostly present as MSU. When serum urate level is in the region of 6,8 mg/dl, MSU crystals start to form. MSU crystals trigger an immune response mainly through activation of the nucleotide-binding oligomerization domain (NOD), leucine-rich repeat (LRR) and pyrin domain-containing protein 3(NLRP3) inflammasome. Among them activation of NLRP3 by tissue-resident macrophages, which recognise MSU crystals as damage-associated molecular patterns (DAMPs), leads to release of active interleukin-1 beta(IL-1β), the key cytokine in gout inflammation [13,14]. Activated IL-1β binds to the IL-1β receptor and induces a signal transduction pathway that activates proinflammatory transcription factors, leading to

amplification of cytokines and chemokines. That results in the recruitment of neutrophils and other immune cells to the site of MSI crystals deposition [1]. Neutrophils engulf MSU crystals and eject their chromatin along with cytosolic and granule protein; that process called NETosis results in the creation of neutrophil extracellular traps (NETs). In addition, a group of enzymes released by neutrophils also process pro-IL-1β into active IL-1β amplifying inflammation [13]. However studies shows that self-limiting nature of acute gout is also a result of high neutrophil densities and accumulation of NETs. In these clusters NETs trap and degrade cytokines and chemokines by NET-bound proteases. This process results in resolution of inflammation in acute gout [13,15].

CLINICAL PRESENTATION OF GOUT

Gout is a chronic crystal deposition disease characterized by the formation and buildup of monosodium urate crystals within tissues such as cartilage, synovium and skin. This process can occur even in the absence of any noticeable clinical symptoms, highlighting that the pathological changes often begin before gout becomes clinically apparent [16].

ASYMPTOMATIC HYPERURICAEMIA WITH MONOSODIUM URATE CRYSTAL DEPOSITS

Hyperuricemia is defined as a serum uric acid level exceeding 6.8 mg/dL [1]. It is most often detected incidentally, as patients typically remain asymptomatic. Only about 5% of individuals with uric acid levels above 9 mg/dL go on to develop gout [17]. Although there is a strong association between serum uric acid levels and the development of gout, elevated levels alone do not confirm or exclude the diagnosis. Many people with hyperuricemia never experience gout, and also, uric acid levels may be normal during acute gout flares. Hyperuricemia is the primary factor promoting the formation of MSU crystals. Once formed, these crystals can stimulate leukocytes and synovial cells to trigger an immune response, resulting in the development of local inflammation [18]. Imaging studies have shown that both the amount and size of urate crystals increase as the condition progresses from asymptomatic hyperuricemia to clinically evident gout. Individuals with hyperuricemia most likely gradually accumulate urate crystals until a threshold is reached that triggers a gout attack [19]. The presence of MSU crystal deposits and the associated subclinical inflammation should be regarded as a form of asymptomatic gout, distinguishing it from asymptomatic hyperuricemia, where no crystal deposition is present [16].

ACUTE GOUT

Some individuals with MSU crystal deposits go on to develop clinical manifestations of gout. The crystals trigger an inflammatory response within the joint or surrounding tissues. Gout commonly presents as an episodic, self-limiting inflammatory arthritis, marked by the rapid onset of severe pain, redness, warmth, swelling, and loss of joint function [17,18,20]. In approximately 80% of initial cases, it appears as an acute monoarthritis, typically reaching peak intensity within 24 to 48 hours [18]. Gout most often affects the lower limbs, with the first metatarsophalangeal (MTP) joint being the classic and most frequent site of acute attacks (50% of initial attacks), this condition is known as podagra. Other frequently involved joints include the tarsal joints, ankles, and knees. Wrists, metacarpophalangeal (MCP) joints, and interphalangeal joints of the hands can also be affected. Less commonly, the hip and shoulder may be involved, while spinal manifestation is extremely rare. Beyond the joints, gout may also lead to inflammation of surrounding soft tissues, such as olecranon bursitis or Achilles tendinitis. In the upper limbs, the olecranon bursa is the most commonly affected site [16,17]. Simultaneous arthritis in multiple joints can occur, particularly in individuals with long-standing, untreated gout or in postmenopausal women [17]. Systemic features are generally minimal or completely absent. However, in certain cases, patients may experience fever and other generalized symptoms [18]. A gout flare is a self-limiting inflammatory episode, with symptoms typically resolving on their own within 7 to 10 days, even without treatment [20]. Acute gout attacks can be triggered by a variety of factors, including acute illnesses, infections and metabolic disturbances. Sudden fluctuations in serum uric acid levels, whether rising or falling, can also provoke flares [18]. An acute attack resolves within a few hours to several days following the initiation of appropriate treatment [17].

INTERCRITICAL PERIOD

After the symptoms of an acute gout attack resolve, the patient enters a remission phase - an asymptomatic period between flares. Despite the absence of symptoms, uric acid levels usually remain elevated, allowing urate crystals to continue accumulating in the tissues. As the disease progresses, these symptom-free intervals tend to shorten, resulting in more frequent flare-ups [21]. Therefore, it is essential to initiate appropriate treatment aimed at lowering uric acid levels. Lowering serum urate levels below 6.8 mg/dL promotes the dissolution of existing urate crystals over time, reducing the frequency of gout flares [22].

CHRONIC GOUT

Untreated gout with recurrent acute attacks eventually progresses to chronic arthropathy, characterized by chronic synovitis, tophus formation and deposition, and ultimately, erosions and joint destruction. It involves the accumulation of solid aggregates of MSU crystals - tophi, in various locations, including joints, bursae, tendons, subcutaneous tissue, and the skin. Tophi most commonly form in areas exposed to pressure or friction [17,22]. These deposits can lead to joint destruction, deformity, and functional impairment. Although they typically develop slowly and asymptomatically, their formation may accelerate significantly in patients using diuretics or those with severe renal disease. The average time for tophi development is approximately 11.6 years from the onset of untreated gout, occurring in 12% of patients after 5 years and in up to 55% after 20 years without treatment [18]. As tophi grow, they can extend into adjacent bone tissue, leading to the development of erosive bone lesions [17].

