Urinary Lithiasis

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Cover Illustration by Christine Schaar
INTRODUCTION

Urinary stones are an ancient phenomenon, found in an Egyptian skeleton approximately 7000 years old. Hippocrates ascribed stones to the ingestion of muddy river water and lime. Galen recognized etiologic factors such as heredity, race, alcohol consumption, and joint disease.

The early 20th century saw advances in understanding of the etiology, chemistry, and bacteriology of various stones, and surgical techniques advanced to a point of relative safety for the patient. The metabolic basis of urinary calculi has been elucidated in the past 30 years, and biochemical etiologic factors can be found in over 95% of stone-forming patients. Medical therapy has developed to a point where appropriate therapy can decrease the expected recurrence rate in a stone-forming population of patients by as much as 90%. Surgical treatment of stones in the kidneys and upper ureters by open incision was necessary until about 1980, whereas lower ureteral stones could be treated to some extent by blind endoscopic procedures, with a success rate of about 80% in appropriately selected patients. The development of extracorporeal shock wave lithotripsy (ESWL), nephroscopy, and small caliber ureteroscopes (both rigid and flexible) has changed the surgical therapy for urolithiasis to the point where it is now rare to perform open surgery for this disease.

This review highlights the modern metabolic approach to stone disease, and the different medical and surgical treatment options for individual cases.

EPIDEMIOLOGY

The prevalence of urinary lithiasis in the U.S. population is about 10%. The lifetime risk is 20% for Caucasian men and about 7% for women, regardless of race. The risk among African American men is about one third the risk among Caucasians. Staghorn calculi occur about twice as often in women as in men due to their association with recurrent urinary tract infection. The annual incidence of urinary calculi is about 1% in the Caucasian male population, principally in those between age 20 and 50 years, with the first episode occurring in the third decade of life. The incidence in summer months is about twice that in winter months. Geographic variations in incidence are well known, with the largest incidence in the United States occurring in the Southeast, particularly in Virginia and the Carolinas, where the incidence is 3 to 4 times higher than in the rest of the country. The incidence is lower in the mountain and desert states (ie, Nevada, Utah, Wyoming, Colorado, Idaho).

The lifetime recurrence rate for urinary stones has been estimated to be between 50% and 80%, with about 10% of recurrences within the first year and an annual rate of 3% to 4% thereafter. The incidence of upper tract stone disease seems to be increasing, whereas the incidence of bladder stones has decreased in developed countries. These trends may be due to higher dietary protein and sugar intake with prosperity. The incidence of stones decreased during World War I and World War II. The incidence in desert troops was high.

In the United States, 70% of urinary calculi are primarily composed of calcium oxalate; half of these are pure and half are a mixture with calcium phosphate. About 6% to 10% are pure calcium phosphate, 10% to 15% are magnesium ammonium phosphate, 8% are uric acid, and 1% to 3% are cystine.

FACTORS UNDERLYING URINARY CALCULUS FORMATION

PHYSICAL CHEMISTRY

Precipitation of a salt in solution occurs when the relative supersaturation is greater than 1. Relative supersaturation is the ratio of the activity product of the ions
in solution to the activity product of those ions in a solution in equilibrium with the solid phase of that salt (called the thermodynamic solubility product). The solubility product varies with the temperature and pH of the solution. The activity coefficients of the constituent ions vary with their concentration and with the concentration of other ionic species in the solution. When supersaturation reaches the formation product, crystals form (Figure 1). The metastable zone is the concentration between the solubility product and the formation product, where crystallization does not occur but preformed crystals will grow. Epitaxy is a process whereby crystals of one salt may be able to precipitate and grow on crystals of another with a similar lattice structure. It probably does not contribute to urinary stone growth.

Stone formation occurs in urine that is continuously or intermittently supersaturated with the particular salt and is deficient in one or more of the recognized inhibitors. These inhibitors include citrate, magnesium, pyrophosphate, glycoproteins (eg, nephrocalcin, Tamm-Horsfall protein), and glycosaminoglycans (eg, chondroitin sulfate, RNA fragments). Calculation of a saturation inhibition index in individual urine samples is mathematically possible and may predict the likelihood of stone occurrence or recurrence. Free particle stone formation is not possible in the human renal tubule because of rapid transit times. Crystal aggregates likely fix to epithelial defects.
or dead cells near the renal papillae (fixed particles). Randall’s plaques are 1- to 2-mm subepithelial calcium deposits in the papillary interstitium, or inspissated collecting ducts, which are found in stone formers in association with infected urine, primarily in patients older than age 50 years.5 They may have a role in fixed particle aggregation of crystals to clinical stone size. Matrix constitutes about 2% to 5% of most stones and may contribute to their formation. Matrix is composed of carbohydrate, glycoprotein, and protein components with an affinity for calcium ions.

**COMMON METABOLIC ABNORMALITIES**

Several metabolic abnormalities are commonly associated with urinary lithiasis (Table 1). The discovery of one or more abnormalities in a particular patient will dictate the future medical treatment of that patient.

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>% Alone</th>
<th>% Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absorptive hypercalciuria</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>Renal hypercalciuria</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Resorptive hypercalciuria</td>
<td>3</td>
<td>8</td>
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<tr>
<td>Unclassified hypercalciuria</td>
<td>15</td>
<td>25</td>
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<tr>
<td>Hyperuricosuric calcium</td>
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<tr>
<td>Hyperoxaluria</td>
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<tr>
<td>Hypocitraturia</td>
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</tr>
<tr>
<td>Hypomagnesuria</td>
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<td>10</td>
</tr>
<tr>
<td>Gouty diathesis</td>
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<td>30</td>
</tr>
<tr>
<td>Cystinuria</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Infection stones</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Low urine volume</td>
<td>10</td>
<td>50</td>
</tr>
</tbody>
</table>

Table 1. Prevalence of Metabolic Abnormalities in Patients with Urinary Lithiasis


Serum calcium may be in the high-normal range. Parathyroid hormone (PTH) levels may be normal or decreased. 1,25-Dihydroxyvitamin D₃ [1,25(OH)₂D₃] levels are increased. The filtered load of calcium is increased and the proportion reabsorbed is decreased due to reduced PTH activity in the loop of Henle, the distal tubule, and the collecting duct. Fasting urinary calcium is less than 0.11 mg/dL glomerular filtrate, and urinary calcium is greater than 0.22 mg/mg creatinine after calcium loading.

Type 2 is a milder form of type 1 in which serum calcium is slightly lower and urinary calcium is not as highly elevated and returns to normal range on a calcium-restricted diet. Type 3 is associated with a renal phosphate leak.8 Serum phosphate decreases to 2 mg/dL or less. A secondary increase of 1,25(OH)₃D₃ is provoked, with a subsequent increase in calcium absorption.

**Renal Hypercalciuria**

Renal hypercalciuria involves a primary defect in the renal tubular reabsorption of calcium. Fasting urinary calcium is elevated, greater than 0.11 mg/dL glomerular filtrate. Serum calcium is slightly reduced, PTH formation is stimulated to the slightly high range, and 1,25(OH)₃D₃ is increased.8

**Resorptive Hypercalciuria**

Hyperparathyroidism is found in 2% to 3% of patients with calcium stones and in about 1 in 2000 patients screened for serum calcium. It is much more common in elderly females. Serum calcium is high, urinary calcium is high on normal and restricted intake, and PTH level is high. PTH is formed in the chief cells of the parathyroid gland, and the N-terminal fragment is the active portion. It stimulates calcium resorption from bone, renal tubular reabsorption of calcium, and intestinal absorption of calcium via increased 1,25(OH)₂D₃. Renal phosphate reabsorption is decreased. About 80% of patients with hyperparathyroidism have a single chief cell adenoma and about 20% have hyperplasia.10 About 4% of patients with hyperparathyroidism develop stones, usually calcium phosphate in type (hydroxyapatite and carbonate apatite).10 Parathyroid scans can localize the site of an adenoma or hyperplasia with 95% accuracy.11 Surgical removal of the offending glands is indicated in most individuals who develop urinary calculi.

**Unclassified Hypercalciuria**

In some cases, it is impossible to discriminate between absorptive and renal hypercalciuria. The urinary calcium is high on normal and restricted calcium intake.
the PTH level is not secondarily stimulated, serum calcium levels are normal, and intestinal calcium absorption is high.

