BMJ Best Practice

Nephrolithiasis

The right clinical information, right where it's needed

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Summary

- Common condition with a 7% to 10% lifetime risk for women and men, respectively.
- Patients typically present with acute renal colic, although some patients are asymptomatic.
- Multiple risk factors include chronic dehydration, diet, obesity, positive family history, specific medicines, and various metabolic abnormalities.
- Non-contrast CT scan of the abdomen/pelvis is the preferred imaging modality.
- Treatment consists of both medical and surgical therapies.
- 24-hour urine tests are recommended for most stone formers to determine cause of stone formation and optimal treatment to help prevent future stone episodes.

BASICS

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]

Epidemiology

The lifetime prevalence of nephrolithiasis is estimated to be between 5% and 12%, with the probability of having a stone varying according to age, gender, race, and geographical location.[5] [6] [7] Nephrolithiasis typically affects adult men more commonly than adult women, with a male to female ratio of 2 or 3:1.[8] [9] [10] However, there is evidence that this difference in incidence between men and women is narrowing.[11] In US men, the highest prevalence of nephrolithiasis is found in white men, followed by Hispanic men, Asian men, and black men.[9] Among US women, the prevalence is highest among white women but lowest among Asian women.[12] Historically, stone occurrence was relatively uncommon before age 20 years but the incidence of stones in children and adolescents is rising. In adults, stone incidence peaks in the fourth to sixth decades of life.[13] Nephrolithiasis has a higher prevalence in hot, arid, or dry climates such as the mountains, desert, or tropical areas. Worldwide, regions of high stone prevalence include the US, British Isles, Scandinavian and Mediterranean countries, northern India and Pakistan, northern Australia, central Europe, portions of the Malay peninsula, and China.[14] Heat exposure and dehydration are risk factors for nephrolithiasis. The prevalence and incident risk of nephrolithiasis are directly correlated with weight and BMI in both genders, although the magnitude of this association is greater in women than in men.[15] [16]

Aetiology

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. 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.[17] Supersaturation depends on urine pH, ionic strength, solute concentration, and solute chemical interaction. The higher the concentration of 2 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.[1] 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, crystallisation may not occur because of prevention from urinary inhibitors. Both urinary calcium and oxalate are important and equal contributors to calcium oxalate stone formation.[18] Several factors increase calcium oxalate supersaturation in urine. These include low urine volume and low citrate, and increased calcium, oxalate, and uric acid.[18]

Pathophysiology

There are differing theories as to the exact pathophysiology of stone formation. 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.[19] Plaques were composed of calcium phosphate/apatite deposits, localised 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 non-stone 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 intra-tubular hydroxyapatite crystals in collecting ducts, with dilation and damage to lining cells proximal to obstruction,[19] 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. This causes nerve endings to stretch and therefore the sensation of renal colic.[1] Pain from urinary calculi can also be due to local inflammatory mediators, oedema, hyperperistalsis, and mucosal irritation.[1]

Classification

Chemical composition of renal calculi

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

- Calcium stones: 80% of renal calculi[2]
- Calcium oxalate: 80% of all calcium stones; risk factors include low urine volume, hypercalciuria, hyperuricosuria, hyperoxaluria, and hypocitraturia
- Calcium phosphate (hydroxy apatite): 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: 10% to 20% of renal calculi; most commonly due to urinary pH <5.5, although hyperuricosuria can also contribute[3]
- 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[2]
- 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. *E coli* is not a urease-producing organism.[4]

Primary prevention

The most important primary prevention measure to help prevent nephrolithiasis is adequate hydration. Fluid intake should be at least 2 to 3 litres per day. Dietary factors are also important. Measures should include decreasing dietary fat, protein, and sodium intake.[1]

Secondary prevention

Long-term dietary modification is essential for preventing future calculi. Aim should be to obtain a 24-hour urine volume of at least 2 litres. 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.[26]

- Fruits, vegetables, and fibres: fruit and vegetable intake should be encouraged because of the beneficial effects of fibre. 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 to 1450 mg oxalate/100 g
    - Nuts, 200 to 600 mg oxalate/100 g
    - Vitamin C is a precursor of oxalate, taking more than 500 to 1000 mg/day is not recommended.
- Animal protein should be limited to 0.8 to 1 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 re-absorption 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 to 360 mg urate/100 g
- Kidneys, 210 to 255 mg urate/100 g
- Poultry skin, 300 mg urate/100 g
- Herring with skin, sardines, anchovies, sprats, 260 to 500 mg urate/100 g.

Where specific metabolic abnormalities exist and are not responsive to dietary modification, specific preventative therapies may be required.[64] These include:

- Uric acid stones: urinary alkalinisation with potassium citrate or sodium bicarbonate
- Hyperuricosuria, recurrent calcium oxalate stones, and normal urine calcium: allopurinol or febuxostat
- Hypercalciuria and recurrent calcium stones: thiazide diuretic with or without potassium supplementation (potassium citrate or potassium chloride)
- Hypocitraturia and recurrent calcium stones: urinary alkalinisation (e.g., potassium citrate; sodium bicarbonate or sodium citrate can be considered if the patient is at risk for hyperkalaemia)
- Hyperoxaluria: oxalate chelator (e.g., calcium, magnesium, or cholestyramine), potassium citrate, pyridoxine
- Cystinuria: urinary alkalinisation 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. Secondary care supervision should be employed as it can produce severe adverse effects such as phlebitis and hypercoagulability.

