Nephrolithiasis

Straight to the point of care
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Summary

Nephrolithiasis (kidney stones) is a common condition, typically affecting adult men more commonly than adult women, although this difference is narrowing.

Patients typically present with acute renal colic, although some patients are asymptomatic.

Multiple risk factors include chronic dehydration, diet, obesity, positive family history, specific medications, and various metabolic abnormalities.

Non-contrast computed tomography scan of the abdomen/pelvis is the imaging modality with the highest sensitivity and specificity to diagnose stones. Plain x-ray (KUB) and renal ultrasound can be utilized for diagnosis in some cases, such as a desire to reduce or eliminate radiation exposure.

Treatment consists of both medical and surgical therapies.

24-hour urine tests are recommended for most stone formers to determine the cause of stone formation and optimal treatment to help prevent future stone episodes.

Definition

Nephrolithiasis refers to the presence of crystalline stones (calculi) within the urinary system (kidneys and ureter). Such renal stones are composed of varying amounts of crystalloid and organic matrix. Ureteric stones almost always originate in the kidney but then pass down into the ureter.[1] [BMJ talk medicine: nephrolithiasis] (https://soundcloud.com/bmjpodcasts/nephrolithiasis?in=bmjpodcasts/sets/bmj-best-practice-clinical)
**Epidemiology**

The lifetime prevalence of nephrolithiasis in the US is estimated to be about 10%.[2] The probability of having a stone varies according to age, sex, race, and geographic location.[2] [3] [4] Nephrolithiasis typically affects adult men more commonly than adult women; however, there is evidence that this difference in incidence between men and women is narrowing.[3] In US men, the highest prevalence of nephrolithiasis is found in white men, followed by Hispanic men, non-Hispanic men, and black men.[2] However, the rate of stone incidence is increasing at a faster rate for black people compared to white, and particularly for black women compared to men.[5] Historically, stone occurrence was relatively uncommon before age 20 years, but the incidence of stones in children and adolescents is rising.[5] In adults, stone incidence peaks between the ages of 40-50 years.[6]

Nephrolithiasis has a higher prevalence in hot, arid, or dry climates, such as the mountains, desert, or tropical areas.[3] [7] Worldwide, regions of high stone prevalence include the US, UK, Scandinavian and Mediterranean countries, northern India and Pakistan, northern Australia, central Europe, portions of the Malay peninsula, and China.[3] Heat exposure and dehydration are risk factors for nephrolithiasis. The prevalence and incident risk of nephrolithiasis are directly correlated with type 2 diabetes, obesity, and variation measures of adiposity variables, including higher waist circumference, and BMI in both sexes, although the magnitude of this association is greater in women than in men.[8] [9] [10]

**Etiology**

Renal stones are crystalline mineral depositions that form from microscopic crystals in the loop of Henle, distal tubules, or the collecting duct. This is usually in response to elevated levels of urinary solutes, such as calcium, uric acid, oxalate, and sodium, as well as decreased levels of stone inhibitors, such as citrate and magnesium.[1] Low urinary volume and abnormally low or high urinary pH also contribute to this process. All of these can lead to urine supersaturation with stone-forming salts and subsequent stone formation.[11] Supersaturation depends on urine pH, ionic strength, solute concentration, and solute chemical interaction. The higher the concentration of two ions, the more likely they are to precipitate out of solution and form crystals. As ion concentrations increase, their activity product reaches the solubility product (Ksp). Concentrations above this point can initiate crystal growth. Once crystals are formed, they either pass out with the urine or become retained in the kidney, where they can grow and stones can form. In urine, even when the concentration of calcium oxalate exceeds the solubility product, crystallization may not occur because of prevention from urinary inhibitors. Both urinary calcium and oxalate are important and equal contributors to calcium oxalate stone formation. Several factors increase calcium oxalate supersaturation in urine. These include low urine volume and low citrate, and increased calcium, oxalate, and uric acid.

**Pathophysiology**

There are differing theories as to the exact pathophysiology of stone formation.[1] Free and fixed particle theories of stone formation are still being debated. Therefore, it is not known whether stones form by deposition of microscopic crystals in the loop of Henle, distal tubules, or the collecting duct. In one study, renal papillary plaques were examined in idiopathic calcium oxalate stone formers.[12] Plaques were composed of calcium phosphate/apatite deposits, localized to the basement membrane of the thin loop of Henle and extending into the papillary interstitium. Once these plaques form, they erode through the urothelium and constitute a stable, anchored surface on which calcium oxalate crystals can nucleate and grow as attached stones. Plaque lesions though reached the basement membrane of collecting ducts, but
did not affect the ductal cells. The papillary surfaces of nonstone formers did not show any plaques. In the same study papillary areas of patients with stones due to obesity-related bypass procedures did not have such plaques, but instead had intratubular hydroxyapatite crystals in collecting ducts, with dilation and damage to lining cells proximal to obstruction,[12] hence indicating that stone formation is a heterogeneous process.

Renal colic from nephrolithiasis is secondary to obstruction of the collecting system by the stone. The stretching of the collecting system or ureter is due to an increase in intraluminal pressure.[13] This causes nerve endings to stretch and therefore the sensation of renal colic. Pain from urinary calculi can also be due to local inflammatory mediators, edema, hyperperistalsis, and mucosal irritation.

**Classification**

**Chemical composition of renal calculi**

There is no formal classification system for renal stones, but they can be classified by composition.[1] For patients with recurrent nephrolithiasis, 24-hour urine measurements allow risk factors to be identified and corrected, which may direct ongoing medical management. A working classification is:

- Calcium stones: 80% of renal calculi
  - Calcium oxalate: 80% of all calcium stones; risk factors include low urine volume, hypercalciuria, hyperuricosuria, hyperoxaluria, and hypocitraturia
  - Calcium phosphate (hydroxy apatite or brushite): 20% of all calcium stones; risk factors include low urine volume, hypercalciuria, hypocitraturia, high urine pH, and associated conditions include primary hyperparathyroidism and renal tubular acidosis
- Uric acid stones: around 10% of renal calculi; most commonly due to urinary pH <5.5, although hyperuricosuria can also contribute
- Cystine stones: 1% of renal calculi; caused by an inborn error of metabolism, cystinuria, an autosomal-recessive disorder that results in abnormal renal tubular re-absorption of the amino acids cystine, ornithine, lysine, and arginine
- Struvite stones: 1% to 5% of renal calculi, also known as infection stones; composed of magnesium, ammonium, and phosphate. They frequently present as staghorn calculi and may be associated with urea-splitting organisms, such as *Proteus*, *Pseudomonas*, and *Klebsiella* species. *Escherichia coli* is not a urease-producing organism.

**Case history**

**Case history #1**

A 45-year-old man presents to the emergency department with a 1-hour history of sudden onset of left-sided flank pain radiating down toward his groin. The patient is writhing in pain, which is unrelieved by position. He also complains of nausea and vomiting.
Other presentations

Many patients with nephrolithiasis are actually asymptomatic, as their stone may be in the kidney and nonobstructing. In these patients, diagnosis may be made following imaging (CT scan, abdominal x-ray, renal ultrasound, etc.) for other reasons. In contrast, other patients may present with gross hematuria, evidence of an obstructive uropathy or sepsis with fever, tachycardia, and hypotension.
# Approach

A diagnosis of nephrolithiasis may be suspected based on the clinical history, physical exam findings, and laboratory test results, and is confirmed with imaging studies.

## Clinical history

Obstructed renal and ureteric stones can cause renal colic: severe, acute flank pain that may radiate to the ipsilateral groin, commonly associated with nausea and vomiting. Rarely, this is accompanied by macroscopic hematuria. As stones pass and get lodged in the distal ureter or intramural tunnel, this can lead to bladder irritation manifested as urinary frequency or urgency. Ipsilateral testicular and groin pain may occur rarely in men with obstructive stones. However, in the absence of obstruction, calculi may be asymptomatic.

## Physical exam

In patients with renal colic, costovertebral angle and ipsilateral flank tenderness may be pronounced. Signs of sepsis, including fever, tachycardia, and hypotension, might indicate an obstructing stone with infection, warranting urgent urology referral.

## Laboratory tests

Initial laboratory tests in all patients with suspected nephrolithiasis are urinalysis, CBC, and serum chemistry to include electrolytes, BUN/creatinine (to assess renal function), calcium, phosphorus, and uric acid. Urinalysis is helpful in confirming a diagnosis of renal stones as microscopic hematuria is present in the majority of patients. However, the absence of hematuria does not exclude nephrolithiasis.[30] Presence of more than 5 to 10 WBCs per high-powered field in urine or pyuria could indicate presence of urinary tract infection or be secondary to inflammation. Urinary crystals of calcium oxalate, uric acid, or cystine may indicate the nature of the calculus, although only cystine crystals are pathognomonic for the underlying type of stones. A urine pH greater than 7 suggests presence of urea-splitting organisms, such as *Proteus*, *Pseudomonas*, or *Klebsiella* species, and struvite stones. A urine pH less than 5.5 suggests uric acid stones.

An elevated WBC count may indicate infection (pyelonephritis or urinary tract infection). Hypercalcemia may suggest hyperparathyroidism as an underlying etiology; hyperuricemia may indicate gout. In women of childbearing age, a pregnancy test should be done prior to imaging with ionizing radiation and to rule out ectopic pregnancy as a cause of symptoms.

Twenty-four-hour urine sampling is not always necessary in a first-time stone former without significant risk for recurrence. However, it is indicated in recurrent stone formers; those with bilateral or multiple stones, history of inflammatory bowel disease, chronic diarrhea, bowel surgery or malabsorption; those with primary hyperparathyroidism, gout or renal tubular acidosis, nephrocalcinosis or stones formed of cystine, uric acid or calcium phosphate; in children; and in interested first-time stone-formers. Basic measurements should include volume, pH, creatinine, calcium, sodium, oxalate, uric acid, and citrate. Analysis of stone composition provides information on chemical composition and etiology. Stones are analyzed after they are extracted during surgery or when patients expel and collect them for analysis. A urine screen for cystine, if the diagnosis of cystinuria is not excluded by stone analysis, should be considered. Serum parathyroid hormone is only measured in cases of high or high-normal serum calcium results.
Imaging

If there is suspicion for nephrolithiasis based on the history, physical exam, and laboratory tests, then imaging is indicated.