Hyperuricosuric Calcium Lithiasis

Some patients with calcium nephrolithiasis have no urinary or serum abnormality other than urinary uric acid levels greater than 600 mg/day. This is probably due to purine dietary excess, with uric acid precipitation and heterogeneous nucleation. Urinary pH less than 5.5 promotes uric acid crystallization, and high urinary uric acid decreases the activity of macromolecular calcium oxalate stone inhibitors. Low urine volume and chronic diarrhea with bicarbonate loss may increase the risk of stone formation.

Hyperoxaluria

Primary hyperoxaluria is an autosomal recessive defect characterized by increased excretion of oxalate (greater than 80 mg/day) and glycolate or t-glycerate. Types 1 and 2 are caused by enzymatic deficiencies in the liver and result in nephrocalcinosis and early renal failure. Gene loci have been identified at 2q37.3 and 9q11, respectively. Type 2 is milder. Liver transplantation is the only curative therapy.

Secondary hyperoxaluria occurs with enteric diseases, intestinal bypass, and other causes of rapid intestinal transit. Fat malabsorption leads to calcium and magnesium binding in the intestine, leaving less calcium and more oxalate to be absorbed. Oxalate is more significant in crystallization than calcium and stones are highly likely. Bile salts also increase intestinal permeability to oxalate. Low urine volume with decreased citrate levels further increases the risk of calculus formation.

Some patients have milder hyperoxaluria associated with high dietary intake of asparagus, spinach, rhubarb, celery, beets, bran flakes, peanut butter, chocolate, cranberries, plums, cola, tea, and vitamin C. Dietary modifications may help.

Metabolic hypokalemic hyperchloremic acidosis, such as that produced by renal tubular acidosis (RTA) type 1, has the opposite effect, and nephrocalcinosis occurs in most patients. In this condition, urinary pH always exceeds 5.5, retained acid is buffered in bone, and there is secondary hypercalciuria and phosphaturia.

Hypomagnesuria

Urinary magnesium excretion less than 50 mg/day may be associated with hypocitraturia. It may be due to low dietary magnesium. Inflammatory bowel disease may be the cause. Magnesium is an inhibitor of calcium oxalate crystallization.

Cystinuria

Cystine is a disulfide consisting of 2 bound cysteine molecules. Cystinuria is present in about 1 in 7000 people. It is an autosomal recessive condition, with 3 types. Type 1 is most common and the gene locus is 2p16.3. Amino acid transport in the intestine and proximal tubule of the kidney is defective, with increased excretion of cystine, ornithine, lysine, and arginine. Cystine is the least soluble of the natural amino acids and cystine stone formation results, accounting for less than 1% of stones in the United States. It accounts for about 8% of pediatric urolithiasis. Homozygotes secrete more than 600 mg/day cystine. Heterozygotes who are incomplete recessives excrete 150 to 300 mg/day. Normal individuals excrete less than 100 mg/day. At a pH of 6.0 to 7.0, urine will dissolve about 300 to 400 mg cystine/L. At a pH of 7.8, about 800 mg/L dissolves. Diagnostic clues are family history, faintly visible stones on plain films, young age (usually less than age 20 years with the first stones), hexagonal crystals on urinalysis, and a positive cyanide nitroprusside test.

Infection Stones

Infection stones are also known as struvite, triple phosphate, or magnesium ammonium phosphate stones. They also may contain carbonate apatite and
hydroxyapatite. Struvite calculi are associated with infection by urease-producing bacteria, most commonly *Proteus* species. Other potential organisms are *Pseudomonas*, *Klebsiella*, *Staphylococcus*, *Ureaplasma urealyticum*, and some anaerobic species. These infections are twice as common in women as in men, occur more often in older patients, and sometimes are associated with the presence of foreign bodies, such as sutures or catheters in patients with neurogenic bladder dysfunction. Urease breaks urea down to ammonium and carbon dioxide, resulting in high urinary pH (greater than 7.2), dissociation of phosphate, and supersaturation with struvite. Struvite stones tend to be large, multiple, and rapidly recurring if the infection is not eliminated. Bacteria are harbored within the stones. Metabolic disorders have been found in about 50% of these cases, and patients should be evaluated for such.16

**Low Urine Volume**

Low urine volume means higher supersaturation levels in the urine, which increases the risk for all stone types. It may be due to low fluid intake, hot weather, excessive sweating, outdoor occupation, or chronic diarrhea.

**EVALUATION OF AN ACUTE STONE EPISODE**

**CASE PRESENTATION**

A 45-year-old man presents to his local emergency room (ER) at 9 PM the day before Thanksgiving. His chief complaint is right flank pain radiating to the right testis, associated with nausea and vomiting.

**History**

The patient reports that the pain started 12 hours ago, primarily in his back. It moved to the flank over the next several hours, with gradually increasing waves of severity. The pain is not relieved in any position or by any movement. The patient also has experienced urinary frequency and mild dysuria for the past 4 hours.

**Physical Examination**

Physical examination reveals a man in obvious distress, writhing uncomfortably on a hard gurney and gaining no relief from attempts at walking. Blood pressure is 150/84 mm Hg, pulse is 110 bpm, and temperature is 98.6°F. No abnormalities are noted on examination, with the exception of a 10-cm scar in the left flank and moderate right flank and lower quadrant tenderness. Examination of the genitalia is normal.

- What initial studies should be obtained in an acute urinary stone episode?
- What evaluation should be performed to identify the etiology of urinary stones?

**INITIAL EVALUATION OF AN ACUTE STONE EPISODE**

**Laboratory Studies**

A complete blood count provides information relevant to possible intra-abdominal inflammatory or hemorrhagic problems. Serum electrolyte, blood urea nitrogen, and serum creatinine measurements are important for evaluating renal function. Serum amylase and lipase measurements evaluate for pancreatitis, and urinalysis assesses the urinary tract.

**Radiologic Studies**

Radiologic studies may be unnecessary if the patient has had many previous stones, the current episode is characteristic of colic, and the laboratory workup is negative except for microscopic hematuria. Otherwise, a plain abdominal film is useful and may confirm the presence of a calculus. More than 90% of stones are radiopaque. Calcium phosphate stones are the most opaque, followed by calcium oxalate monohydrate and calcium oxalate dihydrate stones. Next are triple phosphate and cystine stones. Uric acid stones will not be seen on plain film but can be identified as negative filling defects on intravenous pyelography (IVP) or retrograde pyelography (Figure 2). Stones smaller than 2 or 3 mm and stones overlying bone may be difficult to identify. The prospective sensitivity of radiographic examination of the kidneys, ureter, and bladder (KUB) is 45%, and the specificity is 77%.17 The retrospective sensitivity for KUB after the stone is localized with helical computed tomography (CT) scan is 59%.17 KUB is nevertheless useful in many patients for later follow up of the progress or passage of the stone.

IVP has traditionally been the confirming diagnostic modality in renal colic. Advantages include 1) demonstration of 2 kidneys; 2) visualization of renal size, contours, and anatomy that rule out malignancy; 3) visibility of some functional information; 4) possible discovery of intrarenal and ureteral anomalies that might contribute to stone formation; 5) localizing of the stone relative to different parts of the collecting system, which will be helpful if percutaneous procedures are planned; and 6) information regarding the size of the stone and degree of obstruction. Disadvantages include 1) allergy; 2) poor visualization in unprepped patients and those with abnormal renal function; 3) renal toxicity; and 4) delay in
diagnosis, with possible failure to accurately localize ureteral stones. Prospective IVP sensitivity and specificity in detecting and localizing ureteral stones are 52% and 94%, respectively (Table 2).18

Ultrasonography of the kidneys is rapid and needs no contrast material. Stones larger than 4 to 5 mm produce acoustic shadowing. Hydronephrosis due to ureteral obstruction will be detected. Parenchymal thickness can be assessed. Tumors or cysts may be noted. Other intra-abdominal pathology may be discovered. Detection of the location and size of ureteral stones is poor. Ultrasonography is safe in pregnancy. The presence of a radiologist during the real time examination is critical for best results. Combined with KUB, ultrasonography is valuable in many patients.