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 towards 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 non-obstructing. 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 haematuria, evidence of an obstructive uropathy, or sepsis with fever, tachycardia, and hypotension.

Step-by-step diagnostic approach

A diagnosis of nephrolithiasis may be suspected based on the clinical history, physical examination 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 haematuria. 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 examination

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, FBC, and serum chemistry to include electrolytes, serum urea/creatinine (to assess renal function), calcium, phosphorus, and uric acid. Urinalysis is helpful in confirming a diagnosis of renal stones because microscopic haematuria is present in the majority of patients. However, the absence of haematuria does not exclude nephrolithiasis.[1] Presence of >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.

A raised WBC count may indicate infection (pyelonephritis or UTI). Hypercalcaemia may suggest hyperparathyroidism as an underlying aetiology; hyperuricaemia may indicate gout. In women of childbearing age, a pregnancy test should be done prior to imaging with ionising 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 diarrhoea, 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 aetiology. Stones are analysed 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 examination, and laboratory tests, then imaging is indicated. Non-contrast helical CT (NCCT) scan is the preferred imaging modality due to its high sensitivity and specificity. CT accurately determines presence, size, and location of stones; if it is negative, nephrolithiasis can be ruled out with high likelihood. 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 can also be ordered 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 judgement. In pregnant patients the diagnosis may be made with ultrasound or, in select situations when ultrasound is not adequate, with MRI scans (finding of a filling defect in ureter).

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, although it can be operator dependent and has low sensitivity for diagnosing mid and distal ureteric stones. However, it does have a role as first-line imaging in suspected nephrolithiasis in pregnancy. Transvaginal ultrasound can assist with this by determining if ureteral dilation extends beyond the pelvic brim and it can diagnose stones in the distal ureter. 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. Renal ultrasound also has the advantage of not exposing patients to ionising radiation. MRI is a useful second-line imaging modality that can also be performed without radiation exposure.

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, multicentre study showed no significant difference in high-risk diagnoses, serious adverse events, subsequent emergency room visits, or hospitalisations in those undergoing CT or renal ultrasound in this setting. However, some patients who had an ultrasound did go on to need CT imaging, but it is not clear from this study what factors predicted the need for CT. Further study in this regard would help determine in which patients to use renal ultrasound as an initial diagnostic tool.[25]

According to guidelines published by the American College of Obstetrics and Gynecology, 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 after the first trimester to aid in difficult-to-diagnose cases.[26] [27] Guidelines from the European Association of Urology note that x-ray imaging during the first trimester should be reserved for diagnostic and therapeutic situations in which alternative imaging methods have failed.[26]

An IVP can provide both anatomical 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 IV 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.

According to American Urological Association imaging guidelines for ureteral stones,[28] a low-dose non-contrast CT (<4 mSv) is preferred for patients with a Body Mass Index (BMI) ≤30 kg/m^2, as this limits the potential radiation exposure while maintaining both sensitivity and specificity at 90% or higher. However, low-dose CT is not recommended for those with a BMI >30 kg/m^2, owing to lower sensitivity and specificity in these patients. 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.[29] [30] [31] The guidelines recommend that a standard KUB x-ray should be performed if the stone is not visible on the CT scout, so that patients with stones identifiable on initial KUB x-ray or CT scout can be followed by KUB. Sonogram should be the preferred modality for evaluating children because of radiation risks; however, low-dose CT should be considered if sonogram is non-diagnostic. The guidelines further recommend that renal ultrasonography should be the initial imaging modality of choice during pregnancy. In the first trimester, consideration can be given to MRI without contrast as the second-line imaging modality to identify the level of obstruction and provide estimation of stone size. Low dose CT may be performed for women in the second and third trimesters if ultrasonography is non-diagnostic. This recommendation is further endorsed by the American Congress of Obstetricians and Gynecologists (ACOG), who suggest that an exposure of <5 rads (<50 mGy, a threshold well above the average for a low-dose CT) is not associated with the development of fetal anomalies or fetal loss.[32]

Risk factors

Strong

high protein intake

- A higher energy diet with more protein may be associated with a higher incidence of stones.[1] 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. This promotes calcium salt crystallisation due to urinary saturation of monosodium urate and calcium oxalate/calcium phosphate being increased. Salt excess can also can 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.[9] Among US women, the prevalence is highest among white women but lowest among Asian women.[12]

male sex

- Nephrolithiasis typically affects adult men more commonly than adult women, with a male to female ratio of 2 or 3:1.[8] [9] [10] However, there is evidence that this difference in incidence between men and women is narrowing.[20]

dehydration

- Fluid intake is very important and should be at least 2 to 3 litres per day.[1] In two large observational studies, fluid intake was found to be inversely related to the risk of renal stone formation.[21] [22] 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.[21] [22]
- 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.[18]

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.[1]

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.[18]

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, July through September, with the peak occurring within 1 to 2 months of maximal mean temperatures.[23] [24]
- In the US, prevalence of nephrolithiasis in the south-eastern states ('stone belt') is nearly double that in other areas.

family history

- 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 a family history have a higher incidence of multiple stones and early recurrence.[1]

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, vitamins C and D, protease inhibitors (e.g., indinavir), ephedrine, guaifenesin, triamterene, and sulphadiazine.
- Most of these medications lead to higher urinary levels of calcium, uric acid, sodium, or oxalate, in turn promoting stone formation.

