Nephrolithiasis

Anunta Virapongse, MD, MPH

KEYWORDS

• Nephrolithiasis • Urolithiasis • Ureterolithiasis • Renal calculi • Renal colic
• Medical expulsive therapy • Extracorporeal shock wave lithotripsy

HOSPITAL MEDICINE CLINICS CHECKLIST

1. Acute nephrolithiasis is a common disease that affects 8.8% of people in the United States, and the prevalence of nephrolithiasis is increasing.
2. Risk factors for nephrolithiasis include age, male sex, obesity, diabetes, metabolic syndrome, structural kidney abnormalities, low fluid intake, renal disease and certain gastrointestinal tract diseases.
3. Eighty percent of all stones are calcium oxalate or calcium phosphate.
4. Renal colic is caused by obstruction of the urinary tract, which increases renal pelvic pressures and leads to renal capsular distention, mucosal irritation, stimulation of nocireceptors, and hyperperistalsis.
5. Ultrasonography is recommended as first-line imaging for nephrolithiasis. Computed tomography (CT) scans have a higher sensitivity for detecting stones than ultrasonography; however, use of CT scans has not been shown to improve patient outcomes.
6. Fluids, antiemetics, and pain control with nonsteroidal antiinflammatory drugs and opioids are recommended first-line therapy for acute nephrolithiasis.
7. Medical expulsive therapy to accelerate stone passage with tamsulosin and nifedipine was previously recommended but is controversial.
8. Sepsis caused by obstructive nephrolithiasis is considered a urologic emergency and should be managed with hydration, broad-spectrum antibiotics, and rapid decompression of the genitourinary tract with either percutaneous nephrostomy or retrograde ureteral stent placement.

CONTINUED

Disclosure: The author has nothing to disclose.
Hospital Medicine Section, Division of General Internal Medicine, Department of Medicine, University of Colorado Anschutz Medical Campus, Leprino Building, 4th Floor, Mailstop F-782, 12401 East 17th Avenue, Aurora, CO 80045, USA
E-mail address: Anunta.Virapongse@ucdenver.edu

Hosp Med Clin 5 (2016) 43–57
http://dx.doi.org/10.1016/j.ehmc.2015.08.005
2211-5943/16/$ – see front matter

CONTINUED

9. Extracorporeal shock wave lithotripsy (ESWL) is considered first-line therapy for stones less than 3 cm. Percutaneous nephrolithotomy is first-line therapy for stones greater than 3 cm. Retrograde ureteroscopy has less incidence of repeat therapy and may be a more cost-effective treatment than ESWL.
10. Hospitalists can facilitate creation of inpatient nephrolithiasis pathways and aid in prevention of recurrent stones by educating on dietary modification and initiating metabolic workup and pharmacologic therapies for patients with recurrent stones.

DEFINITIONS

What is the definition of nephrolithiasis?

Nephrolithiasis, or kidney stones, are solid masses made up of crystals formed out of urine precipitants. One or more stones may be present in the genitourinary tract at the same time. Symptoms are caused when the stones occlude the flow of urine from the kidney.[1] Nephrolithiasis, urolithiasis, and ureterolithiasis designate stones in the kidney, urinary tract, and ureter, respectively, although these terms are often used interchangeably in the literature.

What are the characteristics and pathophysiology of the most common types of stones?

Table 1 lists the characteristics of the common types of renal calculi.

EPIDEMIOLOGY

What is the prevalence and incidence of nephrolithiasis?

Nephrolithiasis affects approximately 1 in 11 people in the United States, according to the 2007 to 2010 National Health and Nutrition Examination Survey (NHANES). On average, more than 3600 emergency department (ED) visits for nephrolithiasis occur each day in the United States, with about 20% resulting in hospitalization.[7]

How often do kidney stones recur?

The mean risk of kidney stone recurrence without intervention is 35% at 5 years and 52% at 10 years.[8]

What is the cost of nephrolithiasis?

A 2000 study[9] reviewing claims from 25 large US employers found that total direct and indirect health care expenditures associated with kidney stones, including hospitalization, treatment, and lost workdays, was $5.3 billion annually. However, this number may be an underestimate of the current true cost because a 2009 review of the Nationwide Emergency Department Sample[10] found that ED charges alone for nephrolithiasis were more than $5 billion.