Noncontrast helical CT scanning, using 5-mm collimation and soft tissue windows, is now the gold standard for detection of urolithiasis, particularly for ureteral stones. The cost is equivalent to IVP, and it takes only a few minutes to complete the procedure and obtain results. Without contrast material there is no threat of allergic reaction or renal toxicity. Other intra-abdominal pathology can be evaluated and stone location and size can be accurately determined. All stone types are dense, and Hounsfield units have not been found to be reliable in predicting stone composition or fragility. Stones may be difficult to differentiate from phleboliths or other dense objects (eg, surgical clips), and contrast may be administered in studies that are difficult to interpret. Ureteral stones produce hydronephrosis, ureteral wall thickening at the site of impaction (ie, the rim sign), perinephric fat stranding from edema, and unilateral nephromegaly (Figure 3). The rim sign is present in 50% to 75% of stone cases but rarely if ever with other densities such as phleboliths. In the presence of a detected density, these secondary signs are diagnostic of stone presence. In the absence of a density, the secondary signs are an excellent indication that a stone has recently passed. Sensitivity and specificity of noncontrast helical CT scanning in ureteral stones are both generally noted to be about 95% (see Table 2).

THE SEARCH FOR A CAUSE

Once the diagnosis of urinary lithiasis has been made, patients should undergo testing to determine a cause for the stones. Any stones that spontaneously pass or are surgically removed should be sent for analysis of their composition. The serum should be evaluated for levels of the following: electrolytes, including calcium and magnesium; creatinine; phosphate; uric acid; and PTH. A 24-hour urine study also should be performed; the average normal ranges are listed in Table 3. A 24-hour urine study for cystine normally is less than 100 mg; this study is not necessary unless cystine crystals are present in the urine, stone analysis indicates cystine, or the nitroprusside test is positive. Urine culture

![Figure 2](image)

**Figure 2.** Bilateral retrograde pyelogram showing 2 smooth filling defects in the right renal pelvis, compatible with uric acid stones. This patient had intermittent flank pain, microhematuria, a normal plain abdominal film, and a creatinine of 2.2 g, which prompted retrograde pyelography rather than intravenous pyelography.

### Table 2. Sensitivity and Specificity of Various Radiologic Studies in Ureteral Stones

<table>
<thead>
<tr>
<th>Study</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCHCT</td>
<td>94%</td>
<td>97%</td>
</tr>
<tr>
<td>IVP</td>
<td>52%</td>
<td>94%</td>
</tr>
<tr>
<td>Ultrasonography</td>
<td>19%</td>
<td>97%</td>
</tr>
</tbody>
</table>

should be performed at least once in all patients with urinary calculi and frequently in those with triple phosphate stones. Urinary pH is important for diagnosis of RTA and for follow up in all cases, especially patients who develop uric acid and cystine stones.

**EVALUATION AND DIAGNOSIS OF CASE PATIENT**

**Initial Evaluation in Emergency Room**

Initial blood tests in this patient reveal a leukocyte count of 12,600 but no other abnormalities. Urinalysis reveals 3+ blood on dipstick and 10 to 25 red blood cells per high power field on microscopic examination. At this point, the harried ER physician returns to the patient and completes his history taking. The patient reports that he had kidney stones on 5 occasions since age 21, when he had required an operation to remove a stone from his left ureter. He has since passed 3 stones spontaneously and had 1 removed by a scope procedure done through his penis. He does not know what type of stones these were. He also reports that his father and brother have experienced stone problems. The physician sends the patient to the radiology department for an IVP.

The radiology department contacts the ER physician 2 hours later to report that the IVP showed several small calcifications in the pelvis on plain film and delay in function from the right side. Additional films would be obtained in 1 or 2 hours. The radiologist mentions that there is probably a stone but it was not identified on any of the films so far.

The patient returns to the ER to wait. Because he is still in obvious severe pain, the physician, who now feels reasonably sure that a urinary stone is present, orders 50 mg of meperidine hydrochloride to be given intramuscularly. The patient vomits 15 minutes later and becomes diaphoretic and clammy, with a blood pressure of 90/60 mm Hg. An intravenous drip of normal saline is started at 200 mL/h, and the patient stabilizes, still in severe pain. He is given intravenous ketorolac tromethamine (30 mg) and the pain subsides shortly thereafter, at about 2 AM on Thanksgiving Day. Delayed films are obtained at 4 AM (**Figure 4**), which reveal columnation of the contrast medium in the right ureter down to the uretero-vesical junction. The precise location of the stone is not visible because of overlying contrast in the bladder. Shortly thereafter, the patient passes a small stone and is discharged with a return appointment to a urologist.

**Table 3. Average Normal Ranges for 24-hour Urine Study**

<table>
<thead>
<tr>
<th>Study</th>
<th>Volume: Normal range, 1–2 L; mean, 1.5 L</th>
<th>Creatinine: Male, 1–2 g; female, 0.8–1.8 g</th>
<th>Calcium: Male, ≤ 250 mg; female, ≤ 200 mg</th>
<th>Sodium: 130–315 mEq</th>
<th>Phosphate: 400–1300 mg</th>
<th>Oxalate: 20–40 mg</th>
<th>Citrate: &gt; 640 mg</th>
<th>Magnesium: &gt; 50 mg</th>
<th>Uric acid: &lt; 600 mg</th>
</tr>
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<tbody>
<tr>
<td></td>
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</tbody>
</table>
Subsequent Evaluation by Urologist

The patient sees a urologist, who orders further laboratory studies and a stone analysis. Results are as follows:

- Serum findings: sodium, 139 mEq/L; potassium, 3.0 mEq/L; chloride, 112 mEq/L; bicarbonate, 18 mEq/L; calcium, 10 mg/dL.
- 24-hour urine findings: volume, 930 mL; pH, 5.6; calcium, 130 mg; sodium, 150 mEq; phosphate, 900 mg; oxalate, 75 mg; citrate, 300 mg; magnesium, 10 mg; uric acid, 350 mg.
- Stone analysis: 80% calcium oxalate, 15% calcium phosphate.

Diagnosis

From the patient’s laboratory results, the urologist notes a hyperchloremic, hypokalemic metabolic acidosis with a normal anion gap. She also notes the hyperoxaluria, combined with somewhat low urinary calcium, citrate, and magnesium, and low urine volume. Uric acid is normal. The urologist asks the patient about chronic diarrheal problems and discovers that he has had mild Crohn’s disease since age 18. She concludes that the patient has hyperoxaluria secondary to his Crohn’s disease. This diagnosis likely explains his current and past stone episodes. She recommends dietary calcium supplementation, which will decrease oxalate absorption from the intestine in the patient. This will decrease urinary supersaturation with calcium oxalate and reduce the likelihood of his having future stone episodes.

Dietary Management of Urinary Lithiasis

Case Presentation

A 62-year-old man presents to the ER with left flank pain that developed while he was working outside on a hot July day.
History and Evaluation in ER

The patient is a retired business executive who recently moved to the Southwest with his wife. A week prior to his presentation he began a project involving repainting the exterior of their house and converting the desert landscaping to traditional grass, shrubs, and trees that will remind them of their Iowa roots. He was working outside when the pain developed.

In the ER, a noncontrast helical CT scan is performed, and the patient is diagnosed with a 3-mm ureteral stone. All blood test results are normal, including serum calcium and PTH levels. His 24-hour urine analysis reveals the following: volume, 1.2 L; creatinine, 1.5 g; uric acid, 450 mg; calcium, 270 mg; citrate, 475 mg; oxalate, 30 mg; sodium, 300 mEq. The patient is discharged from the ER with a prescription for oral pain medication and an appointment for follow up with a urologist. He passes the stone 2 days later.

Follow up by Urologist

At the follow-up visit, the urologist reviews the patient’s 24-hour urine studies and notes that his urine volume is somewhat low. Combined with outside work in hot weather, the patient’s urine volume may have been even lower. The results also show mild hypocitraturia, which, along with his urinary calcium level, may have been worsened by high salt intake and sodium excretion. The urologist makes a diagnosis of absorptive hypercalciuria, type 2. As the physician begins to discuss a management approach, the patient states that he believes in natural treatments and would prefer not to take any medication.

- **What dietary advice is appropriate for this patient?**

**COMPONENTS OF DIETARY MANAGEMENT**

**Fluid Intake**

Insensible fluid losses in the average individual are about 1 L/day and increase in outdoor, summer, and exertional conditions. Average urine volume is about 1.5 L; therefore, fluid consumption must be 2.5 L to produce an average urine volume. A higher urine volume will increase tubular transit time, reducing crystal precipitation. Urinary dilution increases citrate excretion and increases the activity of the inhibitor Tamm-Horsfall protein. Supersaturation will also be reduced, with decreased stone risk. The patient should be instructed to measure daily urine output, with a goal of at least 2.5 L/day, evenly spread throughout the 24 hours (to avoid nighttime increases in supersaturation). This advice alone may decrease stone recurrence rate by as much as 60% (stone clinic effect). The relative risk of stone formation in patients with a fluid intake greater than 2.5 L/day is half that of patients with a fluid intake less than 1.6 L/day.

