CLINICAL PRACTICE

Calcium Kidney Stones

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This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.*

A 43-year-old man presents for evaluation of recurrent kidney stones. He passed his first stone 9 years earlier and has had two additional symptomatic stones. Analysis of the first and the last stones showed that they contained 80% calcium oxalate and 20% calcium phosphate. Analysis of a 24-hour urine collection while the patient was not receiving medications revealed a calcium level of 408 mg (10.2 mmol), an oxalate level of 33 mg (367 μmol), and a volume of 1.54 liters; the urine pH was 5.6. The patient had been treated with 20 to 40 mmol of potassium citrate daily since he passed his first stone. How should he be further evaluated and treated?

THE CLINICAL PROBLEM

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In the United States, the prevalence of kidney stones has risen over the past 30 years.[1] By 70 years of age, 11.0% of men and 5.6% of women will have a symptomatic kidney stone. The risk among white persons is approximately three times that among black persons. About 80% of stones are composed of calcium oxalate with variable amounts of calcium phosphate. Diagnosis of a calcium stone requires analysis after passage or removal of the stone. After passage of a first stone, the risk of recurrence is 40% at 5 years and 75% at 20 years. Among patients with recurrent calcium stones who have served as control subjects in randomized, controlled trials of interventions, new stones formed in 43 to 80% of subjects within 3 years.[2-9] Hospitalizations, surgery, and lost work time that are associated with kidney stones cost more than $5 billion annually in the United States.[10] Stone formation is associated with increased rates of chronic kidney disease and hypertension,[11,12] increases that are not completely explained by obesity, which is a risk factor for each of these conditions.[13]

Although many inherited and systemic diseases are associated with calcium kidney stones,[14] most such stones are idiopathic. The majority of patients with idiopathic stones have at least one metabolic abnormality, as identified by 24-hour urine testing. Prevention requires evaluation to identify systemic disease and modifiable factors.

PATHOGENESIS

PHYSICOCHEMICAL FACTORS

Supersaturation, often expressed as the ratio of urinary calcium oxalate or calcium phosphate concentration to its solubility, is the driving force in stone formation. At levels of supersaturation below 1, crystals dissolve, whereas at supersaturation levels above 1, crystals can nucleate and grow, promoting stone formation. Supersaturation is generally higher in patients with recurrent kidney stones than in those without the condition, and the type of stone that is formed correlates with urinary supersaturation. Calcium oxalate supersaturation is independent of urine pH, but calcium phosphate supersaturation increases rapidly as urine pH rises from 6 to 7. Since calcium oxalate stones form over an initial calcium phosphate layer,[15] treatment optimally should lower the supersaturation of both types. Most 24-hour analyses of kidney-stone risk that are performed at specialized laboratories include calculated supersaturation values.

Urine also contains substances that can accelerate or retard urinary crystallization.[16] The only such substance that can be modified in practice at this time is citrate, which can slow the growth of calcium crystals.[17]

Anatomic abnormalities, in particular those that result in urinary stasis (such as ureteropelvic junction obstruction, horseshoe kidney, or polycystic kidney), may precipitate or worsen stone formation.[18] Patients with a single functioning kidney are at particular risk, since stone passage with ureteral obstruction can result in acute kidney failure.

METABOLIC FACTORS

Imbalances between excretions of calcium, oxalate, and water create supersaturation. Hypercalciuria, the most common metabolic abnormality found in patients with recurrent calcium stones, is most often familial and idiopathic[19] and is strongly influenced by diet. Gut calcium absorption is increased in persons with idiopathic hypercalciuria, but serum calcium values remain unchanged, since absorbed calcium is promptly excreted.[20] On a low-calcium diet, such persons often excrete more calcium than they eat,[21] and urinary calcium excretion also rises markedly after the intake of calcium-free nutrients such as simple oral glucose; in such cases, the only source possible is bone. Although hypercalciuria is sometimes divided into subtypes (absorptive, resorptive, and renal leak), this classification is not helpful in guiding treatment. However, measurement of serum calcium is indicated to identify patients with primary hyperparathyroidism.