History & examination factors

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.[33] [34]

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.

haematuria (common)

- Microscopic haematuria is present on urinalysis up to 85% to 90% of cases of nephrolithiasis.[1] Rarely, macroscopic haematuria can be present.

testicular pain (common)

- As stones pass through the ureter, flank pain can radiate towards the groin and testicle, leading to testicular pain.

obesity (common)

- Increased incidence of renal stones is correlated with increased BMI for both genders.

family history (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.

groin pain (uncommon)

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

Diagnostic tests

1st test to order

Test	Result
urinalysis • Microhaematuria is seen in the majority of patients with renal stones.	**may be normal; dipstick positive for leukocytes, nitrates, blood; microscopic analysis positive for WBCs, RBCs, or bacteria**
FBC and differential • A raised WBC may suggest infection (pyelonephritis or UTI).	**variable**
serum electrolytes, urea, and creatinine • These include sodium, potassium, chloride, bicarbonate, creatinine, urea, calcium, uric acid, and phosphorus. • Hypercalcaemia may suggest hyperparathyroidism as an underlying aetiology; hyperuricaemia may indicate gout.	**variable**
urine pregnancy test • Prior to exposure to ionising radiation. • To exclude ectopic pregnancy.	**negative**
non-contrast helical CT scan • Non-contrast helical CT scan (NCCT) is the preferred imaging modality for nephrolithiasis due to its high sensitivity and specificity, and should be ordered as soon as nephrolithiasis is suspected. • A low-dose scan (<4 mSv) is preferred for patients with a body mass index (BMI) ≤30 kg/m^2, as this imaging study limits the potential radiation exposure while maintaining both sensitivity and specificity at 90% or higher. However, low-dose CT is not recommended for those with a BMI >30 kg/m^2, owing to lower sensitivity and specificity in these patients.[28] A size-adjusted, reduced-dose CT protocol has been shown to be 96% sensitive for the detection of ureteral stones requiring intervention in all patients, regardless of BMI.[35] • NCCT accurately determines presence, size, and location of stones; if negative, nephrolithiasis can be ruled out with high likelihood. • According to guidelines published by the American College of Obstetrics and Gynecology, 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 after the first trimester to aid in difficult-to-diagnose cases.[26] [27] Guidelines from the European Association of Urology note that x-ray imaging during the first trimester should be reserved for diagnostic and therapeutic situations in which alternative imaging methods have failed.[26]	**calcification seen in renal collecting system or ureter; hydronephrosis; perinephric stranding (indicative of inflammation or infection)**
stone analysis • Provides information on chemical composition and aetiology. Stones are analysed after they are extracted during surgery or when patients expel and collect them for analysis.	**stone composition**

Other tests to consider

Test	Result
KUB • Plain abdominal film should be ordered initially along with CT scan to determine whether stone is radiolucent. Up to 85% of stones are visible on KUB, although uric acid stones are radiolucent.[36] • 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.[28] • Before definitive surgical therapy, a KUB should be ordered to ensure that patient has not already passed the stone.	**calcification seen within urinary tract**
renal ultrasound • In pregnancy, renal ultrasound is a helpful first-line imaging modality. It should also be the modality of choice for evaluating children because of radiation risk. However, low-dose CT should be considered in children if sonogram is non-diagnostic.[28]	**calcification seen within urinary tract, along with dilation**
IVP • This test has for the most part been replaced by the 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.	**calcification seen within urinary tract or a filling defect seen when dye is passing through the kidney and down the ureter**
24-hour urine monitoring • Helps in determining underlying metabolic cause or aetiology 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.	**increased or decreased values for urinary electrolytes; reduced urine volume**
spot urine for cystine • A urine screen for cystine should be considered if the diagnosis of cystinuria is not excluded by stone analysis.	**cystinuria**

DIAGNOSIS

Differential diagnosis

Condition	Differentiating signs / symptoms	Differentiating tests
Acute appendicitis	• Usually presents with right lower quadrant pain, fever, and signs of peritonitis.	• Urinalysis is negative. • Non-contrast helical CT scan (NCCT) shows dilation of appendix and absence of renal stones.
Ectopic pregnancy	• 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 examination.	• Urine pregnancy test is positive and serum hCG elevated. • Ultrasound reveals presence of mass in fallopian tubes.

