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## Q / Are serum uric acid levels always elevated in acute gout?

### EVIDENCE-BASED ANSWER

**A / NO.** Many patients with acute gout (11%-49%) have normal serum uric acid (SUA) levels (strength of recommendation [SOR]: **A**, prospective cohort studies). Patients taking allopurinol are

significantly more likely to have normal uric acid levels during acute gout attacks (SOR: **B**, extrapolated from prospective cohorts).

### Evidence summary

Six studies have evaluated SUA levels in patients with acute gout. Despite variations in diagnostic approach (clinical criteria vs synovial crystal analysis) and definitions of normal SUA (based on laboratory methods and sex), all 6 studies found normal levels in 11% to 49% of patients with acute gout (TABLE 1).

#### Elevated SUA can be an indicator of gout—or not

A prospective cohort study of 82 patients at a Veterans Administration rheumatology clinic found elevated SUA to be the most sensitive indicator among various clinical criteria for diagnosing acute gout. However, 3 (11%) of the 28 patients who had crystal-proven gout also had a normal SUA.<sup>1</sup>

A second prospective cohort study that evaluated 38 patients during 42 episodes of acute gout in various clinical settings reported a normal SUA in 43% of patients diagnosed on clinical grounds or by joint aspiration.<sup>2</sup>

#### Some patients become hyperuricemic after diagnosis

The largest retrospective cohort study evaluated 226 Korean inpatients with acute gout diagnosed either by synovial crystals or American College of Rheumatology (ACR) criteria (TABLE 2). It found that 12% (27) had

a normal SUA at diagnosis. Interestingly, 81% became hyperuricemic some time after diagnosis.<sup>3</sup>

#### What is a normal SUA value?

Another study reviewed SUA levels in a cohort derived from 2 large prospective RCTs of etoricoxib in patients diagnosed with acute gout by crystal analysis. The proportion of patients with a normal SUA varied substantially according to the definition of a normal value: 32% were normal using a value of 0.48 mmol/L; 11% had normal SUA levels when 0.36 mmol/L was used as the cutoff.<sup>4</sup>

A secondary analysis evaluated the effect of allopurinol on SUA. The proportion of patients on allopurinol with a normal SUA level compared with patients not taking allopurinol was 49% vs 29% using the higher normal cutoff value, and 29% vs 11% using the lower normal value ( $P < .001$ ).<sup>4</sup>

#### Two studies find many gout patients with a normal SUA

A Japanese retrospective cohort study using ACR criteria found that nearly half of patients diagnosed with acute gout had a normal SUA level.<sup>5</sup> A 1967 retrospective examination of Framingham Heart Study data found that one-third of patients clinically diagnosed with gout had a normal level. Some of the patients hadn't been diagnosed at the time their SUA was measured, however.<sup>6</sup>

**TABLE 1**

## Serum uric acid and acute gout: The evidence

Type of cohort (n)	LOE*	Setting	Method of diagnosis	% with normal serum uric acid
Prospective <sup>1</sup> (28)	1b	Veterans Administration rheumatology clinic	Crystal positivity	11%
Prospective <sup>2</sup> (38)	1b	Multiple settings (eg, inpatient, clinic, ED)	Clinical criteria or crystal positivity	43%
Retrospective <sup>3</sup> (226)	2b	Hospitalized patients	Clinical criteria or crystal positivity	12%
Retrospective <sup>4</sup> (339)	2b	Multiple settings	Crystal positivity	32%
Retrospective <sup>5</sup> (41)	2b	Rheumatology clinic	Clinical criteria	49%
Retrospective <sup>6</sup> (69)	2b	Multiple settings	Clinical criteria	33% <sup>†</sup>

ED, emergency department; LOE, level of evidence.

\*1b, prospective cohort study with good follow-up (>80%); 2b, retrospective cohort study or prospective study with poor follow-up.

<sup>†</sup>Not necessarily during acute gout.

**TABLE 2**

## American College of Rheumatology criteria for classifying acute gouty arthritis

- Characteristic urate crystals in the joint fluid (or)
- A tophus proved to contain urate crystals by chemical means or polarized light microscopy (or)
- Six of the following 12 clinical, laboratory, and radiographic phenomena:
  - More than one attack of acute arthritis
  - Maximal inflammation developing within one day
  - Attack of monoarticular arthritis
  - Joint redness
  - First metatarsophalangeal joint is painful or swollen
  - Unilateral attack involving first metatarsophalangeal joint
  - Unilateral attack involving tarsal joint
  - Suspected tophus
  - Hyperuricemia
  - Asymmetric swelling within a joint (radiograph)
  - Subcortical cysts without erosions (radiograph)
  - Negative culture of joint fluid for microorganisms during attack of joint inflammation

Source: Wallace SL et al. *Arthritis Rheum.* 1977.<sup>7</sup>

### Recommendations

The ACR's 1977 criteria for diagnosing gout include hyperuricemia as one potential indi-

cator.<sup>7</sup> The European League Against Rheumatism advises that normal SUA levels may accompany crystal-proven gout because uric

**>**  
**The proportion of patients with normal serum uric acid levels varies substantially, depending on how a normal value is defined.**

acid either acts as a negative acute-phase reactant or increases in renal excretion during acute episodes. They conclude that SUA has

“limited diagnostic value,” especially during acute gout.<sup>8</sup>

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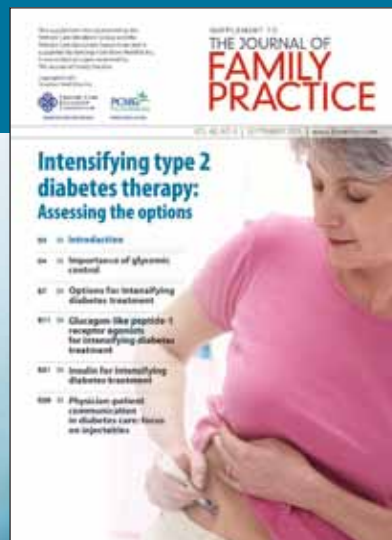
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