Noncontrast helical computed tomography (NCCT) scan is the preferred imaging modality due to its high sensitivity and specificity. Computed tomography (CT) accurately determines presence, size, and location of stones; if it is negative, nephrolithiasis can be ruled out with high likelihood. A low-dose noncontrast CT (<4 mSv) is preferred for patients with a body mass index (BMI) ≤30 kg/m², as this limits the potential radiation exposure while maintaining both sensitivity and specificity at 90% or higher.[31] However, low-dose CT is not recommended for those with a BMI >30 kg/m², owing to lower sensitivity and specificity in these patients. Patients with indinavir and ritonavir stones from anti-HIV medication may have radiolucent stones on CT scan. However, this makes up only a tiny fraction of patients. CT scans are also used when patients with known stones have new onset of renal colic because stones commonly change location or new ones are formed. However, there is a risk of significant radiation exposure with repeated CT scans, and a physician should use his or her judgment.

Plain abdominal radiography (KUB) can determine whether stones are radiopaque and can be used to monitor disease activity. Calcium oxalate and calcium phosphate stones are radiopaque, whereas pure uric acid and indinavir stones are radiolucent and cystine stones are partially radiolucent. The KUB radiograph can suggest the fluoroscopic appearance of a stone, which determines whether it can be targeted with extracorporeal shock wave lithotripsy (ESWL).

Renal ultrasound can be used to diagnose renal stones, particularly in pregnancy or other situations where avoiding radiation exposure is advised, although it can be operator dependent and has low sensitivity for diagnosing mid and distal ureteric stones. The combination of renal ultrasonography with KUB has been proposed as a reasonable initial evaluation protocol when a CT scan cannot be performed or is unavailable. For a known stone-former who has previously had radiopaque stones, it has been suggested that a combination of renal ultrasonography and KUB are a viable option for follow-up imaging; sensitivities of 58% to 100% and specificities of 37% to 100% have been reported for this combination of modalities.[32] [33] [34]

Renal ultrasound and CT have been investigated for their safety and efficacy as an initial diagnostic test for patients who present to the emergency department with suspected nephrolithiasis. The results of a large, multicenter study showed no significant difference in high-risk diagnoses, serious adverse events, subsequent emergency room visits, or hospitalizations in those undergoing CT or renal ultrasound in this setting.[35] Another multicenter randomized trial found that of 1666 patients diagnosed with nephrolithiasis in the emergency department (following abdominal ultrasound or CT), the majority of patients (78%) ultimately had CT performed before elective intervention. Patients whose ultrasound was performed by an emergency department physician were 2.6 times more likely to undergo CT before intervention than those whose ultrasound was performed by a radiologist. Ultrasound as the initial imaging modality did not result in a significant delay to intervention.[36]

An intravenous pyelogram (IVP) can provide both anatomic and functional information on stones and the urinary tract and, before NCCT, was the traditional imaging modality. However, IVP is now less commonly used due to the improved sensitivity of CT scans. Disadvantages include the need for intravenous contrast material, which may provoke an allergic response or renal failure, and the need for multiple delayed films in certain cases and concerns for radiation exposure.
Renal ultrasound is the first-line imaging modality for pregnant patients. For pregnant patients when renal ultrasound is nondiagnostic, transvaginal ultrasound can assist with diagnosis by determining if ureteral dilation extends beyond the pelvic brim; it can also diagnose stones in the distal ureter. Magnetic resonance imaging (MRI), which confers no radiation to the patient, is a second-line imaging modality because stones are not directly visible on MRI and only seen as a filling defect in the collecting system. Radiation doses of <50 mGy have not been associated with increased risk of fetal anomalies or loss; therefore, low-dose protocol CT (<4 mGy) can be used as a last-line option in pregnant women after the first trimester to aid in difficult-to-diagnose cases.[37] [38] [31] [39]

Renal ultrasound should be the preferred modality for evaluating children because of radiation risks; however, low-dose CT should be considered if renal ultrasound is nondiagnostic.[38] [31]

**History and exam**

**Key diagnostic factors**

**acute, severe flank pain (common)**
- Classical renal colic is described as severe, acute flank pain that radiates to the ipsilateral groin. However, cases may have no radiation and some stones are asymptomatic.

**Other diagnostic factors**

**previous episodes of nephrolithiasis (common)**
- More than 50% of patients with renal stones will have another episode within 10 years.[40] [41]

**nausea and vomiting (common)**
- Commonly associated with acute episode.

**urinary frequency/urgency (common)**
- As stones pass and get lodged in the distal ureter or intramural tunnel, this can lead to bladder irritation manifested as urinary frequency or urgency.

**hematuria (common)**
- Microscopic hematuria is present on urinalysis in up to 85% to 90% of cases of nephrolithiasis.[30] Rarely, macroscopic hematuria can be present.

**testicular pain (common)**
- As stones pass through the ureter, flank pain can radiate toward the groin and testicle, leading to testicular pain.

**obesity (common)**
- Increased incidence of renal stones is correlated with increased body mass index (BMI) for both sexes.

**family history of nephrolithiasis (uncommon)**
- May be positive for nephrolithiasis in first-degree relatives. If so, this could suggest an underlying metabolic abnormality.
precipitant medications (uncommon)

- Potential medications that can play a role in formation of renal stones include antacids, carbonic anhydrase inhibitors, sodium- and calcium-containing medications, vitamins C and D, and protease inhibitors.[28]

groin pain (uncommon)

- As stones pass through the ureter, flank pain can radiate toward the groin.

fever (uncommon)

- If also associated with urinary obstruction, urgent decompression is needed. May be a sign of struvite stones, which most commonly occur in association with a urinary infection.

tachycardia (uncommon)

- May indicate urosepsis.

hypotension (uncommon)

- May indicate urosepsis.

costovertebral angle and ipsilateral flank tenderness (uncommon)

- May be pronounced in acute renal colic.

Risk factors

Strong

high protein intake

- A higher energy diet with more protein may be associated with a higher incidence of stones.[14] This is secondary to the increased prevalence of hyperuricosuria, hypocitraturia, and hypercalciuria associated with this diet.

high salt intake

- Higher sodium intake is associated with higher urinary sodium and calcium levels, and decreased urinary citrate.[15] This promotes calcium salt crystallization due to urinary saturation of monosodium urate and calcium oxalate/calcium phosphate being increased. Salt excess can also lead to bone loss, thereby worsening hypercalciuria.

white ancestry

- In US men, the highest prevalence of nephrolithiasis is found in white men, followed by Hispanic men, Asian men, and black men.[16] Among US women, the prevalence is highest among white women but lowest among Asian women.[17]

male sex

- Nephrolithiasis typically affects adult men more commonly than adult women, with a male to female ratio of 2 or 3:1.[18] [16] [19] However, there is evidence that this difference in incidence between men and women is narrowing.[20]
Nephrolithiasis

**Dehydration**

- Fluid intake is very important and should be at least 2-3 liters per day.\[21\] [22] In two large observational studies, fluid intake was found to be inversely related to the risk of renal stone formation.\[23\] [24] A low urine output can produce a higher concentration of urinary solutes, therefore leading to stone formation.

**Obesity**

- Two large prospective cohort studies of men and women found that the prevalence and incident risk of nephrolithiasis were directly correlated with higher weight and BMI in both genders, although the magnitude of the association was greater in women than in men.\[23\] [24]
- Evidence linking obesity with low urine pH and uric acid stones and an association with hypercalciuria could account for an increased risk of uric acid and/or calcium stones in obese patients.\[1\]

**Crystalluria**

- Stone formers (especially calcium oxalate stones) frequently excrete more calcium oxalate crystals in the urine. Increased urinary excretion of cystine, struvite, and uric acid crystals is also a risk factor for stone formation.\[14\]

**Weak occupational exposure to dehydration**

- Dehydration and heat exposure are risk factors for nephrolithiasis. Those exposed to high temperatures demonstrate lower urine volumes and pH, higher uric acid levels, and higher urine specific gravity, leading to higher urinary saturation of uric acid, as well as calcium oxalate. As a result, people exposed to dehydration and heat are at increased risk for forming stones.\[3\] [25]

**Warm climate**

- Seasonal variation in nephrolithiasis is likely related to temperature because of fluid losses through perspiration. It has been reported that the highest incidence of nephrolithiasis is in the summer months, with the peak occurring within 1-2 months of maximal mean temperatures.\[3\] [25]
- In the US, prevalence of nephrolithiasis in the southeastern states (“stone belt”) is nearly double that in other areas.\[26\]

**Family history of nephrolithiasis**

- A positive family history of nephrolithiasis is associated with an increased risk of forming stones. A stone former is twice as likely as a non-stone former to have a first-degree relative with a history of stones. Patients with family history have a higher incidence of multiple stones and early recurrence.\[14\] Studies into possible genetic mutations responsible for inherited forms of nephrolithiasis are ongoing.\[27\]

**Precipitant medications**

- Medications that are associated with an increased risk of stone formation include calcium-containing antacids, carbonic anhydrase inhibitors, sodium and calcium-containing medications, vitamin C, and vitamin D. Most of these medications lead to higher urinary levels of calcium, uric acid, sodium, or oxalate, in turn promoting stone formation. Other medications are poorly soluble with high urinary excretion, favoring direct crystallization and stone formation in urine. These include protease inhibitors (e.g., indinavir, atazanavir), ephedrine, guaifenesin, triamterene, and sulfadiazine.\[28\] Antibiotic
exposure (sulfas, cephalosporins, fluoroquinolones, nitrofurantoin, broad-spectrum penicillins) is associated with an increased likelihood for nephrolithiasis, with the greatest odds for recent exposure and exposure at younger age.[29]

Investigations

1st test to order

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>urinalysis</td>
<td><em>Microhematuria is seen in the majority of patients with renal stones.</em></td>
</tr>
<tr>
<td></td>
<td>may be normal; dipstick positive for leukocytes, nitrates, blood;</td>
</tr>
<tr>
<td></td>
<td>microscopic analysis positive for WBCs, RBCs, or bacteria</td>
</tr>
<tr>
<td>CBC and differential</td>
<td>variable</td>
</tr>
<tr>
<td>serum electrolytes, BUN, and creatinine</td>
<td>variable</td>
</tr>
<tr>
<td>urine pregnancy test</td>
<td>negative</td>
</tr>
<tr>
<td>noncontrast helical CT scan</td>
<td>calcification seen in renal collecting system or ureter; hydronephrosis; perinephric stranding (indicative of inflammation or infection)</td>
</tr>
<tr>
<td>stone analysis</td>
<td>stone composition</td>
</tr>
</tbody>
</table>

