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Editorial

Gout Beyond the Urate Number: An Integrated Approach to Recurrent Shoulder Monoarthritis and Renal Microlithiasis

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A patient with recurrent shoulder monoarthritis despite febuxostat 20 mg/day, serum urate below 5 mg/dL, hypertension treated with bisoprolol and multiple sub-1.5-mm renal calculi poses a familiar clinical dilemma: is this persistent gout, another arthropathy, or a treatment target that has been misunderstood? The answer is not to add drugs reflexively. It is to revisit diagnostic certainty, distinguish circulating urate from established crystal deposits and tailor stone prevention to the stone phenotype.

Pathophysiology: crystals, inflammation and a 'normal' urate result

Gout is a crystal-deposition disease, not simply a raised serum urate result. Sustained urate supersaturation—classically above approximately 6.8 mg/dL at physiologic temperature—permits monosodium urate (MSU) crystals to form in joints and other tissues. Hyperuricaemia most often reflects impaired renal or intestinal urate excretion. Once deposited, MSU crystals activate the NLRP3 inflammasome in innate immune cells, promoting interleukin-1β release and neutrophil recruitment. This inflammatory response produces the flare; crystal burden and inflammatory activity are related, but not interchangeable measures.[1]

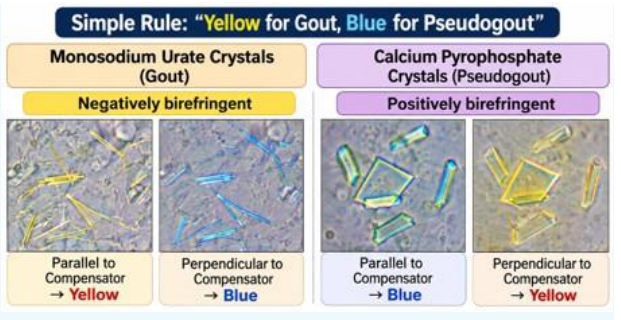
A serum urate below 5 mg/dL during an attack does not exclude gout. In a small prospective study, serum urate was lower during acute attacks than two weeks later, alongside increased urinary urate excretion; associations with inflammatory markers and cortisol are plausible but do not establish a single causal pathway.[2] NICE advises repeating a low urate result at least two weeks after the flare has settled when gout remains likely.[3] Conversely, if repeated intercritical measurements confirm sustained urate below target, persistent attacks should not automatically be labelled 'breakthrough gout': residual crystals may take time to dissolve, but alternative diagnoses must be considered.

Diagnostic strategy: prove the cause of the shoulder attack

The shoulder is less typical than first metatarsophalangeal disease. Calcium pyrophosphate deposition disease (CPPD), septic arthritis, rotator-cuff or periarticular disease and other inflammatory arthritides deserve consideration. When an effusion is present, aspiration during an attack is the most useful next step. Synovial fluid should undergo cell count, Gram stain and culture as well as compensated polarized-light microscopy: MSU crystals are needle-shaped and strongly negatively birefringent, whereas CPP crystals are typically rhomboid and weakly positively birefringent. Finding crystals does not exclude concurrent infection; culture remains important.[3]

If aspiration is not feasible or remains non-diagnostic, ultrasound can identify a double-contour sign or tophus, while dual-energy CT can demonstrate urate deposition. EULAR recommends either modality in the diagnostic assessment of gout; characteristic MSU deposition may establish the diagnosis when fluid analysis is unavailable.[4] In this patient, ultrasound-guided aspiration during the next episode showed typical MSU crystals.

Under polarized microscope rotate the stage for maximum brightness to appear. If the crystals are needle shaped & parallel to the long optical axis and yellow they are gout and if rhomboid weakly blue when parallel they are CPP.



Contemporary management: treat the disease, not a laboratory result

Acute flares should be treated promptly with low-dose colchicine, an NSAID or a glucocorticoid (oral or intra-articular), selected according to kidney function, blood pressure, cardiovascular disease, drug interactions and infection risk. For an accessible shoulder effusion, aspiration followed by intra-articular glucocorticoid can be considered once infection has been reasonably excluded. Colchicine prophylaxis for 3–6 months is recommended when ULT is initiated and may be extended if flares persist; it is not an automatic indefinite prescription.[6]

ULT should generally continue during a flare. Treat-to-target care uses serial serum urate measurements and dose titration, aiming below 6 mg/dL; a lower goal below 5 mg/dL can be considered in severe disease or with frequent ongoing flares.[5,6] Allopurinol is the ACR-preferred first-line ULT, including in chronic kidney disease when started low and titrated carefully. Febuxostat remains an option when allopurinol is unsuitable or ineffective. Its cardiovascular evidence deserves individual discussion: CARES found higher cardiovascular and all-cause mortality with febuxostat in patients with established cardiovascular disease, whereas FAST found non-inferiority for the primary cardiovascular endpoint in a different population.[7,8] ACR conditionally favours an alternative oral ULT, when available, for patients taking febuxostat who have established cardiovascular disease or a new cardiovascular event.[6] In a patient already below target on febuxostat, verify adherence, timing of urate measurements, renal and hepatic function, prior allopurinol history and cardiovascular history before changing treatment.

