

The management of urolithiasis

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Abstract

The incidence and prevalence of urolithiasis is on the rise; though inevitably the increasing availability of cross-sectional imaging has some contribution to this rise in diagnoses, it cannot take all the blame. Urolithiasis is now more commonly being recognized as a symptom of a more systemic disease which has a constellation of presenting signs and complaints. The authors aim to outline the precipitating causes of urolithiasis, along with a comprehensive discussion of the current operative trends available to the practising endourologist. Despite largely being tailored to trainees within Core Training, in parts the discussion will head beyond that what is expected during basic surgical training and move into topics of debate within higher specialist training.

Keywords Metabolic syndrome; percutaneous nephrolithotomy; renal stones; shockwave lithotripsy; ureteroscopy; urolithiasis

The epidemiology of urolithiasis

Urolithiasis affects 1 in 2 people per 1000, per year in the United Kingdom. The prevalence is dependent upon age, sex, race and geography; with a rise seen in the last 25 years regardless of ethnicity and the most prevalent composition being that of calcium oxalate (Table 1). The increased use of imaging modalities is seen as a significant contributor to overall number. There is a lifetime risk between 5% and 10% of developing urinary stone disease in the UK, whereas in the USA this is quoted as 6% in women and 12% in men. Eighty per cent of urinary tract stones are calcium based and seems to disproportionately involve economically active individuals, which inevitably leads to a substantial burden on society. Although traditionally gender ratios are approximated to 2–3:1 (M:F), the latest evidence seems to point to a vast change in this dynamic distribution with a reduction in this difference to less than 2:1 respectively. The incidence – seen as the first ‘stone event’ – is disproportionately higher in Caucasian males. The incidence rises from the age of 20

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Prevalence of composition of calculi

Stone composition	% of renal calculi
Calcium oxalate	80
Struvite (infection related)	2–20
Uric acid	5–10
Calcium phosphate calcium oxalate	10%
Pure calcium phosphate	<1%
Cystine	1%

Table 1

and peaks between 40 and 60 years of age. Women start later (in their 20s) with the incidence peaking earlier before decreasing to 1/1000/year in their late 40–50 years. The percentage recurrence of urolithiasis is a difficult topic to place a blanket value upon due to the heterogeneity of factors involved, with few studies providing reliable data. In general, case series data indicate that 30–40% of patients who are not treated will form another stone within 5 years of the first incidence of stone disease. However, prevention of stone recurrence is very feasible - with randomized trials pointing to a greater than 50% risk reduction.

Dietary risk factors

Diet influences the composition of urine and by inference will directly influence the risk of urolithiasis. Implicated nutrients within the diet include calcium, animal protein, oxalate, sodium, sucrose, fructose, magnesium and potassium.

Calcium: In the past it was presumed that a higher intake of calcium was proportional to the risk of urolithiasis. However, three landmark trials (HPFS, NHS I and NHS II) showed that increased calcium intake was seen as protective of urolithiasis – independent of other risk factors. At first glance, this may seem somewhat counter-intuitive, but a higher calcium intake will subsequently increase dietary oxalate absorption and in effect reduce urinary calcium oxalate excretion. In contrast to dietary calcium, supplemented calcium does not seem to appear to reduce risk in men or younger women and may increase the risk in older women.

Oxalate: The proportion of dietary oxalate that is absorbed ranges from 10% to 50%, with itself affected by concurrent dietary factors (as calcium), intestinal flora and disease. It has a positive correlation with calcium oxalate urolithiasis. Urinary oxalate is also derived from the endogenous metabolism of glycine, hydroxyproline, vitamin C and glycolate.

Potassium: Higher dietary potassium intake was seen as decreasing risk in men and older women – potentially by reducing urine calcium excretion or increasing urinary citrate.

Sodium/sucrose: A higher intake of sodium or sucrose is directly proportional to urinary calcium and independent of calcium intake.

Vitamin C: Ascorbic acid (vitamin C) can be metabolized to oxalate. In a prospective trial, men who consumed greater than

1 g of vitamin C had a greater than 40% risk of stone formation compared to men ingesting lower than the recommended daily allowance. Calcium oxalate stone formers should in general avoid vitamin C supplements.

Animal protein: High levels of animal protein in the diet cause high urinary oxalate, a low pH and low urinary citrate.

Fluid intake: The single most important determinant of urolithiasis risk in the absence metabolic factors is urinary volume. The risk of stone formation is substantially increased when the urine output is less than 1 l/day. Interestingly, increasing water hardness (high calcium content) may reduce risk by concurrently reducing urinary oxalate excretion.

Urinary risk factors

Hypercalciuria: Greater than 300 mg/day in men and 250 mg/day in women on a 1 g/day calcium diet; this is seen in approximately 20%–40% of patients with calcium urolithiasis and is a major factor in calcium oxalate stone formation by increasing the supersaturation of urine. Around 50% of patients with calcium-based urolithiasis will have hypercalciuria. The production of urine with high concentration of calcium can be due to three factors;

- absorptive – due to increased intestinal absorption of calcium
- renal – due to renal leak of calcium
- resorptive – due to bone demineralization.

Dietary calcium restriction is not recommended for stone formers with nephrolithiasis. Diets with a calcium content of 1 g/day, could be protective against the risk of stone formation in hypercalciuric stone forming adults. Moderate dietary salt restriction is useful in limiting urinary calcium excretion and thus may be helpful for primary and secondary prevention of nephrolithiasis. A low-normal protein intake decreases calciuria and is useful in stone prevention.

Hypercalcaemia: It can be said that nearly all hypercalcemia patients who form stones will have primary hyperparathyroidism. However, of those who have hyperparathyroidism – only 1% will tend to form stones.

Hyperoxaluria: Greater than 45 mg/day and is three to four times more common in males than females. However, it is noted that the risk of stone disease begins much below this value. This can be due to primary hyperoxaluria causing increased hepatic production of oxalate or increased oxalate absorption in short bowel syndrome so-called enteric hyperoxaluria – here the gut is over-exposed to bile-salts, leading to an increased permeability to oxalate. A diet low in oxalate and/or a calcium intake which is normal to high, reduces the urinary excretion of oxalate. However, a diet rich in oxalates and/or a diet low in calcium increases urinary oxalate. A restriction in protein intake may also reduce the urinary excretion of oxalate although a vegetarian diet may lead to an increase in urinary oxalate.

Hypocitraturia: Less than 320 mg/day is found in 5–11% of first-time stone formers. Citrate inhibits stone formation by forming a soluble complex with calcium and preventing the agglomeration of calcium oxalate crystals.

Low urine volume: Less than 1 l/day, 12–25% of first-time stone formers will have this abnormality.