Chronic joint swelling, referred to as chronic gouty arthritis, may also be present. This swelling is most commonly caused by persistent effusion resulting from granulomatous inflammation of the synovial membrane induced by MSU crystals. The

natural course of untreated gout leads to more frequent and severe flares and the development of persistent clinical symptoms. However, early diagnosis and appropriate treatment can effectively prevent these outcomes [16].

DIAGNOSIS

The diagnosis of gout has undergone significant changes in recent years, thanks to advances in imaging techniques, a better understanding of the pathophysiology of the disease, and updated guidelines from international scientific societies [23]. The current classification criteria endorsed by the American College of Rheumatology and the European League Against Rheumatism (ACR/EULAR) integrate clinical, imaging, and laboratory domains [24]. According to the assumptions, these criteria can only be used in patients who have had at least one symptomatic episode indicating a gout attack, i.e. swelling, pain or tenderness of a peripheral joint or synovial bursa. The criteria are based on the sum of points assigned to individual clinical, laboratory and imaging parameters; achieving a score of ≥8 points allows for the diagnosis of gout (Table 1). Although formally they are of a classification nature, they are also widely used in clinical practice [23,25].

Table 1. ACR/EULAR 2015 Classification Criteria for Gout

Category	Criteria	Description	Points
Clinical Criteria	Joint involvement	Other joints	0
		Ankle or midfoot (without 1st MTP)	1
		1st MTP involvement	2
	Symptoms during flare	Erythema, tenderness, impaired use	1 each (up to 3)
	Flare pattern	Single typical flare	1
		Recurrent typical flares	2
	Tophi	None	0
		Present	4
Laboratory Criteria	Serum uric acid	< 4 mg/dL	-4
		4 to <6 mg/dL	0
		6 to <8 mg/dL	2
		8 to <10 mg/dL	3
		≥10 mg/dL	4
	MSU crystals in synovial fluid	Absent	-2
		Not examined	0
		Present	Sufficient for diagnosis
Imaging Criteria	MSU deposits	Double contour sign (USG) or DECT	4
	Erosions	≥1 erosion on X-ray (hands/ feet)	4

The gold standard for the diagnosis of gout remains the identification of monosodium urate monohydrate (MSU) crystals in synovial fluid or tophi aspirate using polarized microscopy. This method has 100% specificity and is a sufficient classification criterion according to the 2015 ACR/EULAR guidelines [23]. In a situation where synovial fluid analysis is not possible, the diagnosis is based on clinical features suggestive of gout, in combination with hyperuricemia, which consists of:

- acute, sudden onset (<24 hours) of inflammation of one joint, especially the first metatarsophalangeal joint (MTP),
- skin erythema over the affected joint,
- previous episodes of similar attacks,

- male gender,
- presence of cardiovascular diseases,
- elevated uric acid levels.

Although the threshold of 6 mg/dl (360 µmol/l) is considered the point of plasma uric acid saturation above which the risk of crystallization increases, hyperuricemia alone cannot be the basis for diagnosis. Studies show that only half of patients with valuesabove 10 mg/dl develop symptomatic gout within 15 years. This risk depends on genetic and environmental factors that modulate the processes of crystal nucleation and deposition [23].

When crystal identification is not possible and the clinical picture does not allow for a clear diagnosis, imaging studies are recommended to confirm the presence of MSU deposits and exclude other causes of arthritis [25].

Ultrasonography is the preferred imaging method due to its availability, lack of exposure to radiation, low cost and the ability to visualize:

- double contour sign, which is specific for urate deposits,
- tophi that are not visible in the clinical examination,
- signs of inflammation in Doppler mode.

It is recommended to assess the joints affected by the inflammatory process and bilaterally examine the MTP and knee joints, as typical sites of crystal deposition [25].

Dual-beam computed tomography (DECT) allows for non-invasive detection and characterization of monosodium urate deposits in joints and soft tissues. It is particularly useful in diagnosing difficult cases (e.g. gout), although its availability, cost and need for specialist interpretation limit its use in general practice [25].

Magnetic resonance imaging (MRI) and computed tomography (CT) allow for the assessment of the extent of inflammation, the presence of tophi and joint destruction, but their diagnostic usefulness is limited compared to ultrasound and DECT [23,25].

According to EULAR recommendations, after the diagnosis of gout, the presence of risk factors for hyperuricemia should be routinely assessed, such as:

- obesity,
- chronic kidney disease (CKD),
- medications (thiazide diuretics, low-dose aspirin, cyclosporine, tacrolimus),
- consumption of alcohol, fructose-sweetened beverages, red meat and seafood.

In addition, screening for comorbidities is necessary, including hypertension, type 2 diabetes, coronary heart disease, heart failure and dyslipidemia [25].

Erroneous diagnoses of gout occur with notable frequency; diagnostic accuracy is higher in monoarticular presentations compared with oligoarticular or polyarticular involvement [16,26]. Furthermore, coexistence of crystalinduced arthritis and septic arthritis must always be considered, as identification of crystals in synovial fluid does not categorically exclude concurrent infection [16]. Emerging evidence suggests that gout may not be as mutually exclusive with other chronic inflammatory arthritides as previously thought: MSU crystals have been isolated in patients with various rheumatic diseases, and differentiating acute calcium pyrophosphate crystal arthritis from gout in elderly individuals with established gout can be particularly challenging [16,27].

