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GOUT: FROM HYPERURICEMIA A CHRONIC INFLAMMATORY ARTHRITIS

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ABSTRACT

Gout is a long-standing, progressive inflammatory joint disorder caused by the accumulation of monosodium urate crystals within joints and surrounding tissues due to persistent hyperuricemia. It is among the most common forms of inflammatory arthritis globally, and its prevalence continues to increase as a result of longer life expectancy, altered dietary habits, rising obesity rates, metabolic syndrome, chronic renal impairment, and extensive use of diuretic medications. The underlying pathophysiology of gout is multifactorial, involving abnormalities in uric acid metabolism, crystal deposition, and activation of the innate immune response, particularly through stimulation of the NLRP3 inflammasome, leading to the release of pro-inflammatory mediators such as interleukin-1β. From a clinical perspective, gout typically manifests as recurrent episodes of acute, intense joint pain accompanied by swelling, redness, and tenderness, most frequently involving the first metatarsophalangeal joint. If inadequately managed, the disease may advance to chronic tophaceous gout, resulting in joint damage, deformity, and functional disability. Definitive diagnosis is classically achieved by the detection of monosodium urate crystals in synovial fluid; however, recent advances in imaging techniques, including musculoskeletal ultrasound and dual-energy computed tomography, have significantly improved diagnostic precision, particularly in early or atypical presentations. Therapeutic management of gout includes both the control of acute inflammatory flares and long-term reduction of serum urate levels. Acute episodes are commonly treated with nonsteroidal anti-inflammatory drugs, colchicine, or corticosteroids, whereas long-term management aims to achieve and maintain target urate concentrations using xanthine oxidase inhibitors, uricosuric agents, or novel biologic therapies in resistant cases. Contemporary clinical guidelines support a treat-to-target strategy and highlight the importance of patient education, lifestyle interventions, and effective management of comorbid conditions. Nonetheless, despite the availability of effective therapies, gout remains underrecognized and insufficiently controlled, emphasizing the need for greater awareness, guideline-based care, and a multidisciplinary approach to minimize disease burden and long-term complications.

KEYWORDS: Gout; Hyperuricemia; Monosodium urate crystals; Inflammatory arthritis; NLRP3 inflammasome; Interleukin-1β; Acute gout flare.

INTRODUCTION

Gout is a prevalent form of inflammatory arthritis resulting from the deposition of monosodium urate (MSU) crystals in joints and periarticular tissues due to persistent hyperuricemia.[1] Recognized since ancient times, gout is among the earliest described rheumatologic disorders and has traditionally been linked to excessive dietary intake and underlying metabolic abnormalities.[2] Clinically, the disease is marked by recurrent attacks of acute arthritis, most commonly involving the first metatarsophalangeal joint, and may advance to chronic tophaceous gout with joint damage if not adequately managed.[3]

The underlying pathophysiology of gout is driven by elevated serum uric acid levels arising from either increased urate production or reduced renal elimination.[4] When serum urate concentrations surpass the physiological solubility limit, MSU crystals precipitate within the synovial fluid and surrounding tissues, triggering a pronounced inflammatory response mediated by the innate immune system. Central to this process is the activation of the NLRP3 inflammasome and subsequent release of interleukin-1β[5], which accounts for the intense pain, erythema, and swelling observed during acute gout flares.

Gout is frequently associated with several comorbidities, including hypertension, chronic kidney disease, obesity, diabetes mellitus, and cardiovascular disorders, all of which substantially contribute to disease-related morbidity and diminished quality of life.[6] In recent decades, the global burden of gout has increased significantly, largely due to population aging, lifestyle modifications, and the growing prevalence of metabolic syndrome. Timely diagnosis and effective therapeutic intervention are therefore critical to preventing disease progression, joint destruction, and systemic complications.[7]

Elevated serum urate levels primarily result from enhanced purine metabolism or impaired renal urate excretion.[8] Once urate levels exceed the saturation threshold, MSU crystals form and deposit within joints and periarticular tissues, initiating a robust inflammatory cascade.[9] This cascade involves activation of the NLRP3 inflammasome and the release of pro-inflammatory cytokines, particularly interleukin-1β, which plays a pivotal role in the development of acute gouty inflammation.[10]