Table 1
Characteristics of the common types of renal calculi

Types	Prevalence (%)	Characteristics	Pathophysiology	Appearance on Plain Imaging
Calcium stones • Calcium oxalate • Calcium phosphate	80	Usually mixed calcium oxalate and calcium phosphate Calcium phosphate stones are more difficult to treat with minimally invasive procedures than calcium oxalate Forms in 2–28 wk	Calcium phosphate stones form with urine pH >6 Calcium oxalate stones precipitate around a calcium phosphate layer and are not dependent on urine pH All calcium stones are formed by high excretion of calcium, oxalate, and low excretion of citrate High citrate levels in the urine decrease supersaturation and impede crystal growth	Radiopaque
Uric acid	8–10	Associated with a rich purine diet (meat, fish, and shellfish) Often composite with calcium	Uric acid stones form in normal to low urine pH Patients with uric acid stones have high to high-normal serum uric acid levels	Radiolucent
Struvite stones	10–15	Magnesium ammonium phosphate with components of monoammonium urate or carbonate apatite More common in women than men (2:1 ratio) Forms in the kidney or bladder Large struvite stones in the kidney are termed staghorn calculi If in the kidney, 15% are bilateral Forms in 4–6 wk	Forms after urinary tract infections by urease-producing strains of bacteria such as *Proteus*, *Staphylococcus*, *Pseudomonas*, *Providencia*, and *Klebsiella* Production of urease by bacteria allows the urine pH to increase, precipitating magnesium ammonia and layering of bacterial biofilm to make the stone	Radiopaque
Cystine	1 in adults 25 in pediatric	Rare hereditary disorder Often results in chronic kidney disease	Inability of proximal renal tubule to reabsorb cystine	Radiolucent
Medication-induced (ie, indinavir, atazanavir, darunavir, triamterene, acyclovir)	1–2	—	Precipitates with medication use	Radiolucent (undetectable on computed tomography scan)

Data from Refs.[2–6]

What are the risk factors for developing nephrolithiasis?

Men are at higher risk for nephrolithiasis than women. In the 2007 to 2010 NHANES survey,[11] 10.6% of men had experienced kidney stones, compared with 7.1% of women. Non-Hispanic white people are also at higher risk when compared with Hispanics or non-Hispanic black people. The odds of having a kidney stone range from 1.33 to 1.55 times higher in obese individuals than in those of normal weight.[11,12] The presence of metabolic syndrome (the combination of hyperglycemia, hypertension, and obesity) has been associated with a 71% increased prevalence of nephrolithiasis.[13] Increasing age is also associated with increased risk of kidney stones, as is lower socioeconomic status.[11,13] Diabetes has been correlated to higher risk of stone formation in the United States; however, epidemiologic studies performed in other countries have found this not to be the case.[13]

Other risk factors are listed in **Box 1**.

HISTORY AND EXAMINATION

What are the common presenting symptoms of obstructive nephrolithiasis?

Kidney stones that obstruct the genitourinary tract typically present as the sudden onset of dull and throbbing unilateral flank pain that radiates to the groin area. Visceral symptoms of nausea and vomiting are common and are caused by irritation of the renal plexus, which connects to the mesenteric and celiac plexus at the same spinal level.[16] Gross hematuria is present in a third of these patients. As the stone approaches the ureterovesicular junction (UVJ), the patient may experience dysuria, urinary frequency, and urgency, as well as pain in the lower abdomen radiating to the urethra, testicle, or labia majora.[14,16]

What is the mechanism behind renal colic?

Renal colic is caused by obstruction of the urinary tract, which increases renal pelvic pressures and leads to renal capsular distention, mucosal irritation, stimulation of nocireceptors, and hyperperistalsis.

The pain associated with an attack of renal colic can be divided into 3 phases, which cycle as the stone migrates:[16]

- Onset (0–1.5 hours): ureteral pressure increases as prostaglandins are released and trigger both preglomerular vasodilation, which temporarily increases renal blood flow, and ureteral smooth muscle spasm.
- Plateau (1.5–5 hours): ureteral pressure plateaus as renal blood flow and the glomerular filtration rate begin to decline.
- Abatement (>5 hours): ureteral pressure decreases as preglomerular vasoconstriction further reduces renal blood flow. This vasoconstriction defends the kidney from parenchymal atrophy and results in a decrement in pain.

What are the most common physical examination findings in a patient with nephrolithiasis?

The most common generalized finding is a patient in distress because of pain crisis. There may be tenderness in the costovertebral angle or lower abdomen on palpation, but the abdomen is otherwise soft, nontender. and not distended. The skin may be

Box 1
Risk factors for nephrolithiasis

Structural abnormalities

- Horseshoe kidney
- Ureterocele
- Vesicoureteral reflux
- Calyceal diverticulum
- Ureteral strictures
- Polycystic kidney
- Medullary sponge kidney

Family history

- History of kidney stones in first-degree relative
- Cystinuria
- Dent disease
- Primary hyperoxaluria
- Polycystic kidney disease
- Renal tubular acidosis