NON-PHARMACOLOGICAL TREATMENT

There is a well-established association between serum uric acid levels, obesity, metabolic syndrome, and hyperuricemia. Crosssectional studies have demonstrated a positive correlation between serum uric acid concentrations and body mass index (BMI) [27, 28]. Weight reduction through physical activity and dietary modification leads to a decrease in serum uric acid levels and lowers the risk of gout. Because rapid weight loss induces ketosis, which promotes uric acid reabsorption via the organic anion transporter URAT1, thereby elevating serum uric acid, a gradual reduction in body mass is preferable to abrupt caloric restriction [27]. Although moderateintensity exercise has been linked to lower uric acid levels in obese individuals, it remains unclear whether aerobic activity alone reduces serum uric acid and the incidence of gout. Moreover, physically active men appear to have a lower incidence of gout compared with their sedentary counterparts [27, 29].

Adequate hydration is also recommended for patients with gout, as an internetbased case–crossover study found that consuming at least 1 920 mL of water in the 24 hours preceding an acute gout attack was associated with a 46 % reduction in recurrence frequency [30].

Additional key recommendations include abstaining from alcohol, limiting sugarsweetened beverages, increasing dairy intake, and avoiding organ meats, seafood, and processed meats. Epidemiological research demonstrated that higher dairy consumption correlates with lower serum uric acid and a reduced risk of developing gout. In a cohort of 633 patients with confirmed gout, ingestion of half a cup of cherries (10–12 fruits) or a cherry extract over two days resulted in a 35 % decrease in the likelihood of a subsequent gout attack. Diets rich in vegetables and fruits, particularly cherries, may further reduce serum uric acid levels, and coffee consumption has been inversely associated with hyperuricemia.

Furthermore, supplementation with 500 mg of vitamin C daily for two months increased estimated glomerular filtration rate and lowered serum uric acid [31]. To prevent gout, aim for gradual weight loss through moderate exercise and dietary adjustments, maintain proper hydration, and avoid alcohol and highpurine foods.

PHARMACOLOGICAL TREATMENT

TREATMENT OF ACUTE FLARES

The goal of treating an acute gout flare is to reduce inflammation and alleviate pain. Ideally, treatment should begin within 24 hours of symptom onset to help lessen both the intensity and duration of the episode. Non-drug approaches like rest and applying ice packs can be used alongside anti-inflammatory medications. The primary options for treating a gout flare include nonsteroidal anti-inflammatory drugs (NSAIDs), colchicine, and systemic corticosteroids, all of which have been shown to effectively reduce symptoms during acute flares [32]. Treatment typically lasts 7 to 10 days to avoid recurrence of symptoms. Starting NSAIDs early may resolve the flare with just a single dose. IL-1 antagonists have proven effective in cases of gouty arthritis that do not respond to standard treatments.

NSAIDs are widely used in the treatment of acute gout due to their ability to inhibit cyclooxygenase (COX) enzymes and reduce prostaglandin synthesis, especially COX-2, which is central to pain and inflammation during gout flares [32]. Commonly used NSAIDs include indomethacin (50 mg three times daily), naproxen (500 mg twice daily), and ibuprofen (800 mg three to four times daily), all of which generally provide symptom relief within 4872 hours [33]. Most NSAIDs are equally effective in this indication, and both ACR and EULAR guidelines list them as first-line therapy, provided contraindications are absent [23,34]. When initiated promptly, NSAIDs can shorten the duration of a flare to as little as 3 to 7 days.

Despite their efficacy, NSAIDs carry notable risks, particularly gastrointestinal (ulceration, bleeding), cardiovascular (hypertension, fluid retention), and renal (decreased filtration, sodium retention) [35, 36]. These effects are particularly concerning in elderly patients or those with comorbidities such as heart failure, chronic kidney disease, or peptic ulcer disease. [24]. When used in otherwise healthy individuals, a short-term course is typically well tolerated, especially with attention to dosing and duration. For appropriately selected patients, NSAIDs remain a fast-acting and effective option in acute gout.

Colchicine reduces inflammation in gout by inhibiting neutrophil migration and microtubule polymerization, thus blocking the amplification of the inflammatory cascade [37]. Its effectiveness is highest when administered within the first 24 hours of symptom onset. Historically, high-dose regimens were common but often led to severe gastrointestinal side effects. The AGREE trial established that a low-dose protocol (1.2 mg followed by 0.6 mg after one hour) offers comparable pain relief with significantly fewer adverse effects [33]. This regimen is now endorsed in contemporary guidelines [23].

The therapeutic window of colchicine is narrow. Common side effects include diarrhea and nausea, while severe toxicity can occur in renal or hepatic impairment due to reduced drug clearance [36]. It is contraindicated in severe renal or liver dysfunction and requires caution in moderate cases. Significant drug interactions (e.g. with CYP3A4 or P-glycoprotein inhibitors) may cause colchicine accumulation, increasing the risk of bone marrow suppression or neuromyopathy [34]. Despite these concerns, when used correctly, colchicine is an effective early intervention in acute gout.

Glucocorticoids act through intracellular receptors to modulate gene expression, inhibiting key pro-inflammatory mediators such as NF-B and IL-1 [38]. Their broad anti-inflammatory effect leads to rapid symptom resolution. Commonly used glucocorticoids include oral prednisolone (30-35 mg/day for 5 days), methylprednisolone (dose adjusted by weight or severity), and intra-articular triamcinolone acetonide (20-40 mg depending on joint size), all of which have demonstrated efficacy equivalent to NSAIDs in randomized trials [34,39]. Intra-articular administration is particularly useful in monoarticular flares, especially when sepsis has been ruled out [23]. In cases where multiple joints are involved or oral administration is not feasible, intra-articular glucocorticoid injection remains a highly effective option, particularly when targeting the most symptomatic joints. Intramuscular or intravenous glucocorticoids may also be considered as systemic alternatives in polyarticular flares. Guidelines recognize glucocorticoidsoral, parenteral, or intra-articularas first-line options in acute gout management [23]. A clinical response is often observed within the first 12 to 24 hours of initiation.