Gout is a chronic metabolic and inflammatory disorder caused by sustained hyperuricemia, leading to MSU crystal accumulation in joints, soft tissues, and, in severe cases, other organs.[11] Clinically, it is characterized by episodic acute inflammatory attacks, asymptomatic intercritical periods, and eventual progression to chronic gouty arthritis when inadequately treated.[12] The condition predominantly affects middle-aged and elderly individuals and exhibits a marked male predominance, although the incidence increases among women following menopause.[13]

EPIDEMIOLOGY

Gout represents one of the most prevalent inflammatory arthritic conditions globally, with its occurrence rising consistently over recent decades. This increase is largely attributed to population aging, changes in dietary patterns, and the growing burden of metabolic disorders. In developed nations, gout affects an estimated 1–4% of the adult population, underscoring its significance as a public health issue.[14]

The epidemiology of gout shows marked geographic variation, with the highest prevalence reported in high-income regions such as the United States, the United Kingdom, Australia, and several European countries. Although lower prevalence rates are noted in developing nations, the incidence of gout is increasing in these regions as dietary habits and lifestyles become increasingly westernized.[15]

Gout demonstrates a clear sex-related disparity, occurring more commonly in men than in women, with a male-to-female ratio of approximately 3–4:1. In males, the disease typically manifests during middle adulthood, whereas in females, onset is more common after menopause, likely due to the loss of estrogen's uricosuric effects.[16]

Advancing age is a major risk factor for gout, with incidence rising notably after 40 years of age in men and 60 years in women. Older individuals are more prone to developing chronic, polyarticular disease and frequently present with multiple coexisting medical conditions.[17]

Multiple factors contribute to the development of gout, including obesity, hypertension, chronic kidney disease, diabetes mellitus, excessive alcohol consumption, and diets rich in purines. In addition, the use of certain medications, such as diuretics and low-dose aspirin, is associated with an increased risk of hyperuricemia and gout.[18]

Gout is closely linked to metabolic syndrome and cardiovascular disorders, and affected individuals exhibit higher prevalence rates of hypertension, coronary artery disease, stroke, and chronic kidney disease compared with the general population. These associations significantly contribute to increased morbidity and mortality among patients with gout.[19]

TYPES OF GOUT

Gout is a crystal-associated inflammatory arthritic disorder resulting from the accumulation of monosodium urate (MSU) crystals secondary to hyperuricaemia. Based on the stage of disease and clinical presentation, gout can be categorized into several distinct forms.[20]

1. ASYMPTOMATIC HYPERURICAEMIA

Asymptomatic hyperuricaemia is characterized by elevated serum uric acid concentrations in the absence of clinical symptoms of gout. Although MSU crystal deposition may already be present within joints and soft tissues, affected individuals do not experience overt inflammatory manifestations. Only a subset of patients with asymptomatic hyperuricaemia progresses to clinical gout, with progression influenced by serum urate levels and associated risk factors such as renal impairment and metabolic syndrome.[21]

2. ACUTE GOUTY ARTHRITIS

Acute gouty arthritis represents the most frequent initial manifestation of gout and results from an intense inflammatory reaction to MSU crystals within the joint cavity. It typically presents with sudden onset of severe pain, swelling, erythema, and increased local temperature, most commonly involving the first metatarsophalangeal joint. Although attacks are often self-limiting, recurrence is common if hyperuricaemia is not adequately controlled.[22]

3. INTERCRITICAL GOUT

Intercritical gout refers to the symptom-free period between episodes of acute gouty arthritis. Despite the absence of clinical symptoms during this phase, MSU crystals persist within the joints, and low-grade inflammation may continue. In the absence of effective urate-lowering therapy, intercritical intervals gradually shorten, and acute flares become more frequent.[23]

4. CHRONIC TOPHACEOUS GOUT

Chronic tophaceous gout develops following long-standing uncontrolled hyperuricaemia and repeated acute attacks. This stage is characterized by persistent inflammatory arthritis, progressive joint damage, and the development of tophi—aggregates of MSU crystals that commonly occur in the ears, fingers, elbows, and tendons. Chronic tophaceous gout is associated with significant deformity and functional impairment.[24]