Medical or surgical history

- Bariatric surgery
- Bowel disease (chronic diarrhea, malabsorption)
- Intestinal surgery
- Sarcoidosis
- Gout
- Renal tubular acidosis
- Hypertension
- Diabetes
- Metabolic syndrome
- Obesity
- Primary hyperparathyroidism ± bone disease
- Idiopathic hypercalciuria
- Multiple myeloma
- Hyperthyroidism
- Crohn disease
- Immobilization

Medications

- Medication-induced stones
  - Indinavir
  - Atazanavir
  - Darunavir
  - Triamterene
  - Acyclovir

- Calcium stones
  - Loop diuretics
  - Acetazolamide
  - Theophylline
  - Glucocorticoids
  - Topiramate
  - Calcium supplements
  - Carbonic anhydrase inhibitor
  - Vitamin D
  - Bicarbonate, citrates
- Uric acid stones
  - Thiazides
  - Salicylates
  - Probenicid
  - Allopurinol

Occupational factors

- Lack of toilet facilities
- Dehydration, inability to drink
- Climates with increased temperatures

Dietary factors

- Oxalate load
- Excess salt
- High-protein diets
- Eating disorders
- Grapefruit juice
- High-fructose drinks
- Low calcium intake

Adapted from Refs.[4,6,14,15]

pale, cool, and clammy. Fever is normally not present; if the patient is febrile, this suggests infection. Other abdominal diseases to be considered during examination include acute cholecystitis, abdominal aortic aneurysm, appendicitis, diverticulitis, and gynecologic diseases, all of which may mimic renal colic.[17,18]

DIAGNOSIS

What laboratory studies are most useful in diagnosing nephrolithiasis?

Serum chemistries, serum calcium, and phosphate levels should be recorded for all patients who present with nephrolithiasis to ascertain kidney function at baseline. The presence of hypokalemia and low bicarbonate levels may suggest an underlying renal tubular acidosis. If serum calcium levels are increased, the intact parathyroid hormone level should be sent to evaluate for primary hyperparathyroidism.[6,15,19] Conversely, if the serum calcium and urine calcium levels are low, the 25-hydroxyvitamin D level should be recorded to evaluate for secondary hyperparathyroidism. Hypophosphatemia suggests not only hyperparathyroidism but also mutations in proximal tubular phosphate absorption. Uric acid measurement is useful for managing associated gout.[15]

All patients should receive a urinalysis to rule out infection and determine other causes for kidney disease. Urine pH can help to predict stone type, and urine sediment can identify crystals (**Table 2**).

One or two 24-hour urine tests to detect metabolic abnormalities are also recommended. There is some debate as to whether this test should be performed in patients presenting with stones for the first time, particularly if there are no other comorbidities. 24-hour urine tests should be analyzed for total volume, pH, calcium, oxalate, uric acid, citrate, sodium, potassium, magnesium, ammonia, and creatinine. Urinary cystine should also be measured for patients with a family history of cystinuria.[19] For patients with recurrent stones, repeat 24-hour urine tests should be performed 6 months after initiation of treatment and yearly afterward.[6,15,19]

During acute episodes, patients should be told to strain urine to capture stones to determine the type. Stone analysis can help to give clues as to the cause, determine appropriate treatment plans, and, if recurrent, whether there has been a conversion of stone type (ie, calcium oxalate to struvite in the setting of new infection).[6,19]

What imaging modalities are useful in diagnosing nephrolithiasis?

Ultrasonography should be the initial imaging modality for most patients with suspected nephrolithiasis. Ultrasonography exposes the patient to lower radiation with no differences in high-risk diagnosis, serious adverse events, pain scores, or return hospitalizations and emergency room visits when compared with noncontrast computed tomography (CT).[18,20] CT has a higher sensitivity than ultrasonography for detecting renal stones (96%–98% for CT compared with 45%–57.3% with ultrasonography)[14,20]; however, this does not translate to better patient outcomes.[18] This finding may, in part, be a result of the ability of ultrasonography to detect the presence of hydronephrosis, with sensitivities of 85% to 90%.[14] CT without contrast can be useful for providing additional information on stone size, anatomic abnormalities, and other abdominal disease; consequently, initial imaging with CT should be determined based on clinical judgment.[6]

Imaging should be obtained for all patients with their first kidney stone, an atypical presentation, possible infection, or lack of improvement with conservative management. Confirmatory imaging can be avoided in patients with a known history of nephrolithiasis and no risk factors who are presenting typically with a recurrent stone. These patients can be safely discharged if follow-up is ensured.[14]

For follow-up, either ultrasonography or plain radiography can be used. On plain radiography, 85% to 90% of stones are radiopaque; however, sensitivity ranges from 47% to 69%.[14,21] Despite this finding, radiography is inexpensive, with few

