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# Medical Management and Prevention of Nephrolithiasis

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**ABSTRACT**

Kidney stones have increased in prevalence and pose a significant burden on the US health care expenditure. This article is intended to help primary care physicians in their office management of stone disease by providing an update on the recent advances made in this field.

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**KEYWORDS:** Calcium oxalate stones; Management of stone disease; Nephrolithiasis; Renal colic

In the United States, stone disease accounts for more than 2 million outpatient visits and costs taxpayers more than 2 billion dollars in health care spending.[1] Men have a 3-fold higher lifetime incidence compared to women; indeed, white men have the greatest risk of developing stone disease.[2,3] A key predicament faced by physicians when treating stone disease is the possibility of stone recurrence. The recurrence rate 1 year after an initial stone diagnosis is approximately 15%, but by 5 years the rate increases to approximately 50%. Also, once a stone recurs, the risk of subsequent recurrence is further increased and the interval between recurrences decreases.[1] This article seeks to provide an updated approach to the recognition, diagnosis, and management of renal calculi.

## CLINICAL MANIFESTATIONS

Kidney stones are hard mineral deposits developing in the kidney and usually are found incidentally during routine diagnostic imaging. Most of the symptoms attributed to renal calculi are due to their mechanical effects and obstruction of urine flow. Obstructive stones are symptomatic, whereas nonobstructive stones tend to be asymptomatic aside from occasional hematuria. Pain and hematuria are the most prominent symptoms of stone disease. The characteristic lumbar colicky pain associated with renal calculi is usually rated as "severe" to "very severe" and occurs in spasms lasting a few minutes. Nausea and vomiting can accompany these symptoms. Hematuria can be gross or microscopic. When diagnosing renal colic, an extensive list of alternative diagnoses should be considered (**Table 1**). Fevers and chills may indicate coexisting infection and must be treated with appropriate antipyretics and antibiotics.

## PATHOPHYSIOLOGY

Numerous factors combine to incite stone precipitation in the kidneys. Two different theories have been agreed on the pathophysiology of renal calculi. The first is the theory of super-saturation of the urine with normally soluble minerals, such as calcium, oxalate, and uric acid. Calculi result when ions from the supersaturated urine form microscopic crystals on these foreign bodies, which act as a nidus for stone formation. A second theory applies primarily to the formation of calcium oxalate stones.[4] This postulates that stone-forming materials can precipitate on calcium phosphate containing papillary plaque (Randall's plaque). Stones are predominantly calcium based (75%-80% of all stones); both magnesium ammonium phosphate ("struvite") and uric acid make up approximately 10% of calculi and cystine, or other rare causes account for only a minority (1%).[5]

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**Table 1** Differential Diagnosis of Kidney Stones

| Category | Common Examples |
|---|---|
| Infections | Herpes zoster, pyelonephritis, and diverticulitis |
| Renal disorders | Renal infarct and renal hemorrhage |
| Gastrointestinal disorders | Appendicitis, cholecystitis, duodenal ulcers, and colitis |
| Reproductive system disorders | Men: tumors, epididymitis, and prostatitis<br>Women: ovarian torsion, ovarian cyst, and ectopic pregnancy |

## PRECIPITATING FACTORS

Decreased urinary volume is the main precipitating factor for renal calculi.[6] Reduced fluid intake or strenuous exercise without adequate fluid replacement increases the risk of kidney stones. Obstruction to the flow of urine also can lead to stone formation. Other kidney stones can result from infection and alkaline pH in the urinary tract; these stones are struvite or "infected" stones.

**Table 2** Ancillary Studies in the Diagnosis of Renal Stones

| Study | Notes |
|---|---|
| Basic studies | |
| Serum chemistry | Elevated serum uric acid level indicates hyperuricosuria.<br>Hypercalcemia mandates a serum PTH level to rule out primary parathyroidism. |
| Complete blood count | To rule out infection |
| Urinalysis | Assess hematuria, urine pH, and urine microscopy.<br>Perform 24-h urine collection to detect underlying abnormality of urine composition. |
| Imaging studies | |
| Helical CT urogram | Best initial and gold standard test (95% sensitivity and 98% specificity) for renal colic<br>Uric acid or cystine stones that are radiopaque can be visualized in the CT image.<br>Indinavir stones are invisible with the CT urogram. |
| Ultrasound | Test of choice in pregnancy<br>Distal ureteric calculi $< 5$ mm are not visible. |
| IV urography and kidney ureter bladder radiography | Lack specificity and sensitivity |

CT = computed tomography; IV = intravenous; PTH = parathyroid hormone.