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Other tests to consider

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>plain abdominal radiograph (KUB)</td>
<td>calcification seen within urinary tract</td>
</tr>
</tbody>
</table>
| • Plain abdominal film could be ordered initially along with computed tomography (CT) scan to determine whether stone is radiolucent. Up to 85% of stones are visible on KUB, although uric acid stones are radiolucent.[43]  
  • A KUB x-ray should be performed if the stone is not visible on a CT scout, so that patients with stones identifiable on initial KUB x-ray or CT scout can be followed by KUB.[31]  
  • Before definitive surgical therapy, a KUB should be ordered in an asymptomatic patient to ensure that patient has not already passed the stone. |
| renal ultrasound                    | calcification seen within urinary tract, along with dilation            |
| • In pregnancy, renal ultrasound is the first-line imaging modality. It should also be the modality of choice when there is a desire to reduce or eliminate radiation exposure, such as for evaluation of children. Low-dose computed tomography (CT) can be considered in children if renal ultrasound is nondiagnostic.[31] |
| intravenous pyelogram (IVP)         | calcification seen within urinary tract or a filling defect seen when dye is passing through the kidney and down the ureter |
| • This test has for the most part been replaced by the computed tomography (CT) scan (the new diagnostic standard) for the evaluation and diagnosis of renal stones; however, it is still useful to assess renal function and collecting system drainage. |
| magnetic resonance imaging (MRI)    | filling defect seen in the collecting system                            |
| • Although conferring no radiation to the patient, MRI is a second-line imaging modality because stones are not directly visible on MRI and only seen as a filling defect in the collecting system. It can help to define the level of urinary tract obstruction.[38] |
| 24-hour urine monitoring            | increased or decreased values for urinary electrolytes; reduced urine volume |
| • Helps in determining underlying metabolic cause or etiology for nephrolithiasis. Should be ordered once the patient is stone free.  
  • Basic measurements should include volume, pH, creatinine, sodium, calcium, oxalate, uric acid, and citrate.  
  • Patients with recurrent renal stones should have subsequent periodic 24-hour urine monitoring. |
| spot urine for cystine              | cystinuria                                                              |
| • A urine screen for cystine should be considered if the diagnosis of cystinuria is not excluded by stone analysis. |
## Nephrolithiasis

### Diagnosis

#### Differentials

<table>
<thead>
<tr>
<th>Condition</th>
<th>Differentiating signs / symptoms</th>
<th>Differentiating tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute appendicitis</td>
<td>• Usually presents with right lower quadrant pain, fever, and signs of peritonitis.</td>
<td>• Urinalysis is negative.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Noncontrast helical computed tomography scan (NCCT) shows dilation of appendix and absence of renal stones.</td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
<td>• Woman of childbearing age presents with missed menstrual period, right lower quadrant pain, or pelvic pain with some degree of vaginal bleeding or spotting. Cervical motion tenderness may be present on pelvic exam.</td>
<td>• Urine pregnancy test is positive and serum hCG elevated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ultrasound reveals presence of mass in fallopian tubes.</td>
</tr>
<tr>
<td>Ovarian cyst</td>
<td>• May present with lower pelvic/abdominal discomfort and/or dyspareunia; may be cyclical.</td>
<td>• Abdominal ultrasound shows cystic adnexal lesion; free fluid in the peritoneum.</td>
</tr>
<tr>
<td></td>
<td>• Palpable mass on pelvic exam.</td>
<td>• NCCT shows absence of renal stones.</td>
</tr>
<tr>
<td>Diverticular disease</td>
<td>• May present with left lower quadrant pain or abdominal pain as opposed to flank pain.</td>
<td>• Technetium pertechnetate scan may show enhancement of diverticulum if gastric mucosa is present.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• NCCT shows absence of renal stones.</td>
</tr>
<tr>
<td>Bowel obstruction</td>
<td>• Bowel obstruction patients present with abdominal distension, vomiting, and constipation.</td>
<td>• Abdominal x-ray may show volvulus.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• NCCT shows collapsed bowel with proximal dilation and absence of renal stones.</td>
</tr>
<tr>
<td>Acute pancreatitis</td>
<td>• History of gallstones or alcohol abuse.</td>
<td>• NCCT shows inflammation of the pancreas and absence of renal stones.</td>
</tr>
<tr>
<td></td>
<td>• These patients typically have epigastric pain that radiates to the back, as opposed to flank pain.</td>
<td>• The diagnosis of pancreatitis can usually be distinguished from renal stones on clinical grounds, but in rare cases it might be necessary to measure serum amylase and lipase, which are elevated in pancreatitis and usually normal in stone disease.</td>
</tr>
<tr>
<td>Peptic ulcer disease</td>
<td>• May or may not have a history of peptic ulcer disease. Pain is abrupt, severe in intensity, and may</td>
<td>• Erect chest x-ray and abdominal x-ray may show free air under the diaphragm.</td>
</tr>
<tr>
<td>Condition</td>
<td>Differentiating signs / symptoms</td>
<td>Differentiating tests</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Gastroenteritis                 | • These patients typically have diffuse abdominal pain and no flank pain. Vomiting is prominent and patient may have diarrhea. | • Endoscopy shows peptic ulcer.  
• NCCT shows absence of renal stones. |
| Abdominal aortic aneurysm       | • Pain typically presents as sudden onset of intermittent or continuous abdominal pain, radiating to the back; patient may collapse. | • Ultrasound/CT of the abdomen can show the presence of abdominal aortic aneurysm.     |
| Pyelonephritis                  | • Patients may present with costovertebral angle tenderness and urinary symptoms of dysuria, frequency, and hesitancy; flank pain may radiate to back; fever, chills, fatigue may be present. | • Positive urinalysis and/or urine culture.                                            |
| Tubo-ovarian abscess           | • Patients typically present with acute lower abdominal pain, fevers, and vaginal discharge.    | • Pelvic ultrasound shows multilocular adnexal masses.  
• NCCT shows thick-walled rim-enhancing adnexal masses in the absence of renal stones. |
| Uteropelvic junction obstruction| • Patients may present with intermittent flank or abdominal pain, often worse during brisk diuresis. | • Renal ultrasound or NCCT shows hydronephrosis without a dilated ureter in the absence of a renal stone. |
| Testicular torsion              | • Patients typically present with lower abdominal pain, scrotal pain (testicle), nausea, and/or vomiting. | • Ultrasound shows enlarged, heterogeneous testicle with decreased or absent Doppler flow.  
• NCCT shows enlarged edematous testicle in absence of renal stones. |
| Ovarian torsion                 | • Patients typically present with lower abdominal pain, nausea, and/or vomiting.                  | • Ultrasound shows enlarged, heterogeneous ovary with decreased or absent Doppler flow.  
• NCCT shows enlarged edematous ovary in absence of renal stones. |
## Nephrolithiasis

### Diagnosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Differentiating signs / symptoms</th>
<th>Differentiating tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Musculoskeletal back pain</strong></td>
<td>• Patient may present with unilateral or bilateral middle and/or lower back pain.</td>
<td>• Point tenderness upon muscular palpation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• NCCT is normal with absence of renal stones.</td>
</tr>
<tr>
<td><strong>Mesenteric ischemia</strong></td>
<td>• Patients typically present with acute periumbilical abdominal pain with nausea and vomiting.</td>
<td>• NCCT shows bowel wall thickening, intestinal pneumatosis, portal venous gas, with absence of renal stones.</td>
</tr>
<tr>
<td><strong>Constipation</strong></td>
<td>• Patients typically present with left lower quadrant pain and abdominal distension.</td>
<td>• NCCT shows excessive stool in colon or rectum in absence of renal stones.</td>
</tr>
<tr>
<td><strong>Cholecystitis or biliary colic</strong></td>
<td>• Patient may present with right upper quadrant and/or epigastric pain, fevers, and leukocystosis.</td>
<td>• Abdominal ultrasound will show gallstones with gallbladder wall thickening.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• NCCT shows gallstones, gallbladder wall edema, and high attenuation bile in the absence of renal stones.</td>
</tr>
</tbody>
</table>
Approach

The main goal of initial treatment for an acute stone event is symptomatic relief with hydration and analgesia/antiemetics as needed. If signs and symptoms of infection are present, and the patient has a stone in the kidney or ureter, immediate urologic consultation should be initiated as urinary tract infection in the setting of an obstructing stone is an emergency that requires antibiotics and renal decompression to decrease the chance of life-threatening septic shock.[52] If the patient has a stone present without signs and symptoms of infection, he or she can be managed conservatively with a nonsteroidal anti-inflammatory drug (NSAID) and/or an opioid. NSAIDs have been shown to offer effective pain relief from acute kidney stone related pain with fewer side effects than opioids and acetaminophen.[53] If the pain cannot be managed with conservative therapy, then renal decompression or definitive stone treatment should be considered.[1] There is evidence to support that medical expulsive therapy (MET), namely alpha-blockers, may increase ureteral stone passage rate and decrease the time to stone passage, particularly in distal ureteral stones <10 mm in size.[54] However, if a 4- to 6-week trial of MET has been attempted without successful stone passage, the patient should undergo definitive surgical management.

For patients at risk for, or with a history of recurrent stones, secondary preventive measures should be tailored toward underlying metabolic factors that promote stone formation. For all such patients, dietary modification with adequate hydration is an essential aspect of ongoing management.

Urgent consideration: obstruction and infection

Patients with urinary calculi along with fever and other signs or symptoms of infection need emergency urologic consultation for drainage and intravenous antibiotics. Failure to perform rapid renal decompression can perpetuate urosepsis and result in death. Drainage can be accomplished in two ways. A urologist can place a ureteric stent past the obstruction and achieve drainage. Alternatively, a percutaneous nephrostomy tube can be placed by interventional radiology.