Table 2
Urine sediment crystal characteristics

Appearance	Associated Stone Type	Urinalysis Finding
Rectangular coffin-lid crystals	Struvite stones	Normal
Tetrahedral	Calcium oxalate	Normal
Large flat plates or wedge-shaped prisms	Calcium phosphate	Normal
Hexagonal crystals	Cystinuria	Abnormal
Variable shapes	Uric acid	Normal

Adapted from Goldfarb DS, Arowojolu O. Metabolic evaluation of first-time and recurrent stone formers. Urol Clin North Am 2013;40(1):13–20; and Urinalysis: crystals [Internet]. Available at: http://uoitclinicalbiochemistry.weebly.com/urinalysis-crystals.html. Accessed June 10, 2015.

adverse effects, and can be appropriate for follow-up of stones large enough to be seen on film to confirm passage. Yearly screening of stable patients with ultrasonography or radiography is recommended to assess for new stones or stone growth.[6,15]

Two other imaging modalities, MRI and intravenous pyelography (IVP) can aid in diagnosis. MRI is primarily used in pregnancy as a second-line test when ultrasonography has failed to determine diagnosis. Although MRI does not visualize calculi, it can determine the presence of a dilated ureter and pyelonephritis. MRI can also differentiate between pathologic rather than physiologic hydronephrosis, which occurs as a result of a mass effect between the uterus and the retroperitoneal musculature.[22]

IVP can be used in the emergency setting as an adjunct to plain radiography to visualize filling defects from either radiopaque or radiolucent stones. It can also provide structural and functional information. It has numerous drawbacks, including radiation exposure, risk of nephrotoxicity, and contrast reaction, and should be used only if ultrasonography and CT are unavailable.[14]

MANAGEMENT

What is the immediate management of patients with symptomatic nephrolithiasis?

For patients without evidence of infection or renal dysfunction and stones less than 10 mm, initial treatment consists of fluids, pain control, and antiemetics. Pain control can be achieved through the use of nonsteroidal antiinflammatory drugs (NSAIDs) as well as opioid analgesics.

NSAIDs decrease the production of prostaglandins through blockage of the cyclooxygenase pathway of arachidonic acid, thus decreasing preglomerular vasodilation and renal pelvic pressures.[16] Because of this effect, NSAIDs have been found to have equivalent, if not better, efficacy than opioids in relieving acute renal colic pain.[23] NSAIDs may cause acute kidney injury by compromising renal reserve in patients who are dependent on prostaglandin-mediated vasodilation. Caution should be used when prescribing NSAIDs to elderly patients, pregnant women, and those with acute renal failure, dehydration, and atherosclerosis. Patients with a bleeding diathesis, recent gastrointestinal bleed, or intracranial hemorrhage should also avoid NSAIDs.[14,16,23]

The use of intravenous fluids should be limited to repletion of fluid losses in cases of dehydration and renal insufficiency. No evidence has shown that aggressive infusion of fluids has decreased pain scores or narcotic requirements, decreased the rate of surgical stone removal, or increased the rate of stone passage.[24]

Most patients can be managed conservatively as an outpatient once pain control is achieved and infection and renal damage have been ruled out. Stone size and location help to predict whether the stone will pass spontaneously or will require intervention in the near future.[6,19]

What stone size and location is most likely to pass spontaneously with conservative therapy?

The rate of stone passage depends on the size and location of the stone. In general, stones less than 5 mm have a higher likelihood of passing spontaneously than those greater than 5 mm (**Table 3**).[25] As one might predict, the likelihood of spontaneous stone passage increases as the stone migrates down through the ureter, with the

Table 3
Rate of spontaneous passage of ureteral calculi by size

Stone Size (mm)	Passage Rate (%)
1–4	78
5–7	60
8–9	45
≥10	27
All stone sizes	67

Data from Coll DM, Varanelli MJ, Smith RC. Relationship of spontaneous passage of ureteral calculi to stone size and location as revealed by unenhanced helical CT. Am J Roentgenol 2002;178(1):101–3.

highest likelihood at the UVJ (79%) and the lowest rate at the proximal ureter (48%) for stones of any size.[25]

What is the usefulness of medical expulsive therapy in treating acute nephrolithiasis?

Early initiation of medical expulsive therapy (MET) with calcium channel blockers or α-blockers has been advocated as an adjuvant therapy to conservative therapy; however, recently, MET has come under fire as an effective treatment modality. MET is believed to relax the ureteral smooth muscle and decrease ureteral spasm, thereby promoting stone passage.[16,26–28] In meta-analyses, pooled data[26–28] showed that calcium channel blockers and α-antagonist use decrease time to stone expulsion, pain medication requirements, and pain scores. Patients treated with MET therapy were also found to have a 65% greater likelihood of stone passage than those on standard therapy.[26] Many of the studies included in these reviews had methodological issues.