Condition	Differentiating signs / symptoms	Differentiating tests
Ovarian cyst	• May present with lower pelvic/abdominal discomfort and/or dyspareunia; may be cyclical. • Palpable mass on pelvic examination.	• Abdominal ultrasound shows cystic adnexal lesion; free fluid in the peritoneum. • NCCT shows absence of renal stones.
Diverticular disease	• May present with left lower quadrant pain or abdominal pain as opposed to flank pain.	• Technetium pertechnetate scan may show enhancement of diverticulum if gastric mucosa is present. • NCCT shows absence of renal stones.
Bowel obstruction	• Bowel obstruction patients present with abdominal distension, vomiting, and constipation.	• Abdominal x-ray may show volvulus. • NCCT shows collapsed bowel with proximal dilation and absence of renal stones.
Acute pancreatitis	• History of gallstones or alcohol abuse. • These patients typically have epigastric pain that radiates to the back, as opposed to flank pain.	• NCCT shows inflammation of the pancreas and absence of renal stones. • 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 raised in pancreatitis and usually normal in stone disease.
Peptic ulcer disease	• May or may not have a history of peptic ulcer disease. Pain is abrupt, severe in intensity, and may be localised to right lower quadrant; often related to eating meals.	• Erect CXR and abdominal x-ray may show free air under the diaphragm. • Endoscopy shows peptic ulcer. • NCCT shows absence of renal stones.
Gastroenteritis	• These patients typically have diffuse abdominal pain and no flank pain. Vomiting is prominent and patient may have diarrhoea.	• Stool specimen may be positive for culture. • 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.

Condition	Differentiating signs / symptoms	Differentiating tests
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 oedematous 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 oedematous ovary in absence of renal stones.
Musculoskeletal back pain	• Patient may present with unilateral or bilateral middle and/or lower back pain.	• Point tenderness upon muscular palpation. • NCCT is normal with absence of renal stones.
Mesenteric ischaemia	• Patients typically present with acute peri-umbilical abdominal pain with nausea and vomiting.	• NCCT shows bowel wall thickening, intestinal pneumatosis, portal venous gas, with absence of renal stones.
Constipation	• Patients typically present with left lower quadrant pain and abdominal distension.	• NCCT shows excessive stool in colon or rectum in absence of renal stones.
Cholecystitis or biliary colic	• Patient may present with right upper quadrant and/or epigastric pain, fevers, and leukocytosis.	• Abdominal ultrasound will show gallstones with gallbladder wall thickening. • NCCT shows gallstones, gallbladder wall oedema, and high attenuation bile in the absence of renal stones.

Step-by-step treatment approach

The main goal of initial treatment for an acute stone event is symptomatic relief with hydration and analgesia/anti-emetics as needed. If signs and symptoms of infection are present, and the patient has a stone in the kidney or ureter, immediate urological consultation should be initiated as urinary tract infection in the setting of an obstructing stone is an emergency which requires antibiotics and renal decompression to decrease the chance of life-threatening septic shock.[37] If the patient has a stone present without signs or symptoms of infection, he or she can be managed conservatively with opioids and non-steroidal anti-inflammatory drugs (NSAIDs); 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 and calcium channel blockers, can increase ureteral stone passage rate and decrease the time to stone passage in stones ≤ 10 mm in size.[38] 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 preventative measures should be tailored towards underlying metabolic factors that promote stone formation. For all such patients, dietary modification with adequate hydration is an essential aspect of on-going management.

Urgent consideration: obstruction and infection

Patients with urinary calculi along with fever and other signs or symptoms of infection need emergency urological consultation for drainage and intravenous (IV) 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 ureteric colic includes conservative therapy such as hydration, analgesia (intravenous pain relief with morphine or the NSAID ketorolac), and anti-emetics.

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. Many ureteric stones <10 mm pass spontaneously (68% of stones ≤5 mm pass spontaneously; 47% of stones >5 mm and ≤10 mm pass spontaneously with exact passage rate related to both stone size and location).[39]

Medical expulsive therapy (MET), using an alpha-blocker such as tamsulosin or alfuzosin, may be of benefit in promoting stone passage.[39] [40] [41] [42] The selective alpha-1a receptor antagonist silodosin has also been shown to increase the rate of distal ureteral stone passage.[42] These agents can cause ureteric relaxation of smooth muscle and antispasmodic activity of the ureter leading to stone passage.[43] However, a large, multicentre, randomised, placebo-controlled trial conducted in over 1100 patients with ureteral colic showed that tamsulosin and nifedipine did not increase the likelihood of spontaneous stone passage over a 4-week period.[44] 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 non-contrast 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 anatomical 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, open surgery is now rarely performed.

Calculi between 10 mm and 20 mm are in general treated with extracorporeal shock wave lithotripsy (ESWL) or ureteroscopy as first-line therapy. However for ESWL, the results for lower pole stones are inferior (55%) to upper and mid pole stones (71.8% and 76.5%, respectively).[45] Percutaneous nephrostolithotomy (PCNL) for calculi between 10 mm and 20 mm achieves better stone-free rates for lower pole stones than ESWL (73% versus 57%).[46] Similarly, cystine stones >15 to 20 mm and brushite stones respond poorly to ESWL.[47] 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.[48] 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.[49]

For solitary renal calculi <10 mm, ESWL and ureteroscopy are both valid options. Ureteroscopy or PCNL can be utilised when ESWL fails or in the presence of anatomical abnormalities or other special circumstances.[50]

- 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 anaesthesia. Treatment with tamsulosin appears to be effective in assisting stone clearance in patients with renal and ureteric calculi.[51]While ESWL has been shown to have limited success with lower pole stones there is evidence to suggest that ancillary manoeuvres such as percussion, diuresis, and inversion increase stone-free rates.[52]Contraindications to ESWL treatment include pregnancy, severe skeletal malformations, severe obesity, aortic and/or renal artery aneurysms, uncontrolled HTN, disorders of blood coagulation, and uncontrolled urinary tract infections.[53] [54]

- Ureteroscopy involves placing a small semi-rigid or flexible scope per urethra and into the ureter and/or kidney. Once the stone is visualised, it can be fragmented using a laser 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 anaesthesia 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.