Management of stones <10 mm and no complications

Acute medical treatment for renal or ureteral colic includes conservative therapy, such as hydration, analgesia (an NSAID and/or an opioid), and an anti-emetic.[53] NSAIDs should be offered first-line unless contraindicated (e.g., patients at risk of renal impairment, cardiac failure, gastric ulceration).[38] Parental NSAIDs provide the most sustained pain relief, with fewer adverse effects, when compared with opioids.[53] However, NSAIDs can be offered by any route.[56] Patients with newly diagnosed ureteric stones <10 mm without complicating factors (urosepsis, intractable pain and/or vomiting, impending acute renal failure, obstruction of a solitary or transplanted kidney, or bilateral obstruction) can be managed expectantly.[48] Many ureteric stones <10 mm pass spontaneously, with exact passage rate related to both stone size and location.[59]

MET using an alpha-blocker such as tamsulosin, alfuzosin, or silodosin may be of benefit in promoting larger (but still <10 mm) distal ureteral stone passage; however, efficacy rates have been questioned.[60] These agents can cause ureteric relaxation of smooth muscle and antispasmodic activity of the ureter leading to stone passage.[67] Patients should be made aware that prescribing alpha-blockers for this indication is considered an off-label use of these drugs. Additionally, tamsulosin has been associated with intraoperative floppy iris syndrome, therefore it should not be prescribed if a patient has planned cataract surgery.
If there is spontaneous passage of stones, most pass within 4 to 6 weeks. Surgical intervention is indicated in the presence of persistent obstruction, failure of stone progression, sepsis, or persistent or increasing colic. Such patients in general are followed up with periodic imaging, with either a KUB and renal ultrasound or a noncontrast computed tomography (CT) abdomen and pelvis to monitor stone position and degree of hydronephrosis.

**Management of stones ≥10 mm or smaller stones that fail to pass with MET**

Management can be affected by stone size, location, and composition, in addition to anatomic and clinical features. For larger stones (≥10 mm), and for smaller stones that remain despite conservative therapies, additional surgical treatment is necessary. Historically, open surgery was the only way to remove stones. However, with the development and success of endourology, a term used to describe less invasive surgical techniques that involve closed manipulation of the urinary tract with scopes, open surgery is now rarely performed.

Calculi between 10-20 mm are in general treated with extracorporeal shock wave lithotripsy (ESWL) or ureteroscopy as first-line therapy. However for ESWL, the stone-free rates for lower pole stones are inferior (25%) compared with nonlower pole stones (40%).[68] Percutaneous nephrolithotomy (PCNL) for calculi between 10-20 mm achieves better stone-free rates for lower pole stones than ESWL.[69] Similarly, cystine stones >15-20 mm and brushite stones respond poorly to ESWL.[70] Hence, patients with features predictive of poor outcome, obesity, or a body build not conducive to ESWL, may be advised alternatives such as PCNL or ureteroscopy, which show superior results.[71] Patients with stones >20 mm should primarily be treated with PCNL unless specific indications for an alternate procedure are present. While PCNL is the first-line therapy for large stones, ureteroscopy has been reported to achieve a mean stone-free rate as high as 93.7% (77.0% to 96.7%) for stones >20 mm in size (mean 25 mm) with acceptable overall complication rates (10.1%). However, this requires an average of 1.6 procedures per patient.[72][73]

For solitary renal calculi <10 mm, ESWL and ureteroscopy are both valid options. Ureteroscopy or PCNL can be utilized when ESWL fails, or in the presence of anatomic abnormalities or other special circumstances.[74] A ureteral stent, an internal tube extending from the kidney to the bladder, is often left temporarily in place after ureteroscopy to promote collecting system drainage while any edema from the stone or the procedure resolves. Stents are recommended in cases of functionally or anatomically solitary kidneys, ureteral stricture, noted ureteral injury, or cases with a planned second stage procedure. While stents can be omitted in cases of uncomplicated ureteroscopy, randomized multicenter trials are warranted to better determine which patients can safely undergo ureteroscopy without ureteral stent placement.[75]

- Extracorporeal shock wave lithotripsy (ESWL) is the least invasive method of definitive stone treatment and is suitable for most patients with uncomplicated stone disease. In ESWL, shock waves are generated by a source external to the patient's body and are then propagated into the body and focused on a renal stone. The shock waves break stones by both compressive and tensile forces. The stone fragments then pass out in the urine. Limitations to ESWL include stone size and location. ESWL has the potential benefit of being done under intravenous sedation/analgesia, without need for general anesthesia. Treatment with tamsulosin appears to be effective in assisting stone clearance in patients with renal and ureteric calculi.[76] While ESWL has been shown to have limited success with lower pole stones there is evidence to suggest that ancillary maneuvers such as percussion, diuresis, and inversion increase stone-free
Nephrolithiasis
Management

Contraindications to ESWL treatment include pregnancy, severe skeletal malformations, severe obesity, aortic and/or renal artery aneurysms, uncontrolled hypertension, disorders of blood coagulation, and uncontrolled urinary tract infections.

- Ureteroscopy involves placing a small semi-rigid or flexible scope per urethra and into the ureter and/or kidney. Once the stone is visualized, it can be fragmented using a laser and/or grasped with a basket and removed. The procedure is more invasive than ESWL, but is generally thought to have a higher stone-free rate. General anesthesia is routinely used, and a ureteric stent may be placed at the end of the procedure. The procedure can be safely performed in coagulopathic patients using a holmium laser. Single-use flexible ureteropyeloscopy (FURS) demonstrates comparable efficacy with reusable FURS in treating renal calculi.

- For patients requiring stone removal, both ESWL and ureteroscopy are considered acceptable first-line surgical treatments for stones in the ureter. Ureteroscopic stone-free rates are better than ESWL rates for distal ureteric stones regardless of size and for proximal ureteric stones >10 mm. However, ureteroscopic removal has a higher complication rate and longer hospital stay.

- Percutaneous antegrade ureteroscopy involves percutaneous antegrade removal of ureteric stones, and can be considered in select cases with very large (>15 mm) stones impacted in the upper ureter or when retrograde access is not possible.

- Percutaneous nephrostolithotomy (PCNL) is a minimally invasive form of treatment that is usually reserved for renal and proximal ureteric stones (i.e., in the lower pole) and those that are large (>20 mm), have failed therapy with ESWL and ureteroscopy, or are associated with complex renal anatomy. Percutaneous access into the kidney is gained from the flank. Current evidence indicates that both fluoroscopy and ultrasound (US) guidance may be successfully used for obtaining percutaneous renal access. Combining US and fluoroscopy seems to improve the outcome both with regard to success in achieving access and reducing complications. Once access is gained, a large sheath is placed into the kidney and a nephroscope is used to help remove the stone. For large stones, ultrasound lithotripsy is usually used to break and remove the stone. PCNL usually requires a hospital stay and has more potential complications than either ESWL or ureteroscopy. In stones of 20-30 mm, ESWL is associated with poor stone-free rates (34%) compared to those achieved with PCNL (90%). ESWL is further associated with an increased number of procedures and need for ancillary treatments as the stone size increases.

- Laparoscopic stone removal is another minimally invasive method to remove ureteric or renal stones. However, it is still more invasive, requires a longer hospital stay, and has a much higher learning curve than ureteroscopy or ESWL. With the advances in ESWL and endourologic surgery (i.e., ureteroscopy and PCNL) during the past 20 years, the indications for open stone surgery have markedly diminished. Laparoscopic or open surgical stone removal may still be indicated in rare cases where ESWL, ureteroscopy, and percutaneous ureteroscopy fail or are unlikely to be successful; anatomic deformities preclude a minimally invasive approach; the patient requires concomitant open surgery, pyeloplasty, or a partial nephrectomy; or in patients with a large stone burden requiring a single clearance procedure.

Stones during pregnancy
A symptomatic stone occurs in 1 out of every 200 to 1500 pregnancies with 80% to 90% of these occurring in the second or third trimester. It has been reported that 48% to 80% of stones pass spontaneously during pregnancy.
Pregnant women with renal colic that is not controlled with oral analgesia or with an obstructing stone and signs of infection (fever or urinalysis/urine culture showing a possible urine infection) should receive a ureteric stent or percutaneous nephrostomy tube. Of note, these tubes should be changed more often (every 6 to 8 weeks) due to concern for rapid encrustation as a result of the metabolic changes seen with pregnancy. If the patient has no evidence of infection, definitive therapy with ureteroscopy may be performed and has been demonstrated to be safe.[93] ESWL and PCNL are contraindicated in pregnancy.

**Ongoing medical therapy and dietary modification**

Oral alkalinization therapy with medications such as potassium citrate and sodium bicarbonate may be beneficial in dissolving uric acid stones and preventing uric acid supersaturation. It may be used for treating uric acid stones that do not require urgent surgical treatment, as well as asymptomatic stones. The ideal goal for alkalinization therapy for uric acid stones is to maintain the urine pH between 6.5 and 7.0. Potassium citrate is the first-line therapy. In patients with CHF or renal failure, extra care should be taken when prescribing alkalinization therapy. Alkalinization therapy also plays an important role in preventing calcium and cystine stones.

Long-term dietary modification is essential for preventing future calculi. This modification is centered on increasing fluid intake. At least 2 liters of urine output daily should be recommended to help prevent future episodes of stone formation.[94]

Decreased dietary sodium, protein, and oxalate should be recommended for stone prevention. Increased citrus fruit intake is recommended to prevent stone recurrence.[95] Normal calcium intake (i.e., 1000 mg/day to 1200 mg/day) is recommended.[95] Dietary calcium restriction can lead to less binding of calcium to oxalate in the GI tract, promoting hyperoxaluria and potentiating the risk for stone formation; furthermore, it could have detrimental effects on bone health.

