

# **INTRODUCTION**

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## Epidemiology of pediatric stone disease

Renal stones in childhood are rare in the developed world, representing 1% to 5% of all urinary tract stones. However, in developing countries, the occurrence of renal urolithiasis in children is 30% of all urinary tract stones.<sup>(1-3)</sup>

Renal stones are uncommon in children but an important cause of morbidity and mortality, as highlighted by the recent crisis of melamine induced kidney stones in China. A recent report from the United States suggests that males are more susceptible in their first decade of life; however females become more prone to renal stones in their second decade.<sup>(4)</sup>

In the USA, pediatric urolithiasis accounts for about 1 in 1000 pediatric hospital admissions.<sup>(5)</sup> However pediatric stone disease is considered endemic in developing nations, including India, Turkey, Pakistan, and the Far East. In these areas, ammonium acid urate and uric acid stones predominate, strongly implicating dietary factors.<sup>(6)</sup>

Stone composition in children is strongly associated with geographic and socioeconomic boundaries. In Northern Thailand, for example, there is a very high incidence of pure calcium oxalate stones. This phenomenon occurs because pre masticated glutinous rice is substituted for breast milk. This rice is high in hydroxyproline, a precursor of oxalate.<sup>(7)</sup>

In developing countries, nutritional factors can be a major factor in the formation of stones in poor children. This is caused by diet, high in cereal and low in animal protein, calcium and phosphate, which leads to the formation of urine with a relatively high content of ammonium and urate ions, and consequently to the formation of ammonium acid urate crystals and stones. In countries where there is also a high intake of oxalate from leaves and vegetables, urinary oxalate is increased and, as a result, the ammonium acid urate stones often contain calcium oxalate as well. The stone problem is compounded by low urine volumes resulting in some areas from poor drinking water, and chronic diarrhea, and in others from the hot climate and fluid losses through the skin. Calcium oxalate and uric acid stones are more frequent in males than in females whereas calcium phosphate and struvite stones are more prevalent in females.<sup>(8,9)</sup>

In Europe, the majority of childhood stones are infection related, as seen in 50% to 70% of patients.<sup>(10-11)</sup> These stones are comprised primarily of magnesium ammonium phosphate (struvite) with *Proteus* species being the most frequently cultured organisms.<sup>(11)</sup> In contrast to the reports of pediatric stones in Europe, metabolic disorders are more frequently noted as the cause of childhood urolithiasis in the United States and Scandinavia.<sup>(12-13)</sup>

The anatomic location of these calculi also appears to exhibit strong geographic variations. In Southeast Asia and Africa, bladder calculi are found most frequently, whereas in the United States and Europe upper urinary tract calculi are more common. As societies become more industrialized, there tends to be a shift from lower to upper tract calculi.<sup>(7)</sup>

In developing nations, reports suggest that a metabolic risk factor can be found on urine studies in 84% to 87% of children, most commonly hypercalciuria or hypocitraturia. However, evidence is accumulating that stones in majority of westernized children are calcium based without any evidence of metabolic abnormality on 24 hour urine collection.<sup>(14)</sup>

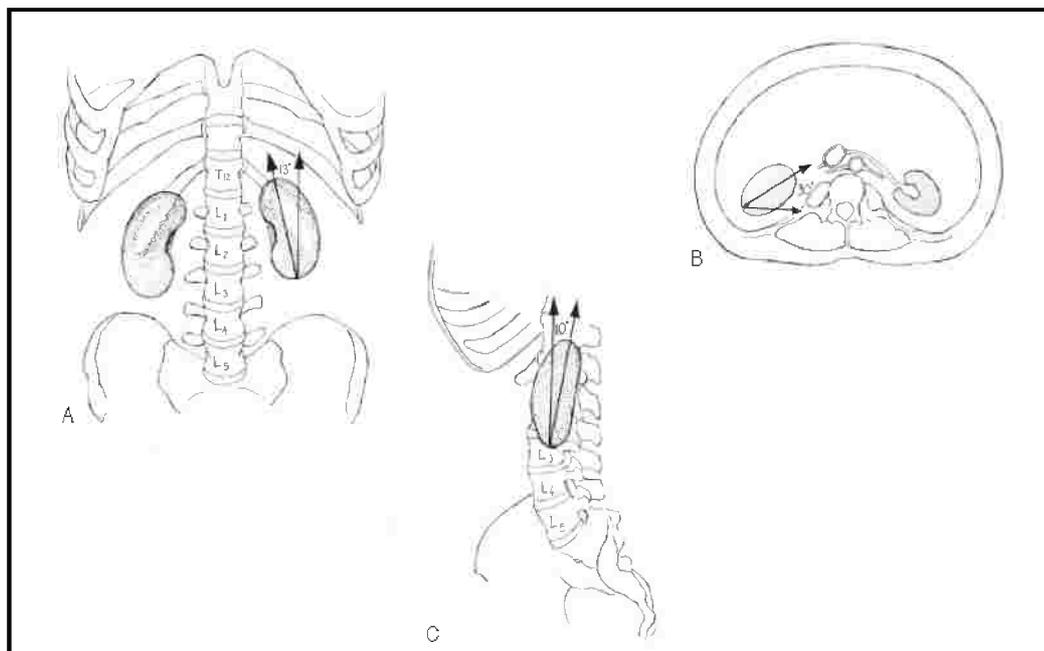
In contrast to adult stone disease, the pediatric population shows only a slight male predominance of stone disease, with some studies showing an equal incidence between boys and girls. In several epidemiological studies analyzing race and pediatric stone disease, it was noted that approx 10% of children with stone disease are African American and approximately 80% are Caucasian.<sup>(15)</sup>

Developmental anomalies of the genitourinary tract may also contribute to the development of urolithiasis. These defects promote stasis of urine and increase the potential for crystallization to occur. Several series have reported the incidence of stones in association with congenital anomalies to range between 20% and 44 %.<sup>(16)</sup>

## Radiologic Orientation of the kidney

The kidneys usually extend from the level of the T12 to L3 vertebrae, being slightly lower in females. The right kidney lies 1 to 2 cm lower than the left. The kidneys are slightly rotated on a vertical axis in three planes: coronal, transverse, and sagittal.