Lemonade and orange juice increase urinary citrate levels and are therefore recommended. Coffee interferes with antidiuretic hormone (ADH) activity, and alcoholic beverages decrease ADH secretion—a desirable effect. Tea and cola drinks have high oxalate contents and may be less advisable. Typical quantities of dairy products do not increase the risk of stone formation or the urinary supersaturation of stone salts. There is no evidence that increased water hardness is associated with higher stone incidence.

**Protein Intake**

High total and animal protein consumption have long been associated with increased risk of urolithiasis. Chronic metabolic acidosis may develop and is associated with high calcium and uric acid excretion in urine, with lower citrate and lower urinary pH. Protein restriction has not been proven to reduce stone incidence.

**Calcium Intake**

Dietary calcium restriction is no longer advised for individuals who develop urinary stones, as decreased bone density and osteoporosis may result. Increased calcium intake has actually been shown to reduce stone risk. This result is probably secondary to increased intestinal binding of oxalate, with decreased urinary oxalate and a decrease in calcium oxalate supersaturation. Thus, moderate increases in dietary calcium can be recommended along with restriction of the oxalate-rich foods previously mentioned.

**Other Dietary Constituents**

No other foods have been consistently shown to affect stone incidence, although high carbohydrate intake increases both urinary calcium and oxalate, whereas vegetables produce a decrease in oxaluria and an increase in citruria and, therefore, may be recommended.

**MEDICAL MANAGEMENT OF CALCIUM STONES**

**CASE PRESENTATION**

A urologist refers a patient to his nephrologist associate. The patient is a 42-year-old man who has had
5 stones over the past 4 years. He underwent ESWL once, ureteroscopy twice, and passed 2 stones spontaneously. The nephrologist orders serum and urinary evaluations. The patient’s serum calcium is 10.2 mg/dL and uric acid is 5.6 mg/dL. His serum PTH level is 20 pg/mL (normal, 10 to 65 pg/mL). A 24-hour urine study reveals the following: volume, 2.22 L; calcium, 489 mg; oxalate, 53 mg; citrate, 244 mg; uric acid, 538 mg. Fasting urinary calcium is less than 0.11 mg/mg creatinine, and post-load urinary calcium is greater than 0.22 mg/mg creatinine.

The nephrologist makes a diagnosis of absorptive hypercalciuria type 1. The patient also has decreased levels of urinary citrate.

• How should this patient be managed at this point?

TREATMENT REGIMENS

Given this patient’s significant procedural history, he certainly warrants the institution of medical therapy. A few options exist.

Thiazide Therapy

Thiazides currently are the mainstay of therapy in absorptive hypercalciuria. Hydrochlorothiazide can be used, starting at a dose of 25 mg/day and increasing to as much as 50 mg twice daily. An alternative is trichlormethiazide 2 mg once or twice daily. The long-term dosage is decided based on urinary calcium monitoring every 3 to 4 months until stable, and then every 6 months. New stone formation rates are reduced by 90%. Side effects include hypokalemia, fatigue, muscle weakness and cramps, impotence, hyperuricemia, and increased serum cholesterol. Side effects are not often severe and rarely prohibit the use of thiazides.

Thiazides promote sodium and calcium reabsorption in the proximal tubule but increase calcium absorption while decreasing sodium absorption in the distal tubule. The overall effect is a decrease in calciuria, diuresis, and contracted intravascular volume. Excessive sodium ingestion will counteract this effect, so dietary salt restriction is advised. There is some evidence that intestinal calcium absorption may decrease on thiazide therapy and that oxalate absorption may secondarily decrease, but it is not conclusive.

Monitoring of urinary calcium may uncover a loss of the hypocalciuric effect after about 2 to 3 years in absorptive hypercalciuria. If this occurs, the thiazide can be stopped for a period of 3 months and then resumed.

Thiazides induce similar metabolic effects and reduction in stone formation in renal calcium leak, which results in hypercalciuria, a slight decrease in serum calcium, and secondary elevation of PTH levels. The effects are specific for this problem and continue long term. Thus, thiazides are unquestionably first-line therapy.

Potassium Citrate

Many patients with hypercalciuria have low levels of the stone inhibitor citrate. Also, therapy with thiazides may result in hypokalemia and hypocitraturia. Such patients will benefit from potassium citrate, which is supplied in 5 and 10 mEq tablets and also in crystal and liquid forms. The dose is 10 to 20 mEq 3 times daily, guided by urinary citrate levels. Both hypokalemia and hypocitraturia are thus treated. The intracellular acidosis produced by thiazide therapy is counteracted, allowing for increased citrate excretion. Citrate complexes with calcium, decreasing calcium oxalate supersaturation. The increased alkali load leads to increased calcium reabsorption and increased urinary pH in the range of 6.5 to 7.0. Citrate directly inhibits calcium oxalate crystallization and also decreases the calcium oxalate precipitation produced by uric acid. Many studies have demonstrated decreased stone formation rates by as much as 90% in patients with hypocitraturia alone, as well as in those with hypercalciuria plus hypocitraturia, and in those with hyperuricosuria alone.

Sodium Cellulose Phosphate

Sodium cellulose phosphate (SCP) is an ion exchange resin that has fallen into disuse to some extent with the popularity of thiazides for hypercalciuria, and also because its use is limited only to those patients with absorptive hypercalciuria. In other patients it may result in secondary hyperparathyroidism because of negative calcium balance. SCP exchanges sodium for calcium in the gut and results in decreased calcium absorption. This renders oxalate more available for absorption. SCP should be used with dietary oxalate restriction. Magnesium citrate may also need to be given, as SCP decreases magnesium absorption. The dose of SCP is 5 g 3 times daily.

Orthophosphate

In patients with absorptive hypercalciuria type 3 (renal phosphate leak), hypophosphatemia leads to increased levels of 1,25(OH)2D3 and intestinal hyperabsorption of calcium. Orthophosphate decreases 1,25(OH)2D3 production and calcium absorption and also produces increased calcium binding, along with increased urinary citrate and pH, all of which reduce calcium oxalate crystallization. Diarrhea is a significant complication. The dose is 500 mg 3 times daily.
A 50-year-old man presents to his urologist with his second urinary stone episode, characterized by right flank pain and hematuria. The patient is 5’7” tall and weighs 332 lb. He complains of sore feet. Radiologic evaluation reveals a small stone in the distal left ureter, which he soon passes in his urine. Stone analysis reveals it to be composed of 95% uric acid. A 24-hour urine evaluation reveals the following: volume, 0.9 L; calcium, 160 mg; citrate, 400 mg; uric acid, 750 mg; pH, 5.2. Serum uric acid is 7.2 mg/dL. Other blood studies are normal.

- What disorder does this patient have and how should it be treated?

CAUSES OF ABNORMALLY HIGH URIC ACID

In many patients with calcium oxalate nephrolithiasis, the only metabolic abnormality discovered is hyperuricosuria. In this patient, who also has low urinary pH and hyperuricemia, gouty diathesis is present and he is forming uric acid stones. His weight and age are typical of those with the onset of gout, a disorder that is thought to have an autosomal dominant inheritance. Nevertheless, blood studies for renal function and to rule out myeloproliferative conditions should be performed.

Humans do not have the liver enzyme uricase, which reduces uric acid to allantoin in other animals. Allantoin is excreted in the urine without complications. Uric acid, on the other hand, may precipitate and induce calcium oxalate or uric acid stone formation. Urate is reabsorbed in both the proximal and distal tubule, and about 10% of the filtered load is excreted in the urine. The pK_{a} of uric acid is 5.75; in a solution below that level, it exists mostly as uric acid, which is relatively insoluble. Above that level, it exists as urate, which is much more soluble. Thus, at a pH of 5.5, urine can dissolve about 100 mg/L of excreted uric acid, whereas at a pH of 7.0 it can dissolve more than 1000 mg/L. (Figure 5). Normal urinary pH is about 6.0 in average individuals. As previously noted, defective ammonium excretion may be the cause of the acidic urine in gouty diathesis. Gouty arthritis occurs in about 25% of these patients.