Hyperuricosuria: Elevated levels of uric acid cause spontaneous precipitation within solution, which can help to act as a ‘scaffold’ for mainly calcium oxalate crystal aggregation and subsequent stone formation. Uric acid exists in solution as uric acid and sodium urate in an ionic balance. Sodium urate is 20 times more soluble than uric acid, but at a pH of 5 less than 20% is sodium urate. This is increased to 50% at a pH of 5.5 and further increased to >90% when the pH goes to 6.5 or greater.

Non-dietary risk factors

Family history/hereditary: common forms of stone disease can be inherited, with the risk of stone formation is 25%–50% higher in individuals with a positive family history of urolithiasis. This contribution is probably as a result of both genetic predisposition as well as similar environmental exposures. Familial renal tubular acidosis (which predisposes to calcium phosphate stones) and cystinuria (predisposition to cysteine stones) are inherited. Cystinuria is an autosomal recessive genetic disorder. It arises from a defect in the cystine/ornithine/arginine/lysine intestinal transport mechanism - leading to excessive cystine within the urine and stone formation.

Systemic disorders: there is a wealth of evidence which points to urolithiasis as a systemic disorder. Furthermore, there are recognized conditions that are associated with calcium-containing stones such as hyperparathyroidism, Crohn’s disease and renal tubular acidosis. Obesity, gout and diabetes (part of the ‘metabolic syndrome’ complex) have also been recently linked to the incidence of renal stone disease - increasing an individual’s BMI increases the risk of stone formation, with other contributory factors controlled.

Ethnicity: individuals of Arabic, Latin American and West Indian descent are more likely to be stone formers than individuals of European descent. Africans have the lowest incidence of urolithiasis.

Environmental factors: while urolithiasis is more common in hot climates, this is confounded by some indigenous populations having a lower prevalence of stones, e.g. African subcontinent, and vice-versa, e.g. Northern Europe. The later discrepancy is thought to relate to the ‘Western lifestyle’ of excessive consumption of animal protein, inadequate fluid intake and sedentary lifestyle.

Pathology of urinary stone disease

Vitamin D acts as a steroidal hormone and is pivotal in maintaining calcium and phosphate haemostasis. Calcium-containing stones result from excessive urinary calcium excretion (hypercalciuria) from either increased intestinal absorption of calcium, increased bone resorption or renal calcium loss. Urine is said to be saturated when the product of the concentrations exceeds that of the solubility product (SP). Below this value, crystallization will not form. Whereas above the SP, spontaneous crystallization

is possible but does not happen due to the inhibitors. Despite these inhibitors, over a certain concentration above the SP the effect of inhibitors ceases to prevent crystallization - this value is called the formation product (FP). Therefore, above this concentration the solute is termed supersaturated. The solute is termed metastable in the concentration range between SP and FP.

Stone formation theories

Fixed-particle theory

This theory favours nucleation of crystals directly upon damaged renal epithelium. The subsequent presence of crystals will further increase fluid turbulence and impede flow – which in turn will either propagate stones locally or ‘filter’ stones that are formed elsewhere in the kidney and become trapped. In time the tubule would become blocked from the accumulation of crystals.

Free-particle theory

Super-saturation of an individual’s urine with calcium oxalate leads to the spontaneous nucleation of crystals, which over time leads to accumulation and subsequent enlargement. However, this theory has been questioned since newly-formed crystals do not remain in the kidney for a sufficient period to allow growth to eventually cause tubular occlusion.

Inhibitor theory

Despite the mechanisms outlined and the commonality of calcium oxalate supersaturation, only a small percentage of us produce stones. Therefore, urine must contain inhibitors of crystallization. This concept was confirmed by Howard and Thomas, who showed that the urine of healthy individuals could prevent the calcification of rat cartilage while that of recurrent calcium oxalate stone formers could not.

Magnesium

This is thought to form strong ionic complexes with oxalate and impacts negatively on calcium oxalate crystal nucleation. In urine, it increases the concentration of oxalate required to require spontaneous calcium oxalate precipitation. However, multiple human trials have failed to show that magnesium administration reduces calcium-based urolithiasis and therefore its beneficial effect is likely to be minor.

Citrate

Studies have shown that citrate inhibits the crystallization of calcium oxalate nucleation and aggregation by binding to calcium to form a complex that forms a soluble compound. Hypocitraturia is seen as a risk factor for urolithiasis.

Diagnosis

Clinical presentation

Renal stones may present with pain or discomfort, while others are found incidentally. Other presentations include persistent non-visible haematuria, intermittent visible haematuria or recurrent urinary tract infections. End-stage complications of infected stones can be life threatening including pyonephrosis, xanthogranulomatous pyelonephritis, perinephric abscesses or

indeed septicaemia. The principal symptom of ureteric colic is excruciating pain – classically described as the patient being unable to get comfortable in contradistinction to the contrasting presentation of a rigid abdomen that causes pain on any movement – as in peritonitis. Despite this, both presentations can often be mistaken for the other – with the clinician having to use a focused history taking to discern the more likely diagnosis within the differential. A special emphasis must be placed on the insidious presentation of the leaking abdominal aortic aneurysm that may present with back/loin and abdominal pain, particularly in elderly patients with a sudden-onset of symptoms. Other differentials to consider during history-taking include (in no particular order):

- ovarian pathology (including torsion in females)
- testicular torsion in males
- diverticular disease
- ectopic pregnancy
- appendicitis
- pyelonephritis/UTI.

Non-visible haematuria is often associated with renal colic, but is common in many other pathologies. Indeed, the lack of haematuria does not always contraindicate the presence of a ureteric stone since the presence of completely obstructed renal unit will not contribute urine to the bladder. Any form of urothelial irritation may cause in non-visible haematuria, which may act to confound the diagnosis – particularly in the presence of retroperitoneal disease that may lead to ureteric inflammation. Similarly, false positives of a non-pathological nature may also include:

- beetroot
- exercise (cycling/running)
- idiopathic.

Radiological investigations

Plain film radiograph: the traditional imaging modality has been plain film radiography. Plain film radiography has an accuracy of 70% (due to variation in the density of differing stone compositions; see [Table 2](#)), but unfortunately cannot assess the degree of obstruction and can confuse phleboliths or vascular calcifications as ureteric calculi. The addition of intravenous contrast (IVU) and serial radiographs increases the diagnostic yield for a plain film radiograph. However, these modalities have largely been superseded by the non-contrast CT KUB. In a bid to reduce radiation exposure associated with serial CT scans, plain radiographs and other modalities still have a part to play in the follow-up of radio-dense stones in the recurrent stone former ([Table 3](#)).