1. **Coronal Projection;** the upper pole is more medial than the lower by an angle of 13° (Fig. 1A).
2. **Transverse Projection** The pelvis and hilum have a more anterior position than the outer convex border by an angle of 30° (Fig1 B).
3. **Sagittal Projection** The long axis of the kidney is angled posteriorly by about 10° (Fig.1 C).



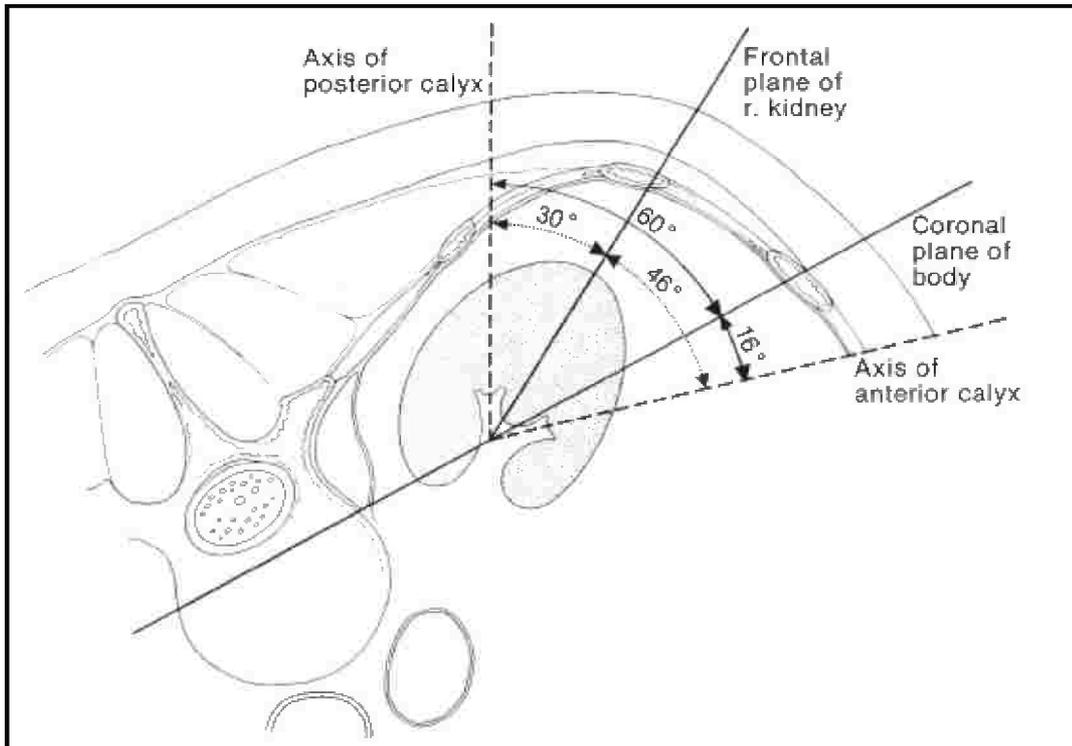
**Fig 1:** Orientation of the kidney in the abdomen from (a) frontal plane (b) axial plane (c) sagittal plane.<sup>(17)</sup>

## Radiologic Orientation for Endourology

### Right Kidney

The orientation of the calyces is variable. At the poles, the angles taken by the necks of the compound or conjoined calyces are not constant, but those in the mid portion of the kidney are aligned in two rows anteriorly and posteriorly at an angle of about  $70^\circ$  to each other (right,  $60^\circ + 16^\circ = 76^\circ$ ; left,  $63^\circ$ ).

From the frontal plane of the kidney, the angles are  $46^\circ$  anteriorly for the axis of the anterior calyces and  $30^\circ$  posteriorly for that of the posterior calyces.