MANAGEMENT OF URIC ACID STONES

In patients without acidic urine, uric acid exists in the urine primarily as monosodium urate, which can induce heterogeneous calcium oxalate nucleation. Whether patients are producing uric acid or calcium oxalate stones, the treatment is essentially the same: water, decreased purine intake, and allopurinol, with or without potassium citrate.

Dietary Measures

Dietary measures would be of some help in this individual. Low urine volume is easily corrected and will reduce the likelihood of future stones. Decreasing purine intake, by avoiding foods such as poultry and fish, may lower his urinary uric acid and, if combined with a decrease of other foodstuffs, may improve his general well-being. Unfortunately, few patients can maintain long-term dietary modifications.

Allopurinol

Allopurinol is a xanthine oxidase inhibitor that reduces uric acid formation from its precursors, xanthine and hypoxanthine, which are excreted in larger quantities but are much more soluble in urine. The serum and urinary uric acid levels drop significantly. The dose is 300 mg/day. Allopurinol has no side effects except for occasional rash and activation of gouty arthritis.

Potassium Citrate

Potassium citrate as added or even sole therapy in this case could be considered with a goal of establishing

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**Figure 5.** Ionization curve of uric acid in solutions of different pH. The pK_a of uric acid is 5.75. Thus, at a pH of 5.75, uric acid will be 50% dissociated. Below that pH level, most will exist as uric acid, and above that level, most will exist as urate, which is highly soluble. Urine at a pH of 7.2 will hold up to 1200 mg of uric acid/L in solution.
a urinary pH of about 6.5 to 6.8. This would increase uric acid solubility without increasing the risk of calcium oxalate nucleation. Patient education is important, particularly in the use of nitrazine paper in monitoring pH and adjusting medication dosage. Citrate is not an inhibitor of uric acid crystallization.

Dissolution of uric acid stones is possible with long-term alkalinization of the urine. It may take several months. Large urine output is helpful, as is decreased dietary purine. Occasionally, a large nonobstructive stone in the kidney may shrink, move, and obstruct a ureter, requiring intervention.

**MANAGEMENT OF CYSTINE STONES**

**CASE PRESENTATION**

An 18-year-old woman presents to her primary care physician with urinary frequency, dysuria, and right-sided back pain. She has had 3 urinary tract infections in the previous year, which responded well to short courses of antibiotics. She has not been sexually active. She spontaneously passed a small stone 1 year ago. She has a brother with a history of 3 stones, with 2 surgical procedures.

Urinalysis reveals 3 to 5 red blood cells and 5 to 10 leukocytes per high power field. Urine culture is positive for *Proteus mirabilis*. The patient is given a prescription for levofloxacin, 250 mg/day for 7 days. She returns for follow up 10 days later, and urinalysis reveals persistent leukocytes and bacteria.

- **What are appropriate next steps in the evaluation of this patient?**

In an 18-year-old patient with recurrent urinary tract infection, radiologic investigation is indicated and in most cases would consist initially of IVP and voiding cystourethrography. An anatomic abnormality is likely with this history and with *Proteus* growing on culture. The patient’s young age and prior history of stone disease, with a family history, leads one to suspect cystinuria. The average age at first stone presentation is 21. Creatinine clearance usually is normal; other metabolic abnormalities (eg, hypercalciuria) will occasionally be found. A previous history of spontaneous stone passage or surgery for stones of unknown composition is not uncommon before the diagnosis is established.

Although urinalysis in this case did not reveal hexagonal crystalluria, this finding is less likely unless the urine is an early morning concentrated specimen; 25% of first morning urine samples show crystalluria. The cyanide-nitroprusside test is a simple method of detecting 24-hour urinary cystine levels greater than 75 mg/L (normal levels are usually less than 50 mg/L). Both the sensitivity and specificity of this test are approximately 80%.

**FURTHER EVALUATION BY NEPHROLOGIST**

The patient is referred to a nephrologist for further evaluation. A voiding cystourethrogram shows no bladder abnormalities and no reflux. A plain abdominal film clearly shows a large intrapelvic stone mass, with apparent masses of smaller stones in the lower and middle calyceal areas of the right kidney. Although the density of the stone is less than a typical large calcium stone, it is clearly visible.

**Figure 6.** Plain abdominal film of a patient with cystinuria showing a large intrapelvic stone mass, with apparent masses of smaller stones in the lower and middle calyceal areas of the right kidney. Although the density of the stone is less than a typical large calcium stone, it is clearly visible.
The suspicion for cystinuria is now strong. In general, it is best not to undertake metabolic evaluation for stone disease if the patient is currently suffering an acute stone episode. However, it is not necessary that the patient be completely free of stones before an evaluation is performed. It is important that she be conducting her life as usual, with typical activities, diet, and fluid intake. The physician must avoid giving dietary and fluid advice or medication to the stone patient prior to workup, or fallacious results may be obtained. In this case, and in any case where dissolution of stones may be a mode of therapy (eg, uric acid or struvite stones), it is advisable to complete the metabolic evaluation immediately.

**METABOLIC WORKUP OF CASE PATIENT**

The nephrologist orders a 24-hour urinary evaluation. Results are as follows: volume, 1.1 L; cystine, 1260 mg; creatinine clearance, 100 mL/min. Urinary pH is 7.2. The nephrologist decides that medical therapy and an attempt to dissolve the stone are indicated.

- **Was the decision to treat medically rather than proceed to surgery appropriate?**

The nephrologist orders a 24-hour urinary evaluation. Results are as follows: volume, 1.1 L; cystine, 1260 mg; creatinine clearance, 100 mL/min. Urinary pH is 7.2. The nephrologist decides that medical therapy and an attempt to dissolve the stone are indicated.

**MEDICAL MANAGEMENT OF CYSTINURIA**

**Hydration and Urinary Alkalization**

Average urine output is approximately 1.5 L/day. At a pH of 7.0, urine will dissolve about 400 mg/L of cystine. At a pH of 7.8, it will dissolve about 800 mg/L. It would seem that urinary cystine levels might be brought to less than saturated by increasing urine volume to about 3 L/day and by alkalinization, which can be achieved with acetazolamide 250 mg twice daily or sodium bicarbonate 15 g/day in divided doses. As sodium increases cystine excretion, potassium citrate would be a preferred mode of alkalinization. In attempts to avoid calcium phosphate and struvite precipitation, the pH target should be about 7.0. The patient must be strongly informed regarding the therapy, in particular to maintain high urine output, low specific gravity, and high alkalinity during sleeping hours. Adherence to this regimen will prevent more stones in about 60% of patients and dissolve old stones in some.

**D-Penicillamine**

Cystine is composed of 2 cysteine molecules joined by a disulfide bond. D-Penicillamine induces a complex with cysteine, which is 50 times more soluble than cystine. 1 g of D-penicillamine will complex about 300 mg of cystine. Dosing begins at 250 mg twice daily and increases to as much as 500 mg 4 times daily in some patients. Stone prevention can be achieved in all patients who can tolerate this regimen with hydration and alkalinization. Dissolution of existing stones is achieved in about 50% of cases, if they are pure cystine. Major drawbacks to D-penicillamine therapy are well known. Nausea, vomiting, and diarrhea are common. Skin rash, fever, proteinuria, and nephrotic syndrome may occur. The typical patients beginning...
treatment are teenagers or young adults, and non-compliance is common. About 30% to 50% stop therapy because of problems.\textsuperscript{29}

**Alpha-Mercaptopropionylglycine**

Alpha-mercaptopropionylglycine (AMPG) is another complexing thiol compound that is effective in reducing urinary cystine saturation. In adults, dosing should begin at 250 mg 3 times daily, not with meals. Urinary cystine levels dictate dosage, with the goal of approximately 300 mg/day of cystine. In children, a reasonable starting dose of AMPG is 15 mg/kg daily. Toxicity of AMPG is less than but similar to that of D-penicillamine. Effectiveness is about the same. Vitamin B\textsubscript{6} deficiency, which may occur with D-penicillamine, is uncommon with AMPG.

**Captopril**

Captopril is an angiotensin-converting enzyme inhibitor with a complexing thiol group that has been found to be effective in some patients with cystinuria.\textsuperscript{30} The side effects are considerably less than with D-penicillamine. Experience with captopril is relatively limited, and the efficacy of this drug is uncertain.