Where specific metabolic abnormalities exist and are not responsive to dietary modification, specific preventive therapies may be required.[51] [96] These include:

- Uric acid stones: urinary alkalinization with potassium citrate or sodium bicarbonate
- Hyperuricosuria, recurrent calcium oxalate stones, and normal urine calcium: allopurinol or febuxostat

  - Febuxostat should only be prescribed for patients who can not tolerate allopurinol or where treatment with allopurinol has failed, and who have been counselled regarding cardiovascular risk.[97]
  - The double-blind Cardiovascular Safety of Febuxostat or Allopurinol in Patients with Gout (CARES) safety trial found that cardiovascular death and all cause mortality were significantly more common among patients taking febuxostat than allopurinol (4.3% vs. 3.2%, HR 1.34 [95% CI 1.03 to 1.73]; 7.8% vs. 6.4%, HR 1.22 [95% CI 1.01 to 1.47], respectively).[98] Treatment group did not differ with respect to a primary composite outcome of cardiovascular events.
  - Febuxostat should be avoided in patients with pre-existing major cardiovascular disease (e.g., myocardial infarction, unstable angina, stroke), unless no other therapy options are appropriate.[99]

- Hypercalciuria and recurrent calcium stones: thiazide diuretic with or without potassium supplementation (potassium citrate or potassium chloride)
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- Hypocitraturia and recurrent calcium stones: urinary alkalinization (e.g., potassium citrate; sodium bicarbonate or sodium citrate can be considered if the patient is at risk for hyperkalemia[100]
- Hyperoxaluria: oxalate chelator (e.g., calcium, magnesium, or cholestyramine), potassium citrate, pyridoxine
- Cystinuria: urinary alkalinization with potassium citrate, thiol binding agent (e.g., tiopronin which is tolerated better than d-penicillamine)
- Struvite stones: urease inhibitor (e.g., acetohydroxamic acid), which is best reserved for complex/recurrent struvite stones in which surgical management has been exhausted.[14] Secondary care supervision should be employed as it can produce severe adverse effects such as phlebitis and hypercoagulability.

Most of these strategies are applied to children with nephrolithiasis, although there is a limited number of well-designed trials in this age group.[101] [102]

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

<table>
<thead>
<tr>
<th>Initial</th>
<th>( summary )</th>
</tr>
</thead>
<tbody>
<tr>
<td>acute renal colic nonpregnant</td>
<td>1st conservative management (hydration, analgesia, and anti-emetic)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Acute</th>
<th>( summary )</th>
</tr>
</thead>
<tbody>
<tr>
<td>confirmed stone: no evidence of obstruction nonpregnant</td>
<td>1st hydration, analgesia, and anti-emetic</td>
</tr>
<tr>
<td>demonstrated bacteriuria</td>
<td>adjunct antibiotic therapy</td>
</tr>
<tr>
<td>stones &lt;10 mm</td>
<td>adjunct surgical decompression</td>
</tr>
<tr>
<td>stones ≥10 mm or failed medical therapy</td>
<td>adjunct medical expulsive therapy (MET)</td>
</tr>
</tbody>
</table>

confirmed stone: with evidence of obstruction nonpregnant

<table>
<thead>
<tr>
<th></th>
<th>1st</th>
</tr>
</thead>
<tbody>
<tr>
<td>hydration, analgesia, and anti-emetic</td>
<td></td>
</tr>
<tr>
<td>plus surgical decompression</td>
<td></td>
</tr>
<tr>
<td>plus surgical removal</td>
<td></td>
</tr>
<tr>
<td>plus antibiotic therapy</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>pregnant</th>
<th>1st</th>
</tr>
</thead>
<tbody>
<tr>
<td>specialist referral</td>
<td></td>
</tr>
</tbody>
</table>
### Ongoing following an acute episode nonpregnant

<table>
<thead>
<tr>
<th>Reason</th>
<th>Type</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>hyperuricosuria and/or uric acid stones</td>
<td>1st</td>
<td>hydration and dietary modification</td>
</tr>
<tr>
<td>hypercalciuria</td>
<td>adjunct</td>
<td>xanthine oxidase inhibitor ± alkalinization therapy</td>
</tr>
<tr>
<td>hypocalciuria</td>
<td>adjunct</td>
<td>diuretics/alkalinization</td>
</tr>
<tr>
<td>hypocitraturia</td>
<td>adjunct</td>
<td>alkalinization</td>
</tr>
<tr>
<td>hyperoxaluria</td>
<td>adjunct</td>
<td>oxalate chelator/alkalinization</td>
</tr>
<tr>
<td>cystinuria</td>
<td>adjunct</td>
<td>alkalinization/thiol binding agent/cystine chelator</td>
</tr>
<tr>
<td>struvite stones</td>
<td>adjunct</td>
<td>urease inhibitor</td>
</tr>
</tbody>
</table>
## Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

### Initial

**acute renal colic nonpregnant**

<table>
<thead>
<tr>
<th>1st</th>
<th>conservative management (hydration, analgesia, and anti-emetic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary options</td>
<td></td>
</tr>
<tr>
<td>» indomethacin: 25-50 mg orally (immediate-release) three times daily when required</td>
<td></td>
</tr>
<tr>
<td>-or-</td>
<td></td>
</tr>
<tr>
<td>» diclofenac sodium: 50 mg orally (immediate-release) three times daily when required; 37.5 mg intravenously every 6 hours when required</td>
<td></td>
</tr>
<tr>
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<tr>
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</tr>
<tr>
<td>--AND/OR--</td>
<td></td>
</tr>
<tr>
<td>» morphine sulfate: 2.5 to 10 mg intravenously/intramuscularly/subcutaneously every 2-6 hours when required</td>
<td></td>
</tr>
<tr>
<td>--AND--</td>
<td></td>
</tr>
<tr>
<td>» ondansetron: 4 mg intravenously every 8-12 hours when required</td>
<td></td>
</tr>
</tbody>
</table>

**Acute medical treatment for suspected renal or ureteric colic includes conservative therapies such as hydration, analgesia (a nonsteroidal anti-inflammatory drug [NSAID] such as diclofenac, indomethacin, or ketorolac, and/or an opioid such as morphine), and an anti-emetic (e.g., ondansetron).[55]**

**NSAIDs should be offered first-line unless contraindicated (e.g., patients at risk of renal impairment, cardiac failure, gastric ulceration).[38] [56] [57] [Evidence C] Parental NSAIDs provide the most sustained pain relief, with fewer adverse effects, when compared with opioids.[53] [58] However, NSAIDs can be offered by any route.[56] [Evidence C] Examples are listed above.**

»
Acute

**confirmed stone: no evidence of obstruction nonpregnant**

<table>
<thead>
<tr>
<th>1st</th>
<th>hydration, analgesia, and anti-emetic</th>
</tr>
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</table>

» Patients with newly diagnosed ureteric stones <10 mm without complicating factors (urosepsis, intractable pain and/or vomiting, impending acute renal failure, obstruction of a solitary or transplanted kidney, or bilateral obstruction) can be managed expectantly.[48]

» Conservative treatment for confirmed stones with renal or ureteric colic includes hydration, analgesia (nonsteroidal anti-inflammatory drugs [NSAIDs] such as diclofenac, indomethacin, or ketorolac, and/or an opioid such as morphine), and an anti-emetic (e.g., ondansetron).[55]

» NSAIDs should be offered first-line unless contraindicated (e.g., patients at risk of renal impairment, cardiac failure, gastric ulceration).[38] [56] [57] [Evidence C] Parental NSAIDs provide the most sustained pain relief, with fewer adverse effects, when compared with opioids.[53] [58] However, NSAIDs can be offered by any route.[56] [Evidence C] Examples are listed above.

»

- demonstrated bacteriuria

<table>
<thead>
<tr>
<th>adjunct</th>
<th>antibiotic therapy</th>
</tr>
</thead>
</table>

Treatment recommended for SOME patients in selected patient group
Nephrolithiasis Management

Acute

► If infection is present, but no obstruction or signs of sepsis, the patient can be treated with conservative therapy and antibiotics.

► Empiric antibiotic therapy should be started pending sensitivity results based on urinalysis cultures. The empiric regimen depends on various factors, including the type of infection, patient factors, and local antibiotic resistance patterns; consult local guidelines for more information on choice of antibiotics.

adjunct surgical decompression

Treatment recommended for SOME patients in selected patient group

► Patients with urinary calculi along with fever and other signs or symptoms of infection need emergency urologic consultation for drainage and intravenous antibiotics.

► Drainage can be accomplished in two ways. In the acute setting, a urologist can place a ureteric stent past the obstructing stone and achieve renal drainage. Alternatively, percutaneous nephrostomy by an interventional radiologist may be performed. Failure to perform rapid renal decompression can lead to urosepsis and death.

adjunct medical expulsive therapy (MET)

Treatment recommended for SOME patients in selected patient group

Primary options

► tamsulosin: 0.4 mg orally once daily

OR

► alfuzosin: 10 mg orally once daily

OR

► silodosin: 8 mg orally once daily

► There is evidence to support that MET can increase ureteral stone passage rate and decrease the time to stone passage in stones <10 mm in size.[54]

► Using an alpha-blocker, such as tamsulosin, alfuzosin, or silodosin may be of benefit in promoting larger (but still <10 mm) distal ureteral stone passage; however, efficacy rates have been questioned.[64] [61] [62] [60] [63] [103] [104] [105]
### Management

#### Acute

<table>
<thead>
<tr>
<th>stones ≥10 mm or failed medical therapy</th>
<th>adjunct surgical removal</th>
</tr>
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<tr>
<td>Treatment recommended for SOME patients in selected patient group</td>
<td></td>
</tr>
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<td>For smaller stones that fail conservative therapies (e.g., uncontrolled symptoms, failure of stone to progress, or persistent obstruction), additional surgical treatment is necessary.</td>
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<td>Percutaneous nephrostolithotomy (PCNL) is minimally invasive and usually reserved for renal and proximal ureteric stones (i.e., in the lower pole) and those that are large (&gt;20 mm), have failed therapy with ESWL and ureteroscopy, or are associated with complex renal anatomy.[48]</td>
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<td>Laparoscopic or open surgical stone removal may be considered in rare cases where ESWL, ureteroscopy, and percutaneous ureteroscopy fail, or are unlikely to be successful.</td>
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</table>

#### confirmed stone: with evidence of obstruction nonpregnant

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<td>Primary options</td>
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<td>» indomethacin: 25-50 mg orally (immediate-release) three times daily when required</td>
</tr>
<tr>
<td>» diclofenac sodium: 50 mg orally (immediate-release) three times daily when required</td>
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</table>
**Acute**

<table>
<thead>
<tr>
<th>Management</th>
<th></th>
</tr>
</thead>
</table>
| **required**: 37.5 mg intravenously every 6 hours when required  
**-or-**  
» ketorolac: consult specialist for guidance on dose  
**--AND/OR--**  
» morphine sulfate: 2.5 to 10 mg intravenously/intramuscularly/subcutaneously every 2-6 hours when required  
**--AND--**  
» ondansetron: 4 mg intravenously every 8-12 hours when required |

- Patients with obstructed urinary calculi with infection require emergency urologic consultation and surgical drainage, with intravenous antibiotics and supportive measures (hydration, analgesia with a non steroidal anti-inflammatory drug such as diclofenac, indomethacin, or ketorolac, and/or an opioid such as morphine, and an anti-emetic such as ondansetron) as necessary.