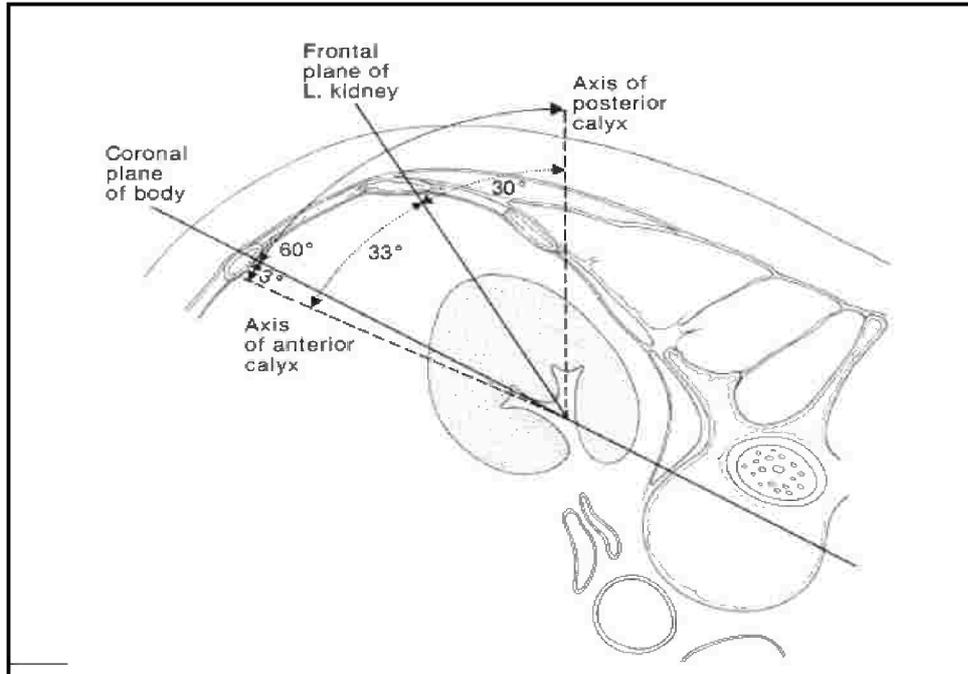


**Fig 2:** Orientation axis of anterior and posterior calyces of right kidney to coronal plane of the body.<sup>(17)</sup>

### Left kidney

The angle of the axis of the anterior calyceal angle is  $3^\circ$  anterior to the coronal plane of the body. The typical anterior set of calyces lies close to the coronal plane. Therefore, most portions of an anterior calyx are visualized on a urogram of a supine subject, whereas the posterior calyces appear end-on. The angle of the axis of the posterior calyx is 60 degrees posteriorly from the coronal plane.

From the frontal plane of the kidney, the anterior calyces have an angle of  $33^\circ$  anteriorly; the posterior calyces have a similar angle of  $30^\circ$ , but posteriorly. However, there is great variation in calyceal morphology and arrangement.

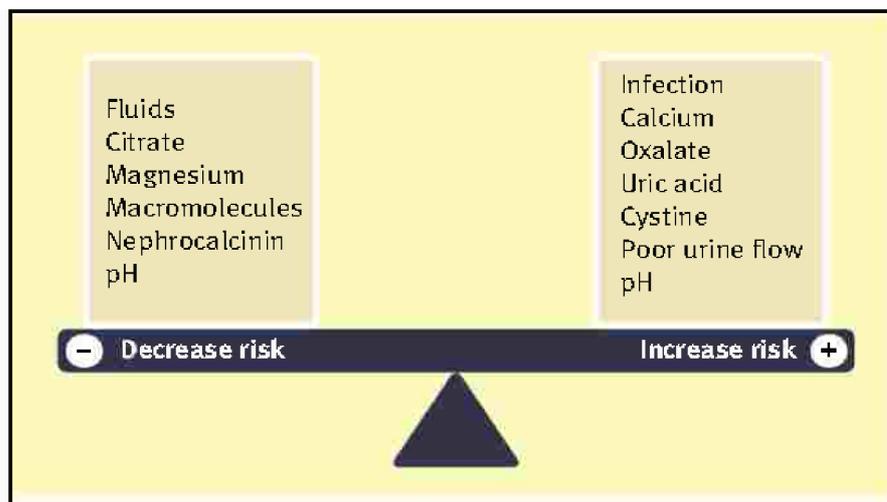


**Fig 3:** Orientation axis of anterior and posterior calyces of left kidney to coronal plane of the body.<sup>(17)</sup>

### Pathogenesis of stone formation

Similar to the adult population, the most common metabolic etiology of pediatric stone disease is hypercalciuria. Further, a positive family history of stone disease has been reported in 52% of children with idiopathic hypercalciuria. Other studies have found abnormalities in urinary citrate and oxalate concentrations in children with urolithiasis. In a study of 78 children between 1 and 15 yr of age with calcium stones, hypocitraturia was 4.3 times more common than in healthy controls.<sup>(18)</sup>

The crystallization of ions, their subsequent growth and aggregation lead to stone formation. This multi-factorial process is influenced by concentration of urinary ions, urine volume and flow, urinary pH and the balance of molecules that promote and inhibit stone formation.<sup>(4)</sup>



**Fig 4:** Shows factors that increase and decrease risk of crystallization.<sup>(4)</sup>

In a prolithogenic environment, a nidus or nucleus develops from crystallization of ions or around a foreign particle, such as bacteria. The nidus may then aggregate into a stone through precipitation or crystal growth, a process called nucleation. Nucleation of stones can be homogeneous or heterogeneous, with common ions including calcium, phosphate, oxalate, citrate and uric acid. This is of practical importance as a nidus is easily dissolved by medical treatment or a change in urinary environment. Mature, fully formed stones are extremely difficult to dissolve with medical therapy. The majority of renal stones are composed of calcium oxalate (45-65%) and calcium phosphate (14-30%). Struvite (magnesium ammonium phosphate), cystine and uric acid stones make up the remaining 5-10 %.<sup>(4)</sup>

## **Calcium stones**

Calcium stones are usually made from calcium oxalate or calcium phosphate. Supersaturation of calcium (hypercalciuria) and oxalate (hyperoxaluria) or decreased concentration of inhibitors, such as citrate (hypocitraturia), plays a major role in the formation of calcium oxalate stones.<sup>(19)</sup>