- For patients requiring stone removal, both ESWL and ureteroscopy are considered acceptable first-line surgical treatments for stones in the ureter[39] Ureteroscopic stone-free rates are better than ESWL rates for distal ureteric stones regardless of size (overall 94% versus 74%) and for proximal ureteric stones >10 mm. The stone-free rates for mid-ureteric stones are not significantly different between ureteroscopy and ESWL. ESWL had significantly better stone-free rates for proximal ureteric stones <10 mm compared to ureteroscopy.[39]

- 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.[39] [55] [56]

- 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.[57] Percutaneous access into the kidney is gained from the flank and then a large sheath is placed into the kidney. Once this is done, 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 mm to 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.[58]

- Laparoscopic and open surgical stone removal: 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 endourological 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,[39] anatomical 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.[26]

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.[59] It has been reported that 48% to 80% of stones pass spontaneously during pregnancy.[27] [60]

Abdominal ultrasonography is the initial imaging study of choice to diagnose a stone in a pregnant patient; however, it can be difficult to differentiate between physiological dilation of the kidney and ureter, and that secondary to stone disease. Transvaginal ultrasound can assist with this by determining if ureteral dilation extends beyond the pelvic brim and it can diagnose stones in the distal ureter. MRI is a useful second-line imaging modality that can be performed without radiation exposure. According to guidelines published by the American College of Obstetrics and Gynecology, 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 after the first trimester to aid in difficult-to-diagnose cases.[26] [27] Guidelines from the European Association of Urology and the American Urological Association note that x-ray imaging during the first trimester should be reserved for diagnostic and therapeutic situations in which alternative imaging methods have failed.[26] [39]

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 must be changed every 4 to 6 weeks due to rapid encrustation that occurs 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.[61] ESWL and PCNL are contraindicated in pregnancy.

Ongoing medical therapy and dietary modification

Oral alkalinisation 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 alkalinisation therapy 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 alkalinisation therapy. Alkalinisation 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 centred on increasing fluid intake. At least 2 litres of urine output daily should be recommended to help prevent future episodes of stone formation.[62]

Decreased dietary sodium, protein, and oxalate should be recommended for stone prevention. Increased citrus fruit intake is recommended to prevent stone recurrence.[63] Normal calcium intake (i.e., 1000 mg/day to 1200 mg/day) is recommended.[63] 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 preventative therapies may be required.[64] These include:

- Uric acid stones: urinary alkalinisation with potassium citrate or sodium bicarbonate
- Hyperuricosuria, recurrent calcium oxalate stones, and normal urine calcium: allopurinol or febuxostat
- Hypercalciuria and recurrent calcium stones: thiazide diuretic with or without potassium supplementation (potassium citrate or potassium chloride)
- Hypocitraturia and recurrent calcium stones: urinary alkalinisation (e.g., potassium citrate; sodium bicarbonate or sodium citrate can be considered if the patient is at risk for hyperkalaemia)[65]
- Hyperoxaluria: oxalate chelator (e.g., calcium, magnesium, or cholestyramine), potassium citrate, pyridoxine
- Cystinuria: urinary alkalinisation 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. Secondary care supervision should be employed as it can produce severe adverse effects such as phlebitis and hypercoagulability.

Treatment details overview

Consult your local pharmaceutical database for comprehensive drug information including contraindications, drug interactions, and alternative dosing. (see Disclaimer)

Presumptive		(summary)
Patient group	**Tx line**	**Treatment**

Presumptive (summary)

acute renal colic non-pregnant	1st	conservative management (hydration, pain control, and anti-emetics)

Acute (summary)

Patient group	Tx line	Treatment
confirmed stone: no evidence of obstruction non-pregnant	1st	hydration, pain control, and anti-emetics
demonstrated bacteriuria	adjunct	antibiotic therapy
	adjunct	surgical decompression
stones ≤10 mm	adjunct	medical expulsive therapy (MET)
stones ≥10 mm or failed medical therapy	adjunct	surgical removal
confirmed stone: with evidence of obstruction non-pregnant	1st	hydration, pain control, and anti-emetics
	plus	surgical decompression
	plus	surgical removal
with infection	plus	antibiotic therapy
pregnant	1st	specialist referral

Ongoing (summary)

Patient group	Tx line	Treatment
following an acute episode non-pregnant	1st	hydration and dietary modification
hyperuricosuria and/or uric acid stones	adjunct	alkalinisation/allopurinol
hypercalciuria	adjunct	diuretics/alkalinisation
hypocitraturia	adjunct	alkalinisation
hyperoxaluria	adjunct	oxalate chelator/alkalinisation
cystinuria	adjunct	alkalinisation/thiol binding agent/cystine chelator
struvite stones	adjunct	urease inhibitor