Radio-opaque calculi on X-ray KUB

Radio-opaque	Calcium oxalate
Partially opaque	Cystine, magnesium ammonium phosphate (Struvite)
Radio-lucent	Uric acid, xanthine, indinavir (Invisible on CT)

Table 2

Effective dosages used in the investigation of ureteric colic

Examination	Effective dosage (mSv)	Background equivalent (2 mSv/yr)
XRAY KUB	0.6	16 weeks
XRAY IVU	3.0	1 yr
CT Abdo/pelvis	15	1.5 yrs
Ultra low dose CT KUB	1.2	15 weeks
Normal dose CT KUB	5	41 weeks

Table 3

Ultrasonography: the role of ultrasonography is important in patient groups where radiation needs to be kept to a minimum such as the young or pregnant patient; similarly, ultrasonography is useful in the follow-up of recurrent stones. In expert hands, the sensitivity of detecting calculi is upwards of 95%, with the larger stones becoming more obvious to see. Renal calculi appear as echogenic foci with either a twinkle artefact or posterior acoustic shadowing. Proximal and distal/VUU ureteric stones can often be clearly identified, but the rest of the ureter is often obscured by bowel gas, which significantly lowers sensitivity. Despite some ultrasonographers using ureteric ‘jets’ from the ureteric orifices as a surrogate marker for lack of obstruction, this may be prone to error due to the risk of incomplete obstruction – which can still cause long-term renal damage. The addition of colour-Doppler ultrasonography permits a calculation of the ‘resistive index’ (RI) within the intrarenal vessels, which is proportional to the pressure within the collecting system. Thus measurement of RI can increase the sensitivity and specificity for the diagnosis of an obstructed kidney in the context of acute renal colic.

Computed tomography (CT): non-contrast CT KUB is now the gold standard in the detection of urolithiasis and is recommended in the acute and outpatient setting due to its superior sensitivity and specificity, approaching 99–100%. Advantages over other modalities include the speed at which it can be performed; alternate pathology from non-urological systems can be detected, no intravenous contrast is required and information is provided on size/density of stone and presence/absence of hydronephrosis. The main limitations to CT KUB include cost and the increased patient exposure to radiation (Table 3). Small sub-3 mm stone can be missed if they fall between the imaged tissue planes or ‘slices’. Stones made from protease inhibitor ‘indinavir’, used as part of the anti-retroviral regimen in HIV treatment, may be undetectable on non-contrast CT KUB. Pelvic calcifications and phleboliths adjacent to the ureter can sometimes be mistaken for distal ureteric stones especially in the patient with a paucity of intra-abdominal fat. In this circumstance occasionally a ‘urographic’ phase is required with the addition of intravenous contrast to highlight the ureter.

Further refinement in CT technology enables ‘low-dose’ CT defined as <3 millisieverts (mSv) and ‘ultralow-dose’, <1 mSv, achieved by reducing the current to the radiation source. The reduced radiation exposure comes at the expense of decreasing image resolution limiting its use in obese patients and in the diagnosis of

alternate non-stone pathology. For point of reference and comparison, the average person is exposed to 2.4 mSv over a whole year and a transatlantic flight would provide 0.08 mSv radiation exposure.

Measuring the Hounsfield units (HU) on a non-contrast CT scan can approximate the composition of a stone. The HU is a radiological quantitative scale of radiodensity. Water is given the HU of 0, bone is 1000 HU and air is –1000HU. Typically, uric acid stones have a HU of 200–500 HU, whereas calcium oxalate stones are 600–1200 HU. Such information can be useful when planning intervention, for example, the likely success of extracorporeal shockwave lithotripsy. Above 1000 HU, extracorporeal shock wave lithotripsy (ESWL) is unlikely to be successful. Novel dual-energy CT scanners provide simultaneous scanning at differing voltages enabling increasingly sensitive estimation of stone composition.

Magnetic resonance imaging (MRI): the role of MRI in stone disease is limited partly due to high cost and lack of availability in the emergent setting, but also because the sensitivity of MRI for urolithiasis is around 82% and thus inferior to CT KUB. Stones are not obviously identified on MRI but when used they are best recognized using T2-weighted sequencing. There may be a role for MRI as an adjunct to ultrasonography in the pregnant patient. Pregnancy is associated with a physiological hydronephrosis, predominantly on the right side, secondary to a gravid uterus. MRI can be useful to differentiate between a truly obstructed kidney with a ureteric calculus versus pregnancy related hydronephrosis. However, when faced with a septic pregnant patient with an apparent hydronephrosis it is best to decompress the kidney with a nephrostomy and not delay management while awaiting an MRI scan.

Metabolic screening: is useful to identify those patients with urolithiasis and correctable metabolic disorders. Screening can be divided into basic and full metabolic screening and includes both urine and plasma sampling. Basic screening is expected for all patients presenting with stone disease in the clinic or emergency setting and is recommended by European Association guidelines. Testing includes serum creatinine and electrolytes, serum uric acid, serum adjusted calcium and, if there is a concern over sepsis or acute colic, the full blood count and C-reactive protein should also be tested. Urinalysis and microscopy, culture and sensitivity should be performed in all stone patients. Often overlooked is the urine pH and specific gravity, important because the changes in urine pH and increase in solute concentration can precipitate crystallization and supersaturation leading to stone formation. The following patients should undergo full metabolic testing as they have a high chance of recurrence;

- young patients (under 25)
- strong family history
- 100% composition stones found on stone analysis
- anatomical urinary tract abnormalities
- multiple recurrences
- bilateral formed stones
- short time between recurrences.

Full screening includes additional serum testing of phosphate, bicarbonate, parathyroid hormone and vitamin D. It also includes 24-hour urine collections with patients providing two separate

24-hour collections on consecutive days. Intake and physical activity should reflect the patient's normal routine. One collection container should include hydrochloric acid and be tested for volume, calcium, oxalate, citrate, magnesium, creatinine and phosphate. The second collection container should include sodium azide and be tested for volume, pH, urate, cystine/homocysteine, sodium, protein, creatinine and potassium.

Ureteric stones

Indications for intervention

- Pain (failure to respond to analgesia).
- Fever.
- Impaired renal function.
- Social reasons (young, active patients that are required for childcare or work. It is mandatory for airline pilots to be stone free before resuming work).
- Prolonged unrelieved obstruction (spontaneous passage usually takes 4–6 weeks).
- Solitary kidney

The majority of ureteric stones can be managed conservatively allowing the calculus to pass spontaneously. It is generally accepted that conservatively managed patients require follow-up imaging to ensure the stone has passed. The above indications describe the situations when intervention is required. The primary goal of intervention is to ensure decompression of the kidney and this can be achieved via a general anaesthetic retrograde insertion of a double-JJ stent or through the insertion of a percutaneous nephrostomy. In the non-septic patient, with the correct equipment, trained staff and favorable stone location it is possible to perform primary ureteroscopy and laser fragmentation of ureteric calculus in the emergency setting – in fact, the latest NICE and GIRFFT recommendations point towards this now becoming the 'gold standard' of care.