## **Hypercalciuria**

Hypercalciuria is defined by a 24-hour urinary calcium excretion of more than 4 mg/kg/day in a child weighing less than 60 kg. In infants younger than 3 months, 5 mg/kg/day is considered to be the upper limit of normal for calcium excretion.<sup>(19)</sup>

Hypercalciuria is the most common cause of metabolic stone disease and is found in more than 50% of children with urinary stones.<sup>(20)</sup> Hypercalciuria can be classified as either idiopathic or secondary. Idiopathic hypercalciuria is diagnosed when clinical, laboratory, and radiographic investigations fail to delineate an underlying cause. Secondary hypercalciuria occurs when a known process produces excessive urinary calcium. In secondary (hypercalcaemic) hypercalciuria, a high serum calcium level may be due to increased bone resorption (hyperparathyroidism, hyperthyroidism, immobilization, acidosis, metastatic disease) or gastrointestinal hyper absorption (hypervitaminosis D).<sup>(21)</sup>

Secondary causes of hypercalciuria should be particularly considered if there is a positive family history, failure to thrive, rickets, renal dysfunction, proteinuria, dysmorphic features or a poor response to therapy. Secondary hypercalciuria occurs when a known process produces excessive urinary calcium such as increased bone resorption (hyperparathyroidism, hyperthyroidism, immobilization, acidosis, metastatic disease, McCunee-Albright syndrome), gastrointestinal hyper absorption (hypervitaminosis D, sarcoidosis, milk-alkali syndrome) or lack of renal tubular re-absorption (Dent's disease, Bartters syndrome or renal tubular acidosis).<sup>(4)</sup>

A good screening test for hypercalciuria compares the ratio of urinary calcium to creatinine. The normal calcium-to-creatinine ratio in children is less than 0.2. If the calculated ratio is higher than 0.2, repeat testing is indicated. Neonates and infants have a higher calcium excretion and lower creatinine excretion than older children. If the follow-up ratios are normal, then no additional testing for hypercalciuria is needed. However, if the ratio remains elevated, a timed 24-hour urine collection should be obtained and the calcium excretion calculated.<sup>(19,22)</sup>

The 24-hour calcium excretion test is the criterion standard for the diagnosis of hypercalciuria. If calcium excretion is higher than 4 mg/kg/day (0.1 mmol/kg/day), the diagnosis of hypercalciuria is confirmed and further evaluation is warranted. Further evaluation includes levels of serum bicarbonate, creatinine, alkaline phosphatase, calcium, magnesium, pH, and parathyroid hormone. Freshly voided urine should be measured for pH.<sup>(19,21,23)</sup>

A 24-hour urine collection should also be collected for measurement of calcium, phosphorus, sodium, magnesium, citrate and oxalate. Meanwhile dietary manipulations should be tried to normalize urine calcium. Urinary calcium may change with restriction of sodium in the diet, especially when it is higher than normal.<sup>(24)</sup>

Initial management of hypercalciuria is always to increase fluid intake and urinary flow. Dietary modification is a mandatory part of effective therapy. The child should be referred to a dietician to assess accurately the daily intake of calcium, animal protein, and sodium. Dietary sodium restriction is recommended as well as maintenance of calcium intake consistent with the daily needs of the child. A brief trial of a low-calcium diet can be carried out to determine if exogenous calcium intake is contributing to high urinary calcium. However, great caution should be used when trying to restrict calcium intake for long periods.<sup>(25)</sup>

Hydrochlorothiazide and other thiazide-type diuretics may be used to treat hypercalciuria at a dosage of 1-2 mg/kg/day.<sup>(26, 27)</sup> Citrate therapy is also useful if citrate levels are low or if hypercalciuria persists, despite other therapies.<sup>(28)</sup>

### **Hyperoxaluria**

Oxalic acid is a metabolite excreted by the kidneys. Only 10-15% of oxalate comes from diet. Normal school children excrete less than 50 mg (0.57 mmol)/1.73m<sup>2</sup>/day, while infants excrete four times as much. Hyperoxaluria may result from increased dietary intake, enteric hyper absorption (as in short bowel syndrome) or an inborn error of metabolism.<sup>(26, 29)</sup>

Two types of primary hyperoxaluria have been identified. These two types of enzymatic deficiencies are characterized by calcium oxalate nephrolithiasis, nephrocalcinosis, and renal failure.<sup>(4)</sup>

Type I primary hyperoxaluria occurs due to a deficiency of the hepatic peroxisomal enzyme, alanine glyoxylate aminotransferase. This metabolic defect is more common and results in increased urinary excretion of oxalic acid, glyoxylic acid, and glycolic acid. The amount of residual enzyme activity determines the clinical onset of urolithiasis and progressiveness of renal insufficiency, with death often occurring before 20 years of age in the most severe form. Type II primary hyperoxaluria occurs because of deficiencies in hepatic D-glycerate dehydrogenase and glyoxylate reductase activity. Urinary excretion of glycolic acid is normal, and there is a marked increase in the excretion of L-glycerate and oxalate. Type II hyperoxaluria appears to behave in a more indolent and benign fashion with a better long-term prognosis than for type I.<sup>(30)</sup>

Other forms of hyperoxaluria, secondary or acquired hyperoxaluria, as mentioned earlier, may be due to hyper absorption of oxalate in inflammatory bowel syndrome, pancreatitis and short bowel syndrome. Yet, the majority of children who have high levels of oxalate excretion in urine may not have any documented metabolic problem or any dietary cause. This is known as idiopathic 'mild' hyperoxaluria, with urine oxalate levels elevated only mildly in these cases.<sup>(26)</sup>