The level of oxalate excretion is modestly higher among patients with recurrent calcium stones than among those without the condition, possibly because of increased oxalate absorption in the gut.[22] The intake of ascorbic acid and a high level of protein may increase oxalate production.[23] Because calcium binds with oxalate in the gut and hinders its absorption, oxalate is more readily absorbed when dietary calcium is low.[23] This may be why a low-calcium diet does not successfully prevent stone recurrence.[24]

Citrate chelates calcium in the urine, decreasing supersaturation and reducing the growth of crystals[17]; hypocitraturia is a risk factor for stone formation. Distal renal tubular acidosis, hypokalemia, and the use of carbonic anhydrase inhibitors (e.g., topiramate) lead to hypocitraturia, but the cause of this condition in most patients with recurrent kidney stones is unknown.[25] Hyperuricosuria, often from high dietary intake of purines, is thought to promote the formation of calcium stones by reducing the solubility of calcium oxalate.[26]

HISTOPATHOLOGY

Intraoperative papillary biopsy specimens obtained from patients with recurrent kidney stones show that the pattern of crystal deposition differs according to the type of stone. Idiopathic calcium oxalate stones form over regions of interstitial calcium phosphate deposits (Randall's plaque) on the papillary surface,[27] whereas idiopathic calcium phosphate stones are associated with crystal deposits in inner medullary collecting ducts that contain mainly apatite,[28,29] sometimes mixed with other crystals. (For additional details, see the Supplementary Appendix, available with the full text of this article at NEJM.org.)

STRATEGIES AND EVIDENCE

Patients with recurrent calcium stones should be evaluated to rule out systemic disease and guide preventive therapy. Evaluation includes history taking directed at detecting potential causes of stones (Table 1). All stones should be analyzed to classify the type and to detect conversion from one stone type to another — for example, from calcium oxalate to struvite in the presence of infection or to calcium phosphate if the urinary pH rises in response to treatment.[30]

Computed tomography (CT) without the use of contrast material provides information regarding the presence, size, and location of stones, as well as ruling out anatomic abnormalities and providing a baseline for assessing whether subsequent stones that are passed are old or new (with the latter indicating a need for improved preventive treatment). Given the expense and radiation exposure of CT, renal ultrasonography

Table 1. Key Coexisting Medical Conditions, Medication Use, Diet, and Other Factors Associated with Calcium Kidney Stones.

Variable	Features	Type of Kidney Stone	
		Calcium Oxalate	Calcium Phosphate
Medical or surgical history			
Bowel disease	Chronic diarrhea, malabsorption	Yes	
Intestinal surgery	Small-bowel resection, ileostomy	Yes	
Bariatric surgery	Duodenal switch, Roux-en-Y gastric bypass	Yes	
Sarcoidosis		Yes	Yes
Gout		Yes	
Renal tubular acidosis			Yes
Bone disease or fracture	Primary hyperparathyroidism, idiopathic hypercalciuria, myeloma	Yes	Yes
Immobilization	Trauma, prolonged illness	Yes	Yes
Hyperthyroidism	Untreated, iatrogenic	Yes	Yes
Renal anomaly	Urinary stasis	Yes	Yes
Medications			
Topiramate	Seizures, migraine		Yes
Calcium supplements	Antacids, dietary supplement	Yes	Yes
Carbonic anhydrase inhibitor	Glaucoma		Yes
Alkali	Bicarbonate, citrate		Yes
Vitamin D		Yes	Yes
Occupational or recreational factor			
Dehydration	Hot environment, inability to drink	Yes	Yes
Dietary factor			
Oxalate loads	Nuts, spinach, ascorbic acid	Yes	
Excess salt	Prepared foods, snack foods	Yes	Yes
Eating disorders	Vomiting, use of laxatives	Yes	Yes
Strange diets*	Protein powder, sugar loads	Yes	Yes
Family history			
History of kidney stones in a first-degree relative	Idiopathic hypercalciuria, primary hyperoxaluria	Yes	Yes

* Strange diets include very restrictive choices of food or the use of a large number or amount of supplements.

or abdominal plain radiography may be used in follow-up imaging of known stones, although these methods are less sensitive than CT.