- If obstruction is present without infection, the patient can be managed conservatively; if the pain cannot be managed with a nonsteroidal anti-inflammatory drug (if renal function normal) and/or an opioid, then decompression should be considered.[1] If obstruction is present with infection decompression and antibiotics are essential to minimize risk for life-threatening sepsis.

- NSAIDs should be offered first-line unless contraindicated (e.g., patients at risk of renal impairment, cardiac failure, gastric ulceration).[38] [56] [57] [Evidence C] Parental NSAIDs provide the most sustained pain relief, with fewer adverse effects, when compared with opioids.[53] [58] However, NSAIDs can be offered by any route.[56] [Evidence C] Examples are listed above.

**plus surgical decompression**

Treatment recommended for ALL patients in selected patient group

- Patients with urinary calculi along with fever and other signs or symptoms of infection need emergency urologic consultation for drainage and intravenous antibiotics.

- Drainage can be accomplished in two ways. In the acute setting, a urologist can place a ureteric stent past the obstructing stone and achieve renal drainage. Alternatively, percutaneous...
### Acute

Nephrostomy by an interventional radiologist may be performed.

**plus surgical removal**

Treatment recommended for ALL patients in selected patient group

- For smaller stones that fail conservative therapies (e.g., uncontrolled symptoms, failure of stone to progress, or persistent obstruction), additional surgical treatment is necessary.

- Extracorporeal shock wave lithotripsy (ESWL) and ureteroscopy are considered first-line treatments. However, ureteroscopy in general is associated with better stone-free rates than ESWL.

- Percutaneous antegrade ureteroscopy involves percutaneous antegrade removal of ureteric stones, and can be considered in select cases with very large (>15 mm) stones impacted in the upper ureter or when retrograde access is not possible.

- Percutaneous nephrostolithotomy (PCNL) is minimally invasive and usually reserved for renal and proximal ureteric stones (i.e., in the lower pole) and those that are large (>20 mm), have failed therapy with ESWL and ureteroscopy, or are associated with complex renal anatomy.[48]

- Laparoscopic or open surgical stone removal may be considered in rare cases where ESWL, ureteroscopy, and percutaneous ureteroscopy fail, or are unlikely to be successful.

**with infection**

**plus antibiotic therapy**

Treatment recommended for ALL patients in selected patient group

**Primary options**

- **gentamicin**: 1.5 mg/kg intravenously every 8 hours
  
  OR
  
  - **ampicillin**: 2 g intravenously every 6 hours
    
    - **and**
    
    - **gentamicin**: 1.5 mg/kg intravenously every 8 hours
      
      OR
      
      - **cefuroxime sodium**: 750-1500 mg intravenously every 8 hours
        
        - **or**
## Acute

| » cefotetan: 1-2 g intravenously every 12-24 hours  
  -or-  
  » ceftriaxone: 1-2 g intravenously every 24 hours  
  -AND--  
  » gentamicin: 1.5 mg/kg intravenously every 8 hours |

OR

| » ceftriaxone: 1-2 g intravenously every 24 hours |

### Secondary options

| » piperacillin/tazobactam: 3.375 g intravenously every 6 hours  
  Dose consists of 3 g of piperacillin plus 0.375 g of tazobactam.  
OR  
  » piperacillin/tazobactam: 3.375 g intravenously every 6 hours  
  Dose consists of 3 g of piperacillin plus 0.375 g of tazobactam.  
  -and-  
  » gentamicin: 1.5 mg/kg intravenously every 8 hours |

» Patients with urinary calculi along with fever and other signs or symptoms of infection need emergency urologic consultation for drainage and intravenous antibiotics.

» Empiric broad-spectrum antibiotic therapy should be started pending sensitivity results based on urinalysis cultures.[38] Empiric regimens differ across locations, and local guidance with the aid of a local antibiogram should be sought.

» Patients should be treated with 14 days of culture-specific antibiotics.

---

### pregnant

**1st specialist referral**

» The principles of treatment for the acute stone episode are similar in pregnant and nonpregnant patients. However, analgesics, antibiotics, anti-emetics, and intravenous fluids are given relative to their safety and risk for that
particular trimester. For example, nonsteroidal anti-inflammatory drugs should be avoided, particularly during the first and third trimesters. Alpha-blockers (e.g., tamsulosin) are not recommended as there are no adequate and well-controlled studies in pregnant women.

- Similarly antibiotics are given according to their risk benefit ratio.

- Temporary measures for symptomatic obstruction or intractable symptoms include a ureteric stent or percutaneous nephrostomy tube. However, they need frequent changes because of increased encrustation risk. If the patient has no evidence of infection, definitive therapy with ureteroscopy may be performed and has been demonstrated to be safe.\[^{[93]}\]

  Extracorporeal shock wave lithotripsy (ESWL) and percutaneous nephrostolithotomy (PCNL) are contraindicated in pregnancy.
## Nephrolithiasis

### Ongoing

#### following an acute episode nonpregnant

**hydration and dietary modification**

- Long-term dietary modification is essential for preventing future calculi. This modification is centered on increasing fluid intake. At least 2 liters of urine output daily should be recommended to help prevent future episodes of stone formation.[94]

- Decreased dietary sodium, protein, and oxalate should be recommended for stone prevention. Increased citrus fruit intake is recommended to prevent stone recurrence.[95]

- Normal calcium intake is recommended.[95] Dietary calcium restriction can lead to less binding of calcium to oxalate in the GI tract, promoting hyperoxaluria and increased stone formation.[106]

#### hyperuricosuria and/or uric acid stones

**adjunct xanthine oxidase inhibitor ± alkalinization therapy**

Treatment recommended for SOME patients in selected patient group

**Primary options**

- **potassium citrate**: 30-60 mEq/day orally given in 3-4 divided doses OR

- **allopurinol**: 100-300 mg orally once daily

**Secondary options**

- **sodium bicarbonate**: 4 g orally initially, followed by 1-2 g every 4-6 hours, maximum 16 g/day OR

- **sodium bicarbonate**: 4 g orally initially, followed by 1-2 g every 4-6 hours, maximum 16 g/day
  - **allopurinol**: 100-300 mg orally once daily
Ongoing

Tertiary options

» febuxostat: 40-80 mg orally once daily
An increased risk of death has been reported with febuxostat compared to allopurinol. The FDA recommends that febuxostat should only be prescribed in patients who cannot tolerate, or have failed treatment with, allopurinol. US Food and Drug Administration. FDA adds Boxed Warning for increased risk of death with gout medicine Uloric (febuxostat). 21 February 2019 [internet publication]. https://www.fda.gov/Drugs/DrugSafety/ucm631182.htm

» Hyperuricosuria is treated with allopurinol. Elevated urinary uric acid levels (>800 mg/day) promote calcium oxalate and uric acid stones. Allopurinol is effective; it may work especially well in patients with gout. Febuxostat is an alternative agent which, at high dose, lowers urinary uric acid to a greater extent than allopurinol.[107] Febuxostat should only be prescribed for patients who can not tolerate allopurinol or when treatment with allopurinol has failed, and who have been counselled regarding cardiovascular risk.[97] Febuxostat should be avoided in patients with pre-existing major cardiovascular disease (e.g., myocardial infarction, unstable angina, stroke), unless no other therapy options are appropriate.[99] The double-blind Cardiovascular Safety of Febuxostat or Allopurinol in Patients with Gout (CARES) safety trial found that cardiovascular death and all cause mortality were significantly more common among patients taking febuxostat than allopurinol (4.3% vs. 3.2%, HR 1.34 [95% CI 1.03 to 1.73]; 7.8% vs. 6.4%, HR 1.22 [95% CI 1.01 to 1.47], respectively).[98] Treatment group did not differ with respect to a primary composite outcome of cardiovascular events.

» Uric acid stones are treated with alkalinization therapy, with or without allopurinol. Oral alkalinization therapy with medications such as potassium citrate and sodium bicarbonate may be beneficial for dissolving uric acid stones and preventing uric acid supersaturation. It may be used for treating uric acid stones that do not require urgent surgical treatment, as well as asymptomatic stones. The ideal goal for alkalinization therapy is to maintain urine pH between 6.5 and 7.0. In patients with CHF or renal failure, extra care should be taken when prescribing alkalinization therapy. Potassium citrate is first-line therapy.
<table>
<thead>
<tr>
<th>Ongoing</th>
<th>hypercalciuria</th>
<th>adjunct</th>
<th>diuretics/alkalinization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Treatment recommended for SOME patients in selected patient group</td>
</tr>
<tr>
<td>Primary options</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>chlorthalidone: 25-50 mg orally once daily</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>hydrochlorothiazide: 25-50 mg orally twice daily</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>indapamide: 1.25 to 2.5 mg orally once daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary options</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>potassium citrate: 10-20 mEq orally three to four times daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Given until urinary calcium normalizes.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Thiazide diuretics are generally combined with potassium citrate to prevent the development of hypokalemia and hypocitraturia associated with this therapy.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hypocitraturia</td>
<td>adjunct</td>
<td>alkalinization</td>
<td></td>
</tr>
<tr>
<td>Treatment recommended for SOME patients in selected patient group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary options</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>potassium citrate: 30-60 mEq/day orally given in 4 divided doses</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypocitraturia is treated with oral alkalinization therapy.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hyperoxaluria</td>
<td>adjunct</td>
<td>oxalate chelator/alkalinization</td>
<td></td>
</tr>
<tr>
<td>Treatment recommended for SOME patients in selected patient group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary options</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>calcium carbonate: 1-2 g/day orally given in 3-4 divided doses Dose refers to elemental calcium.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>calcium citrate: 1-2 g/day orally given in 3-4 divided doses Dose refers to elemental calcium.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Ongoing

OR

» **potassium citrate**: 30-60 mEq/day orally given in 4 divided doses

OR

» **magnesium oxide**: 400-800 mg orally two to three times daily

OR

» **cholestyramine**: 2-4 g orally four times daily

OR

» **pyridoxine (vitamin B6)**: 250-500 mg orally once daily

> For patients with elevated urinary oxalate level secondary to small bowel or ileal disease, oral administration of calcium with meals is recommended.[108]

> Cholestyramine is also effective for hyperoxaluria due to intestinal disease, but is poorly tolerated.