5. SECONDARY GOUT

Secondary gout arises due to identifiable underlying conditions or external factors that either increase uric acid production or reduce renal urate excretion. Common causes include chronic kidney disease, myeloproliferative disorders, excessive alcohol consumption, and the use of medications such as diuretics. Clinically, secondary gout resembles primary gout; however, effective management requires treatment of both hyperuricaemia and the underlying precipitating condition.[25]

ETIOLOGY

1. Increased Uric Acid Production

Excessive uric acid synthesis is a major contributor to gout and occurs as a result of heightened purine metabolism. This may arise from high consumption of purine-rich foods such as red meat, seafood, and organ meats, or from increased endogenous purine breakdown observed in conditions including myeloproliferative disorders, hemolytic anaemia, psoriasis, and chemotherapy-associated tumor lysis syndrome.[26]

2. Reduced Renal Excretion of Uric Acid

Impaired renal elimination of uric acid is the most frequent cause of hyperuricaemia leading to gout. Decreased urate clearance may occur in chronic kidney disease, dehydration, lactic acidosis, and hypothyroidism. Diminished excretion results in elevated serum uric acid levels and subsequent monosodium urate crystal deposition in tissues.[27]

3. Genetic Susceptibility

Genetic predisposition plays a significant role in gout pathogenesis. Polymorphisms in genes encoding urate transporters, such as URAT1 and GLUT9, lead to defective renal urate handling and reduced excretion. Individuals with a positive family history have a markedly increased risk of developing gout.[28]

4. Dietary Influences

Dietary patterns have a strong impact on serum uric acid concentrations. Intake of purine-rich foods, excessive consumption of fructose-sweetened beverages, and alcohol intake increase uric acid production and impair renal excretion, thereby precipitating gout flares.[29]

5. Alcohol Intake

Alcohol consumption promotes hyperuricaemia by enhancing uric acid generation and reducing its renal elimination. Metabolism of ethanol increases lactate production, which competitively inhibits renal urate excretion. Beer further exacerbates the condition due to its high purine content.[30]

6. Obesity and Metabolic Syndrome

Obesity is associated with increased uric acid production and reduced renal clearance. Insulin resistance, a hallmark of metabolic syndrome, further decreases urate excretion. Comorbid conditions such as hypertension, diabetes mellitus, and dyslipidaemia are commonly observed in patients with gout.[31]

7. Drug-Induced Hyperuricaemia

Several medications increase the risk of gout by reducing uric acid excretion or enhancing its production. These include thiazide and loop diuretics, low-dose aspirin, cyclosporine, pyrazinamide, ethambutol, and cytotoxic agents used in chemotherapy.[32]

8. Chronic Kidney Disease

Chronic kidney disease serves as both a predisposing factor and a complication of gout. Reduced glomerular filtration rate and tubular dysfunction impair uric acid excretion, leading to sustained hyperuricaemia and recurrent episodes of gouty arthritis.[33]

9. Secondary Medical Conditions

Secondary gout may arise from underlying systemic disorders such as hypertension, hypothyroidism, lead poisoning (saturnine gout), and post-organ transplantation states. These conditions disrupt uric acid metabolism or renal handling, thereby increasing susceptibility to gout.[34]

RISK FACTORS

1. Male Sex and Increasing Age

Gout predominantly affects men compared to women, largely due to the uricosuric action of oestrogen in

premenopausal females. In both sexes, the risk of developing gout rises with advancing age as renal urate excretion gradually declines and the prevalence of associated comorbidities increases.[35]

2. Genetic Susceptibility

A family history of gout significantly elevates the risk of disease development. Genetic variations involving renal urate transporter genes, particularly URAT1 and GLUT9, impair uric acid handling by the kidneys, resulting in elevated serum urate concentrations and increased susceptibility to gout.[36]