Metabolic testing should be done after the resolution of the acute episode of stone passage, when patients have resumed their usual diet and activity. Evaluation includes a blood test to screen for hypercalcemia, chronic kidney disease, and renal tubular acidosis. Analysis of a 24-hour urine collection to detect metabolic abnormalities should preferably be performed twice, since mineral excretions may vary from day to day.[31] Tables 2 and 3 provide a suggested framework for testing and interpretation. Whether to evaluate patients after a single kidney-stone episode is controversial, although it seems prudent to rule out systemic disease, especially in patients with a first stone before adulthood.

TREATMENT

MANAGEMENT OF SYMPTOMATIC STONES

Stones that have formed in kidneys do not require removal or fragmentation unless they cause obstruction, infection, serious bleeding, or persistent pain. Ureteral stones of less than 10 mm in

Table 2. Diagnostic Testing for Patients with Recurrent Kidney Stones.*

Measurement	Normal Value or Range for Adults	Purpose
Blood testing		
Calcium	8.8–10.3 mg/dl	Detection of primary hyperparathyroidism, excessive vitamin D intake, sarcoidosis
Phosphate	2.5–5.0 mg/dl	Detection of primary hyperparathyroidism
Creatinine	0.6–1.2 mg/dl	Detection of chronic kidney disease
Bicarbonate	20–28 mmol/liter	Detection of renal tubular acidosis
Chloride	95–105 mmol/liter	Detection of renal tubular acidosis
Potassium	3.5–4.8 mmol/liter	Detection of renal tubular acidosis, eating disorders, gastrointestinal disease
Urine collection over 24-hour period		
Volume	>1.5 liter/day	Detection of low volume as cause of stones
Calcium	<300 mg/day for men, <250 mg/day for women; <140 mg/g creatinine/day	Detection of hypercalciuria
Oxalate	<40 mg/day	Detection of hyperoxaluria
pH	5.8–6.2	Calculation of calcium phosphate and uric acid supersaturation, diagnosis of renal tubular acidosis
Phosphate	500–1500 mg/day	Calculation of calcium phosphate supersaturation
Citrate	>450 mg/day for men, >550 mg/day for women	Detection of low citrate level and diagnosis of renal tubular acidosis; calculation of calcium phosphate supersaturation
Uric acid	<800 mg/day for men, <750 mg/day for women	Detection of hyperuricosuria as cause of stones; calculation of uric acid supersaturation
Sodium	50–150 mmol/day	Diet counseling; calculation of supersaturation
Potassium	20–100 mmol/day	Use of potassium salts; calculation of supersaturation
Magnesium	50–150 mg/day	Detection of malabsorption; calculation of supersaturation
Sulfate	20–80 mmol/day	Calculation of supersaturation; measure of net acid production
Ammonium	15–60 mmol/day	Calculation of supersaturation
Creatinine	20–24 mg/kg/day for men, 15–19 mg/kg/day for women	Comparison of actual with predicted creatinine to assess the completeness of the urine collection
Protein catabolic rate†	0.8–1.0 g/kg/day	Estimation of protein intake
Calculated supersaturation‡		
Calcium oxalate	6–10	Guidance of treatment
Calcium phosphate	0.5–2	Guidance of treatment
Other screening tests		
Urinary cystine screening§	Negative	Detection of cystinuria
Stone analysis		Basic classification of condition