When faced with an infected, obstructed kidney the question of whether to perform a retrograde stent or nephrostomy insertion may be decided by logistics and the availability of an on-call interventional radiologist. The advantages of nephrostomy insertion is the rapid decrease in renal pelvis pressure with immediate drainage of pus/infected urine, also nephrostomy insertion can be performed under local anaesthetic thus in the unstable patient, where general anaesthetic may be risky, this is the preferred option. On the negative side some patients cannot tolerate a nephrostomy bag and prefer a stent as it is 'internalized'. Furthermore, there is a greater risk of bleeding and viscus injury with nephrostomy insertion compared to retrograde stent insertion. Still, to date, the seminal work by Margaret Pearle and associates is the best evidence we have in comparison between both strategies – benefits of stent insertion included lower length of stay and pain requirements; however, the pecuniary burden was almost double that of nephrostomy insertion. While either drainage method is useful in stabilizing the patient neither method treats the underlying calculus and the patients will require further treatment to be stone free.

Medical therapy – dissolution

Uric acid stones

Uric acid stones are likely secondary to a purine-rich diet. Fifty per cent of patients have concomitant gout, while the other 50%

have a high protein, low fluid lifestyle. Classically these stones form in concentrated acidic urine. Therefore, therapy which revolves around dissolution includes urinary alkalization, hydration, modification of diet and allopurinol. Urine output is recommended to be at least 2 l per day and the urine is alkalinized with potassium citrate 10 ml TDS (pH 6.5–7). Allopurinol is recommended when urinary uric acid excretion is greater than 1.2 g/day or in patients with hyperuricaemia.

Cystine: cystinuria requires lifelong follow-up and can be debilitating because of the speed of stone production. Most patients will readily excrete greater than 1 g of cystine per day. Cystine's solubility in acidic preparations is low, the aim of dissolution therapy is to hydrate and alkalize the urine. A further treatment strategy is the addition of drugs that convert cystine to compounds that are more soluble at lower pH values. Cystine stones are exceedingly hard and usually do not respond well to ESWL, hence if there is treatment failure with dissolution therapy then usually flexible uretero-rensoscopy or percutaneous nephrolithotomy is required.

Medical therapy – expulsive

It is thought that ureteric peristalsis is a key component in stone passage. In the presence of an obstructed stone, the natural pathways of peristalsis are disrupted, resulting in uncoordinated peristalsis that actually hinders passage of the stone. Non-steroidal anti-inflammatories (NSAIDs) lower ureteral activity and thereby provide excellent analgesia by reducing the pain of colic. Within the sympathetic nervous system, α -1 fibres are excitatory and subsequent blockage results in smooth muscle relaxation and contraction frequency. However, since the sympathetic nervous system only modulates activity, the intrinsic peristaltic activity to urothelium continues. There is great heterogeneity in the quality of trials performed under the auspices of evaluating medical expulsive therapy (MET). Indeed, Hollingsworth et al. (2006) only included 9 of over 400 studies analysed as of a sufficient quality to include within their subsequent meta-analysis. Overall, there was a 65% relative risk reduction of stone passage compared to placebo for alpha-adrenoceptor antagonists. Similarly, Parsons et al. (2007), showed that patients taking α -antagonists were 44% more likely to pass their stone spontaneously than those who were not on treatment. In recent years, the introduction of MET to help treat the passage of ureteric stones has become a cornerstone in the management of distal ureteric stones. Indeed, a meta-analysis of randomized controlled trials concluded that the smooth muscle relaxant drugs tamsulosin and nifedipine assisted both stone passage and analgesic requirements in those who were managed expectantly with ureteric colic. However, the most recent randomized multi-centre trial has not shown benefit in MET (SUSPEND, 2015), and therefore despite their wide use, there is still no conclusive evidence for the use of MET.

Extracorporeal shockwave lithotripsy

Introduced in the early 1980s, ESWL has transformed the management of urolithiasis. There are four components to any ESWL system; the generator, the focusing device, the coupling medium (to the body) and the type of imaging used to detect the stone

(fluoroscopy and/or ultrasound). Shockwaves are generated by a source external to the patients and are transmitted with the help of a coupling medium (usually water) through to the patient's skin. From here, they converge by passing through soft tissues to the point of maximum intensity – focused onto the stone. The waves are composed of a sharp peak in positive pressure followed by a trailing negative pressure wave; this causes stone fragmentation by the combination of shearing and cavitation. Cavitation bubbles created on the surface of the stone by the waves, implode on the stone surface – causing high-speed jets that erode the stone's surface. Firing the lithotripter at a high rate will cause the second wave to hit the newly formed cavitation bubbles before they implode. This 'bubble cloud' results in absorption and dissipation of energy to help further fragment the stone. The types of shockwave generators have not changed through the years and consist of either electrohydraulic, electromagnetic or piezoelectric generators (Figure 1). Initially this form of treatment required general anaesthesia, but with the onset of modern generators ESWL today consists of day case 20-minute procedure, covered with oral analgesia. The sensation is often likened to a stretched rubber band snapping against skin. If the stone is positioned near bone (e.g. rib), treatment may be considered to be uncomfortable due to the resonance of the waves created by colliding with the bone. The majority of renal stones can be treated with ESWL in a minimally invasive fashion and is thus often the first line of treatment in the management of urolithiasis.

Absolute contraindications to ESWL:

- pregnancy
- bleeding diathesis
- urinary tract infection (UTI)
- aortic or renal artery aneurysm.

Relative contraindications (where ESWL has a lower success rate) include:

- horseshoe kidney (due to the higher insertion of the ureter on the renal pelvis)
- obesity
- hard (>1000 Hounsfield units), large (>1 cm), lower pole stones
- stone situated within a calyceal diverticulum
- pelviureteric Junction obstruction (failure of passage of stone)
- malformation (e.g. spina bifida) make it impossible to adequately position the patient upon the table.

