

## Hyperuricosuric Calcium Oxalate Kidney Stones

It is common for a patient to have mixed uric acid and calcium oxalate stones, or to pass uric acid stones at some times and calcium oxalate at others. Gout is often an associated feature. Overall, approximately 5% of all stones are mixed calcium oxalate and uric acid. Excess excretion of uric acid in the urine is thought to be the pathologic link, and this syndrome has been named hyperuricosuric calcium oxalate nephrolithiasis. In solution, crystals of uric acid and sodium hydrogen urate appear to promote calcium oxalate crystallization. The exact mechanisms underlying this observation, and whether it occurs in human urine, remain controversial. Among proposed mechanisms uric acid and sodium hydrogen urate crystals appear to inactivate urinary calcium oxalate crystal growth inhibitors, soluble uric acid appears to decrease spontaneous nucleation of calcium oxalate (by a “salting out” mechanism), and any uric acid crystals that form in the kidney could occlude tubules, promote stasis, and thereby promote retention of calcium oxalate crystals in the kidney.

The urinary profile of patients who excrete mixed uric acid/calcium oxalate stones is intermediate between those who excrete pure calcium stones, and those who excrete uric acid stones. The average urinary pH is, on average, lower than that of pure calcium oxalate stone formers (pH 5.7 vs. 6.0), favoring precipitation of uric acid, and perhaps indirectly promoting calcium oxalate crystallization. Urinary citrate excretion is also reduced. This more acidic urine, which is most pronounced in the early morning when urine is also maximally concentrated, is likely to be at least as important as the absolute quantity of uric acid excreted.

Treatment includes high fluid intake and moderate ingestion of purines and animal protein. If hyperuricosuria cannot be controlled by diet alone, allopurinol is a useful treatment strategy. At a dose of 300 mg per d, a 30-40% reduction in uric acid excretion is typical. A 3-yr placebo-controlled trial clearly demonstrates that treatment of hyperuricosuric calcium oxalate stone-formers with allopurinol reduces the formation of new stones by 51%. Because allopurinol does not alter other urinary constituents (e.g., oxalate or calcium) and has no effect on calcium oxalate crystal growth, it is overwhelmingly likely that the allopurinol is effective because it reduces urinary uric acid excretion. The major side effect of allopurinol is a hypersensitivity rash, which occurs in about 2% of patients. In a small number (0.01%) a severe, life-threatening reaction can develop. Typically, adverse effects occur in the first weeks, and all patients should be advised to stop the medication at the first sign of itching or rash. An alternative treatment strategy is oral citrate to raise the urinary pH, thereby preventing uric acid crystallization. A preliminary study suggests that oral citrate may in fact be an effective strategy, although whether citrate would be an effective treatment in those hyperuricosuric calcium oxalate stone-formers with normal or high urinary citrate levels remains unknown. It may be possible to prescribe the citrate as a single nighttime dose (e.g., 30-60 mEq), to prevent an acidic urinary pH early in the morning however, this strategy has not been rigorously examined in hyperuricosuric calcium oxalate stone-formers, nor compared to other treatment strategies.

Information taken by permission from: *Essential Urology: A Guide to Clinical Practice*, edited by Jeannette M. Potts, 2004.