**MEDICAL MANAGEMENT OF CASE PATIENT**

After 3 months of therapy with hydration, alkalination, and AMPG, the patient returns for follow up. A 24-hour urine study reveals urine volume is now 3 L, pH is 7.2, and cystine is 250 mg. The plain abdominal film is unchanged, and urine culture again grows *Proteus*, although the patient is asymptomatic. She is tolerating AMPG well. She is referred to a urologist.

- What should be done now?

**SURGICAL MANAGEMENT OF CYSTINURIA**

The plain film in this case suggests that the patient has a staghorn calculus with a single large stone in the renal pelvis and a large bulk of many small stones in the lower and middle pole calyces. Some small stones also are seen in the upper calyces. One option for surgical therapy is open surgery, which involves a major flank incision, a long hospitalization and recovery period, and quite likely retained stones. However, less invasive options are available and would be preferred. Minimally invasive therapy became the routine for cystine stones in the early 1980s, with the development of ESWL and percutaneous nephrolithotomy techniques. Percutaneous nephrolithotomy, possibly followed by ESWL, currently is the recommended treatment for staghorn calculi.\textsuperscript{31}

ESWL in this particular patient would first require placement of a ureteral double-J catheter to avoid steinstrasse and ureteral obstruction by fragments. Several sessions of ESWL would probably be required, particularly considering the well-known difficulty in fragmenting cystine stones. Cystine stones tend to fragment into relatively large pieces, which commonly stick in the ureter or remain in the kidney.

In this case, percutaneous management should be the initial treatment. Access through the lower pole will allow removal of stones in that area and in the renal pelvis with a rigid nephroscope and ultrasound fragmentation. The advantage of simultaneous suction removal of fragments is obvious. For stones or fragments that can not easily be reached with rigid nephroscopy, a flexible scope with Holmium laser can be used. Grasping or basketing of sizable fragments will save some operative time. Patience in the performance of this surgery can not be over-stressed to ensure complete stone removal, with the avoidance of intrarenal bleeding and collecting system tears with extravasation, which may occur and limit one’s surgical vision and thoroughness. A second percutaneous access may be considered in some cases but is not necessary in this patient.

**SURGICAL TREATMENT OF CASE PATIENT**

The bulk of the stone is removed by ultrasonic disintegration. The remaining fragments and smaller stones are removed by Holmium lithotripsy, basketing, and irrigation intraoperatively. The stone responds quickly to ultrasound. Although quick response is not always the case, in this instance it was probably due to the stone composition of 60% cystine and 40% struvite, as found later.

**OPTIONS FOR MANAGEMENT OF INTRARENAL STONES**

**CASE PRESENTATION**

A 51-year-old woman presents to her local ER with gross hematuria and severe right flank pain. She has a temperature of 100°F and a leukocyte count of 12,600. Serum chemistry values all are normal. Evaluation reveals a right-sided renal pelvic stone measuring 4.0 cm by 2.3 cm. The patient has no prior stone history and no other significant past medical history. A double-J stent is placed for relief of pain and fever (Figure 8).

- What modalities are used to address intrarenal stones?
EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY

ESWL was developed in 1980, and the first shock wave machine used in the United States was the Dornier HM3 lithotriptor. Subsequent generations of shock wave machines have allowed for multifunctionality, better use of operating room space, different modalities of stone visualization, and monitored analgesia rather than general anesthesia. The newer machines are inferior to the HM3 in lithotripsy effectiveness but more useful in general urologic practice. There is little difference in effectiveness among most of the newer machines.

Procedure

ESWL relies upon the generation of a shock wave from an electromagnetic, piezoelectric, or electrohydraulic source. The shock wave is then focused (via an acoustic lens, concave piezoelectric dish, or ellipsoid reflector, respectively) at an area where the stone is located. The shock wave aperture is the area of skin penetrated by the shock wave. Wider apertures are associated with less pain. The focal zone of the shock wave is the second important attribute and indicates the size of the effective stone fragmentation area. Larger zones have higher energy and pressure and may require fewer shocks to fragment a stone. The shock wave is coupled to the patient with a water cushion to avoid dissipation of energy at interfaces, and the stone is positioned in the focal area by use of fluoroscopic or ultrasound imaging. In most cases, particularly in ureteral stones, fluoroscopy is superior to ultrasound because it affords better visualization of the stone (ie, it is easier for the urologist to interpret) and better monitoring of stone fragmentation.

The small acoustic difference between water and various tissues accounts for the relative lack of tissue damage with shock waves. The large acoustic difference between stones and the surrounding tissues accounts for the fragmentation of stones. Reflection and refraction of the shock wave at the posterior surface of the stone increases fracture lines and fragmentation.

Long-term complications of ESWL are unusual and generally mild. Gross hematuria is common immediately after ESWL, along with hematoma and some pain at the entry site. Steinstrasse may occur with larger stones and consists of an obstructive accumulation in the ureter of small or larger stone fragments. This problem can be avoided by the pretreatment placement of a double-J stent, which can be left in place until most of the fragments pass (usually in 1 or 2 weeks). Occasionally, perinephric hematoma or pancreatitis occurs. It was originally thought that secondary hypertension might be common after ESWL, but there is no evidence of this. Renal function is not affected in the long term, even with bilateral simultaneous ESWL.

Success Rates

All types of stones can be treated with ESWL; the most difficult to fragment are cystine, calcium oxalate monohydrate, and calcium oxalate dihydrate stones. Struvite is the softest, followed by calcium phosphate and uric acid. Unfortunately, calculus composition cannot be predicted from plain films at present. Smooth, homogeneous dense stones are more likely to be calcium oxalate monohydrate or calcium phosphate. History and urine studies may foretell cystine stones. Urea-splitting organisms in the urine indicate struvite. Future developments in CT may assist in identifying stone type and hardness and, thus, planning therapy.

Morbid obesity may render ESWL ineffective if the stone cannot be focused. Some machines have weight limits, or the size and thickness of the patient may make it impossible to focus the stone. A dry run prior to giving anesthesia or analgesia will assist in making this determination.

In general, intrarenal stones smaller than 2 cm will be successfully fragmented in 1 session of ESWL in 60% to 90% of cases, whereas stones 2 cm or larger require retreatment in 30% to 50% of cases. For calyceal...
stones, the retreatment rate is about 5% for stones smaller than 1 cm, 10% for 1- to 2-cm stones, and about 35% for 2- to 3-cm stones. Lower pole stones have a lower stone-free status with ESWL than stones in other portions of the kidney, with a 30% to 50% failure rate. Factors mitigating against ESWL success for lower pole calyceal stones are an infundibulopelvic angle less than 70°, long infundibulum (longer than 3 cm), and narrow infundibulum (less than 0.5 cm). In these situations, fragments tend to remain immobile, and secondary procedures often are necessary.

A statistic sometimes quoted for a method of stone treatment is the efficiency quotient (EQ), the equation for which is:

$$\text{EQ} = \frac{\% \text{ stone free}}{\% \text{ retreatments} + \% \text{ auxiliary procedures} + 100}$$

The EQ for renal stones treated by ESWL alone varies from 0.66 for stones measuring 1 cm or less, to 0.62 for 1- to 2-cm stones, to 0.27 for 2- to 3-cm stones, to 0.16 for stones measuring 3 cm or more. The EQ for lower pole stones is less for stones of all sizes than the EQ for stones of all sizes in other parts of the collecting system.

Stone-free status of the patient is judged by plain film at 3 months in most series. CT scans are likely to show greater numbers of residual fragments. Some reports indicate ESWL success rates in the kidney as low as 47% (using residual fragments larger than 2 mm as the criterion of failure) and recommend percutaneous treatment for stones larger than 1.5 cm. Staghorn stones can be successfully fragmented with ESWL alone. Various authors report stone-free rates ranging from 45% to 65%, with an average number of procedures ranging from 1.5 to 3.3. The percentage of cases requiring auxiliary procedures, such as ureteroscopy, stent insertions, and percutaneous tubes, ranges from 30% to 80% in these series. Definitions of staghorn stones are variable. Definitions of success and stone-free rates are also quite variable, although residual fragments less than 3 mm are often discounted because of expected passage. With struvite stones this is not adequate, and all attempts should be to render the patient totally stone free to prevent recurrences secondary to the bacteria retained within fragments. ESWL monotherapy is not recommended for treatment of staghorn stones.