Pacemakers are not contraindicated in ESWL treatment. For patients on antiplatelet drugs (e.g. aspirin) will require these stopping before the commencement of treatment. Simple renal cysts, or indeed stones in polycystic kidneys are not a contraindication. Special recognition has to be given to the stones that have a low propensity to fragment – namely those of calcium oxalate monohydrate variety (but also to a lesser extent Cystine and Brushite stones). ESWL can be performed for stones within the kidney and the ureter. However, the latest evidence points to ESWL best suited to proximal ureteric stones less than 10 mm compared to that of semirigid ureteroscopy. Experimental evidence suggests that shockwaves are not as efficacious in treating ureteric calculi as compared renal-sited calculi; the lack of sufficient stone–fluid interface is thought to account for the poorer fragmentation rate. ESWL is not recommended to treat an

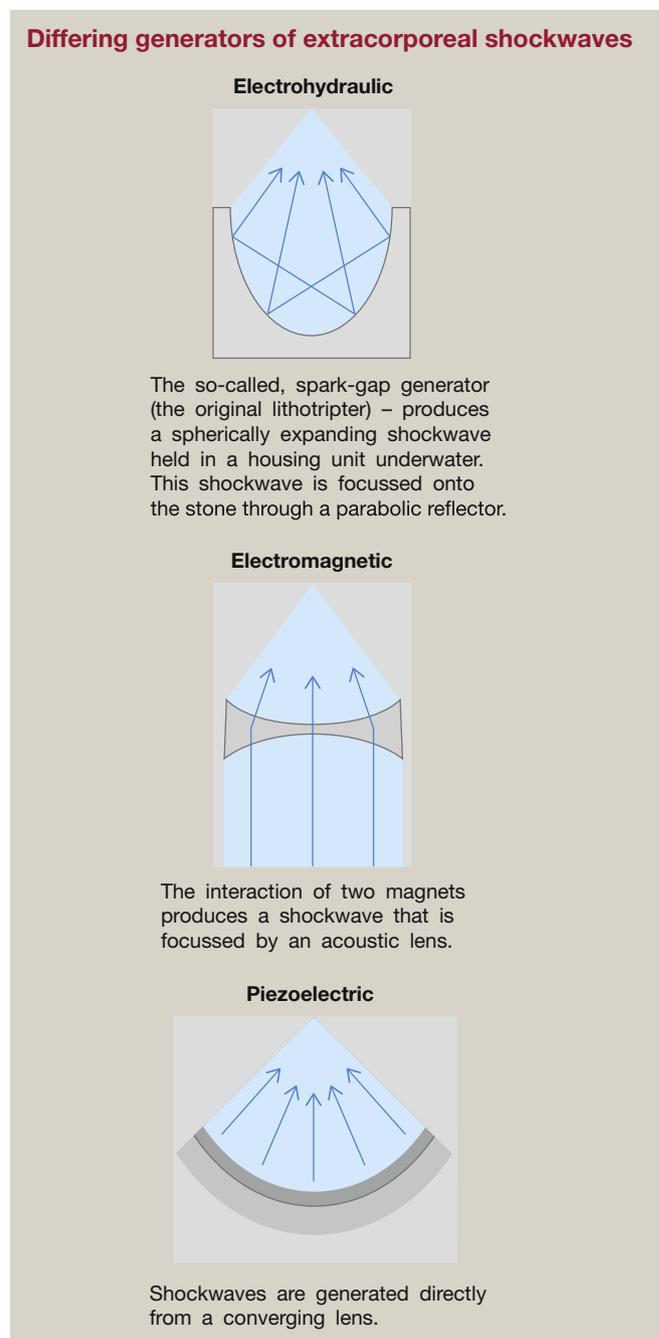


Figure 1

obstructed, infected renal system – in this setting nephrostomy drainage or ureteric stent placement is advocated.

The indications for ESWL revolve around the stone size and position. It is usually the first-line approach in patients with stone burden less than 10 mm and in children. In renal stone burden between 10 and 20 mm; it could be considered if other approaches are deemed to be a higher complication risk.

Complications of ESWL

Immediate – complications related to fragmented stones. *steinstrasse* (German for 'stone street'), occurs due to the passage

of multiple fragments down the ipsilateral ureter causing obstruction. Patients present with ureteric colic and although a conservative approach is recognized as a treatment option, it inevitably requires decompression of their renal tract through the retrograde insertion of a ureteric stent due to ongoing pain or a nephrostomy. The advantage of a nephrostomy is that it allows the oedema from ureteric obstruction to settle and normal peristalsis to resume—increasing the possibility of spontaneous stone passage and reducing the need for a further procedure or two (ureteroscopy followed by removal of the ureteric stent at a later date). However, in reality patients are less willing to maintain a nephrostomy on an outpatient basis than a ureteric stent. The larger and/or harder the stone – the more likely the presentation.

Infection – the disruption of the integrity of the stone will often release bacteria held within its lattice structure. These are then free to enter the blood stream and cause a transient bacteraemia, which can occasionally progress to septicaemia if uncontrolled. Other infective complications include a UTI, perinephric abscess formation and more severe complications including multiorgan failure and death. Patient selection for ESWL is key. Those who have a propensity to produce infection-stones should be covered with antibiotics prophylactically prior to the procedure. The use of prophylactic antibiotics in non-infection stones as routine prophylaxis varies amongst differing units, with the majority favouring a single dose pre-procedure.

Tissue injury: renal – bleeding (causing intrarenal or extrarenal haematoma) and oedema are the two most common manifestations of renal injury. Occasionally, patients may experience visible haematuria which is usually self-limiting. Parenchymal injury is thought to be mediated through a vasoconstrictive response resulting in a reduced flow and subsequent reduction in glomerular filtration rate. Injury may be reduced by employing a lower frequency (optimal ranges from 60 to 120 Hz).

Percutaneous nephrolithotomy

Since it was originally described over 60 years ago, percutaneous nephrolithotomy (PCNL) has become established as the preferred approach to tackling large stone burdens within the renal collecting system (such as [Figure 2](#)). It offers a reduced morbidity rate, lower length of stay and cost to the previous method of open pyelolithotomy. It offers the removal of the renal stone as a whole or in fragments through a specifically created tract between the skin surface and the collecting system of the kidney.

The approach to percutaneous access is considered crucial in PCNL planning and can define operative length, need for further procedures and complications rate. In general, the kidneys lie obliquely between T12 and L2/3, with the right lying lower than the left due to the presence of the liver. Each kidney's long axis is parallel with the lateral border of the psoas, ensuring that the upper pole calyces more medial and posterior than the inferior poles.

There are three major calyceal groups to each kidney; upper, middle and lower. The upper and lower calyces are generally clustered together, while the middle is arranged in anterior or posterior sets that arise directly from the renal pelvis (62%) or as an offshoot from either the upper or lower pole systems (38%). Each renal artery divides into anterior and posterior branches;



Figure 2 ‘Staghorn’ calculus involving all of the calyces branching from the renal pelvis. PCNL was undertaken as the preferred operative intervention.

the anterior then subdivides into four segmental branches that supply the superior and inferior poles as well as the anterior upper and middle portions of the kidney. The posterior division supplies the remaining areas of the kidney.

Segmental arteries then further subdivide and branch into lobar, interlobar, arcuate and interlobular arteries. Brodel’s line is an avascular plane that runs in the watershed catchment area between both anterior and posterior vascular supplies of the kidney. It is located posterior to the lateral convex border of the kidney and is considered the safer route for percutaneous access into the renal collecting system. There are several critical structures surrounding each kidney. On the left – the adrenal gland, spleen, pancreas, stomach and descending colon. While on the right – adrenal gland, ascending colon, liver and duodenum. However, with both kidneys lying in such close proximity to the pleura and diaphragm, the greatest risk in supracostal puncture is that of a pneumothorax. This can be mitigated by avoiding supra – 11th punctures.