* Blood testing for renal tubular acidosis, chronic kidney disease, and hypercalcemia, along with urinary cystine screening and kidney-stone analysis, are appropriate for all patients with recurrent kidney stones. Collection of urine over a 24-hour period is appropriate if medical prevention of kidney-stone formation is planned. To convert the values for calcium to millimoles per day, multiply by 0.025. To convert the values for phosphate to millimoles per day, multiply by 0.0323. To convert the values for creatinine to micromoles per day multiply by 0.00884. To convert the values for urinary oxalate to micromoles per day, multiply by 11.11. To convert the values for urinary citrate to mmol per day, multiply by 0.0052. To convert the values for urinary uric acid to millimoles per day, multiply by 0.00595. To convert the values for urinary magnesium to mmol per day, multiply by 0.0411. To convert the values for urinary urea nitrogen to moles per day, multiply by 0.0357.

† The protein catabolic rate is calculated by multiplying the urea nitrogen excretion in grams per day by 6.25 and dividing by body weight in kilograms.

‡ Supersaturation is expressed as the ratio of urinary calcium oxalate or calcium phosphate concentration to its solubility.

§ Urinary cystine was tested with the use of the cyanide nitroprusside test. A negative test means that the cystine concentration is less than 75 mg per liter.

Table 3. Primary Causes of Calcium Kidney Stones and Their Treatments.*

Cause	Key Abnormality					
	Serum Calcium	Serum Parathyroid Hormone	Urine Calcium	Urine pH	Urine Citrate	Urine Oxalate
Idiopathic calcium oxalate	Normal	Normal	Normal or increased	Normal	Normal or decreased	Normal or increased
Idiopathic calcium phosphate	Normal	Normal	Normal or increased	Increased	Normal or decreased	Normal
Primary hyperparathyroidism	Increased	Increased	Increased	Increased	Normal	Normal
Sarcoidosis	Increased	Decreased	Increased	Normal	Normal	Normal
Lithium use	Increased	Increased	Increased	Increased	Normal	Normal
Oral supplementation with calcium or vitamin D	Normal or increased	Normal	Increased	Normal	Normal	Normal
Ileostomy	Normal or decreased	Normal	Decreased	Decreased	Decreased	Normal
Short-bowel syndrome	Normal or decreased	Normal	Decreased	Decreased	Decreased	Increased
Bariatric surgery	Normal or decreased	Normal	Decreased	Normal	Decreased	Increased
Renal tubular acidosis	Normal	Normal	Normal or increased	Increased	Decreased	Normal

* NA denotes not available because histologic analyses have not been reported for patients with the listed conditions.

diameter may be followed with conservative treatment in the absence of fever, infection, or renal failure, if pain is controlled. Opioid analgesics and nonsteroidal antiinflammatory agents are both effective for pain control in acute colic. Therapy with drugs that block α_1-adrenergic receptors or calcium-channel blockers may facilitate passage of ureteral stones.[32] In general, stones larger than 10 mm in diameter will not pass, and those smaller than 5 mm will; stones from 5 mm to 10 mm have variable outcomes. Stones in the distal ureter are more likely to pass than those located more proximally.

If stones do not pass, there are several surgical options for removal.[33] Data to guide surgical recommendations are derived largely from meta-analyses of small trials. For ureteral stones, the treatment of choice is either shock-wave lithotripsy or ureteroscopy with laser lithotripsy. Stone-free rates are better with ureteroscopy, but complication rates are higher, including sepsis and ureteral injury. For stones lodged in the kidney, the size, location, and presumed composition play a role in determining treatment. Not all stone types fragment equally well; for example, calcium oxalate monohydrate and brushite stones are more resistant to fragmentation than calcium oxalate dihydrate or apatite stones. Shock-wave lithotripsy and ureteroscopy are frequently used for smaller stones. Percutaneous nephrolithotomy may be used for single large stones (above 2 cm) or a large or obstructing stone burden. This procedure requires general anesthesia and hospitalization and carries more risk of complications, including bleeding and infection, than other techniques but can result in a stone-free kidney.[34] Open or laparoscopic procedures are occasionally used for stone removal in challenging cases.