The stone composition is calcium oxalate in approximately 70% of patients, uric acid in 20%, and the remainders are composed of mixed or miscellaneous constituents. The majority of cases present in late childhood or adolescents with recurrent stones and nephrocalcinosis. The condition is often only detected once renal function is impaired, with diagnosis commonly made after end-stage renal failure. Children under the age of one may present with failure to thrive, renal stones, anemia and metabolic acidosis. Systemic oxalate deposition, systemic oxalosis, occurs in blood vessels, retina, myocardium, bone marrow and eventually throughout the body.<sup>(4)</sup>

The diagnosis is made upon laboratory findings of severe hyperoxaluria and clinical symptoms. The definitive diagnosis requires liver biopsy to assay the enzyme activity. Treatment of hyperoxaluria consists of promotion of high urine flow and restriction of oxalate in diet. Use of pyridoxine may be useful in reducing urine levels, especially in type I primary hyperoxaluria.<sup>(26,29)</sup>

### **Hypocitraturia**

Citrate is a urinary stone inhibitor. Citrate acts by binding to calcium and by directly inhibiting the growth and aggregation of calcium oxalate as well as calcium phosphate crystals. Thus, low urine citrate may be a significant cause of calcium stone disease. In adults, hypocitraturia is the excretion of citrate in urine of less than 320 mg/day (1.5 mmol/day) for adults; this value must be adjusted for children depending on body size.<sup>(31,32)</sup>

The most common cause for hypocitraturia in children is renal tubular acidosis (RTA). Three types of RTA have been described. Only RTA I have been associated with nephrolithiasis.<sup>(33)</sup> An incomplete form of RTA has been described as an inability to acidify urine with no evidence of systemic acidosis. These patients also secrete high levels of urinary calcium and low levels of urinary citrate, making them susceptible to nephrocalcinosis and recurrent nephrolithiasis.<sup>(34-36)</sup>

Environmental factors that lower urinary citrate include a high-protein intake and excessive salt intake. Many reports emphasize the significance of hypocitraturia in pediatric calcium stone disease. Presence of hypocitraturia ranges from 30% to 60% in children with calcium stone disease.<sup>(32)</sup>

Hypocitraturia usually occurs in the absence of any concurrent symptoms or any known metabolic derangements. It may also occur in association with any metabolic acidosis, distal tubular acidosis or diarrhoeal syndromes. Due to the increased stone risk in hypocitraturia, the restoration of normal citrate levels is advocated to reduce stone formation. Although some studies have shown that citrate replacement therapy reduces the risk of stone formation in an adult population, there are few relevant studies in children. Hypocitraturia is treated by potassium citrate at a starting dose of 1 mEq/kg, given in two divided doses.<sup>(32)</sup>

### **Uric acid stones**

Uric acid stones are responsible for urinary calculi in 4-8% of children. A daily output of uric acid of more than 10 mg/kg/day is considered to be hyperuricosuria.<sup>(26)</sup>

Uric acid is the final product of purine metabolism. Uric acid excretion is greatest in newborns and decreases with age until adolescents. Hyperuricosuria is familial or idiopathic with normal serum uric acid or caused by inborn errors of purine metabolism, high cell turn over states, disorders of the proximal tubule and inherited disorders of the urate transporter in the proximal tubule.<sup>(4)</sup> The formation of uric acid stones is dependent mainly on the presence of acidic urinary composition. Uric acid remains in an undissociated and insoluble form at a pH of less than 5.8.<sup>(26)</sup>

Uric acid stones are non-opaque stones, and plain radiographs are insufficient for uric acid stones. Alkalinization of urine is the mainstay of prevention for uric acid stones. Potassium citrate preparations are useful as alkalinizing drugs. Maintaining a urine pH of 6 to 6.5 is sufficient for prevention of uric acid stones.<sup>(26)</sup>

### **Cystine stones**

Cystinuria is the cause of 5-10% of pediatric stones with half of the affected patients developing stones in their lifetime. Incidence peaks in the 2nd and 3rd decade of life and declines during adulthood. Patients develop recurrent, often bilateral renal stones, chronic urinary tract infections and renal dysfunction often leading to end-stage renal failure.<sup>(4)</sup>

Cystinuria is a complex autosomal recessive disorder, which results in a defect in the transporter of L-cystine and the dibasic amino acids ornithine, arginine and lysine (remembered with the mnemonic COLA!) in the proximal tubule of the kidney.<sup>(4)</sup>

Only cystine is insoluble at urinary pH and its precipitation results in stone formation. Cystine stones are faintly radio-opaque and may be difficult to identify by as a plain film. They are also hard in texture and more difficult to disintegrate by extracorporeal shock-wave lithotripsy (ESWL).<sup>(37)</sup>

The medical treatment for cystine stones aims to reduce cystine saturation in urine and increase its solubility. The initial treatment consists of maintaining a high urine flow and the use of alkalinizing agents, such as potassium citrate to maintain urine pH at above 7.0. If this treatment fails, the use of D-penicillamine or  $\alpha$ -mercaptopyropionol glycine may reduce cystine levels in urine and prevent stone formation. Use of these drugs can be associated with severe side effects, such as bone marrow depression and nephrotic syndrome.<sup>(37)</sup>