Patient preparation and assessment prior to PCNL is crucial in any intended procedure. Routine laboratory investigations include an assessment of renal function, haemoglobin and a relevant, recent mid-stream specimen of urine. Any anticoagulants should be noted at the time of clinic and an appropriate plan should be in place at the time of pre-assessment, including any ‘bridging’ schemes for anticoagulants such as clopidogrel/warfarin/rivaroxaban, which would include liaising directly with the resident haematologist. All cases will require a recent group and save, but not an active cross-matched sample. Patients with significant stone burden or indeed those with an anatomically abnormal urinary tract, will often culture a mixed growth within the urine cultures. In this instance, it is useful to liaise directly with the resident microbiologist to tailor an antibiotic regimen

that is suited to the case – in many cases this will involve reviewing previous MSUs for culture and sensitivities and advice based on induction administration with backup treatment if systemic sepsis encountered.

Once the target calyx is chosen, the position on the overlying skin is marked and a small blade puncture is made. An 18G/15 cm angiographic (Kellert) needle is advanced into the chosen calyx with combined fluoroscopy and ultrasound. In some patients, needle puncture of the collecting system will encounter foul-smelling urine or indeed frank pus. In these instances, it is advised to deploy a nephrostomy tube to ensure adequate drainage and abandon the procedure. A sample should always be taken for culture and in some instances where urine does not drain directly post-puncture due to a low-pressure system; retrograde injection of saline via the ureteric catheter should introduce urine through the needle sheath.

Currently, there is no evidence as yet to identify supine over prone PCNL as the superior technique in achieving lowest stone free rates. There are clear advantages of supine PCNL: anaesthetic considerations in morbidly obese patients, reduction in intra-ocular pressures, difficult manoeuvrability due to fixed flexion deformities of the limbs or spine and the ability to approach the stone burden both in an antegrade and retrograde manner by use of the urethra. However, there are also advantages to the prone approach: the ability to hydro-distend the collecting system to allow for better vision and manoeuvrability. The first step in PCNL is to establish retrograde access with the placement of ureteric catheter (usually 5/6 Fr) – this allows the option to hydro-distend collapsed collecting systems or indeed retrograde inject contrast to aid the localization of the preferred calyx for puncture. Patient position for the placement of the ureteric catheter varies from the on-table frogs-leg position which is preferred for a flexible cystoscopy-guided entry, to full lithotomy. After satisfactory placement of the ureteric catheter, a concurrent urethral catheter is placed alongside to adequately drain the bladder during this procedure – this allows monitoring of urine output and prevents excessive fluid accumulating within the bladder through an antegrade approach. The ureteric catheter also acts as an obstruction to prevent debris passing down the ureter, as well as providing the operating surgeons the ability to flush any debris that may have accumulated in its path retrograde into the view of the nephroscope. Some endo-urologists describe the use of an occlusion balloon to prevent stone debris from passing down the ureter as well as keeping the collecting system dilated pre-puncture.

Once a calyx is punctured with the needle, the core of the needle is cannulated with a guidewire, which is passed through the infundibulum of the calyx, into the renal pelvis and through the pelviureteric junction into the ureter in an antegrade approach. The wire is subsequently exchanged to a 'super-stiff' guidewire, upon which the tract is dilated to a sufficient caliber (usually 26 Fr–28 Fr) to allow an access sheath to be inserted down the track into the calyx. Typically for kidneys with a high stone burden, PCNL is preferred due to the alignment of the nephroscope with the long axis of the kidney – which allows manipulation of the scope into the upper calyces, renal pelvis, lower calyces, pelvi-ureteric junction and proximal ureter. Occasionally in staghorn calculi, parallel lie calyces make some stones inaccessible through a single track approach and therefore

require multiple punctures to ensure adequate manoeuvrability of the nephroscope to access all stone-bearing calyces. The patient is then usually turned prone, while taking utmost care to protect the airway/eyes and the ureteric catheter. The anaesthetist will lead patient positioning, with supports placed under the chest, pelvis, knees and ankles. Patient warming, anti-DVT stockings and pneumatic compression devices are ensured. Stone fragmentation usually occurs through the use of a combination ultrasonic and pneumatic lithotripter – which allows efficient fragmentation of large stone and ultrasound assisted fracture and suction of smaller and/or softer stones. Occasionally, with an appropriately placed track – an endoscopic grasper can simply remove the stone without requiring significant fragmentation (Figure 3). Following the PCNL, a nephrostomy tube is usually placed and can range from an 8 Fr 'pigtail' locking-nephrostomy, a Foley catheter (used in urethral catheterization), to a large 28 Fr drainage tube. The use of the nephrostomy tube is primarily to aid in drainage and tamponade the nephrostomy track. If prolonged drainage is wished, a double-J can be deployed.

Modern advances in PCNL approaches have largely concentrated on reducing the size of the dilated track down in a bid to reduce the risk of postoperative bleeding and pain. The terminology is described below along with the access sheath size.

- >22 Fr standard PCNL
- <22 Fr mini-PCNL
- 11-13 Fr ultra-mini PCNL
- 10-14 Fr super-mini PCNL
- 8 Fr mini-micro PCNL
- <5 Fr micro-PCNL.

Such a small tracts necessitates the use of a laser to fragment the stone in to small pieces with saline irrigation to flush the pieces down the sheath. In some specialist centres combined approaches are employed utilizing retrograde flexible ureteroscopy simultaneously with PCNL to aid in calyceal puncture and improved stone clearance but this is far from standard. This 'combi' PCNL approach is often performed in a modified

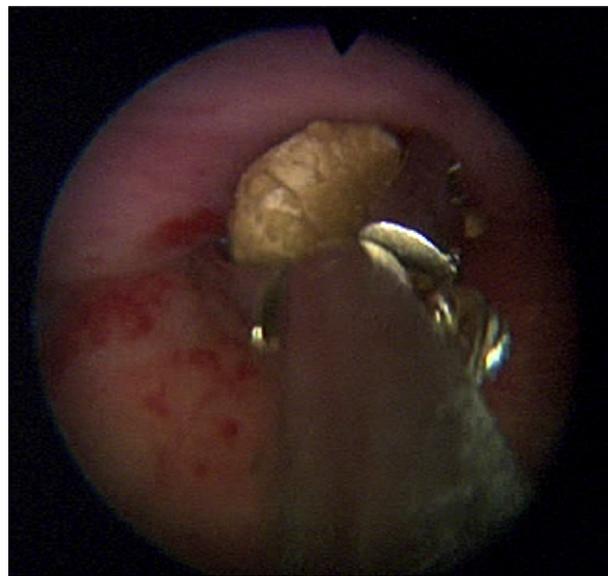


Figure 3 Intraoperative screen capture of stone retrieval with endoscopic graspers through a nephroscope, within the renal pelvis.

supine/lithotomy position and requires two theatre stacks with two different teams working in tandem. It has the benefit of intraoperative translocation of stone burden in order to reduce the number of percutaneous tracts used – particularly useful when dealing with significant stone burden in multiple, parallel-calices.