PREVENTION OF IDIOPATHIC CALCIUM OXALATE STONES

Prevention of recurrent stones requires decreasing urinary supersaturation, which is generally achieved by raising urine volume and lowering calcium and oxalate excretion. It should be recognized that urinary abnormalities are graded risk factors, and thresholds for the definition of normal urinary function are not absolute cutoffs.[35] Table 4 summarizes treatment strategies.

		Supersaturation			Tissue Changes		Treatment
Urine Uric Acid	Urine Volume	Calcium Oxalate	Calcium Phosphate	Uric Acid	Interstitial Plaque	Collecting-Duct Plugging	
Normal or increased	Normal or decreased	High	Normal or high	Normal or high	Increased	Not present	Thiazide for idiopathic hypercalciuria; potassium citrate for calcium oxalate (and perhaps calcium phosphate) stones; allopurinol for hyperuricosuria; sodium restriction and possible protein or oxalate restriction; increased fluid intake
Normal	Normal	High	High	Normal	Normal	Increased	
Normal	Normal	High	High	Low	Increased	Increased	Parathyroid surgery
Normal	Normal	High	High	Normal	NA	NA	Glucocorticoids, possible ketoconazole
Normal	Normal	High	High	Normal	NA	NA	Discontinuation of lithium
Normal	Normal	High	High	Low	NA	NA	Discontinuation of supplements
Normal	Decreased	High	Low	High	Increased	Increased	
Normal	Decreased	High	Low	High	Normal	Increased	Fluids, alkali; supplements to reduce urine oxalate excretion for the short-bowel syndrome and bariatric surgery
Normal	Normal	High	Normal	Normal	Normal	Increased	
Normal	Increased	Normal	High	Low	Normal	Increased	Alkali, possible thiazides

(For additional details regarding treatment trials, see Table 1 in the Supplementary Appendix.)

A randomized trial of increased fluid intake that was targeted to maintain a daily urine volume of more than 2 liters showed a significant reduction in recurrent stone passage among patients with first-time kidney stones.[36] A target urine volume of 2 to 2.5 liters is reasonable and can be achieved by an increased intake of fluids, especially water, although most low-sodium, low-carbohydrate fluids are acceptable in moderation for this purpose.

In a randomized, controlled trial involving Italian men with hypercalciuria,[24] a diet that was low in animal protein (52 g per day), sodium (50 mmol per day), and oxalate (200 mg per day) with normal calcium intake (1200 mg per day) was associated with a reduction in stone formation of almost 50% over a period of 5 years, as compared with a diet that was low in calcium (400 mg per day) and oxalate. In contrast, in a U.S. trial, a low-protein diet did not reduce stone recurrence during a 4.5-year period, but compliance with the diet was poor and dietary sodium was not restricted.[37] A low-sodium diet can significantly decrease excretion of both calcium and oxalate,[38] but data on the effect of a sodium-restricted diet alone on stone recurrence are lacking. Calcium restriction should be avoided in patients with hypercalciuria, since it may result in a reduction in bone mineral density[39] and an increased rate of fracture.[40]

Thiazide-type diuretics decrease urine calcium excretion, and in randomized, controlled trials, these medications significantly reduced recurrence rates of calcium stones by more than 50% during a 3-year period, as compared with placebo.[2,4,6,9] Long-acting agents like chlorthalidone and indapamide are effective with once-daily doses, whereas twice-daily doses are recommended for hydrochlorothiazide.

Hyperoxaluria may occur when dietary calcium is low or oxalate intake is unusually high or (less commonly) when oxalate is overproduced. Dietary oxalate restriction to less than 100 mg per day and the avoidance of an intake of ascorbic acid above 100 mg per day are prudent if hyperoxaluria is present. Foods that are very high in oxalate include spinach, rhubarb, wheat bran, chocolate, beets, miso, tahini, and most nuts. (A list of the oxalate content of various foods is available at www.ohf.org under Resources.) Marked

Table 4. Treatment Recommendations for the Prevention of Idiopathic Calcium Kidney Stones in Adults.