Treatment options

Presumptive

Patient group	Tx line	Treatment
acute renal colic non-pregnant	**1st**	**conservative management (hydration, pain control, and anti-emetics)** » Acute medical treatment for suspected renal or ureteric colic includes conservative therapies such as hydration, analgesia (non-steroidal anti-inflammatory drugs such as ketorolac are used initially if normal renal function), and an anti-emetic. **Primary options** » crystalloids **--AND--** » ketorolac: 30 mg intravenously initially, followed by 15 mg every 6-8 hours for 3 days only **-and/or-** » morphine sulphate: 1-5 mg intravenously every 4 hours when required **--AND--** » ondansetron: 4 mg intravenously every 8 hours when required

Acute

Patient group	Tx line	Treatment
confirmed stone: no evidence of obstruction non-pregnant	**1st**	**hydration, pain control, and anti-emetics** » Acute medical treatment for confirmed stones with renal or ureteric colic includes conservative therapies such as hydration, analgesia (non-steroidal anti-inflammatory drugs such as ketorolac are used initially if normal renal function), and an anti-emetic. **Primary options** » crystalloids **--AND--** » ketorolac: 30 mg intravenously initially, followed by 15 mg every 6-8 hours for 3 days only **-and/or-** » morphine sulphate: 1-5 mg intravenously every 4 hours when required **--AND--** » ondansetron: 4 mg intravenously every 8 hours when required
demonstrated bacteriuria	**adjunct**	**antibiotic therapy**

TREATMENT

Acute

Patient group	Tx line	Treatment
		» If infection is present, but no obstruction or signs of sepsis, the patient can be treated with conservative therapy and antibiotics. » Empirical antibiotic therapy should be started pending sensitivity results based on urinalysis cultures. **Primary options** » trimethoprim/sulfamethoxazole: 160/800 mg orally twice daily for 1-2 weeks Dose refers to trimethoprim component. **OR** » nitrofurantoin: 100 mg orally twice daily for 1-2 weeks
	adjunct	**surgical decompression** » Drainage can be accomplished in 2 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.
stones ≤10 mm	adjunct	**medical expulsive therapy (MET)** » 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.[38] » Using an alpha-blocker, such as tamsulosin or alfuzosin or silodosin, may be of benefit in promoting stone passage.[39] [40] [41] [42] However, a large, multicentre, randomised, placebo-controlled trial conducted in over 1100 patients with ureteral colic showed that tamsulosin and nifedipine did not increase the likelihood of spontaneous stone passage over a 4-week period.[44] » These agents should be given for 4 to 6 weeks or until the stone is passed. If the stone has still not passed by that time, surgical intervention is recommended. **Primary options** » tamsulosin: 0.4 mg orally once daily **OR** » alfuzosin: 10 mg orally once daily **OR**

Acute

Patient group	Tx line	Treatment
		» silodosin: 8 mg orally once daily
stones ≥10 mm or failed medical therapy	**adjunct**	**surgical removal** » 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.[57] » 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.
confirmed stone: with evidence of obstruction non-pregnant	**1st**	**hydration, pain control, and anti-emetics** » Patients with obstructed urinary calculi with infection require emergency urological consultation and surgical drainage, with intravenous antibiotics and supportive measures (hydration, analgesia, and anti-emetics) as necessary. » If obstruction is present without infection, the patient can be managed conservatively; if the pain cannot be managed with non-steroidal anti-inflammatory drugs (if renal function normal) and opioids, then decompression should be considered.[1] If obstruction is present with infection decompression and antibiotics are essential to minimise risk for life-threatening sepsis. **Primary options** » crystalloids **--AND--** » ketorolac: 30 mg intravenously initially, followed by 15 mg every 6-8 hours for 3 days only

TREATMENT

Acute

Patient group	Tx line	Treatment
		-and/or- » morphine sulphate: 1-5 mg intravenously every 4 hours when required **--AND--** » ondansetron: 4 mg intravenously every 8 hours when required
	plus	**surgical decompression** » Drainage can be accomplished in 2 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.
	plus	**surgical removal** » 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.[57] » 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** » Patients with urinary calculi along with fever and other signs or symptoms of infection need emergency urological consultation for drainage and intravenous antibiotics. » Empirical broad-spectrum antibiotic therapy should be started pending sensitivity results based on urinalysis cultures.

Acute

Patient group	Tx line	Treatment
		Primary options » ampicillin: 2 g intravenously every 6 hours for 7-10 days **-or-** » ampicillin/sulbactam: 3 g intravenously every 6 hours for 14 days Dose consists of 2 g of ampicillin plus 1 g of sulbactam. **-or-** » piperacillin/tazobactam: 2.25 to 4.5 g intravenously every 6 hours for 7-10 days Dose consists of 2, 3 or 4 g of piperacillin plus 0.25, 0.375 or 0.5 g of tazobactam. **--AND--** » gentamicin: 1.5 mg/kg intravenously every 8 hours for 7-10 days **Secondary options** » ceftriaxone: 1 g intravenously every 24 hours for 14 days
pregnant	**1st**	**specialist referral** » The principles of treatment for the acute stone episode are similar in pregnant and non-pregnant patients. However, analgesics, antibiotics, anti-emetics, and intravenous fluids are given relative to their safety and risk for that particular trimester. Non-steroidal anti-inflammatory drugs should not be used during the first or second trimester. Alpha-blockers (e.g., tamsulosin) are US Food and Drug Administration (FDA) pregnancy category B. » 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.[61] Extracorporeal shock wave lithotripsy (ESWL) and percutaneous nephrostolithotomy (PCNL) are contraindicated in pregnancy.