**Percutaneous Nephrolithotomy**

Percutaneous nephrolithotomy (PCNL) has been in use since the late 1970s, and its results have improved as technology has advanced. PCNL is applicable to stones in every location and of every size within the kidney and ureter. Uncontrolled bleeding diathesis and untreated infections are the only contraindications. Intracorporeal lithotripsy is particularly indicated for larger or harder stones, those in calyceal diverticula, and for ESWL failures.

**Success Rates**

Stone-free rates with PCNL are about 90% for cases involving stones up to 3 cm and as high as 75% for larger stones; retreatment rates are about 10% for smaller stones and 25% for those larger than 2 cm. The EQs are 0.8 for stones smaller than 2 cm and 0.6 for stones 2 cm or larger. These results represent a considerable advantage in overall success when compared to ESWL. The rapid resolution of the stone and treatment episode result in less days of debility for the patient, reduced pain and perhaps cost, and an earlier return to normal activities.

**Surgical Procedure**

Anatomic variations (eg, horseshoe kidneys) require great care when planning the percutaneous access. Morbid obesity may make entrance to the collecting system difficult, as the instruments may not be long enough, and anesthesia problems are more likely in the prone position in obese patients. The lateral position may be preferable and may also allow for a shorter track into the kidney (overcoming the problem of instrument length), as the pannus falls away. A larger skin incision will also allow for the surgeon to push the instruments further into the subcutaneous tissues and thus gain easier access to the collecting system.

The safest access is through a lower pole calyx. The middle third provides good access to a large portion of the collecting system. Upper pole access allows for evacuation of stones with rigid instrumentation from upper and lower calyces and from the renal pelvis, with relative ease. Upper pole access achieved from above the 12th rib is complicated by hydrothorax about 10% of the time. Such fluid collections usually resolve spontaneously but may require a chest tube. With large stones or difficult infundibular or calyceal anatomy, 2 or perhaps even 3 percutaneous sticks may be required to reach all calculus material, although the availability of flexible instrumentation has rendered the need for multiple sticks unusual.
Energy Sources Commonly Used

**Ultrasound.** Ultrasonic probes can be passed only through rigid endoscopes with offset eyepieces. Ultrasonic waves are generated when an electric current is applied to a piezoceramic crystal. Vibrational energy is generated that is transmitted along the length of the probe. The drilling effect created by this process is applied to the stone when the probe is held directly on it, or in very close proximity. As surrounding tissue does not vibrate with the probe, there is little danger of tissue damage from the energy applied, but the probe can certainly be pushed too hard against stone or tissue and produce perforations and tears. Forceful use will incite bleeding, which obscures vision and may cause the operation to finish prematurely. The larger probes used for nephroscopy are hollow and allow application of suction to remove stone fragments as they are broken off the main stone. Most stones respond well, although some cystine and calcium oxalate monohydrate stones may be resistant. Probes become quite hot during use, and it is advisable to have 2 probes available to allow for exchange and cooling. Use of ultrasound for ureteral stones is not common, as the smaller probes required do not allow for suction channels to remove fragments.

Stones in calyceal diverticula can be treated by direct puncture and dilation into the diverticulum. For removal of solitary calyceal stones, access directly into the involved calyx produces excellent results, whereas access through another calyx with a direct route to the involved area is also satisfactory (eg, upper pole access for lower pole stones). Excessive cranking of the instrument is to be avoided, as it tends to produce mucosal tears and bleeding.

**Electrohydraulic lithotripsy (EHL)** is the least expensive method of fragmenting urinary calculi. Its greatest use is in the treatment of bladder stones, but EHL can be used for ureteral and renal stones as well, with smaller and more flexible probes. A spark gap is present at the end of the probe. Discharge in a liquid medium produces water vaporization and a cavitation bubble that generates 3 shock waves: an expansion, contraction, and rebound wave. The probe is held about 1 mm from the stone for best fragmentation effect. If held directly on the stone, there is no cavitation; if too far from the stone, the energy dissipates. Fibers are relatively rapidly consumed, and for large or hard stones there should be many replacements on hand. EHL use has declined since the Holmium laser became more widely available.

**Laser lithotripsy.** External energy excites atoms within a laser. Electrons then develop a higher, unstable energy state and emit photons that collide with other photons, giving rise to 2 photons of the same wavelength and direction. The wavelength, energy, and pulse duration of different lasers vary.

In the Nd:YAG laser, the stone is heated, forming a plasma that expands to produce a shock wave, vaporizing the surface of the stone and fragmenting it. Stone fragmentation rates of 55% to 80% are reported, but it is not effective for hard stones. The pulsed-dye laser is more effective but very expensive. The Ho:YAG laser uses photothermal energy, emitting pulses of 2100-nm light that drill into stones or tissue when directly applied. Fragmentation rates approach 100% for urinary stones, although the process is sometimes slow. Pulse frequency and voltage can be varied to produce greater energy. Guidewires and stone baskets can be broken and must not be directly touched by the fiber. Fibers of different width permit the Ho:YAG laser to be used through the larger rigid and smallest flexible scopes, thus expanding its capacity to fragment essentially any stone in any location within the urinary tract. The tissue-cutting capability of the laser permits opening of obstructive narrowing in the ureteropelvic junction or ureter after stone has been removed. This may be an important adjunct in some cases.

Management of Leftover Stones and Fragments

The first step is to establish whether the stone is completely removed. Extra care at the end of the surgical procedure to explore the collecting system thoroughly may discover significant fragments that might have been left behind. It can not be emphasized enough that patience, care, and suspicion of residual stone contribute hugely to success with percutaneous surgery. Residual stone should be removed initially rather than later. Even if the stone is easily fragmented and removed in the renal pelvis with rigid instrumentation and ultrasound, the calyces should be examined for fragments that may have run away to hide in far corners.

Postoperatively, on day 1 or 2, radiologic examination should be performed. Plain film is inadequate in assessing for residual fragments; at a minimum, plain film tomograms should be obtained. An antegrade pyelogram should be obtained to confirm renal drainage through the ureter and to rule out perforations and leakage prior to tube removal. CT without contrast is well known to be more sensitive than plain films in revealing stones and fragments and perhaps should be the examination of choice.

Significant residual fragments may require ESWL to break them to removable or passable size. Alternatively, a second percutaneous nephroscopy, with or without
sedation and analgesia, will usually be possible and all fragments may be removed with baskets and grasping forceps.

• How should this patient’s 4-cm stone be managed?

The patient already has a double-J stent inserted, so this case could be considered for ESWL as primary treatment, with the expectation that obstructive steinstrasse would not be a problem. The stone, however, appears smooth and dense and may well be calcium oxalate monohydrate, which is difficult to break with ESWL. Quite likely, 2 or more sessions would be required, and even then it might not be adequately fragmented. Percutaneous access through an upper or middle calyx would allow the stone to be removed by ultrasonic lithotripsy, possibly with assistance from a Ho:YAG laser if it is particularly hard. With such a stone in the renal pelvis, the expectation would be for complete removal with nephrostomy tube drainage for 1 or 2 days postoperatively.

Figure 9. Plain abdominal film of a patient with a staghorn calculus.

increased renal function dictates that the left kidney be preserved.

• What are appropriate treatment options for this patient?

OPTIONS FOR SURGICAL MANAGEMENT

Growth of struvite (infection) stones can be extremely rapid; thus, if a stone is removed but fragments remain, a new staghorn may form within 3 months. Conservative management of struvite staghorns is ill advised because of problems with symptomatic pyelonephritis, pain, intra- and periureteral abscess, and occasional sepsis and death. ESWL monotherapy is inadequate in such cases. On average, 2 to 3 procedures render only 50% of patients stone free, and auxiliary procedures are necessary in 50% to 80% of cases. Percutaneous monotherapy requires an average of about 2 procedures to achieve 70% to 80% stone-free status and may require 2 or 3 access sites.