3. Hyperuricaemia

Sustained elevation of serum uric acid levels is the most critical risk factor for gout. As serum urate concentrations increase—particularly beyond the saturation threshold of approximately 6.8 mg/dL—the probability of monosodium urate crystal formation rises markedly.[37]

4. Dietary Influences

Diets rich in purines, including red meat, seafood, and organ meats, contribute to increased uric acid synthesis. Additionally, intake of fructose-containing beverages elevates serum urate levels by accelerating purine metabolism, thereby increasing the risk of gout.[38]

5. Alcohol Intake

Alcohol consumption, especially beer and distilled spirits, is strongly linked to gout. Alcohol enhances uric acid production and reduces renal urate excretion through lactate accumulation, resulting in hyperuricaemia and triggering acute gout flares.[39]

6. Obesity and Metabolic Syndrome

Obesity is an independent predictor of gout, associated with both increased uric acid production and impaired renal clearance. Features of metabolic syndrome, including insulin resistance, hypertension, and dyslipidaemia, are commonly associated with elevated serum urate levels and gout.[40]

7. Chronic Kidney Disease

Reduced kidney function leads to diminished uric acid excretion, causing persistent hyperuricaemia and heightened risk of gout. Chronic kidney disease also complicates disease management and increases the likelihood of recurrent acute gout attacks.[41]

8. Medications

Several widely prescribed medications predispose individuals to gout by disrupting uric acid metabolism. These include thiazide and loop diuretics, low-dose aspirin, cyclosporine, tacrolimus, pyrazinamide, and ethambutol.[42]

9. Associated Medical Conditions

Comorbid conditions such as hypertension, diabetes mellitus, hypothyroidism, psoriasis, and cardiovascular disease are linked to an increased risk of gout. These disorders influence uric acid synthesis or excretion and commonly coexist with hyperuricaemia.[43]

MODIFIABLE RISK & FACTORS

1. Alcohol Consumption

Alcohol consumption, especially beer and distilled spirits, represents an important modifiable risk factor for gout. Alcohol promotes hyperuricaemia by increasing uric acid production and impairing renal urate excretion through lactate accumulation. Limiting or avoiding alcohol intake has been shown to reduce serum urate levels and lower the frequency of gout flares.[44]

2. Obesity and Excess Body Weight

Excess body weight contributes to elevated serum uric acid levels by enhancing uric acid synthesis and decreasing renal elimination. Weight loss achieved through dietary modification and regular physical activity is associated with reductions in serum urate concentrations and a decreased severity and recurrence of gout attacks.[45]

NON-MODIFIABLE RISK FACTORS

1. Genetic Predisposition

Genetic susceptibility plays a central role in gout pathogenesis. Variations in genes encoding urate transporters, including URAT1 and GLUT9, disrupt renal urate handling and lead to hyperuricaemia. Individuals with a family history of gout are at a significantly increased risk of developing the disease.[46]

2. Ethnicity

Ethnic background influences the prevalence of gout, reflecting underlying genetic predisposition. Higher rates of gout have been documented among Pacific Islanders, Māori populations, and individuals of African descent compared with Caucasian groups.[47]

SIGNS AND SYMPTOMS

Gout is an inflammatory joint disorder resulting from the deposition of monosodium urate (MSU) crystals in joints and soft tissues due to sustained hyperuricemia. Clinically, it is characterized by recurrent episodes of acute arthritis and may progress to chronic joint involvement and disability if inadequately managed.[48]

The hallmark manifestation of gout is acute gouty arthritis, which typically has a sudden onset, often during the night or early morning hours. Severe joint pain rapidly intensifies within the first 24 hours and is frequently described as throbbing or excruciating, with extreme sensitivity to touch. Acute attacks may be triggered by factors such as alcohol intake, purine-rich meals, trauma, surgery, or intercurrent medical illnesses.[49]

The first metatarsophalangeal joint of the great toe, known as podagra, is the most commonly affected site. Other frequently involved joints include the ankles,

knees, wrists, fingers, and elbows. Affected joints exhibit marked inflammation, presenting with swelling, erythema, warmth, and severe tenderness, often mimicking septic arthritis or cellulitis.[49]