Treatment	Mechanism of Action	Dose	Selection Criteria	Potential Complications
Fluids	Lowers supersaturation by dilution of solutes	Adequate to maintain urine volume >2 liters daily	Useful for all patients; possible sole treatment for patients with a single stone episode	Need to avoid fluids containing excess salt or carbohydrates
Diet	Lowers supersaturation by decreasing calcium and oxalate excretion; maintains bone mineral, prevents hyperoxaluria	Sodium, <100 mmol/day; protein, <0.8–1 g of animal protein/kg/day; oxalate, <100 mg/day; calcium, 800–1000 mg/day	Recommendations for sodium and protein especially useful in patients with hypercalciuria or hyperuricosuria; for oxalate in patients with hyperoxaluria; and for calcium in all patients with calcium stones	Difficulty in maintaining diet; should obtain calcium from dietary sources and avoid supplements
Thiazide-type diuretic	Lowers supersaturation by decreasing calcium excretion	Chlorthalidone, 12.5–50 mg/day; indapamide, 1.25–2.5 mg/day; hydrochlorothiazide, 12.5–25 mg twice daily	Patients with hypercalciuria; may be useful for some with normocalciuria	Hypokalemia, reduced blood pressure (may be desirable); allergy and sun sensitivity
Potassium alkali	Lowers supersaturation by chelating calcium; inhibits growth of calcium crystals	Potassium citrate, 10–20 mmol two or three times daily	Patients with hypocitraturia	Need to monitor urine pH and calcium phosphate supersaturation; avoid supersaturation of >1
Allopurinol	Lowers urinary uric acid concentration, which may improve solubility of calcium salts	100–300 mg/day (may be taken once daily)	Patients with hyperuricosuria and calcium stones	Allergy (may be severe)

hyperoxaluria should prompt consideration of malabsorption or one of the primary hyperoxaluria syndromes.[41]

Two randomized trials have shown substantial reductions in stone recurrence among patients with hypocitraturia who were treated with potassium alkali three times daily.[3,7] One trial of sodium–potassium citrate had negative results.[8] Potassium alkali may be safely combined with thiazide[9,42] when indicated, but no trials have compared the combination against either agent alone for the prevention of stone recurrence.

Hyperuricosuria can decrease the solubility of calcium oxalate and increase the incidence of calcium oxalate stones. Allopurinol (at a dose of 300 mg daily) decreased stone recurrence in a randomized trial involving patients with idiopathic calcium oxalate stones who had hyperuricosuria.[5] A reduction in the intake of protein (and therefore purine) is also prudent but has not been explicitly tested among patients with hyperuricosuria and recurrent kidney stones.

In long-term clinical follow-up, preventive treatment resulted in persistent reductions in stone recurrence during a period of 20 years or more.[43] However, compliance tended to wane over time, with rates of nonadherence approaching 20% per year.[44]

PREVENTION OF CALCIUM PHOSPHATE STONES

Most calcium stones consist of more than 90% calcium oxalate with trace amounts of calcium phosphate, but the proportion of calcium phosphate in stones has increased over time.[45,46] Idiopathic calcium phosphate stones (more than 50% calcium phosphate) are more common among women and are associated with alkaline urine pH, a condition whose cause is not well understood. Mild abnormalities in urine acidification may be present, although metabolic acidosis is uncommon.[46,47] Some patients convert from the formation of calcium oxalate stones to the formation of calcium phosphate stones. In one study, such patients had a urine pH that was more alkaline (>6.2) at baseline than those who continued to produce calcium oxalate stones.[30] Calcium phosphate stones are associated with poorer stone-free rates after percutaneous nephrolithotomy and with more shock-wave lithotripsy treatments than are calcium oxalate stones.[46,48]

Among patients with calcium phosphate stones, treatment is similar to that of patients with calcium oxalate stones except that potassium alkali should be used cautiously because it raises urine pH, potentially worsening calcium phosphate supersaturation. Levels of urine pH and citrate and the degree of supersaturation should be assessed after starting therapy. If the citrate level does not rise and the degree of supersaturation worsens, the medication is unlikely to be of benefit.