### **Infection stones (struvite stones)**

Infection-related stones constitute nearly 5% of the urinary stones in children. Renal stones precipitated by infection are classically caused by urease-producing organisms, most commonly *Proteus* spp. Urease breaks down urea into ammonia and carbon dioxide and increases urinary pH which precipitates the formation of phosphate-based stones. *Staphylococcus aureus*, *Klebsiella* spp. and *Pseudomonas* spp. less commonly produce urease. These organisms result in the formation of struvite and calcium phosphate stones. Struvite stones are common and often present as staghorn calculi.<sup>(4)</sup>

In the alkaline environment triple phosphates form, and eventual outcome is the super saturation of magnesium ammonium phosphate and carbonate apatite that lead to stone formation. In addition to bacterial elimination, stone elimination is essential for treatment because stones will harbor infection inside, and antibiotic treatment will not be effective. Consideration should be given to investigate any congenital problem that causes stasis and infection. Genitourinary tract anomalies predispose to formation of such stones.<sup>(4)</sup>

## **Clinical presentation and diagnostic evaluation**

### **Clinical presentation**

Adults typically present to medical services with excruciating renal colic and hematuria. This is not the case in children, especially the very young.<sup>(4)</sup>

An Italian study reported that approximately 70% of children under the age of eight presented with central or diffuse abdominal pain. Only 29% presented with flank pain, compared to 85% of children over eight years of age.<sup>(4)</sup>

- Abdominal pain is the primary complaint in the majority of patients. Pain typical of renal colic is more reliable in older children, with younger children presenting with non-specific abdominal pain, sub-acute pain or recurrent abdominal pain.
- Macroscopic hematuria is another common presenting complaint but only 30% present with both abdominal pain and macroscopic hematuria.
- Microscopic hematuria may be the sole indicator, and this is more common in children.
- Other important presenting symptoms are dysuria, vomiting or urinary retention. Children often present with non-specific symptoms.
- Importantly 20% of children with renal stones are totally asymptomatic and are identified incidentally during investigations for urinary tract infections or unrelated problems. Early detection is desirable to reduce potential renal damage, relieve debilitating symptoms if present, and finally if it is found that the stone(s) are an inherited metabolic etiology it allows siblings to be screened early. In some cases, urinary infection may be the only finding leading to radiological imaging in which a stone is identified.<sup>(4,6)</sup>

### **Imaging**

- Many radio-opaque stones can be identified with a simple abdominal flat-plate examination.
- High resolution US is the first choice method for detecting and monitoring childhood urolithiasis.
- Non contrast helical CT may have an additional diagnostic role in clinically suspected renal, ureteral or bladder stones not clearly defined by US and particularly in the evaluation of equivocal findings suspicious for ureteral calculi, provided this assessment will have therapeutic implications.<sup>(37)</sup> If no stone is found but symptoms persist, spiral CT scanning is indicated. The most sensitive test. It is safe and rapid, with 97% sensitivity and 96% specificity.<sup>(39-41)</sup>
- Intravenous pyelography is rarely used in children but sometimes used to delineate the calyceal anatomy before percutaneous or open surgery.<sup>(41)</sup>

### **Metabolic evaluation**

Due to the high incidence of predisposing factors for urolithiasis in children and high stone recurrence rates, every child with urinary stone should be given a complete metabolic evaluation.<sup>(32,42,43)</sup>

Pediatric urolithiasis is often associated with metabolic abnormalities that can lead to recurrent stone episodes. In the first 5 years of life, the incidence rate of stone recurrence has been reported to range between 30% and 50%. Today, metabolic evaluation is recommended when pediatric stone disease occurs even for the first time.<sup>(44-46)</sup>

### **Metabolic evaluation includes**

- Family and patient history of metabolic problem, Previous or recurrent urinary tract infection, Immobility, Diet, Fluid intake, Prematurity (Increased urinary levels of prolithogenic factors), Prolithogenic drugs (e.g. diuretics, chemotherapeutic agents, salicylates, corticosteroids, vitamin A/D).
- Past medical history.
- Analysis of stone composition. Complete blood count, electrolytes, blood urea nitrogen, creatinine, calcium, phosphorus, alkaline phosphatase, uric acid, total protein, albumin, parathyroid hormone (if there is hypercalcemia).
- Spot urine analysis (to detect infection or microscopic hematuria) and culture, including ratio of calcium, uric acid, oxalate, cystine, citrate, and magnesium to creatinine.
- Urine tests, including a 24-hour urine collection for calcium, phosphorus, magnesium, oxalate, uric acid citrate, cystine, protein, and creatinine clearance.

### **Interventional Management**

With the advance of technology stone management has changed from open surgical approach to endoscopic techniques that are less invasive. Deciding the form of treatment depends on the number, size, location, composition and anatomy of the urinary tract.<sup>(43,47,48)</sup>

### **Extracorporeal shock-wave lithotripsy**

Since the initial report on shock-wave lithotripsy (SWL) by Newman et al.<sup>(49)</sup> in adults, much experience has accumulated on its use in children. Many reports confirm that SWL can be performed in children with no suspicion of long-term morbidity of the kidney.<sup>(50-53)</sup>

The mean number of shock waves for each treatment in children is about 1800 and 2000 and the mean power set varies between 14 kV and 21 kV. The use of ultrasonography and digital fluoroscopy has significantly decreased the radiation exposure and it has been shown that children are exposed to significantly lower doses of radiation compared to adults.<sup>(47,54,55)</sup> Concerns about anesthesia do not seem to be a problem anymore because of advances in technique and medication, even in the infant period. The type of anesthesia should be general or dissociative for children under 10 years of age, whereas conventional intravenous sedation or patient-controlled analgesia is an option for older children who are able to co-operate.<sup>(56)</sup>