Steroids are particularly valuable in patients with contraindications to NSAIDs or colchicine, such as those with renal insufficiency or gastrointestinal disorders [36]. While transient side effects such as hyperglycemia, fluid retention, and mood alterations can occur, glucocorticoids avoid many of the risks associated with NSAIDs. Studies have shown that short-term steroid use in gout is generally safe and well tolerated, making them an effective and practical option for a broad range of patients [34, 39].

Interleukin-1 (IL-1) antagonists have demonstrated efficacy in treating refractory cases of gouty arthritis, especially when patients do not respond to conventional therapies such as nonsteroidal anti-inflammatory drugs, colchicine, and corticosteroids. IL-1 is a key pro-inflammatory cytokine involved in gouty inflammation, and targeting it has become an innovative approach in managing the condition. Among the IL-1 inhibitors, anakinra, rilonacept, and canakinumab have been studied extensively [40].

Anakinra, which acts as an interleukin-1 receptor antagonist, has become a promising treatment for hospitalized individuals suffering from acute gout and calcium pyrophosphate (CPP) crystal arthritis, especially those with complicated medical conditions. Conventional treatments like NSAIDs, colchicine, and corticosteroids are often unsuitable or not well-tolerated by these patients. Anakinra offers quick clinical relief, with 75% of cases experiencing significant improvement or complete resolution within four days of starting treatment. The medication has demonstrated a favorable safety profile, even among high-risk groups such as those with active infections, recent surgeries, or organ transplants, groups usually

excluded from clinical trials. Importantly, anakinra seems safe for patients with chronic kidney disease or end-stage renal disease, addressing a significant limitation of standard treatments. Although its direct cost is higher, the potential to reduce hospital stays and complications suggests it may be cost-effective in certain situations [40].

Rilonacept, an inhibitor of interleukin-1, has proven effective in preventing gout flares, particularly when starting uric acid-lowering therapy (ULT). Research has indicated that rilonacept significantly decreases the occurrence of gout flares during the initial months of ULT [41,42]. For example, a phase III trial revealed that rilonacept notably lowered the average number of gout flares per patient compared to a placebo and also resulted in fewer days with gout flares [41]. Another study found that administering rilonacept in doses of 80 mg and 160 mg led to a marked reduction in gout flares, with a greater percentage of patients remaining flare-free compared to those on a placebo [42]. Furthermore, rilonacept was generally well-tolerated, with the most frequent side effects being mild reactions at the injection site [43]. However, in the treatment of acute gouty arthritis, rilonacept, whether used alone or with indomethacin, did not significantly surpass indomethacin alone in reducing pain in a controlled trial [42]. Thus, while rilonacept is effective in preventing flares associated with the start of ULT, its effectiveness in treating acute flares may be limited compared to other options.

Meanwhile, canakinumab, a monoclonal antibody targeting IL-1β, has been effective for both reducing pain and inflammation during acute gout attacks and lowering the risk of recurrent episodes [44]. Clinical trials have shown its effectiveness in managing acute flares, providing quick and lasting pain relief while significantly lowering the risk of recurrent episodes. Notably, in an 8-week dose-ranging study, the 150 mg dose of canakinumab was more effective than glucocorticoids in reducing pain and inflammation [45,46]. Beyond acute management, canakinumab has also shown potential in preventing flares during the initiation of urate-lowering therapy, outperforming colchicine in this regard. Regarding safety, although some concerns have been raised, canakinumab generally has a tolerability profile similar to existing treatments like glucocorticoids [46,47,48].

Overall, IL-1 blockers present a viable treatment alternative for patients with contraindications or intolerance to standard therapies, and their use in clinical practice, particularly in cases of refractory gouty arthritis, is supported by substantial evidence.

URATE-LOWERING THERAPIES

Gout is a chronic inflammatory disease caused by hyperuricemia, which causes the formation of monosodium urate crystals in the joints and other sequelae. Treatment of gout is aimed not only at controlling pain and recurring attacks, but primarily at resolving the underlying causes of crystal deposition and the associated side effects of deposits, including tophi. A key outcome is the secondary effect, which occurs as a result of urinary tract activity when blood levels are below the saturation threshold, usually <6 mg/dl, and in patients with advanced disease, even <5 mg/dl [43].

According to the 2020 American College of Rheumatology guidelines, pharmacological treatment of chronic gout should be initiated in all patients with tophi, kidney stones, gout-related joint damage, and those who have experienced two or more attacks within a year. The first-line drug is allopurinol, a xanthine oxidase inhibitor, used in low initial doses (e.g., 100 mg/day, or even 50 mg/day in patients with chronic kidney disease), with gradual increases until the target uric acid level is achieved [43].

In cases of allopurinol intolerance or ineffectiveness despite the maximum dose (usually 800 mg/day), febuxostat, also a xanthine oxidase inhibitor, is an alternative. Febuxostat is more effective than allopurinol in lowering uric acid levels, but its cardiovascular safety has been controversial. The CARES study, which included over 6,000 patients with gout and cardiovascular disease, demonstrated that although febuxostat did not increase the risk of composite cardiovascular events compared with allopurinol, it was associated with increased cardiovascular and all-cause mortality. In light of these results, febuxostat should be used with caution, particularly in patients with a history of heart disease or stroke [46].

In patients with chronic, refractory gout, particularly those with massive tophi deposits or frequent flare-ups despite maximal conventional therapy, pegloticase may be used. This recombinant uricase, administered intravenously every two weeks, catalyzes the breakdown of uric acid into soluble allantoin. Clinical trials have demonstrated its high efficacy, with a significant percentage of patients achieving uric acid levels <6 mg/dL and a reduction or complete disappearance of tophi. However, pegloticase is associated with a high risk of immunological reactions (including anaphylactic reactions) and the development of neutralizing antibodies, which may limit its efficacy. Therefore, therapy should be closely monitored, with uric acid levels monitored before each infusion [49,50].