In May, 2015, a multicenter randomized double-blinded placebo-controlled trial involving 1167 participants across 24 UK hospitals was published in *The Lancet*.[29] This trial, the SUSPEND (Spontaneous Urinary Stone Passage Enabled by Drugs) study, randomized patients presenting with acute symptomatic nephrolithiasis to tamsulosin, nifedipine, or placebo treatment groups. After 4 weeks, no difference was found between these groups in rate and time of stone passage, use of analgesics, and health status. Because of the high-powered nature of this study, the use of MET therapy with tamsulosin and nifedipine seems to have little to no therapeutic benefit in the treatment of acute nephrolithiasis.

Although MET therapy using tamsulosin and nifedipine may be discouraged, selective α_{1a}-antagonists (silodosin) might have promise for treatment of distal kidney stones. On a subgroup analysis in a 2015 study,[30] the percentage of distal stone passage was 69% on silodosin compared with 46% on placebo ($P = .01$). The goal sample size was not reached, which limits these findings.

What are the indications for urology consultation?

Urology should be urgently consulted for patients with evidence of sepsis related to urinary tract infection, evidence of acute renal failure, anuria, or history of solitary functioning kidney. Obtain urology input in cases of intractable pain unresponsive to conservative therapy and serious hematuria. For patients who can be managed as outpatients with conservative therapy, outpatient urology follow-up should be

scheduled for definitive treatment in case of inability to pass the stone and also for metabolic evaluation and stone analysis.[14]

What is the management of patients presenting with sepsis with an obstructing stone?

Patients presenting with sepsis caused by an upper urinary tract infection require emergent intervention and decompression. As with all septic patients, broad-spectrum antibiotics and intravenous resuscitation should be initiated immediately. Pathogens to be considered include *Escherichia coli*, *Klebsiella*, *Proteus*, *Enterobacter*, and *Citrobacter*.[14] Imaging should be performed to determine the location and size of the stone, as well as presence of hydronephrosis or pyelonephritis. The presence of pyonephrosis is associated with high mortality and risk of kidney loss and should be suspected in septic patients with a history of diabetes, immunosuppression, and structural abnormalities.[14,31]

Decompression can be achieved by either placement of a retrograde ureteral stent or percutaneous nephrostomy. Both procedures are comparable in outcomes. In a small study of 42 patients,[31] both studies had similar hospital stay durations, time to normalization of white blood cell count, and time to normal temperature.

What are the urologic interventions for an obstructing stone?

Table 4 compares and contrasts the urologic interventions available for obstructing stones.

Extracorporeal shock wave lithotripsy (ESWL) uses shock waves to disintegrate stones, which then are expelled through the urine. Stone-free rates for this procedure vary depending on location and size of the stone, ranging from 86% to 89% in the renal pelvis, 37% to 68% in the lower calyx, 51% to 91% in the middistal ureter, and 32% to 78% in the proximal ureter[32,33] ESWL is first-line therapy for stones less than 3 cm in diameter.[32]

Retrograde ureteroscopy, or retrograde intrarenal surgery (RIRS), uses a flexible scope that is inserted through the bladder and into the renal collecting system. Using laser lithotripsy, the stones are fragmented and passed into the urine.[34] The indications for this procedure are broad and there are few contraindications.[32] It is considered second-line therapy to ESWL in treatment of moderate-sized stones.

Percutaneous nephrolithotomy (PCNL) uses a small-caliber nephrostomy catheter to pass a nephroscope from the flank into the renal collecting system. The stone is removed by placement of tools through the nephroscope.[34] PCNL is indicated for patients with a large stone burden, lower kidney pole stones, and less common stone types (ie, cystine). Because this procedure requires general anesthesia, PCNL has a higher analgesic requirement, higher length of stay, and higher bleeding rates.[34,35]

Laparoscopic lithotomy can be used as an alternative for treatment of large impacted or multiple stones when RIRS and ESWL fail or PCNL is unavailable. One small study[36] has shown that laparoscopic lithotomy is comparable with PCNL in terms of stone-free rates and hospital stay duration. More blood loss is associated with laparoscopic lithotomy.