Complications: the most common postoperative complication from PCNL is the systemic inflammatory response syndrome, although progression to full sepsis is unusual. Other risks include bleeding requiring transfusion (5%) or embolization (0.5%–1.5%) and adjacent organ injury. Further complications include fluid overload, hypothermia, inward sheath migration, nephron-cutaneous fistulae and mortality. Bleeding can occur both from the renal parenchyma and from arterial injury during puncture. Classically sudden bleeds causing large drops in haemoglobin present within the first 24–48 hours after nephrostomy tube removal and clot dislodgement after tube tamponade. The second peak in incidence is secondary to spontaneous bleeding from arterio-venous malformations or pseudoaneurysms from iatrogenic injury. Venous bleeding can often be controlled by clamping the nephrostomy tube for tamponade. However, if fresh blood is persistent with systemic compromise one should suspect an arterial injury. Diabetes, the number of tracts, prolonged operative time, infection stones, and so on, all increase the chance of postoperative complications. Injury to pleural structures are best treated with a thoracic drain. The management of a thoraco-pleural fistula reflects the general principles of fistula treatment – and ensures adequate drainage both from the kidney via a nephrostomy and the chest via a chest drain. Damage to the colon usually occurs as a result of the passage of the access sheath through the viscus and into the kidney. This can be managed by a ureteric stent to drain urine and withdrawing the access sheath back to the colon to the point of perforation. If there is no distal colonic obstruction (and leakage is contained within the retroperitoneum) colonic perforation should resolve spontaneously – and this can be confirmed with a contrast examination through the nephrostomy tube at a later point.

Retrograde endoscopic management

The rigid ureteroscope allows direct visualization of the ureter and is the ideal instrument for managing ureteric stones. Small stones can be directly ‘basketed’ out; however, the majority will need to be fragmented with a laser fibre to facilitate removal. The flexible uretero-roscope (FUR) allows access to the calyces of the kidney and is useful for managing renal stones in the 0.5cm–1.5 cm range or in those with larger stone burden where PCNL is contraindicated. A ureteric access sheath can be inserted over a guidewire to enable drainage of the renal pelvis and multiple passes of the FUR when renal stones are fragmented and basketed. FUR is a key component to the urologist’s armamentarium; this has continued to evolve with the development of better optics (fibre optic to digital sensor tip), deflection, irrigation flow and durability (Figure 4). Accordingly, the clinical indications and inclusion criteria for therapy has expanded to reflect these achievements (Table 4).

Currently the repair costs of maintaining a FUR service is high and the equipment itself is expensive running in to several

£10,000s. The highest risk of scope damage is while treating lower pole stones in situ (laser damage) and issues surrounding packaging re-processed scopes and their transport. More recently a single-use disposable FUR has been developed to tackle the issue of maintenance and sterilization. Studies have shown comparable image quality, ergonomics, stone clearance rates and favourable cost comparison. It is likely that these disposable scopes will become more commonplace.

The holmium-YAG laser

This holmium laser is passed through an yttrium-aluminium garnet (YAG) crystal, which gives it the wavelength of 2100 nm (infrared, invisible spectrum). It delivers pulsatile energy that allows lithotripsy to be performed. Its penetrative depth is between 0.3 and 0.4 mm, so the risk of perforation through urothelium is low. The laser radiation is absorbed by water in the stone causing a vapour pressure that fragments the stone described as the photo-thermal effect. Various laser fibres exist but for FURs a 200–300 micron fibre is recommended. Laser generators allow for the manipulation of laser setting to create different energy effects:

- Fragmentation – uses high energy (Joules) with low frequency (Hertz) to create small stone pieces that subsequently need to be basketed out.
- Dusting – with low energy and high frequency break the stones into tiny pieces which later pass spontaneously.
- Pop corning – with high energy and high frequency breaks larger fragments into smaller ones.

The decision on laser settings depends upon surgeon preference, stone composition/size and stone location. The generally accepted approach is to start on low settings such as 0.6 J × 6 Hz and adjust accordingly as the stone responds. Some instances – such as a hostile PUJ – make basketing a large stone difficult and risks traumatizing; in such instances dusting and period of diuresis may be more favourable.

Complications of retrograde surgery

The most common complication encountered is the inability to access calculi particularly when the ureter has not been pre-stented and is too tight to facilitate passing of instruments. Further complications include infection/sepsis, bleeding, injury



Figure 4 Fluoroscopic (intraoperative) image of a flexible ureteroscope examining the lower pole of the kidney.

Approaches and considerations

	ESWL	FURS	PCNL
Stone size	<1 cm	0.5–1.5 cm	1 cm+
Anatomy	Not suitable for abnormal anatomy (horseshoe, PUJ stricture)	Difficult in urinary diversions	Antegrade access allows suitable approach to kidney and ureters
Stone composition	Better efficacy with softer stones	All, except hard lower pole stones which may be hard to access or require multiple attempts	All

Table 4

to the ureter, manifesting immediately with perforation or complete avulsion (very rare). Later complications including ureteric stricture are relatively unlikely (0.5%); but are more common when the stone has been impacted or injury has been caused by either the access sheath or during use of the laser. Eighty per cent of people experience stent symptoms and can significantly impact the quality of life. Alpha-adrenoceptor blockers and anticholinergic medications can play a limited role in alleviating symptoms, but as a whole – the younger male patient suffers the most – presumed due to the tightness of this cohorts ureters. Stents may also become blocked or migrate and require removal or replacement.

Open surgery for the management of urolithiasis

In the modern era of minimally invasive techniques, the uses and indications for open surgery are dwindling, with less than 0.5% of stone-related procedures done via the open route. However, in countries with limited access to modern amenities and complex stone-burden presentations, the open approach is still utilized to excellent effect.

According to the European Association of Urology/American Urological Association, the indications for open treatment are:

- Complex stone burden requiring multiple PCNL tracts and/or multiple staged procedures.
- Treatment failure using endourological techniques.
- Patient choice (preferring a single procedure).
- Intra-renal anatomical abnormalities requiring concomitant surgical correction (PUJ obstruction).
- Large stone burden within children – requiring only one anaesthetic procedure.
- Skeletal deformity – contractures hampering endourological access.

In most cases, a flank approach is the incision of choice, with the patient positioned in a lateral position and the table ‘broken’ such that access to the flank is made more apparent. The skin is incised above the 10th to the 12th rib, with great care used to avoid the neuro-vascular bundle that comes associated with the rib’s inferior lip.