AREAS OF UNCERTAINTY

Treatment trials for calcium stones have not looked specifically at outcomes in patients with calcium phosphate stones. Dietary recommendations to increase fluids, lower salt and protein intake, and maintain a normal intake of calcium are supported by an Italian randomized trial,[24] but no women were included in this study, and it is unclear whether many Americans can comply with the necessary dietary pattern sufficiently to successfully prevent stones. The Dietary Approaches to Stop Hypertension (DASH)–Sodium diet, when modified to remove high-oxalate foods, replicates many of the features of the study diet and may provide a model to follow, but its effects on stone recurrence have not been explicitly studied.[49] Stone formation is associated with an increased risk of bone disease, chronic kidney disease, and hypertension, but it is not known whether effective stone prevention decreases these risks.

GUIDELINES

Guidelines of the American Urological Association (www.auanet.org) recommend that patients who require surgery for ureteral stones should be informed about benefits and risks of all current treatment approaches. Shock-wave lithotripsy and ureteroscopy with laser lithotripsy are both considered acceptable first-line treatments, although ureteroscopy achieves greater stone-free rates. Percutaneous access and open or laparoscopic surgery are used as needed for selected cases. The guidelines do not address evaluation or treatment to prevent recurrent stones.

CONCLUSIONS AND RECOMMENDATIONS

Preventive treatment to decrease stone recurrence is indicated for patients with recurrent calcium stones, such as the patient in the vignette. If systemic disease is not present, treatment should focus on metabolic abnormalities uncovered during the workup, such as hypercalciuria, hypocitraturia, hyperuricosuria, or hyperoxaluria. Although data comparing specific supersaturation targets are lacking, a logical strategy is to lower calcium oxalate and calcium phosphate supersaturation to the low end of the normal range.

Patients should be advised to increase fluid intake to at least 2 liters daily and reduce sodium intake to 2300 mg and protein intake to 0.8 to 1 g per kilogram of body weight per day, since these dietary interventions have reduced stone recurrence in randomized trials. Calcium intake should not be reduced below the recommended intake for sex and age and should be supplied by food rather than by supplements, which may increase the risk of stone formation. In many patients, medication is also needed; the choice of medication is influenced by the metabolic abnormalities identified, the type of stone, and the preference of patients.

The stones of the patient in the vignette contain 20% phosphate, despite a low urine pH while the patient was not receiving medications; the increased phosphate level may reflect his previous treatment with citrate. Both hypocitraturia and hypercalciuria may contribute to his stone formation. In addition to the recommendations above, we would initiate therapy with a thiazide-type diuretic (e.g., 25 mg of chlorthalidone daily) to lower the urinary calcium level. A reduction in sodium intake will also reduce a thiazide-induced loss of potassium.

A follow-up 24-hour urine collection and serum chemical analysis should be performed in 4 to 6 weeks to assess the efficacy of treatment and possible side effects, particularly hypokalemia, which can worsen hypocitraturia. If potassium supplementation is needed, it may be added as potassium alkali, but the urine pH level and the level of calcium phosphate supersaturation should be monitored. If the level of calcium phosphate supersaturation rises and is consistently above 1, potassium chloride should be substituted. Primary treatment with potassium alkali would be an alternative to a thiazide but may not lower the level of urinary calcium phosphate supersaturation as effectively. Ongoing attention is warranted at follow-up visits to monitor whether the patient is adhering to preventive recommendations.

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