Antihypertensive selection is an opportunity for risk reduction, not a mandate to switch every patient. ACR conditionally recommends replacing hydrochlorothiazide when feasible and preferentially choosing losartan when clinically appropriate.[6] In a large observational study, losartan and calcium-channel blockers were associated with a lower risk of incident gout, whereas diuretics and beta-blockers were associated with a higher risk.[7] These associations do not justify stopping bisoprolol when needed for heart failure, ischaemic heart disease or arrhythmia, nor do they make losartan a replacement for ULT. If blood pressure and comorbidities permit, losartan or a calcium-channel blocker may be considered.

Renal microlithiasis: phenotype before prescription

Tiny asymptomatic renal stones do not ordinarily require shock-wave lithotripsy or ureteroscopy. Confirm number, location, size and absence of obstruction or infection, and use ultrasound surveillance where suitable. The AUA 2026 guideline suggests repeat imaging at 6–12 months initially; EAU guidance supports observation of asymptomatic calyceal stones with periodic imaging.[10–12] Gout does not prove that these stones are uric acid: calcium oxalate stones are common, and composition should be established if a stone is passed or retrieved.

Given multiple stones and gout, assess renal function, electrolytes, urinalysis and urine pH; consider 24-hour urine testing for volume, pH, calcium, oxalate, uric acid, citrate, sodium and creatinine, particularly with recurrence or other high-risk features.[10,12] Encourage fluid intake sufficient to produce at least 2.5 L of urine daily, unless contraindicated. Maintain normal dietary calcium with meals rather than restricting it, since calcium binds oxalate in the gut. Reduce excess sodium and non-dairy animal protein when indicated by stone chemistry, and limit sugar-sweetened drinks and excessive fructose. Blanket avoidance of bakery products or chocolate, or claims that dietary trans fats directly prime joint inflammasomes, are not supported as specific gout treatments.[6,10]

Potassium citrate should be targeted, not prescribed solely because gout and tiny stones coexist. It is appropriate when uric-acid stones with persistently acidic urine or hypocitraturia are demonstrated. Because low urine pH, rather than excess uric-acid excretion alone, commonly drives uric-acid stones, febuxostat should not be escalated solely as first-line stone therapy.[11] For uric-acid stone prevention, the AUA 2026 guideline recommends titrating urine pH to 6.0–6.5; higher targets may be used under supervision to dissolve confirmed uric-acid stones, while recognising that over-alkalinisation can promote calcium-phosphate stones.[11] With concurrent losartan, monitor serum potassium and renal function because renin–angiotensin system blockade can increase potassium retention.[13]

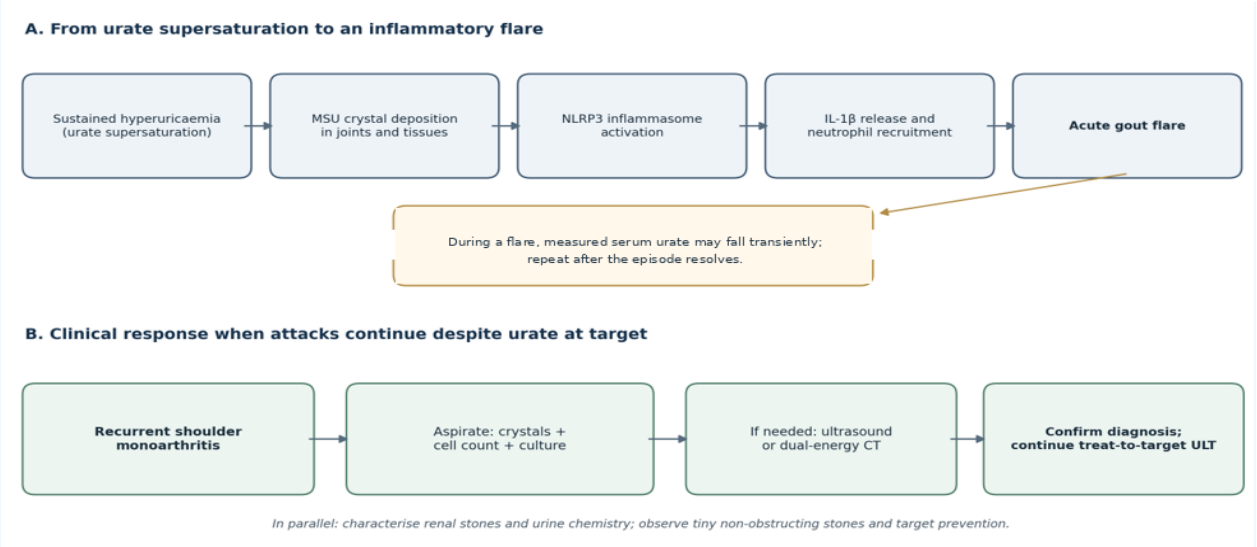


Figure 1: *Simplified pathophysiology and clinical decision pathway. MSU, monosodium urate; ULT, urate-lowering therapy.*

Conclusion

The central lesson is diagnostic discipline. A low serum urate is encouraging but cannot identify the cause of a shoulder attack, and gout does not establish the composition of a renal stone. Confirm the arthritis (Figure 1), maintain evidence-based treat-to-target ULT, select antihypertensive therapy around the whole cardiovascular indication, and manage microlithiasis by surveillance and metabolic phenotype. This integrated approach avoids unnecessary procedures and medication while addressing crystal disease and long-term risk.

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