Stones in the bladder

A stone can form in the bladder from:

- bladder outflow obstruction e.g. benign prostatic enlargement
- foreign objects, e.g. retained stitch, catheterization

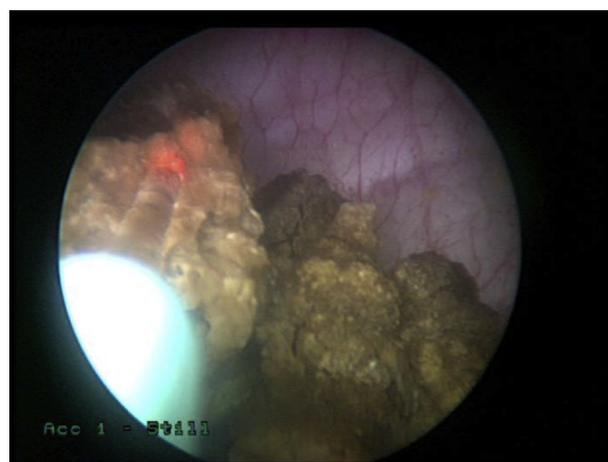


Figure 5 Laser fragmentation of bladder stone.

- failure of passage of upper tract calculi
- neuropathic lower urinary tract.

In general, a stone that is small enough to pass down the ureter into the bladder is usually small enough to pass through the urethra. More often than not, the stone is often not noticed during spontaneous passage. However, patients may feel or an exacerbation of voiding/storage lower urinary tract symptoms. Stones less than 2 cm can often be treated endoscopically (Figure 5). Larger stones may require a staged procedure or indeed an open cystolithotomy. The endoscopic approach can be either through the use of the Mauermayer ‘stone-punch’ or more recently through the use of the holmium laser which can fragment any stone. The traditional use of electrohydraulic shock-wave lithotripsy is now considered to be the least preferred option due to the risk of mucosal injury. It is important to treat the cause of the stone, to prevent future recurrences.

Conclusion

There has been more than a 50% increase in documented urolithiasis episodes and a greater than 100% increase in ureteroscopic stone treatments in the last 10 years. There is a higher risk of renal stones with so-called ‘Western diets’; a largely sedentary lifestyle combined in a diet rich in sugar or salt, high protein and low fibre diet. The socio-economic burden of stone disease is set to rise as individuals live longer with unhealthy lifestyles. There is an inevitable link between metabolic syndrome and stone production, just as there is a link between obesity and uric acid

stone formation. Despite accounting for confounding factors, there is still an increasing incidence of urolithiasis along with a decreased time to recurrence within the obese population. Insulin resistance decreases the production of ammonia which alters urinary acidification and brings about a lowered urinary pH. Indeed, the rate of prevalence of type-2 diabetes in uric acid stone formers is much higher than the general population (30–40% versus 5–10%) and subsequently, there is growing evidence that urolithiasis may be in fact a systemic disorder representing the interaction of multiple metabolic risk factors.

Surgeons-in-training have to be vigilant in the identification and the swift management of the infected, obstructed kidney. This unforgiving condition, will rapidly progress to multiple organ failure followed by death if not identified in a timely manner. Thus, this diagnosis, much like a leaking abdominal aneurysm is for abdominal pain and hypotension, must always be considered when loin pain and pyrexia are part of the presenting picture. ◆

FURTHER READING

- Chaussy C, Schmiedt E. Extracorporeal shock wave lithotripsy (ESWL) for kidney stones. An alternative to surgery? *Urol Radiol* 1984; **6**: 80e7.
- Clayman R. Dietary factors and the risk of incident kidney stones in younger women. nurses' health study II. *J Urol* 2005; **173**: 479e479.
- Kavanagh J. Supersaturation and renal precipitation: the key to stone formation? *Urol Res* 2006; **34**: 81e5.
- Khan S. Modulators of urinary stone formation. *Front Biosci* 2004; **9**: 1450e5.
- Lingeman JE, Matlaga BR, Evan AP. Surgical management of upper urinary tract calculi. In: Wein A, ed. *Campbell-Walsh urology ninth edition review*. Philadelphia: Saunders/Elsevier, 2007.
- Percutaneous nephrolithotomy made easier: a practical guide, tips and tricks. *BJU Int* 2008; **102**: 1178e1178.
- Pickard R, Starr K, MacLennan G, et al. Use of drug therapy in the management of symptomatic ureteric stones in hospitalised adults: a multicentre, placebo-controlled, randomised controlled trial and cost-effectiveness analysis of a calcium channel blocker (nifedipine) and an alpha-blocker (tamsulosin) (the SUSPEND trial). *Health Technol Assess* 2015; **19**: 1e172.
- Prezioso D, Strazzullo P, Lotti T, et al. Dietary treatment of urinary risk factors for renal stone formation. A review of CLU working Group. *Arch Ital Urol Androl* 2015; **87**: 105.
- Sakhaee K. Recent advances in the pathophysiology of nephrolithiasis. *Kidney Int* 2009; **75**: 585e59.
- Shoma A, Eraky I, El-Kenawy M, El-Kappany H. Percutaneous nephrolithotomy in the supine position: technical aspects and functional outcome compared with the prone technique. *Urology* 2002; **60**: 388e92.
- Skolarikos A, Alivizatos G, de la Rosette J. Extracorporeal shock wave lithotripsy 25 years later: complications and their prevention. *Eur Urol* 2006; **50**: 981e90.
- Skolarikos A, de la Rosette J. Prevention and treatment of complications following percutaneous nephrolithotomy. *Curr Opin Urol* 2008; **18**: 229e34.
- Soucie J, Coates R, McClellan W, Austin H, Thun M. Relation between geographic variability in kidney stones prevalence and risk factors for stones. *Am J Epidemiol* 1996; **143**: 487e95.
- Stables DP. Percutaneous nephrostomy: technique, indications, and results. *Urol Clin* 1982; **9**: 15e29.
- Taylor E. Dietary factors and the risk of incident kidney stones in men: new insights after 14 years of follow-up. *J Am Soc Nephrol* 2004; **15**: 3225e32.
- Tawfik E, Bagley D. Management of upper urinary tract calculi with ureteroscopic techniques. *Urology* 1999; **53**: 25e31.
- Thiruchelvam N, Mostafid H, Ubhayakar G. Planning percutaneous nephrolithotomy using multidetector computed tomography urography, multiplanar reconstruction and three-dimensional reformatting. *BJU Int* 2005; **95**: 1280e4.
- Turney BW, Reynard JM, Noble JG, Keoghane SR. Trends in urological stone disease. *BJU Int* 2012; **109**: 1082e7, <https://doi.org/10.1111/j.1464-410X.2011.10495.x>.