**Table 3** Treatment Options for Stone Disease

| Acute Medical Management | |
|---|---|
| Pain relief | Ketorolac tromethamine<br>IV morphine sulfate<br>Oral hydrocodone and oxycodone along with NSAIDs as outpatient management |
| Anti-emetic therapy | Metoclopramide HCL and prochlorperazine |
| Straining urine | Patients are asked to strain their urine for several days and bring in any stone that passes. |
| Chronic medical management | |
| Expulsive therapy | Useful in passing stones $< 3$ mm<br>Calcium channel blockers (eg, nifedipine)<br>Alpha-blockers (nonselective [terazosin] and alpha-1 selective [tamsulosin]) |
| Prevention of stone formation | Alkalinizing agents (potassium citrate and sodium bicarbonate)<br>When dissolving uric acid or cystine stones, maintain pH between 6.5 and 7, because pH $> 7.5$ precipitates calcium to form stones, even with normal calcium excretion.<br>Allopurinol therapy for hyperuricosuria |

IV = intravenous; NSAID = nonsteroidal anti-inflammatory drug; HCL = hydrochloride.

## DIAGNOSIS

A detailed history is essential in aiding diagnosis of renal calculi. A personal or family history of stone disease should raise a red flag for kidney stones. A history of hyperparathyroidism; recurrent urinary tract infections; renal tubular acidosis; gastrointestinal diseases, including diarrhea; and prior urologic surgeries should be sought. A history also should include the patient's fluid intake and dietary and medical history, including drugs that the patient is taking. The basic studies to be initiated when suspecting renal stones are listed in **Table 2**.

## TREATMENT

One of the key factors determining further management of stone diseases is the presence of any coexisting infection or obstruction. Once these have been ruled out, the majority of patients with suspected kidney stones can be managed conservatively with pain medication and hydration until they pass the stone (**Table 3**). Chances that the stone will pass are contingent on the size and position of the calculi; smaller and more distal stones pass easily. In fact, 85% of stones less than 3 mm spontaneously pass through with the aid of medical expulsive therapy. An emergency urology consultation for possible surgical management is necessary for signs of infection, acute