Systemic manifestations, including fever, malaise, and leukocytosis, may accompany acute attacks, particularly in severe or polyarticular presentations, which can complicate clinical diagnosis.[50]

With recurrent untreated flares, gout may progress to chronic gouty arthritis. This stage is characterized by persistent joint pain, stiffness, limited range of motion, and progressive structural damage. Chronic disease often involves multiple joints and results in significant functional impairment.[51]

In advanced or long-standing gout, tophi may develop due to the accumulation of MSU crystals in soft tissues. These nodular deposits are commonly found on the pinna of the ear, fingers, toes, olecranon bursae, and Achilles tendon, and may lead to joint deformity, skin ulceration, nerve compression, or secondary infection.[52]

Acute gouty arthritis remains the most frequent clinical presentation, marked by sudden onset of intense joint pain that rapidly worsens over a few hours. The pain is often described as sharp, burning, or unbearable, severely restricting movement or contact with the affected joint.[53]

The first metatarsophalangeal joint is involved in most initial episodes, followed by the midfoot, ankles, knees, wrists, fingers, and elbows. Signs of acute inflammation include swelling, erythema, warmth, and tense, shiny skin over the affected joint, closely resembling infectious arthritis.[54]

During acute flares, systemic features such as fever, chills, fatigue, leukocytosis, and elevated inflammatory markers, including C-reactive protein, may be present and complicate differentiation from septic arthritis.[55]

As gout progresses, repeated acute episodes lead to intercritical periods, during which patients remain asymptomatic. Without appropriate urate-lowering therapy, these symptom-free intervals shorten, eventually progressing to chronic inflammatory arthritis.[56]

Chronic gout is characterized by ongoing joint inflammation, morning stiffness, reduced mobility, and progressive joint destruction due to continuous crystal deposition. Multijoint involvement is common, significantly affecting functional status and quality of life.[57]

In long-standing uncontrolled disease, tophi develop as firm, irregular nodules composed of urate crystals. Common sites include the helix of the ear, fingers, toes, olecranon and prepatellar bursae, and the Achilles tendon. Complications of tophaceous gout include joint deformity, ulceration, infection, and nerve compression syndromes.[58]

COMPLICATIONS

When gout is inadequately managed, it can give rise to multiple local and systemic complications involving the joints, soft tissues, and kidneys. Recurrent episodes of acute inflammation lead to progressive structural damage and contribute significantly to long-term morbidity.[59]

One of the most important complications is chronic gouty arthritis, which develops following repeated untreated or poorly controlled acute attacks. This condition is characterized by ongoing joint inflammation, persistent pain, stiffness, restricted mobility, and irreversible joint damage resulting from continuous deposition of monosodium urate crystals.[60]

Tophaceous gout represents a defining feature of advanced, uncontrolled disease. Tophi are firm, irregular nodules composed of urate crystals that accumulate within soft tissues, commonly affecting the fingers, toes, ears, olecranon bursae, and Achilles tendon. These deposits may result in joint deformities, limitation of movement, skin ulceration, secondary infections, and compression of adjacent nerves.[61]

Renal involvement is another significant complication of gout. Sustained hyperuricemia may lead to uric acid stone formation, presenting clinically with renal colic, hematuria, or urinary obstruction. Furthermore, long-term urate crystal deposition within renal tissues can cause gouty nephropathy, contributing to the progression of chronic kidney disease.[62]

Severe inflammatory responses during acute gout flares can occasionally lead to diagnostic challenges or delayed treatment, increasing the risk of adverse outcomes such as joint destruction or unnecessary surgical procedures when the condition is mistaken for septic arthritis.[63]

In addition to musculoskeletal and renal complications, gout is associated with an elevated risk of cardiovascular and metabolic disorders, including hypertension, coronary artery disease, heart failure, diabetes mellitus, and metabolic syndrome. These associated conditions significantly contribute to increased morbidity and mortality among patients with gout.[64]

DIAGNOSIS

The diagnosis of gout relies on an integrated assessment of clinical manifestations, laboratory investigations, and imaging findings. Establishing an accurate diagnosis is crucial to distinguish gout from other inflammatory joint disorders, particularly septic arthritis and rheumatoid arthritis.[65]