> Treatment with potassium citrate can fix the metabolic acidosis and hypokalemia that may be present and can increase the urinary citrate.

> Pyridoxine is indicated in primary hyperoxaluria.

### Cystinuria

**Adjunct**

**alkalinization/thiol binding agent/cystine chelator**

Treatment recommended for SOME patients in selected patient group

**Primary options**

» **potassium citrate**: 30-60 mEq/day orally given in 4 divided doses

**Secondary options**

» **tiopronin**: 800 mg/day orally in 3 divided doses, adjust dose according to response, usual dose is 1000 mg/day

OR

» **penicillamine**: 250 mg orally four times daily

> The goal for treatment of cystinuria is to decrease urine levels to <250 mg/L.
Management

<table>
<thead>
<tr>
<th>Ongoing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Conservative therapy involves increased hydration to keep urine output at ≥3 L/day in order to reduce the saturation of cystine and decreased sodium intake.</strong></td>
</tr>
<tr>
<td><strong>Alkalization of urine with potassium citrate leads to an increase in the solubility of cystine, although a substantial increment in solubility does not occur unless the pH is &gt;7.5.</strong></td>
</tr>
<tr>
<td><strong>If conservative therapy and alkalinization fail, chelating agents such as tiopronin or penicillamine should be used. Tiopronin has a better adverse-effect profile than penicillamine and is therefore the preferred therapy.</strong>[109]</td>
</tr>
</tbody>
</table>

---

**Struvite stones**

**Adjunct urease inhibitor**

Treatment recommended for SOME patients in selected patient group

**Primary options**

- **acetohydroxamic acid:** 250 mg orally three to four times daily

  - Acetohydroxamic acid, a urease inhibitor, may reduce the urine saturation of struvite and therefore prevent stone formation. It is best reserved for complex and recurrent struvite stones under secondary care supervision.

  - This medication has a high rate of adverse effects including deep vein thrombosis, tremors, and headaches.[14]

---

**Primary prevention**

The most important prevention measure to help prevent nephrolithiasis is adequate hydration.[21] [22] Fluid intake should be at least 2-3 liters per day. Dietary factors are also important. Measures should include decreasing dietary fat, protein, and sodium intake.

**Secondary prevention**

Fluid intake should be increased to maintain a urine output of more than 2 liters per day.[115] Long-term dietary modification is essential for preventing future calculi. Aim should be to obtain a 24-hour urine volume of at least 2 liters. Orange juice is able to bring the urinary citrate levels up much more than lemon juice because of its high potassium content.

Diet should be balanced with contributions from all food groups, without excesses of any kind.[38]

- Fruits, vegetables, and fibers: fruit and vegetable intake should be encouraged because of the beneficial effects of fiber. The alkaline content of a vegetarian diet also gives rise to a desirable increase in urinary pH.
An excessive intake of oxalate-rich products should be limited or avoided to prevent an oxalate load. This includes fruit and vegetables rich in oxalate such as wheat bran. This is particularly important in patients in whom a high oxalate excretion has been demonstrated. The following products have a high content of oxalate:

- Rhubarb, 530 mg oxalate/100 g
- Spinach, 570 mg oxalate/100 g
- Cocoa, 625 mg oxalate/100 g
- Tea leaves, 375-1450 mg oxalate/100 g
- Nuts, 200-600 mg oxalate/100 g
- Vitamin C is a precursor of oxalate, taking more than 500-1000 mg/day is not recommended.

Animal protein should be limited to 0.8 to 1.0 g/kg body weight. An excessive consumption of animal protein may give rise to hypercalciuria, hypocitraturia, low pH, hyperoxaluria, and hyperuricosuria.

Calcium intake should not be restricted unless there are very strong reasons because of the inverse relationship between dietary calcium and calcium stone formation. The minimum daily requirement for calcium is 800 mg and the general recommendation is 1000 mg/day (refers to elemental calcium). Calcium supplements are not recommended except in cases of enteric hyperoxaluria.

A high consumption of sodium causes hypercalciuria by reduced proximal tubular reabsorption of calcium. Urinary citrate is reduced. The risk of forming sodium urate crystals is increased and the effect of thiazide in reducing urinary calcium is counteracted by a high sodium intake. The daily sodium intake should not exceed 3 g.

The intake of food particularly rich in urate should be restricted in patients with hyperuricosuric calcium oxalate stone disease, as well as in patients with uric acid stone disease. The intake of urate should not exceed 500 mg/day. Examples of food rich in urate include:

- Calf thymus, 900 mg urate/100 g
- Liver, 260-360 mg urate/100 g
- Kidneys, 210-255 mg urate/100 g
- Poultry skin, 300 mg urate/100 g
- Herring with skin, sardines, anchovies, sprats, 260-500 mg urate/100 g.

Where specific metabolic abnormalities exist and are not responsive to dietary modification, specific preventive therapies may be required.[51] These include:

- Uric acid stones: urinary alkalinization with potassium citrate or sodium bicarbonate
- Hyperuricosuria, recurrent calcium oxalate stones, and normal urine calcium: allopurinol or febuxostat

An increased risk of death has been reported with febuxostat compared to allopurinol.[98] Febuxostat should only be prescribed for patients who can not tolerate allopurinol or where treatment with allopurinol has failed, and who have been counselled regarding cardiovascular risk.[97] In July 2019, the UK Medicines and Healthcare products Regulatory Agency issued a reminder to avoid treatment with febuxostat in patients with pre-existing major cardiovascular disease, unless no other therapy options are appropriate.[99]

- Hypercalciuria and recurrent calcium stones: thiazide diuretic with or without potassium supplementation (potassium citrate or potassium chloride)
- Hypocitraturia and recurrent calcium stones: urinary alkalinization (e.g., potassium citrate; sodium bicarbonate or sodium citrate can be considered if the patient is at risk for hyperkalemia)
- Hyperoxaluria: oxalate chelator (e.g., calcium, magnesium, or cholestyramine), potassium citrate, pyridoxine
• Cystinuria: urinary alkalinization with potassium citrate, thiol binding agent (e.g., tiopronin which is tolerated better than d-penicillamine)
• Struvite stones: urease inhibitor (e.g., acetohydroxamic acid), which is best reserved for complex/recurrent struvite stones in which surgical management has been exhausted.[14] Secondary care supervision should be employed as it can produce severe adverse effects such as phlebitis and hypercoagulability.

Patient discussions

Patients with nephrolithiasis should be advised to have a fluid intake of at least 2.0 to 2.5 liters per day, a low-protein diet, and a low-sodium diet to prevent nephrolithiasis.[114]
Monitoring

After stone passage or successful medical/surgical treatment, patients with risk of recurrence should be evaluated metabolically with serum studies and 24-hour urine for metabolic studies to determine whether any metabolic abnormalities exist that predispose to recurrent stone formation. Patients can then alter their diet/lifestyle or be placed on the appropriate medication if needed. Patients with cystine stones are more likely to require additional urologic interventions over time despite medical therapy and close follow-up.[113]

Periodic 24-hour urine monitoring should be performed to assess the efficacy of dietary/lifestyle changes and medications. Imaging with noncontrast computed tomography (CT) scan or KUB should be carried out every 6-12 months to monitor for recurrence or increase in the size of existing stones.
## Complications

<table>
<thead>
<tr>
<th>Complications</th>
<th>Timeframe</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>post-percutaneous nephrostolithotomy (PCNL) bleeding</strong></td>
<td>short term</td>
<td>medium</td>
</tr>
<tr>
<td>Can occur from creation of nephrostomy tract when gaining access to the kidney. A nephrostomy tube will usually tamponade the bleeding in the immediate postoperative period. Gross hematuria a week after PCNL should be evaluated with renal arteriogram to evaluate for pseudoaneurysm or arterial-venous fistula which can be treated with embolization.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>post-extracorporeal shock wave lithotripsy (ESWL) hematoma</strong></td>
<td>short term</td>
<td>low</td>
</tr>
<tr>
<td>Occurs due to disruption of blood vessels around and near kidney by shock waves. Managed conservatively with expectant management and blood transfusion if needed.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>post-ESWL, PCNL, or ureteroscopy treatment urosepsis</strong></td>
<td>short term</td>
<td>low</td>
</tr>
<tr>
<td>Should be treated with intravenous antibiotics and vasoactive medication when needed. Perform imaging to rule out obstruction or abscess.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>post-ESWL steinstrasse</strong></td>
<td>short term</td>
<td>low</td>
</tr>
<tr>
<td>Occurs due to stone fragments obstructing ureter and subsequent fragments not being able to pass. Patient may need a stent to adequately drain the kidney or a nephrostomy tube which facilitates spontaneous stone passage.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>post-ESWL, PCNL, or ureteroscopy ureteric injury</strong></td>
<td>short term</td>
<td>low</td>
</tr>
<tr>
<td>Can occur from scope, laser, or basket causing ureteric damage. Short-term ureteric stent is recommended.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>visceral organ injury</strong></td>
<td>short term</td>
<td>low</td>
</tr>
<tr>
<td>Can occur from creation of nephrostomy tract leading to bowel or liver injury.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>pneumothorax</strong></td>
<td>short term</td>
<td>low</td>
</tr>
<tr>
<td>May occur from creation of the nephrostomy tract with violation of the pleural cavity. Should be treated with a chest tube.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ureteric stricture</strong></td>
<td>long term</td>
<td>low</td>
</tr>
<tr>
<td>Can be a long-term sequela from ureteric injury. Patient may need subsequent procedure such as dilation or incision of the stricture.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Nephrolithiasis is a lifelong disease process. The rate of recurrence of nephrolithiasis is 50% at 5 years.\textsuperscript{[1]} The patients at highest risk for recurrence are frequently those who are not compliant with medical therapy and dietary/lifestyle modifications, or where underlying metabolic abnormalities exist. Residual stone fragments from surgery will usually spontaneously pass as long as their size is $<4$ mm.