The efficacy of ESWL versus PCNL has been compared in the literature. In a 2014 systematic review,[33] PCNL was found to be a more definitive treatment of kidney stones compared with ESWL, although more complications were reported with PCNL. More recently, a retrospective cohort study between ESWL and RIRS[37] found that, after adjusting for confounders, 11% of patients underwent repeat procedure with ESWL compared with 0.3% of patients undergoing RIRS. Given these findings,

Table 4
Minimally invasive therapeutic interventions for treatment of symptomatic renal calculi

Intervention	Size (Diameter)	Location/Use	Contraindications	Complications
Extracorporeal shock wave lithotripsy (ESWL)	<3 cm	Less successful for renal lower pole stones or beneath the pelvic bone	Pregnancy, severe skeletal malformation, severe obesity, urinary tract obstruction distal to the stone, aortic or renal artery aneurysms	Fragments lodged in ureter (steinstrasse), hematoma, infection and sepsis, possible acute pancreatitis
Retrograde ureteroscopy	Any but success decreases with size	Used in obesity, pregnancy, renal anatomic abnormalities (ie, ectopic or horseshoe kidney)	Untreated infections and bleeding diathesis	Minor ureteral perforation, ureteral injury, bleeding, infection, residual stones, stent discomfort
Percutaneous nephrolithotomy	Any, best for >3 cm	Best for lower renal pole stones, proximal ureteral stones. Gold standard for struvite staghorn calculi	Uncorrected coagulopathy, pregnancy	Bleeding, increased pain compared with ESWL, urinary tract infection, perforation

Adapted from Refs.[3,32,35,38]

although ESWL is considered first-line therapy, providers may elect to pursue RIRS first for more definitive therapy from a cost-effectiveness perspective.

What are the dietary recommendations for long-term management of nephrolithiasis?

Both the American College of Physicians and the American Urologic Association have made recommendations for dietary modification to prevent calcium kidney stones:

- Increase fluid intake to produce of 2 to 2.5 L of urine daily.[19,39]
- Although the evidence is weak, patients should also avoid drinking soft drinks, particularly those with phosphoric acid (colas).[19]
- Stay on a normal-calcium diet and limit sodium intake.[39] Although seemingly counterintuitive, low-calcium diets increase the risk of stone formation, because calcium is needed to bind with oxalate in the gut to prevent absorption and stone formation.[24]
- However, excess dietary calcium should be avoided, because that can lead to stone formation.[39]
- Patients with calcium oxalate stones should limit oxalate-rich foods so as to avoid hyperoxaluria.[19]
- Increase fruits and vegetables and limit nondairy animal protein to increase urinary citrate production to prevent calcium stones; limit dietary purine to prevent uric acid stones.[19]
- For patients with cystine stones, oral fluid intake should be increased to 4 L per day to decrease cystine concentration, as well as decreasing sodium intake to 100 mEq (2300 mg) daily and limiting animal protein, which contains cystine.[19]

What are the medical recommendations for long-term management of nephrolithiasis?

For the prevention of calcium stones, thiazide diuretics, citrates, and allopurinol have all been found to decrease recurrence of stones. For patients with no urinary abnormalities but with recurrent stones, potassium citrate and thiazides should be offered.[19] In the case of uric acid stones, the goal is to use medications to increase urinary pH. In these patients, the low urinary pH, rather than hyperuricosuria, precipitates uric acid stones.[5]

For struvite stones, the mainstay of therapy is minimally invasive stone removal. Further stones are prevented and residual stones are treated by antibiotic therapy, and to some degree, by urease inhibitors. In patients with cystine stones, dietary modifications and urinary alkalization are the first-line therapy for prevention of stones.[19]

See **Table 5** for additional details.

PERFORMANCE IMPROVEMENT

What is the role of hospitalists in the care of a patient with nephrolithiasis?

Depending on institutional culture, hospitalists may be called on to manage acute nephrolithiasis patients in lieu of or in conjunction with their urology colleagues. Hospitalists can assist in the development of nephrolithiasis pathways to streamline the initial evaluation and medical management of these patients and to ensure appropriate triage for intervention. For inpatients with recurrent kidney stones, hospitalists should consider initiating the workup for metabolic causes with a 24-hour urine test, as well as prescribing preventive pharmaceutical and dietary therapies if previous