An important aspect of long-term gout treatment is the prevention of attacks, which may worsen during the initial phase of ULT treatment due to mobilization of urate deposits. For this purpose, the use of colchicine (e.g., 0.5–1 mg/day), NSAIDs, or low-dose glucocorticosteroids for at least 3 to 6 months after initiating uric acid-lowering therapy is recommended [45].

Nonpharmacological interventions, including patient education, lifestyle changes, and dietary modifications, are essential components of chronic gout treatment. A systematic review found that weight loss, increased physical activity, and reduced alcohol consumption, particularly beer, are strongly associated with lower uric acid levels and reduced attack frequency [51]. Weight loss reduces uric acid production and improves renal excretion, which translates into better control of hyperuricemia. Reducing the intake of purines (e.g., red meat, seafood), alcohol, and high-fructose beverages, as well as following a Mediterranean or DASH diet, have been shown to be beneficial in reducing urate levels and the risk of gout episodes [51,52]. Patient education regarding these changes increases treatment adherence and is integral to effective, integrated gout care.

Regular monitoring of uric acid levels, assessing for the presence of tophi, and strict adherence to treatment recommendations allow not only for disease control but, in many cases, for achieving remission – a state in which attacks

cease, uric acid levels remain stably low, and symptoms subside or minimize [45].

DISCUSSION

The pathogenesis of gout is fundamentally driven by the supersaturation of monosodium urate crystals, whose deposition within joint and periarticular tissues activates the NLRP3 inflammasome and triggers intense neutrophil-mediated inflammation [1,2]. Although joint fluid analysis remains the diagnostic gold standard [3], current clinical practice increasingly employs ultrasonography, particularly the double-contour sign, and dual-energy computed tomography for the detection of subclinical deposits when synovial sampling is not feasible [4,5].

The management of acute flares relies on the early initiation of nonsteroidal anti-inflammatory drugs, colchicine, or glucocorticoids, all of which demonstrate high efficacy in symptom relief but carry specific safety concerns related to cardiovascular, gastrointestinal, or renal comorbidities [6,7]. For patients intolerant of these agents, interleukin-1 inhibitors such as anakinra, rilonacept, or canakinumab represent an effective alternative, although their high cost and limited availability restrict widespread use [8,9]. Long-term urate-lowering therapy remains the cornerstone of disease control. Allopurinol is the first-line agent, while febuxostat serves as an alternative in cases of intolerance or contraindication, though its cardiovascular safety remains under discussion following the results of the CARES trial [10,11]. Pegloticase is reserved for refractory cases and demonstrates excellent biochemical efficacy, but its immunogenicity limits long-term applicability [12]. A summary of currently used pharmacological agents is presented in Table 2.

Table 2. Pharmacological agents used in gout management

Drug class	Example agents	Mechanism of action	Typical dosage range	Main indications	Key contraindications / cautions	Selected references
Nonsteroidal anti-inflammatory drugs (NSAIDs)	Naproxen, Indomethacin, Ibuprofen	Inhibition of COX-1 and COX-2 enzymes, suppression of prostaglandin-mediated inflammation	Naproxen 500 mg twice daily; Indomethacin 50 mg three times daily	Acute gout flares	Peptic ulcer, renal insufficiency, cardiovascular disease	[12], [18], [22]
Colchicine	Colchicine	Inhibition of microtubule polymerization, reduction of neutrophil migration	1 mg initially, then 0.5 mg after 1 hour (max 1.5 mg per attack)	Acute gout attacks, flare prophylaxis during ULT initiation	Severe renal/ hepatic disease, gastrointestinal intolerance	[14], [19], [25]
Glucocorticoids	Prednisone, Methylprednisolone	Anti-inflammatory through inhibition of cytokine transcription and leukocyte activation	Prednisone 30–40 mg/ day, taper over 5–10 days	Acute gout (when NSAIDs/ colchicine contraindicated)	Diabetes, infection, osteoporosis	[20], [23]
Xanthine oxidase inhibitors	Allopurinol, Febuxostat	Inhibition of xanthine oxidase, reducing uric acid synthesis	Allopurinol 100–300 mg/ day; Febuxostat 40–80 mg/ day	Long-term urate-lowering therapy	Severe hepatic/ renal dysfunction, hypersensitivity (Allopurinol); cardiovascular risk (Febuxostat)	[5], [8], [27]
Uricase agents	Pegloticase	Enzymatic oxidation of uric acid to allantoin	8 mg IV every 2 weeks	Refractory chronic gout	G6PD deficiency, infusion reactions, high immunogenicity	[28], [29]

Drug class	Example agents	Mechanism of action	Typical dosage range	Main indications	Key contraindications / cautions	Selected references
IL-1 inhibitors	Anakinra, Canakinumab, Rilonacept	Blockade of IL-1–mediated inflammation	Anakinra 100 mg/day SC for 3 days; Canakinumab 150 mg SC single dose	Acute flares resistant to standard therapy	Infection, neutropenia, cost limitations	[30], [31], [33]

Current literature highlights several unresolved issues that continue to shape the discussion on gout management. The treatment threshold for asymptomatic hyperuricemia remains uncertain [13]. The optimal target level of serum urate also varies among guidelines, with ACR recommending levels below 6 mg/dL and EULAR suggesting lower thresholds for patients with tophi [14,15]. The use of prophylactic colchicine during urate-lowering therapy, although supported by evidence, raises concerns about long-term tolerability [16,17]. Furthermore, the influence of metabolic comorbidities on therapeutic response and the potential cardiovascular implications of xanthine oxidase inhibitors require further clarification [18,19].

Non-pharmacological strategies, including dietary purine restriction, gradual weight reduction, adequate hydration, and moderation of alcohol intake, remain essential components of comprehensive management [20,21]. Nevertheless, adherence to lifestyle modification remains low in clinical practice [22]. Complementary non- pharmacological and lifestyle strategies are summarized in Table 2.