The Return of Kidney Stones (ROKS) nomogram can be used to help to predict the risk of a second kidney stone.\textsuperscript{[112]}
# Diagnostic guidelines

## International

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Published by</th>
<th>Last published</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microhемaturia (<a href="https://www.auanet.org/guidelines">https://www.auanet.org/guidelines</a>)</td>
<td>American Urological Association; Society of Urodynamics, Female Pelvic Medicine &amp; Urogenital Reconstruction</td>
<td>2020</td>
</tr>
<tr>
<td>Surgical management of stones (<a href="https://www.auanet.org/guidelines">https://www.auanet.org/guidelines</a>)</td>
<td>American Urological Association; Endourology Society</td>
<td>2016</td>
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<tr>
<td>CUA guideline on the evaluation and medical management of the kidney stone patient (<a href="https://www.cua.org/guidelines">https://www.cua.org/guidelines</a>)</td>
<td>Canadian Urological Association</td>
<td>2016</td>
</tr>
<tr>
<td>Urolithiasis (<a href="https://uroweb.org/guideline/urolithiasis">https://uroweb.org/guideline/urolithiasis</a>)</td>
<td>European Association of Urology</td>
<td>2020</td>
</tr>
</tbody>
</table>
# Treatment guidelines

## International

<table>
<thead>
<tr>
<th>Title</th>
<th>Published by</th>
<th>Last published</th>
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<tbody>
<tr>
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<td>European Association of Urology</td>
<td>2020</td>
</tr>
</tbody>
</table>
Online resources

Evidence tables

What is the clinical effectiveness of nonsteroidal anti-inflammatory drugs (NSAIDs) in managing acute pain in people with symptomatic renal or ureteric stones?[56]

This table is a summary of the analysis reported in a guideline (underpinned by a systematic review) that focuses on the above important clinical question.

View the full source guideline (https://www.nice.org.uk/guidance/ng118/evidence)

Evidence C *

Confidence in the evidence is very low or low where GRADE has been performed and the intervention may be more effective/beneficial than the comparison for key outcomes. However, this is uncertain and new evidence could change this in the future.

Population: People with symptomatic renal or ureteric stones

Intervention: NSAIDs

Comparison: Opioid or acetaminophen or antispasmodic or placebo

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Effectiveness (BMJ rating)†</th>
<th>Confidence in evidence (GRADE)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs versus placebo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain (visual analogue scale [VAS]; 0-10), change &amp; final scores: follow-up 25 minutes to 10 days; range of scores: 0-10</td>
<td>Favors intervention</td>
<td>Very Low</td>
</tr>
<tr>
<td>Pain relief (VAS; 0-10): follow-up 180 minutes; range of scores: 0-10</td>
<td>Favors intervention</td>
<td>Moderate</td>
</tr>
<tr>
<td>Need for rescue medication: follow-up 25 minutes</td>
<td>Favors intervention</td>
<td>Low</td>
</tr>
<tr>
<td>No pain relief: follow-up 25 minutes</td>
<td>Favors intervention</td>
<td>Moderate</td>
</tr>
<tr>
<td>Pain relief, partial or complete: follow-up 25-30 minutes</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
</tbody>
</table>

NSAIDs versus paracetamol
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Effectiveness (BMJ rating)</th>
<th>Confidence in evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain (numerical rating scale [NRS] or VAS): follow-up 30 minutes; range of scores: 0-10</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
<tr>
<td>Reduction in pain by 50% or in NRS pain score &gt;3: follow up 30 minutes</td>
<td>No statistically significant difference</td>
<td>High</td>
</tr>
<tr>
<td>Persistent pain: follow-up 60 minutes</td>
<td>Favors intervention</td>
<td>Moderate</td>
</tr>
<tr>
<td>Pain relief</td>
<td>No statistically significant difference</td>
<td>Low or Very Low</td>
</tr>
<tr>
<td>Need for rescue medication: follow-up 30 minutes</td>
<td>Favors intervention</td>
<td>Moderate</td>
</tr>
<tr>
<td>Minor adverse events (unspecified, vomiting, abdominal pain, dizziness, epigastric pain)</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
<tr>
<td>NSAIDs versus opioids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain (VAS &amp; NRS), final and change scores: at 30-60 minutes; range of scores: 0-10</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
<tr>
<td>Pain (VAS) (at 30 minutes; range of scores: 1-10) or need for rescue medication (at 30-40 minutes)</td>
<td>Favors intervention</td>
<td>Very Low</td>
</tr>
<tr>
<td>Pain relief (no pain relief, partial pain relief, or complete pain relief): up to 60 minutes follow-up/at discharge</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
<tr>
<td>Persistent pain: at 60 minutes</td>
<td>Favors intervention</td>
<td>High</td>
</tr>
<tr>
<td>Reduction in pain NRS score &gt;3 at 30 minutes</td>
<td>No statistically significant difference</td>
<td>High</td>
</tr>
<tr>
<td>Reduction in pain by 50% at 30 minutes</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
</tbody>
</table>
### Evidence tables

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Effectiveness (BMJ rating)†</th>
<th>Confidence in evidence (GRADE)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major adverse events (significant side effects): follow-up not reported</td>
<td>No statistically significant difference</td>
<td>Low</td>
</tr>
<tr>
<td>Minor adverse events[^d]</td>
<td>Occurs more commonly with opioids compared with NSAIDs (favors intervention)</td>
<td>Moderate to Very Low[^d]</td>
</tr>
<tr>
<td>Minor adverse events (urinary retention) at 60 minutes</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
<tr>
<td>Minor adverse events (pain at injection site) at 12 hours</td>
<td>Occurs more commonly with intramuscular NSAIDs compared with intramuscular opioids (favors comparison)</td>
<td>Low</td>
</tr>
</tbody>
</table>

**NSAIDs versus antispasmodics**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Effectiveness (BMJ rating)†</th>
<th>Confidence in evidence (GRADE)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain (VAS, 0-10); follow-up 40 minutes; range of scores: 0-10</td>
<td>No statistically significant difference</td>
<td>Low</td>
</tr>
<tr>
<td>Complete pain relief: follow-up 30 minutes</td>
<td>Favors intervention</td>
<td>Low</td>
</tr>
<tr>
<td>Need for rescue medication: follow-up 40-60 minutes</td>
<td>No statistically significant difference</td>
<td>Very Low</td>
</tr>
<tr>
<td>Minor adverse events (sleepiness)</td>
<td>Occurs more commonly with antispasmodics compared with NSAIDs (favors intervention)</td>
<td>Moderate</td>
</tr>
<tr>
<td>Minor adverse events (dizziness)</td>
<td>No statistically significant difference</td>
<td>Low</td>
</tr>
</tbody>
</table>

### Recommendations as stated in the source guideline

Offer an NSAID by any route as first-line treatment for adults, children, and young people with suspected renal colic.

**Note**

- Most of the studies evaluated an intravenous or intramuscular route of administration, with just one study using an oral preparation and four studies using a rectal preparation. The guideline committee acknowledged that the latter two are more commonly used and that the results may not reflect practice in the UK; however, they also noted that the evidence was not sufficient to include any one route of administration in the recommendation.

- The outcome of partial pain relief at discharge was graded as low-quality evidence while complete pain relief at discharge/unclear time point was graded as very low-quality evidence. Three randomized controlled...
Nephrolithiasis

Evidence tables

Trials underpinned these outcomes (one for partial pain relief and two for complete pain relief), showing no statistically significant difference between treatment groups.

- Follow-up times range from 60 minutes to 14 days for unspecified and vomiting outcomes, but are not reported for abdominal pain, dizziness, and epigastric pain.

- Minor adverse events include: unspecified at 14 days; nausea and vomiting at 30 minutes to 24 hours; vomiting, nausea, dizziness with unclear time point or not reported; and sleepiness at 1-24 hours or not reported. The evidence underpinning these outcomes ranged from moderate to very low quality.

* Evidence levels

The Evidence level is an internal rating applied by BMJ Best Practice. See the EBM Toolkit (https://bestpractice.bmj.com/info/evidence-tables/) for details.

Confidence in evidence

A - High or moderate to high
B - Moderate or low to moderate
C - Very low or low

† Effectiveness (BMJ rating)

Based on statistical significance, which demonstrates that the results are unlikely to be due to chance, but which does not necessarily translate to a clinical significance.

‡ Grade certainty ratings

<table>
<thead>
<tr>
<th>High</th>
<th>The authors are very confident that the true effect is similar to the estimated effect.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>The authors are moderately confident that the true effect is likely to be close to the estimated effect.</td>
</tr>
<tr>
<td>Low</td>
<td>The authors have limited confidence in the effect estimate and the true effect may be substantially different.</td>
</tr>
<tr>
<td>Very Low</td>
<td>The authors have very little confidence in the effect estimate and the true effect is likely to be substantially different.</td>
</tr>
</tbody>
</table>

BMJ Best Practice EBM Toolkit: What is GRADE? (https://bestpractice.bmj.com/info/toolkit/learn-ebm/what-is-grade/)
Key articles


References


References


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Please note that recommended formulations and doses may differ between drug databases drug names and brands, drug formularies, or locations. A local drug formulary should always be consulted for full prescribing information.

Treatment recommendations in BMJ Best Practice are specific to patient groups. Care is advised when selecting the integrated drug formulary as some treatment recommendations are for adults only, and external links to a paediatric formulary do not necessarily advocate use in children (and vice-versa). Always check that you have selected the correct drug formulary for your patient.

Where your version of BMJ Best Practice does not integrate with a local drug formulary, you should consult a local pharmaceutical database for comprehensive drug information including contraindications, drug interactions, and alternative dosing before prescribing.

Interpretation of numbers

Regardless of the language in which the content is displayed, numerals are displayed according to the original English-language numerical separator standard. For example 4 digit numbers shall not include a comma nor a decimal point; numbers of 5 or more digits shall include commas; and numbers stated to be less than 1 shall be depicted using decimal points. See Figure 1 below for an explanatory table.

BMJ accepts no responsibility for misinterpretation of numbers which comply with this stated numerical separator standard.

This approach is in line with the guidance of the International Bureau of Weights and Measures Service.

Figure 1 – BMJ Best Practice Numeral Style
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