Table 5
Long-term management by stone type

Type	Treatment	Pathophysiology
Calcium stones	Thiazides	Decrease calcium excretion Best for patients with hypercalciuria Decreases risk of stone recurrence when compared with placebo (24.9% vs 48.5%)
	Potassium alkalis Potassium citrate Potassium-magnesium citrate Potassium-sodium citrate	Binds with calcium Reduces stone recurrence from 52.3% to 11.1% when compared with placebo Best for patients with hypocitraturia and low urinary pH Potassium citrate is preferred over sodium citrate because increased sodium load can increase calcium excretion
	Allopurinol	Decreases uric acid concentration Best for patients with hyperuricosuria and normal urine calcium levels
Uric acid stones	Potassium citrate	First-line therapy Dissolves uric acid stones Prevents uric acid recurrence Goal urine pH is 6 with potassium citrate therapy
Struvite stones	Antibiotics after minimally invasive stone removal, with broad-spectrum antibiotics on day before surgery and 1–2 h postoperatively	Give antibiotics specific to organism for 1–2 wk Low-dose suppression has been recommended, but dose and duration remain unclear, ranging from 3 to 6 mo or 1 to 2 y. Requires monthly urine cultures for 3 mo after antibiotic cessation
	Urease inhibitors (acetohydroxamic acid)	Best for nonsurgical candidates Used also to treat residual stone fragments postoperatively Delays time to stone recurrence from 9 to 15 mo and can reduce stone growth Severe side effect profile (tremor, phlebothrombosis)
Cystine stones	Potassium citrate	Alkalinizes the urine to goal pH of 7.0
	Cystine-binding thiol drugs	Second-line therapy if diet and potassium citrate are ineffective
	α-Mercaptoproponylglycine (tiopronin)	Tiopronin is better tolerated than D-penicillamine, but contraindicated in pregnancy and patients with blood disorders
	D-Penicillamine	

Adapted from Refs.[3,5,6,19,39,40]

stone composition is known. Hospitalists should work closely with urology to ensure timely follow-up.

CLINICAL GUIDELINES

- Pearle MS, Goldfarb DS, Assimos DG, et al. Medical management of kidney stones: AUA guideline. J Urol 2014;192(2):316–24.
- Qaseem A, Dallas P, Forciea MA, et al; Clinical Guidelines Committee of the American College of Physicians. Dietary and pharmacologic management to prevent recurrent nephrolithiasis in adults: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2014;161(9):659–67.

REFERENCES

1. Kidney stones: MedlinePlus Medical Encyclopedia [Internet]. Available at: http://www.nlm.nih.gov/medlineplus/ency/article/000458.htm. Accessed June 2, 2015.
2. Dixon A, Jones J. Radiopaedia.org: Urolithiasis [Internet]. Available at: http://radiopaedia.org/articles/urolithiasis. Accessed June 13, 2015.
3. Flannigan R, Choy WH, Chew B, et al. Renal struvite stones–pathogenesis, microbiology, and management strategies. Nat Rev Urol 2014;11(6):333–41.
4. Izzedine H, Lescure FX, Bonnet F. HIV medication-based urolithiasis. Clin Kidney J 2014;7(2):121–6.
5. Reichard C, Gill BC, Sarkissian C, et al. 100% uric acid stone formers: what makes them different? Urology 2015;85(2):296–8.
6. Worcester EM, Coe FL. Calcium kidney stones. N Engl J Med 2010;363(10):954–63.
7. Foster G, Stocks C, Borofsky MS. Emergency department visits and hospital admissions for kidney stone disease, 2009: statistical brief #139 [Internet]. In: Healthcare cost and utilization project (HCUP) statistical briefs. Rockville (MD): Agency for Health Care Policy and Research (US); 2006. Available at: http://www.ncbi.nlm.nih.gov/books/NBK100827/. Accessed August 1, 2015.
8. Uribarri J, Oh MS, Carroll HJ. The first kidney stone. Ann Intern Med 1989;111(12):1006–9.
9. Saigal CS, Joyce G, Timilsina AR. Direct and indirect costs of nephrolithiasis in an employed population: opportunity for disease management? Kidney Int 2005;68(4):1808–14.
10. Ghani KR, Roghmann F, Sammon JD, et al. Emergency department visits in the United States for upper urinary tract stones: trends in hospitalization and charges. J Urol 2014;191(1):90–6.
11. Scales CD, Smith AC, Hanley JM, et al, Urologic diseases in America project. Prevalence of kidney stones in the United States. Eur Urol 2012;62(1):160–5.
12. Taylor EN, Stampfer MJ, Curhan GC. Obesity, weight gain, and the risk of kidney stones. JAMA 2005;293(4):455–62.
13. Jeong IG, Kang T, Bang JK, et al. Association between metabolic syndrome and the presence of kidney stones in a screened population. Am J Kidney Dis 2011;58(3):383–8.
14. Graham A, Luber S, Wolfson AB. Urolithiasis in the emergency department. Emerg Med Clin North Am 2011;29(3):519–38.
15. Goldfarb DS, Arowojolu O. Metabolic evaluation of first-time and recurrent stone formers. Urol Clin North Am 2013;40(1):13–20.
16. Travaglini F, Bartoletti R, Gacci M, et al. Pathophysiology of reno-ureteral colic. Urol Int 2004;72(Suppl 1):20–3.
17. Kang HW, Lee SK, Kim WT, et al. Natural history of asymptomatic renal stones and prediction of stone related events. J Urol 2013;189(5):1740–6.
18. Smith-Bindman R. Ultrasonography vs. CT for suspected nephrolithiasis. N Engl J Med 2014;371(26):2531.
19. Pearle MS, Goldfarb DS, Assimos DG, et al. Medical management of kidney stones: AUA guideline. J Urol 2014;192(2):316–24.
20. Kanno T, Kubota M, Sakamoto H, et al. Determining the efficacy of ultrasonography for the detection of ureteral stone. Urology 2014;84(3):533–7.
21. Mutgi A, Williams JW, Nettleman M. Renal colic: utility of the plain abdominal roentgenogram. Arch Intern Med 1991;151(8):1589–92.
22. Masselli G, Derme M, Laghi F, et al. Imaging of stone disease in pregnancy. Abdom Imaging 2013;38(6):1409–14.