Initial concern about the relatively smaller anatomy of children disappeared with the considerably good results of many reports. One of these studies concluded that renal stones greater than 20 mm need more than one session, the pediatric ureter was found to be at least as efficient as the adult for transporting stone fragments after ESWL.<sup>(57)</sup>

Localization of the calculi has been described as a significant factor affecting the success rates in different studies. Stones in renal pelvis and upper ureter seem to respond better to SWL. In these mentioned sites, the stone clearance rates are nearly 90%. However, SWL was found to be less effective for caliceal stones particularly the lower caliceal stones. Several studies reported stone-free rates for isolated lower caliceal stones varying between 50% and 62 %.<sup>(58-61)</sup>

Although stenting does not affect stone clearance, overall complication rates are higher and hospital stay is longer in the unstented patient.<sup>(62-63)</sup> Stenting is essential in solitary kidneys undergoing SWL treatment. Children with a large stone burden have a high risk of developing Stein-strasse and urinary obstruction and should be followed more closely for the risk of prolonged urinary tract obstruction after SWL. Post-SWL stent or nephrostomy tube placement may be needed in prolonged obstruction.<sup>(32,64)</sup>

Stone-free rates are significantly affected by various factors. Regardless of the location, as the stone size increases, the stone-free rates decrease and re-treatment rate increases. The stone-free rates for < 1 cm, 1-2 cm, > 2 cm and overall, were reported as nearly 90%, 80%, 60% and 80%, respectively. As the stone size increases, the need for additional sessions increases.<sup>(62-66)</sup>

Even those with staghorn calculi can be treated successfully with SWL monotherapy. Lottmann et al.<sup>(63)</sup> reported a stone-free rate of 82.6% higher in younger children. Al-Busaidy et al.<sup>(64)</sup> achieved similar success rates (79%) in children with staghorn calculi. The latter authors also evaluated the effect of prophylactic ureteral stents on stone-free and complication rates. The findings revealed that stenting did not affect the stone clearance; however, in the unstented patient group complication rates were higher (1% vs. 21%) and hospital stay was longer.<sup>(65)</sup>

Focusing on these relatively lower success rates, Tan et al.<sup>(67)</sup> noted that stone clearance is closely related with lower calyceal anatomy (infundibulopelvic angle and length). Alternatively, the results of the study by Onal et al.<sup>(61)</sup> suggested that calyceal pelvic anatomy in pediatric lower pole stones has no significant impact on stone clearance after SWL. Contrary to these findings, excellent results, such as 92%, had also been reported in the literature for lower calyceal stones.<sup>(58)</sup>

In treatment of urinary stone disease, complete removal of stone is essential. Historically, with SWL, the term clinically insignificant residual fragments “CIRF” was used to refer to fragments  $\leq 4$ mm associated with sterile urine in an otherwise asymptomatic patient that would pass spontaneously.<sup>(68)</sup> However, this term was not accepted by some authors because fragments have the potential to cause obstruction and are an important risk factor for stone growth and recurrence.<sup>(69)</sup>

Some studies have addressed the value of medical therapy on the outcome of residual fragments. Fine et al reported 50% stone re-growth in patients with CIRFs, was decreased to 16% with medical management.<sup>(70)</sup> Cicerello et al and Soygur et al demonstrated the benefit of potassium citrate therapy in the clearance of residual stone fragments.<sup>(71,72)</sup> Strem et al reviewed the natural history of CIRFs in 160 patients and observed that 43.1% of patients had a symptomatic stone event and/or required intervention after SWL.<sup>(73)</sup>

Tan et al.<sup>(74)</sup> reported a decreased stone-free rate in patients who had metabolic or anatomic risk factors (31.7% vs. 69.4%). Therefore, treatment of underlying causative factors and follow-up after SWL is of great importance.

In children with sterile preoperative urine cultures, antibiotic prophylaxis to decrease the infectious complications is not recommended. However, every effort should be made to sterilize the urine before ESWL, ureteroscopy, or percutaneous nephrolithotomy, as stated by Wu and Docimo.<sup>(75)</sup>

Complications arising from SWL in children are usually self-limiting and transient. The most common complications are:

- Renal colic;
- Transient hydronephrosis;
- Dermal ecchymosis;
- Urinary tract infection;
- Formation of Stein-strasse;
- Sepsis;
- Rarely, hemoptysis.<sup>(75)</sup>

## **Percutaneous nephrolithotomy**

SWL is the first choice for treating most renal pediatric stones. However, percutaneous renal surgery can be used for larger and complex stones. Pre-operative evaluation, indication and surgical technique are similar in children compared to adults. Percutaneous nephrolithotomy is used as monotherapy in most cases, but is also used as an adjunctive procedure to other therapies.<sup>(75)</sup>

Since the mid-1970s percutaneous nephrolithotomy (PCNL) has gained popularity and replaced open surgery in adults. A decade later, use of the same technique with the same instruments in seven children was first reported by Woodside et al.<sup>(76)</sup> the use of adult-sized instruments, in association with an increased number of tracts and sheath size, seems to increase blood loss. However, the development of small-caliber instruments means that PCNL can be used in children. Percutaneous nephrolithotomy has some advantages for children (particularly smaller children), such as smaller skin incision, single-step dilation and sheath placement, good working access for pediatric instruments, variable length, and lower cost.<sup>(75,77)</sup>