Table 2. Non-pharmacological and lifestyle interventions in gout management

Intervention category	**Specific recommendations**	**Expected effect on serum uric acid and disease course**	**Supporting evidence / notes**	**Selected references**
Dietary modification	Limit intake of purine-rich foods (red meat, organ meats, shellfish); reduce fructose-sweetened beverages; increase consumption of low-fat dairy products, vegetables, and whole grains	Decrease in serum uric acid levels; reduced frequency of gout flares	Consistent with ACR and EULAR recommendations; supported by observational and interventional studies	[10], [16], [21], [24]
Alcohol moderation	Avoid or limit beer and spirits; moderate wine intake if tolerated	Reduction of hyperuricemia and risk of acute attacks	Alcohol (especially beer) increases urate production and decreases renal excretion	[7], [12], [20]
Weight management	Gradual weight reduction through calorie control and balanced nutrition	Decrease in serum urate levels and flare frequency; improved metabolic comorbidities	Weight loss improves renal urate clearance and insulin sensitivity	[9], [14], [18], [22]
Hydration	Maintain adequate water intake (at least 2–2.5 L/day if not contraindicated)	Enhanced uric acid excretion; reduced risk of crystal precipitation	Adequate hydration promotes renal clearance and reduces stone formation	[11], [15], [25]
Physical activity	Regular moderate aerobic exercise (e.g., walking, swimming, cycling); avoid joint overstrain during acute flares	Improves overall metabolic health, reduces obesity-related hyperuricemia	Physical activity beneficial for cardiovascular and metabolic comorbidities	[8], [13], [19]

Patient education and adherence	Long-term adherence to diet, hydration, and pharmacotherapy; avoidance of self-discontinuation of ULT	Sustained urate control and lower risk of chronic tophaceous gout	Patient education is key to long-term disease control	[5], [17], [23], [26]

Combining pharmacological and behavioral interventions appears to yield the most favorable long-term outcomes, yet additional studies are needed to identify the most effective and sustainable approaches [23]. An overview of the diagnostic and therapeutic stages of gout is provided in Table 3.

Table 3. Diagnostic and therapeutic stages in gout management

Clinical stage	Key clinical features	Diagnostic approach	Therapeutic strategy	Main objectives	Selected references
Asymptomatic hyperuricemia	Elevated serum uric acid > 6.8 mg/dL without symptoms	Routine biochemical testing; assessment of comorbidities and risk factors	Lifestyle modification; pharmacotherapy only in selected high-risk cases	Prevent crystal deposition and metabolic complications	[2], [6], [10]
Acute gout flare	Sudden onset of monoarthritis (often first metatarsophalangeal joint), swelling, redness, severe pain	Synovial fluid analysis (MSU crystals); ultrasound "double-contour sign"	NSAIDs, colchicine, or glucocorticoids; IL-1 inhibitors in refractory cases	Rapid inflammation control and pain relief	[4], [8], [12], [15]
Intercritical period	Symptom-free interval between attacks	Monitoring serum uric acid; imaging for urate deposits	Initiate or adjust urate-lowering therapy; continue prophylactic colchicine	Maintain urate below target and prevent new flares	[5], [9], [13], [17]
Chronic tophaceous gout	Persistent hyperuricemia with tophi, joint deformities, and chronic pain	Ultrasound, dual-energy CT, or MRI for tophi visualization; renal function evaluation	Long-term ULT (allopurinol, febuxostat, or pegloticase); surgical removal of large tophi if indicated	Dissolve urate deposits, prevent disability and joint destruction	[7], [11], [14], [18]
Comorbid management	Association with metabolic syndrome, renal disease, hypertension, cardiovascular disorders	Comprehensive metabolic evaluation	Coordinated pharmacologic and lifestyle therapy addressing both gout and comorbidities	Reduce systemic inflammation and overall morbidity	[3], [10], [16], [19]

LIMITATIONS

This review is narrative in nature and not a systematic meta-analysis. It is based primarily on international peer-reviewed publications. To improve regional relevance and completeness of the analysis, inclusion of national epidemiological and clinical data from Poland is recommended in future updates [24].

In summary, recent advances in research have expanded the understanding of gout as a systemic inflammatory disease driven by NLRP3 inflammasome activation and complex metabolic interactions [25]. Integration of pharmacological, lifestyle, and preventive strategies remains essential for achieving long-term disease control and reducing the global and regional burden of gout [26,27].

CONCLUSIONS

Gout management relies on an integrated approach combining rapid anti-inflammatory treatment during acute attacks with long-term correction of hyperuricemia. Early diagnosis through synovial fluid analysis and imaging allows timely intervention, while sustained urate-lowering therapy adjusted to renal function and comorbidities promotes gradual dissolution of urate deposits and prevents joint damage. Low-dose colchicine or NSAIDs at therapy initiation reduce the

risk of paradoxical flares.

Equally important are lifestyle-based measures, including gradual weight reduction, balanced diet, regular physical activity, proper hydration, and limitation of purine-rich foods and alcohol, which synergize with pharmacological treatment to improve long-term outcomes. Continuous monitoring of serum uric acid, regular follow-up, and structured patient education promote adherence and treatment success.

Recent research (2020–2025) underscores the systemic nature of gout and the need for an individualized, multidisciplinary approach that integrates metabolic, cardiovascular, and musculoskeletal perspectives. The findings summarized in this review provide clinicians with an updated framework for evidence-based management and highlight the importance of preventive strategies in reducing the global health and socioeconomic burden of gout.

DISCLOSURE

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The authors declare no conflict of interest.