Sandwich therapy has been advocated. In this approach, initial PCNL is performed with the objective of using a single percutaneous access to avoid bleeding risks and to remove all stone that can be easily and directly reached, without attempting to enter all infundibula and calyces that contain stone. The residual calyceal stones are then treated by ESWL, and a subsequent PCNL is performed to remove residual stone using rigid or flexible instruments. In one study, complete stone-free status was achieved in 70% of patients undergoing sandwich therapy, with no significant fragments in the remaining 30%; renal function remained stable or improved in 96% of patients, and stone recurrences were noted in 22% over a mean follow up of 2.5 years.
Open surgery for staghorn calculi (or other stones) is rarely performed. Partial nephrectomy may be considered on occasion for bulky lower pole stones, where future problems might be anticipated if a dilated, diseased portion of kidney is left by PCNL.

For very large staghorns, particularly with multiple infundibula and calyces involved, it may be wise to perform extended pyelolithotomy or anatrophic nephrolithotomy. Extreme obesity may preclude other methods of treatment. Failure of PCNL to fragment a large hard stone is another indication, but this should not now occur with the availability of Ho:YAG lasers.

Stone-free rates of 90% are possible with open surgery,\(^4\) which is superior to rates with endoscopic treatment. Stone-free status is achieved in 1 procedure as opposed to perhaps 2 or 3 procedures endoscopically. The cost for open surgery is less than that for PCNL or combination therapy for large stones. There is economic benefit in some instances from the shorter recovery time with PCNL. Renal functional impairment is not a major factor with either modality, although renal atrophy following anatrophic nephrolithotomy has been reported,\(^4\) with as much as 30% to 50% loss of function.

Extended pyelolithotomy may be the preferable open procedure for staghorns, with radial nephrotoomies as necessary to reach calyceal stones. Radiologic confirmation of stone-free status intraoperatively is vital, and flexible nephroscopy also is very helpful as an operating room tool to confirm that all stone has been removed. Patients with very complex staghorn calculi should be counseled that open surgery is a viable alternative, and the urologist should consider it when faced with an obviously challenging case that might require more than 2 or 3 endoscopic or ESWL procedures.

**CASE PRESENTATION**

A 42-year-old woman presents to the ER with right flank pain. IVP reveals a 7-mm stone in the distal segment of the right ureter and left lower pole calcifications measuring 30 mm × 11 mm at the largest dimensions (Figure 10, Figure 11). The right stone is obstructive and causes considerable renal colic. The patient also has intermittent pain on the left side, and a review of previous abdominal radiographs reveals that the stone mass in her left kidney probably is 2 stones in different lower pole calyces. Her urine is sterile, and blood results are all normal. Metabolic evaluation is postponed until the acute situation resolves.

**Should this patient’s right stone be treated immediately or allowed to pass?**

The overall rate of passage of ureteral stones is approximately 60%.\(^5\) Rates of passage vary with location in the ureter, and were 22%, 46%, and 71%, respectively, for the upper, middle, and lower thirds.\(^5\) The average time to passage was 17 days, ranging from 0 to 300 days. Smaller stones obviously pass more quickly than larger stones. More than 90% of stones that are 2 mm or smaller and located in the lower or middle third of the ureter will pass spontaneously, compared to 60% of 3- to 4-mm stones and 50% of 5- to 6-mm stones. Larger stones often will not pass within any reasonable time frame. The important dimension is the width of the stone.

Most patients are willing to wait for a short period to see if their stone will pass. If the stone is small, the patient can be assured that passage is highly likely and encouraged to strain all urine, avoid large fluid intake, and control pain with oral medication. With stones larger than 5 mm, one must be realistic about the time frame, the uncertainty, and the impact of intermittent bouts of pain on the patient’s life. Stone pain is at its worst in the first 24 hours and then tapers off, but severe pain may occur every few hours, days, or weeks while awaiting passage. If infection develops, immediate intervention is indicated. Prolonged observation may lead to loss of some or all of that kidney’s function.

In this patient’s case, intervention seems indicated for the right ureteral stone both because of its size and because the left-sided stones may be treated at the same session.

**What intervention is appropriate for managing the patient’s right stone?**

**EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY**

ESWL is possible for distal ureteral stones. Visualization of the stone may sometimes be difficult. Stone-free rates are approximately 85% to 90% and retreatment rates about 10% to 20%. Complications are few, and anesthesia is not necessary. For mid-ureteral stones, success rates are closer to 60%. Stone-free results for upper ureteral stones are good—approximately 80% in situ and 90% if the stone is initially pushed back into the kidney by catheter manipulation.
Ureteroscopy is increasingly used as instruments have become smaller and more flexible and as urologists gain experience with the techniques involved. Semirigid (Figure 12) and flexible ureteroscopes of 7 French size allow relatively easy access to the lower and upper ureter, and the flexible scopes can be passed up to the kidney to access stones in the pelvis or any calyces. Balloon dilation of the orifice and intramural tunnel facilitates introduction of the scope, although it is frequently unnecessary with the smaller scopes. Placement of a safety guide wire is mandatory, and a second wire can be placed over which to pass a flexible ureteroscope. The ureteroscope should not be advanced unless the lumen is in view and should not be pushed onward if there is any resistance. Mucosal tears or complete avulsion might result, rendering the rest of the procedure troublesome. Placement of a sheath is useful when dealing with stones in the middle or upper ureter or kidney, which might require removing and reinserting the instrument.

Small stones in the distal ureter can be removed by basket. For stones 5 mm or larger, basketing should not be done unless the orifice and intramural tunnel have been dilated. For stones above the iliac vessels, it is safer to fragment them and basket the pieces or allow spontaneous passage.Fragmentation of stones with EHL is usually successful, but perforation of the ureter is possible, and use of the Ho:YAG laser is safer and very successful. Impacted larger stones should never be basketed because of the possibility of ureteral avulsion, a disastrous complication. Ureteroscopic success rates should be close to 100% in all segments of the ureter.

In one recent series, ESWL was compared to ureteroscopy in a randomized fashion for distal ureteral stones.4 In those patients with stones 5 mm or smaller, stone-free status was achieved in a mean of 0.2 days with ureteroscopy and 10.8 days with ESWL; 15% of ESWL patients required retreatment. For stones larger than 5 mm, mean time to stone-free status was 3 days for ureteroscopy and 9 days for ESWL; 5% of ESWL
patients required retreatment. Satisfaction with therapy was 100% for ureteroscopy patients and 85% for ESWL.

**MANAGEMENT OF CASE PATIENT**

Ureteroscopic treatment with a Ho:YAG laser is undertaken with rapid success and removal of all significant fragments of the right ureteral stone.

- **What should be done about the stones in the patient’s left kidney?**

  In the absence of the right distal ureteral stone, ESWL or PCNL might be the treatment of choice for this patient’s lower pole calculi. In this particular patient, however, who already had an anesthetic and was positioned for ureteroscopy, the left side should be tackled at the same session with a flexible ureteroscope and laser lithotripsy. When this procedure is done, it is exceedingly important to spend some extra time breaking the stone into the smallest pieces possible. Care should be taken to whittle on the outer margins of the stone, to avoid creating larger fragments that could perhaps be left behind.

  The flexible ureteroscope can be introduced relatively easily into upper and mid-pole calyces (Figure 13). Entry into lower pole calyces is more difficult but can be accomplished 80% to 90% of the time with a combination of active and passive deflection. It is more difficult when it contains a laser fiber, which limits its flexibility somewhat. The smallest fiber should be used and introduced before the instrument is flexed, as introduction after the scope is flexed may tend to damage the inner channel, requiring expensive repairs and taking the instrument out of commission for some time. EHL fibers are not quite as stiff and may allow easier passage around angles in the collecting system, but bleeding is more easily started and may limit one’s visibility and ability to complete the procedure.

Ureteroscopic treatment of intrarenal stones is quite feasible, particularly for stones smaller than 1 cm. For those up to 2 cm, it may be successful but is more likely to leave residual significant fragments. Overall success in one series was 81% in a single session and 93% after a second procedure when required. Stones in calyceal diverticula may be successfully treated, but the neck of the diverticulum should be seen on radiograph and should be dilated to facilitate the procedure.

**CONCLUSION**

The surgical therapy of stone disease has changed greatly over the past 20 years with advances in ESWL and
endoscopic instrumentation. Open surgery is now rare, and it seems likely that ureteroscopic therapy will become more common. Virtually all patients can be successfully treated surgically, with relatively little morbidity. Many ureteral stones will pass spontaneously if given a chance. Conservative therapy of intrarenal stones is frequently complicated by infection and stone growth. Most importantly, we should remember to evaluate the patients for metabolic problems, as appropriate treatment is 90% effective in prophylaxis.

REFERENCES