Ongoing

Patient group	Tx line	Treatment
following an acute episode non-pregnant	1st	**hydration and dietary modification** » Long-term dietary modification is essential for preventing future calculi. This modification is centred on increasing fluid intake. At least 2 litres of urine output daily should be recommended to help prevent future episodes of stone formation.[62] » Decreased dietary sodium, protein, and oxalate should be recommended for stone prevention. Increased citrus fruit intake is recommended to prevent stone recurrence.[63] » Normal calcium intake is recommended.[63] Dietary calcium restriction can lead to less binding of calcium to oxalate in the GI tract, promoting hyperoxaluria and increased stone formation.[66]
hyperuricosuria and/or uric acid stones	adjunct	**alkalinisation/allopurinol** » 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.[67] » Uric acid stones are treated with alkalinisation therapy, with or without allopurinol. Oral alkalinisation therapy with medicines 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 alkalinisation 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 alkalinisation therapy. Potassium citrate is first-line therapy. **Primary options** » potassium citrate: 30-60 mEq/day orally given in 3-4 divided doses **OR** » allopurinol: 100-300 mg orally once daily **OR** » potassium citrate: 30-60 mEq/day orally given in 3-4 divided doses **-and-** » allopurinol: 100-300 mg orally once daily

Ongoing

Patient group	Tx line	Treatment
		Secondary options » febuxostat: 40-80 mg orally once daily **OR** » 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 **-and-** » allopurinol: 100-300 mg orally once daily
hypercalciuria	**adjunct**	**diuretics/alkalinisation** » Given until urinary calcium normalises. » Thiazide diuretics are generally combined with potassium citrate to prevent the development of hypokalaemia and hypocitraturia associated with this therapy. **Primary options** » chlortalidone: 25-50 mg orally once daily **OR** » hydrochlorothiazide: 25-50 mg orally twice daily **OR** » indapamide: 1.25 to 2.5 mg orally once daily **Secondary options** » potassium citrate: 10-20 mEq orally three to four times daily
hypocitraturia	**adjunct**	**alkalinisation** » Hypocitraturia is treated with oral alkalinisation therapy. **Primary options** » potassium citrate: 30-60 mEq/day orally given in 4 divided doses
hyperoxaluria	**adjunct**	**oxalate chelator/alkalinisation** » For patients with elevated urinary oxalate level secondary to small bowel or ileal disease, oral

TREATMENT

Ongoing

Patient group	Tx line	Treatment
		administration of calcium with meals is recommended.[68] » Colestyramine is also effective for hyperoxaluria due to intestinal disease, but is poorly tolerated. » Treatment with potassium citrate can fix the metabolic acidosis and hypokalaemia that may be present and can increase the urinary citrate. » Pyridoxine is indicated in primary hyperoxaluria. **Primary options** » calcium carbonate: 1-2 g/day orally given in 3-4 divided doses Dose refers to elemental calcium. **OR** » calcium citrate: 1-2 g/day orally given in 3-4 divided doses Dose refers to elemental calcium. **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** » colestyramine: 2-4 g orally four times daily **OR** » pyridoxine: 250-500 mg orally once daily
cystinuria	**adjunct**	**alkalinisation/thiol binding agent/cystine chelator** » The goal for the treatment of cystinuria is to decrease urine levels to <250 mg/L. » 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. » Alkalinisation 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 >7.5. » If conservative therapy and alkalinisation fail, chelating agents such as tiopronin or penicillamine should be used. Tiopronin has a better adverse-effect

Ongoing

Patient group	Tx line	Treatment
		profile than penicillamine and is therefore the preferred therapy.[69] » Captopril (which has chelation effects) is a third-line agent to treat cystinuria, although no long-term clinical trials have shown its efficacy. **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 **Tertiary options** » captopril: 75-150 mg/day orally given in 3 divided doses
struvite stones	**adjunct**	**urease inhibitor** » 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 medicine has a high rate of adverse effects including DVT, tremors, and headaches.[1] **Primary options** » acetohydroxamic acid: 250 mg orally three to four times daily

Recommendations

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.

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

Patient instructions

Patients with nephrolithiasis should be advised to have a fluid intake of at least 2 litres per day, a low-protein diet, and a low-sodium diet to prevent nephrolithiasis.[71]

Complications

Complications	Timeframe	Likelihood
post-percutaneous nephrostolithotomy (PCNL) bleeding	**short term**	**medium**
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 haematuria a week after PCNL should be evaluated with renal arteriogram to evaluate for pseudoaneurysm or arterial-venous fistula which can be treated with embolisation.		
post-extracorporeal shock wave lithotripsy (ESWL) haematoma	**short term**	**low**
Occurs due to disruption of blood vessels around and near kidney by shock waves. Managed conservatively with expectant management and blood transfusion if needed.		
post-ESWL, PCNL, or ureteroscopy treatment urosepsis	**short term**	**low**
Should be treated with intravenous antibiotics and vasoactive medication when needed. Perform imaging to rule out obstruction or abscess.		
post-ESWL steinstrasse	**short term**	**low**
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.		
post-ESWL, PCNL, or ureteroscopy ureteric injury	**short term**	**low**
Can occur from scope, laser, or basket causing ureteric damage. Short-term ureteric stent is recommended.		