The definitive method for diagnosing gout is the detection of monosodium urate (MSU) crystals in

synovial fluid or aspirated material from a tophus using polarized light microscopy. These crystals are characteristically needle-shaped and exhibit strong negative birefringence, a finding that is highly specific for gout.[66]

In routine clinical practice, gout is frequently diagnosed on the basis of characteristic clinical features, especially in patients presenting with sudden onset of severe monoarticular arthritis involving the first metatarsophalangeal joint. Supporting features include marked erythema, swelling, extreme tenderness, warmth of the joint, and rapid progression of symptoms.[67]

Measurement of serum uric acid levels is commonly performed during evaluation; however, hyperuricemia alone is not diagnostic. Serum urate levels may be normal during acute gout flares, and elevated levels can also be present in individuals without gout. Nevertheless, persistently elevated serum urate concentrations increase the likelihood of gout when interpreted in the appropriate clinical context.[68]

Imaging modalities are useful adjuncts in diagnosis, particularly in patients with chronic disease or atypical presentations. Plain radiographs in advanced gout may reveal joint space narrowing and characteristic punched-out erosions with overhanging margins. Ultrasonography can demonstrate the double-contour sign, while dual-energy computed tomography (DECT) allows direct visualization of urate crystal deposition.[69]

When crystal analysis is not possible, validated clinical diagnostic tools such as the American College of Rheumatology/European Alliance of Associations for Rheumatology (ACR/EULAR) classification criteria are employed to enhance diagnostic accuracy.[70]

Overall, the diagnosis of gout requires careful correlation of clinical findings with laboratory and imaging evidence to differentiate it from other inflammatory and infectious arthropathies. Early and precise diagnosis is essential to initiate appropriate therapy and prevent long-term joint damage and systemic complications.[71]

Identification of MSU crystals in synovial fluid or tophaceous material remains the gold standard diagnostic technique. Under polarized microscopy, the presence of negatively birefringent, needle-shaped crystals provides definitive confirmation of gout.[72]

In situations where joint aspiration cannot be performed, diagnosis is often based on typical clinical presentation. Hallmark features include abrupt onset of severe monoarticular inflammation, intense pain, swelling, erythema, and warmth, most frequently involving the first metatarsophalangeal joint.[73]

Serum uric acid estimation forms an important component of the diagnostic workup. Although neither sensitive nor specific on its own, persistently elevated serum urate levels support the diagnosis of gout when correlated with characteristic clinical features.[74]

TREATMENT

The management of gout comprises three key components: control of acute inflammatory attacks, long-term urate-lowering therapy, and lifestyle modification. The main objectives are rapid relief of pain and inflammation during acute flares and prevention of recurrent attacks and complications by maintaining serum uric acid levels below 6 mg/dL (360 µmol/L).[75]

Acute gout flares should be treated promptly with anti-inflammatory medications. Non-steroidal anti-inflammatory drugs (NSAIDs), including indomethacin, naproxen, and ibuprofen, are considered first-line therapy in the absence of contraindications. Colchicine is most effective when initiated within the first 24 hours of symptom onset, with low-dose regimens preferred to reduce gastrointestinal adverse effects. Corticosteroids, administered orally, intra-articularly, or intramuscularly, are recommended for patients who are unable to tolerate NSAIDs or colchicine, particularly those with renal dysfunction or peptic ulcer disease.[76]

Long-term urate-lowering therapy (ULT) is indicated in patients with frequent gout attacks, tophaceous gout, chronic gouty arthritis, or uric acid nephrolithiasis. Xanthine oxidase inhibitors, such as allopurinol, are the preferred first-line agents as they decrease uric acid synthesis. Febuxostat is an alternative for patients who are intolerant to allopurinol. Uricosuric agents, including probenecid, may be used in selected patients with adequate renal function by enhancing renal urate excretion.[77]