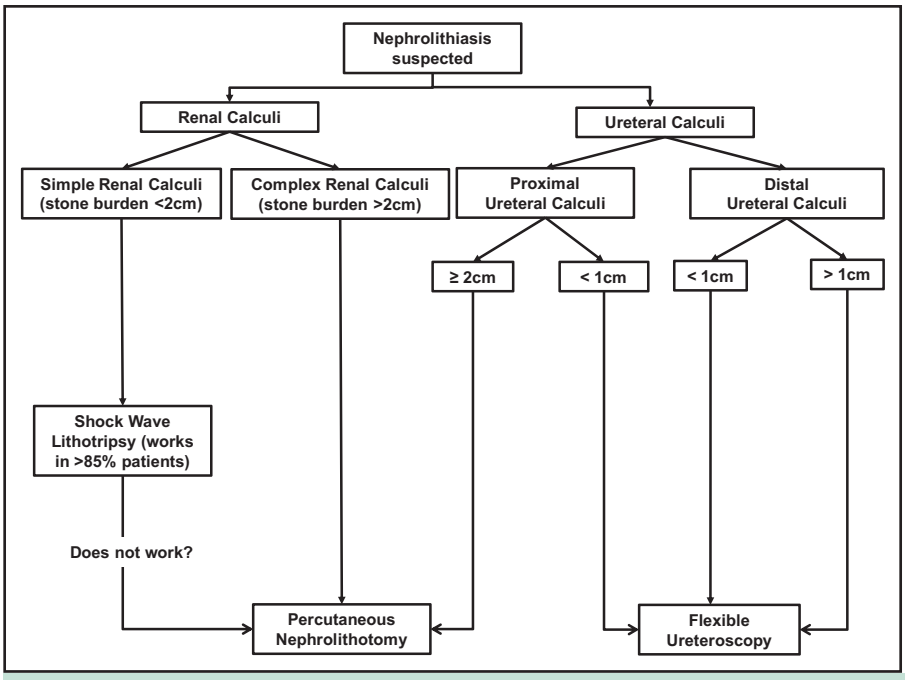


**Figure 1** Steps in diagnosis and treatment of renal and ureteral calculi (Adapted from Miller NL et al,[8] Ramakumar et al,[9] and Lingeman JE et al[10]).

kidney injury, or intractable pain with severe nausea or vomiting. All patients presenting with possible kidney stones should be instructed to strain their urine for several days and recover any stone that passes. **Table 3** lists the acute and chronic medical management of renal stones.

## SURGICAL MANAGEMENT

Surgery is necessary for stones larger than 8 mm because these rarely pass out spontaneously. When a patient presents with signs and symptoms of obstruction and infection secondary to stone disease, emergency surgical relief with ureteral stent placement is undertaken. In patients with sig-

**Table 4** Common Biochemical Abnormalities in Recurrent Nephrolithiasis

| Abnormality | Pathophysiology | Therapy | Notes |
|---|---|---|---|
| Increased calcium excretion (men > 300 mg/d, women > 250 mg/d) | Hyperparathyroidism<br>Hyper 1,25-$(OH)_2D_3$ vitaminosis<br>Granulomatous diseases<br>Lithium therapy<br>Idiopathic | Thiazide-like diuretics<br>Hydrochlorothiazide 6.25-12.5 mg (1/4-1/2 of 25-mg tablets) BID<br>Chlorthalidone 12.5 mg/QD<br>Indapamide 2.5 mg/QD | Blood pressure will decrease on diuretics.<br>Monitor for hypokalemia. |
| Decreased citrate (<300 mg/d) | Hypokalemia<br>Diet rich in animal protein and sodium<br>Renal tubular acidosis | Potassium citrate15-45 mEq BID to maintain pH at 6.0-7.0 | Void pH > 7.5 |
| Increased oxalate excretion (>40 mg/d) | Fat malabsorption<br>Dietary hyperoxaluria<br>Idiopathic hyperoxaluria<br>Genetic defects (rare) | Oxalate binder: OTC calcium carbonate<br>Low oxalate diet | |
| Excessive uric acid production (men > 800 mg/d and women > 750 mg/d) | Increased dietary purine<br>High-fructose sweeteners<br>Acidic urine (pH <5.5)<br>Gout<br>Low urine volume | Allopurinol (target uric acid < 6.0 mg/dL)<br>Low purine diet<br>Potassium citrate to alkalinize urine | Avoid probenicid, angiotensin-receptor blockers, and aspirin. |

BID = twice per day; OTC = over the counter; QD = once per day.

nificant morbidities in whom the stone cannot be bypassed with a stent, percutaneous nephrostomy is performed (**Figure 1**). Surgical management also varies on the type of stone. The American Urological Association recommends ureteroscopy and extracorporeal short-wave lithotripsy as first-line treatments for ureteral stones and percutaneous nephrolithotomy for staghorn calculi.[7]

## PROPHYLAXIS

The American Urological Association recommends restricting dietary calcium, sodium, animal proteins, and oxalate to prevent future stone formation.[7] A simple and effective recommendation to these patients is to instruct them to increase fluid intake to render the urine "clear and colorless." Recurrent renal stones mandate metabolic evaluation, including 24-hour urine collection to develop an appropriate therapeutic plan (**Table 4**). A regimen of potassium-citrate 15 to 30 mEq twice per day is commonly used, because it successfully corrects multiple stone-forming abnormalities (acidic urine, low citrate excretion, and uric acid precipitation) simultaneously.

## CONCLUSIONS

Early recognition and treatment initiation for renal stones will benefit patients acutely, and the use of prophylactic measures will prevent future recurrences and complications.

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