REFERENCES

1. Dalbeth N, Gosling AL, Gaffo A, Abhishek A. Gout. *Lancet.* 2021;397(10287):1843–1855. doi:10.1016/S0140-6736(21)00569-9
2. Dehlin M, Jacobsson L, Roddy E. Global epidemiology of gout: prevalence, incidence, treatment patterns and risk factors. *Nat Rev Rheumatol.* 2020;16(7):380–390. doi:10.1038/s41584-020-0441-1
3. Tang X, Deng D, Wu Q. Global, regional, and national burden of gout among older adults (≥65) from 1990 to 2021 and projections for 2050. *Front Public Health.* 2025;13:1540190. doi:10.3389/fpubh.2025.1540190
4. Zhu Y, Pandya BJ, Choi HK. Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007–2008. *Arthritis Rheum.* 2011;63(10):3136–3141. doi:10.1002/art.30520
5. Burke BT, Köttgen A, Law A, et al. Physical function, hyperuricemia, and gout in older adults. *Arthritis Care Res (Hoboken).* 2015;67(12):1730–1738. doi:10.1002/acr.22648
6. Zhu B, Wang Y, Zhou W, et al. Trend dynamics of gout prevalence among the Chinese population, 1990–2019: a joinpoint and age–period–cohort analysis. *Front Public Health.* 2022;10:1008598. doi:10.3389/fpubh.2022.1008598
7. Strohmaier WL, Bonkovic-Őszi J. Are there seasonal variations in renal colic in uric acid stone formers in Germany? *World J Urol.* 2022;40(8):2099–2103. doi:10.1007/s00345-022-04058-4

8. McCormick N, Rai SK, Lu N, Yokose C, Curhan GC, Choi HK. Estimation of primary prevention of gout in men through modification of obesity and other key lifestyle factors. *JAMA Netw Open.* 2020;3(11):e2027421. doi:10.1001/jamanetworkopen.2020.27421
9. Jung SM, Jung SH, Lee SN, et al. The impact of lifestyle on cardiovascular risk in patients with gout: a population-based cohort study. *Eur Heart J Qual Care Clin Outcomes.* 2025;11(4):397–405. doi:10.1093/ehjqcco/qcae048
10. Hatano M, Okada A, Sasabuchi Y, et al. Gout incidence in metformin versus sodium-glucose co-transporter-2 inhibitor users: a retrospective cohort study. *Rheumatology (Oxford).* 2025;64(7):4164–4171. doi:10.1093/rheumatology/keaf136
11. Zhu M, Wang X, Peng Z, et al. The role of the estimated glomerular filtration rate and body roundness index in the risk assessment of uric acid–lowering therapy–resistant gout in US adults: evidence from the National Health and Nutrition Examination Survey (2007–2018). *Ren Fail.* 2025;47(1):2441398. doi:10.1080/0886022x.2024.2441398
12. Duan L, Zhong J, Yang Y, Zhu X. Editorial: advances in pathogenesis and therapies of gout. *Front Immunol.* 2022;13:890204. doi:10.3389/fimmu.2022.890204
13. Ahn EY, So MW. The pathogenesis of gout. *J Rheum Dis.* 2025;32:8–16. doi:10.4078/jrd.2024.0054
14. Martinon F, Pétrilli V, Mayor A, et al. Gout-associated uric acid crystals activate the NALP3 inflammasome. *Nature.* 2006;440:237–241. doi:10.1038/nature04516
15. Schauer C, Janko C, Munoz LE, et al. Aggregated neutrophil extracellular traps limit inflammation by degrading cytokines and chemokines. *Nat Med.* 2014;20(5):511–517. doi:10.1038/nm.3547
16. Perez-Ruiz F, Castillo E, Chinchilla SP, Herrero-Beites AM. Clinical manifestations and diagnosis of gout. *Rheum Dis Clin North Am.* 2014;40(2):193–206. doi:10.1016/j.rdc.2014.01.003
17. Ragab G, Elshahaly M, Bardin T. Gout: an old disease in new perspective—a review. *J Adv Res.* 2017;8(5):495–511. doi:10.1016/j.jare.2017.04.008
18. Grassi W, De Angelis R. Clinical features of gout. *Reumatismo.* 2012;63(4):238–245. doi:10.4081/reumatismo.2011.238
19. Robinson PC. Gout—an update of aetiology, genetics, co-morbidities and management. *Maturitas.* 2018;118:67–73. doi:10.1016/j.maturitas.2018.10.012
20. Dalbeth N, Choi HK, Joosten LAB, et al. Gout. *Nat Rev Dis Primers.* 2019;5(1):69. doi:10.1038/s41572-019-0115-y
21. Engel B, Just J, Bleckwenn M, Weckbecker K. Treatment options for gout. *Dtsch Arztebl Int.* 2017;114(13):215–222. doi:10.3238/arztebl.2017.0215
22. Sivera F, Andres M, Dalbeth N. A glance into the future of gout. *Ther Adv Musculoskelet Dis.* 2022;14:1759720X221114098. doi:10.1177/1759720X221114098
23. Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. *Ann Rheum Dis.* 2017;76(1):29–42. doi:10.1136/annrheumdis-2016-209707
24. Errata. *Arthritis Rheumatol.* 2016;68(2):515. doi:10.1002/art.39536
25. Richette P, Doherty M, Pascual E, et al. 2018 updated European League Against Rheumatism evidence-based recommendations for the diagnosis of gout. *Ann Rheum Dis.* 2020;79(1):31–38. doi:10.1136/annrheumdis-2019-215315
26. Pérez Ruiz F, Ruiz López J, Herrero Beites AM. Influencia de la historia natural de la enfermedad en el diagnóstico previo en pacientes con gota [Influence of the natural history of disease on a previous diagnosis in patients with gout]. *Reumatol Clin.* 2009;5(6):248–251. doi:10.1016/j.reuma.2008.12.013
27. Oliviero F, Scanu A, Galozzi P, et al. Prevalence of calcium pyrophosphate and monosodium urate crystals in synovial fluid of patients with previously diagnosed joint diseases. *Joint Bone Spine.* 2013;80(3):287–290. doi:10.1016/j.jbspin.2012.08.006
28. Kakutani-Hatayama M, Kadoya M, Okazaki H, et al. Nonpharmacological management of gout and hyperuricemia: hints for better lifestyle. *Am J Lifestyle Med.* 2015;11(4):321–329. doi:10.1177/1559827615601973
29. Williams PT. Effects of diet, physical activity and performance, and body weight on incident gout in ostensibly healthy, vigorously active men. *Am J Clin Nutr.* 2008;87(5):1480–1487. doi:10.1093/ajcn/87.5.1480
30. Neogi T, Chen C, Chaisson C, Hunter DJ, Zhang Y. Drinking water can reduce the risk of recurrent gout attacks. Paper presented at: ACR Annual Scientific Meeting; October 16-21, 2009; Philadelphia, PA.
31. Zhang Y, Neogi T, Chen C, Chaisson C, Hunter DJ, Choi HK. Cherry consumption and decreased risk of recurrent gout attacks. *Arthritis Rheum.* 2012;64(12):4004–4011. doi:10.1002/art.34677
32. Shekelle PG, Okunogbe A, Newberry SJ, et al. Management of gout: a systematic review in support of an American College of Physicians clinical practice guideline. *Ann Intern Med.* 2017;166(1):37–51. doi:10.7326/M160570
33. van Durme C, Wechalekar MD, Landewé RB, et al. Non-steroidal anti-inflammatory drugs for acute gout. *Cochrane Database Syst Rev.* 2021;12:CD010120. doi:10.1002/14651858.cd010120.pub3
34. Terkeltaub RA, Furst DE, Bennett K, et al. Efficacy of low-dose colchicine for acute gout flare: results of a randomized, controlled trial. *Arthritis Rheum.* 2010;62(4):1060–1068. doi:10.1002/art.27327
35. Cronstein BN, Sunkureddi P. Mechanistic aspects of inflammation and clinical management of inflammation in acute gouty arthritis. *J Clin Rheumatol.* 2013;19(1):19–29. doi:10.1097/RHU.0b013e31827d8790
36. Sadiq NM, Robinson KJ, Terrell JM. Colchicine. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025 Jan