FOLLOW UP

Complications	Timeframe	Likelihood
visceral organ injury	**short term**	**low**
Can occur from creation of nephrostomy tract leading to bowel or liver injury.		
pneumothorax	**short term**	**low**
May occur from creation of the nephrostomy tract with violation of the pleural cavity. Should be treated with a chest tube.		
ureteric stricture	**long term**	**low**
Can be a long-term sequela from ureteric injury. Patient may need subsequent procedure such as dilation or incision of the stricture.		

Prognosis

Nephrolithiasis is a lifelong disease process. The rate of recurrence of nephrolithiasis in first-time stone formers is 50% at 5 years and 80% at 10 years.[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.[70]

Diagnostic guidelines

Europe

Guidelines on urolithiasis

Published by: European Association of Urology **Last published:** 2016

Guidelines on paediatric urology

Published by: European Association of Urology **Last published:** 2016

North America

Medical management of kidney stones

Published by: American Urological Association **Last published:** 2014

Summary: This guideline provides recommendations on the diagnosis of kidney stones.

ACR Appropriateness Criteria: hematuria

Published by: American College of Radiology **Last published:** 2014

Summary: Rates radiological diagnostic procedures from most appropriate to least appropriate for haematuria.

ACR Appropriateness Criteria: acute abdominal pain and fever or suspected abdominal abscess

Published by: American College of Radiology **Last published:** 2012

Summary: Rates radiological diagnostic procedures from most appropriate to least appropriate for acute abdominal pain and fever or suspected abdominal abscess.

Treatment guidelines

Europe

Guidelines on urolithiasis

Published by: European Association of Urology **Last published:** 2016

Summary: Comprehensive, evidence-based guideline on all aspects of the diagnosis, management, and prevention of urolithiasis. Includes management of urolithiasis in children and in pregnant women. Includes the AUA/EAU 2007 guideline on management of ureteric calculi.

Interventional treatment for urolithiasis

Published by: European Association of Urology **Last published:** 2016

Summary: These guidelines describe recent recommendations on treatment indications and the choice of modality for ureteral and renal calculi.

GUIDELINES

Europe

Guidelines on paediatric urology

Published by: European Association of Urology **Last published:** 2016

Laparoscopic nephrolithotomy and pyelolithotomy

Published by: National Institute for Health and Care Excellence **Last published:** 2007

Summary: Limited evidence suggests that these procedures are adequately safe and efficacious. They should be used only by surgeons with advanced laparoscopic skills, working with a multidisciplinary team. Most patients with renal stones can be managed by less invasive treatments.

North America

Surgical management of stones

Published by: American Urological Association **Last published:** 2016

Summary: Provides guidelines for the surgical management of patients with kidney and ureteral stones including recommendations for adult and paediatric patients as well as pregnant patients.

Prevention of recurrent nephrolithiasis: dietary and pharmacologic options

Published by: American College of Physicians **Last published:** 2015

Summary: The American College of Physicians has provided recommendations regarding management of recurrent nephrolithiasis using diet and medication.

Medical management of kidney stones

Published by: American Urological Association **Last published:** 2014

Summary: This guideline provides recommendations on the medical management of kidney stones.

Opioids in the management of chronic non-cancer pain: an update of American Society of the Interventional Pain Physicians' (ASIPP) guidelines

Published by: American Society of Interventional Pain Physicians **Last published:** 2008

Summary: Covers opioids use for chronic non-cancer pain, with the conclusion that evidence is variable for use lasting more than 6 months.

Oceania

Kidney stones

Published by: Caring for Australians with Renal Impairment (CARI) **Last published:** 2007

Summary: A series of 7 guidelines covering clinical diagnosis of kidney stones; cystine stones; kidney stone epidemiology; metabolic evaluation; prevention of recurrent calcium nephrolithiasis; radiological diagnosis of kidney stones; uric acid stones.

Key articles

- Pearle MS, Calhoun EA, Curhan GC. Urologic diseases in America project: urolithiasis. J Urol. 2005;173:848-857. Abstract
- Moore CL, Daniels B, Ghita M, et al. Accuracy of reduced-dose computed tomography for ureteral stones in emergency department patients. Ann Emerg Med. 2015;65:189-98.e2. Abstract
- Preminger GM, Tiselius HG, Assimos DG, et al; EAU/AUA Nephrolithiasis Guideline Panel. 2007 guideline for the management of ureteral calculi. J Urol. 2007;178:2418-2434. Full text Abstract
- Pearle MS, Goldfarb DS, Assimos DG, et al.; American Urological Association. Medical management of kidney stones: AUA guideline. J Urol. 2014;192:316-324. Full text Abstract

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