Initiation of ULT can precipitate acute gout flares due to mobilization of urate stores. Therefore, prophylactic therapy with low-dose colchicine or NSAIDs is recommended during the initial phase of treatment, typically for 3–6 months. Regular monitoring of serum uric acid levels is essential, and ULT doses should be adjusted to achieve and maintain target urate concentrations.[78]

Lifestyle modification serves as an important adjunct to pharmacological therapy. Patients are advised to limit consumption of purine-rich foods, alcohol—particularly beer—and fructose-sweetened beverages. Weight reduction, adequate hydration, and optimal management of comorbid conditions such as hypertension, diabetes mellitus, and dyslipidaemia contribute to improved gout control and reduced flare frequency.[79]

The primary goal in treating acute gout attacks is rapid suppression of inflammation and pain. NSAIDs remain commonly used first-line agents, while colchicine is effective when administered early during an attack. Corticosteroids are reserved for patients with

contraindications to NSAIDs or colchicine and can be administered through various routes depending on clinical circumstances.[80]

Urate-lowering therapy is recommended for patients with recurrent attacks, tophi, chronic inflammatory arthritis, or renal involvement. Xanthine oxidase inhibitors, including allopurinol and febuxostat, remain the cornerstone of therapy by reducing uric acid production, while uricosuric agents such as probenecid are used in carefully selected patients. These medications are intended for long-term use and should generally not be initiated during an acute gout flare.[81]

Prophylactic therapy during the initiation of ULT is critical, as sudden changes in serum urate levels can provoke acute attacks. Low-dose colchicine or NSAIDs are commonly prescribed for several months until serum urate levels stabilize and the risk of flares diminishes.[82]

Non-pharmacological interventions play a supportive but essential role in gout management. These include weight control, avoidance of alcohol—especially beer—restriction of purine-rich foods, adequate fluid intake, and appropriate management of associated metabolic and cardiovascular conditions. Patient education and adherence to treatment are vital for long-term disease control.[83]

Overall, gout management involves coordinated treatment of acute attacks, sustained urate-lowering therapy, and lifestyle interventions. The overarching goals are to alleviate acute symptoms, prevent recurrence, reduce serum uric acid levels, and minimize long-term complications such as tophi, joint destruction, and renal impairment.[84]

PHARMACOLOGICAL TREATMENT

Pharmacological management of gout focuses on controlling acute inflammatory episodes, preventing recurrent flares, and lowering serum uric acid concentrations to minimize joint damage and the development of tophi. Selection of drug therapy depends on the stage of disease, attack frequency, renal function, and the presence of associated comorbid conditions.[85]

Treatment of acute gout attacks primarily involves anti-inflammatory agents. Non-steroidal anti-inflammatory drugs (NSAIDs), including indomethacin, naproxen, and ibuprofen, are regarded as first-line therapy. Colchicine is most effective when administered early in the course of an attack and is commonly used in patients who are unable to tolerate NSAIDs. Corticosteroids, administered orally, intramuscularly, or via intra-articular injection, are recommended when both NSAIDs and colchicine are contraindicated or ineffective.[86]

Urate-lowering therapy (ULT) is recommended for patients with frequent gout flares, chronic gouty arthritis, tophaceous deposits, or renal involvement. Xanthine oxidase inhibitors such as allopurinol and febuxostat are the preferred agents and act by decreasing uric acid production. Uricosuric drugs, including probenecid, enhance renal urate excretion and may be used in carefully selected patients with preserved kidney function. ULT is intended for long-term use and should generally not be initiated during an acute gout attack.[87]

Prophylactic therapy during the initiation of ULT is an essential aspect of treatment, as rapid alterations in serum urate levels can trigger acute gout flares. Low-dose colchicine or low-dose NSAIDs are therefore recommended for several months when starting urate-lowering agents to reduce the risk of flare development.[88]

Management of severe or treatment-refractory gout may require the use of newer therapeutic agents. Pegloticase, a recombinant uricase enzyme, is indicated for patients with severe chronic gout that is resistant to conventional therapy and acts by converting uric acid into the more soluble metabolite allantoin. In addition, interleukin-1 inhibitors such as anakinra and canakinumab may be considered in selected patients with frequent or refractory gout flares who fail to respond to standard treatments.[89]

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