19. https://www.ncbi.nlm.nih.gov/books/NBK431102/

37. Slobodnick A, Shah B, Krasnokutsky S, Pillinger MH. Update on colchicine, 2017. *Curr Rheumatol Rep.* 2017;19(7):20. doi:10.3899/jrheum.140458
38. Barnes PJ. How corticosteroids control inflammation: Quintiles Prize Lecture 2005. *Br J Pharmacol.* 2006;148(3):245–254. doi:10.1038/sj.bjp.0706736
39. Janssens HJ, Janssen M, van de Lisdonk EH, et al. Use of oral prednisolone or naproxen for the treatment of gout arthritis: a double blind, randomised equivalence trial. *Lancet.* 2008;371(9627):1854–1860. doi:10.1016/s0140-6736(08)60799-0
40. Liew JW, Gardner GC. Use of anakinra in hospitalized patients with crystal-associated arthritis. *J Rheumatol.* 2019;46(10):1345–1349. doi:10.3899/jrheum.181018
41. Sundy JS, Weinstein SP, Wu R, et al. Rilonacept for gout flare prevention in patients receiving uric acid-lowering therapy: results of RESURGE, a phase III, international safety study. *J Rheumatol.* 2014;41(8):1703–1711. doi:10.3899/jrheum.131226
42. Terkeltaub RA, Baraf HS, Wang J, et al. Rilonacept in the treatment of acute gouty arthritis: a randomized, controlled clinical trial using indomethacin as the active comparator. *Arthritis Res Ther.* 2013;15(1):R25. doi:10.1186/ar4159
43. Mitha E, Weinstein SP, Luo S-F, et al. Rilonacept for gout flare prevention during initiation of uric acid-lowering therapy: results from the PRESURGE-2 international, phase 3, randomized, placebo-controlled trial. *Rheumatology.* 2013;52(7):1285–1292. doi:10.1093/rheumatology/ket114
44. Schlesinger N. Anti-interleukin-1 therapy in the management of gout. *Curr Rheumatol Rep.* 2014;16(2):398. doi:10.1007/s11926-013-0398-z
45. FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology guideline for the management of gout. *Arthritis Care Res (Hoboken).* 2020;72(6):744–760. doi:10.1002/acr.24180
46. White WB, Saag KG, Becker MA, et al. Cardiovascular safety of febuxostat or allopurinol in patients with gout. *N Engl J Med.* 2018;378(13):1200–1210. doi:10.1056/NEJMoa1710895
47. So A, De Meulemeester M, Arulmani U, et al. Canakinumab for the treatment of acute flares in difficult-to-treat gouty arthritis: results of a multicenter, phase II, dose-ranging study. *Arthritis Rheum.* 2010;62(10):3064–3076. doi:10.1002/art.27600
48. Dumusc A, So A. Interleukin-1 as a therapeutic target in gout. *Curr Opin Rheumatol.* 2015;27(2):156–163. doi:10.1097/BOR.0000000000000143
49. Schlesinger N, Lipsky PE. Pegloticase treatment of chronic refractory gout: update on efficacy and safety. *Semin Arthritis Rheum.* 2020;50(3 Suppl):S31–S38. doi:10.1016/j.semarthrit.2020.04.011
50. Sundy JS, Baraf HSB, Yood RA, et al. Efficacy and tolerability of pegloticase for the treatment of chronic gout in patients refractory to conventional treatment: two randomized controlled trials. *JAMA.* 2011;306(7):711–720. doi:10.1001/jama.2011.1169
51. Moi JHY, Sriranganathan MK, Edwards CJ, Buchbinder R. Lifestyle interventions for chronic gout. *Cochrane Database Syst Rev.* 2013;2013(6):CD010039. doi:10.1002/14651858.CD010039.pub2
52. Yokose C, McCormick N, Choi HK. Dietary and lifestyle-centered approach in gout care and prevention. *Curr Rheumatol Rep.* 2021;23(7):51. doi:10.1007/s11926-021-01020-y

back