23. Holdgate A, Pollock T. Nonsteroidal anti-inflammatory drugs (NSAIDS) versus opioids for acute renal colic [Internet]. Cochrane Database Syst Rev 2005;(2):CD004137; Available at: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004137.pub3/abstract. Accessed June 11, 2015.
24. Worster AS, Bhanich Supapol W. Fluids and diuretics for acute ureteric colic [Internet]. Cochrane Database Syst Rev 2005;(2):CD004926; Available at: http://onlinelibrary.wiley.com.hsl-ezproxy.ucdenver.edu/doi/10.1002/14651858.CD004926.pub3/abstract. Accessed June 12, 2015.
25. Coll DM, Varanelli MJ, Smith RC. Relationship of spontaneous passage of ureteral calculi to stone size and location as revealed by unenhanced helical CT. Am J Roentgenol 2002;178(1):101–3.
26. Seitz C, Liatsikos E, Porpiglia F, et al. Medical therapy to facilitate the passage of stones: what is the evidence? Eur Urol 2009;56(3):455–71.
27. Hollingsworth JM, Rogers MA, Kaufman SR, et al. Medical therapy to facilitate urinary stone passage: a meta-analysis. Lancet 2006;368(9542):1171–9.
28. Campschroer T, Zhu Y, Duijvesz D, et al. Alpha-blockers as medical expulsive therapy for ureteral stones. Cochrane Database Syst Rev 2014;(4):CD008509.
29. Pickard R, Starr K, MacLennan G, et al. Medical expulsive therapy in adults with ureteric colic: a multicentre, randomised, placebo-controlled trial. Lancet 2015;386(9991):341–9.
30. Sur RL, Shore N, L'Esperance J, et al. Silodosin to facilitate passage of ureteral stones: a multi-institutional, randomized, double-blinded, placebo-controlled trial. Eur Urol 2015;67(5):959–64.
31. Pearle MS, Pierce HL, Miller GL, et al. Optimal method of urgent decompression of the collecting system for obstruction and infection due to ureteral calculi. J Urol 1998;160(4):1260–4.
32. Wignall GR, Canales BK, Denstedt JD, et al. Minimally invasive approaches to upper urinary tract urolithiasis. Urol Clin North Am 2008;35(3):441–54, viii.
33. Srisubat A, Potisat S, Lojanapiwat B, et al. Extracorporeal shock wave lithotripsy (ESWL) versus percutaneous nephrolithotomy (PCNL) or retrograde intrarenal surgery (RIRS) for kidney stones. Cochrane Database Syst Rev 2014;(11):CD007044.
34. AUA university: kidney stones [Internet]. Available at: http://www.auanet.org/education/kidney-stones.cfm. Accessed June 13, 2015.
35. Kumar A, Kumar N, Vasudeva P, et al. A prospective, randomized comparison of shock wave lithotripsy, retrograde intrarenal surgery and miniperc for treatment of 1 to 2 cm radiolucent lower calyceal renal calculi: a single center experience. J Urol 2015;193(1):160–4.
36. Topaloglu H, Karakoyunlu N, Sari S, et al. A comparison of antegrade percutaneous and laparoscopic approaches in the treatment of proximal ureteral stones. Biomed Res Int 2014;2014:691946.
37. Scales CD, Lai JC, Dick AW, et al. Comparative effectiveness of shock wave lithotripsy and ureteroscopy for treating patients with kidney stones. JAMA Surg 2014;149(7):648–53.
38. De Cógáin M, Krambeck AE, Rule AD, et al. Shock wave lithotripsy and diabetes mellitus: a population-based cohort study. Urology 2012;79(2):298–302.
39. Qaseem A, Dallas P, Forciea MA, et al, Clinical Guidelines Committee of the American College of Physicians. Dietary and pharmacologic management to prevent recurrent nephrolithiasis in adults: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2014;161(9):659–67.
40. Medscape: thiola-tiopronin [Internet]. Available at: http://reference.medscape.com/drug/thiola-tiopronin-342857. Accessed June 13, 2015.