As monotherapy, PCNL is considerably effective and safe. The reported stone-free rates in the recent literature are between 86.9% and 98.5% after a single session. These rates increase with adjunctive measures, such as second-look PCNL, SWL and URS. Even in complete staghorn cases, a clearance rate of 89% has been achieved following a single session.<sup>(78-83)</sup>

In one study, none of the patients studied with DMSA (2, 3-dimercaptosuccinic acid) renal scan had renal scarring, and all except one of 72 renal units experienced improvement (or at least stabilization of renal function) on DTPA (diethylenetriamine-penta-acetic acid) scan after PCNL.<sup>(81)</sup>

The advancement in technology will additionally decrease renal and body-wall trauma, which will result in less pain, reduced severity or risk of complications, and shorter hospital stays, including the possibility of performing “tubeless” outpatient PCNLs as mentioned by Jackman et al.<sup>(77)</sup>

Moreover, in a study by Salah et al reported that simultaneous bilateral PCNL can be performed with the same efficacy and safety as in adults. However, they emphasized that they collected a huge amount of experience before attempting such an operation in children.<sup>(84)</sup>

The most frequently reported complications of PCNL in children are bleeding, post-operative fever or infection, and persistent urinary leakage. Bleeding requiring transfusion in the modern series is reported in less than 10%<sup>(85-90)</sup> and is closely associated with stone burden, operative time, sheath size and the number of tracts.<sup>(91)</sup> Post-operative infectious complications, such as fever with or without documented UTI, are reported as less than 15%, and the origin of fever is not always found to be the infection.<sup>(90,92)</sup>

However, PCNL may present problems in infants and preschool-age children because of the small size and mobility of the pediatric kidney, friable renal parenchyma, and the small size of the collecting system.<sup>(93)</sup> But with the availability of smaller sized instruments, miniaturized PCNL (‘mini-perc’) through a 13F or 14F sheath has become possible<sup>(94-96)</sup>, with decreased transfusion rates. This miniaturization has been further developed into the technique of ‘micro-perc’ using a 4.85F ‘all-seeing needle’. This technique is still experimental and enables the stone to be fragmented by a laser in situ and left for spontaneous passage.<sup>(97)</sup>

As experience has accumulated in adult cases, new approaches have also started to be applied in children, including tubeless PCNL. This technique has been used in uncomplicated surgery for stones smaller than 2 cm, with patients left either with an indwelling catheter or double J stent in the ureter<sup>(87,92)</sup> or totally tubeless.<sup>(98)</sup>

The mean postoperative hospital stay is not different from adults; it has been reported as 2 days in all the fore-mentioned studies and is exceedingly shorter than open surgery. The lesser invasive nature of this technique should make it become a promising alternative to open surgery in treatment of renal calculi in children.<sup>(98)</sup>

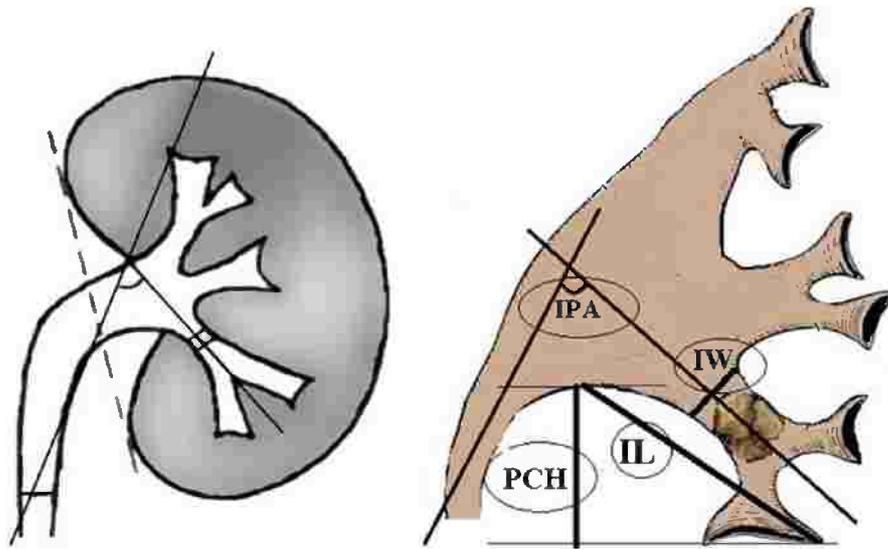
## **Ureteroscopy**

Treating ureteral stones with ureteroscopy in children was not made popular until Ritchey et al<sup>(99)</sup> and Shepard et al<sup>(100)</sup> successfully described its use in 1988. The first well-documented series of pediatric ureteroscopic procedures was reported in 1990.<sup>(101, 102)</sup> Initial attempts were limited to lower ureteral stones. Once smaller and flexible instruments became available, accessing any location in the urinary tract became possible. In addition, ureteroscopy provided the diagnosis and treatment of rare renal and ureteral pathologies (i.e. fibro-epithelial polyps).<sup>(103)</sup>

The technique used in children is similar to the one used in adults. It is strongly recommended that guide wires are used and the procedure is performed using direct vision. Routine balloon dilation of ureterovesical junction and ureteral stenting are controversial. In general, ureteric dilatation is being performed much less and only in selected cases. There is a tendency to use hydro-dilation more because it is similarly effective.<sup>(101-106)</sup>

Although extracorporeal shockwave lithotripsy is still used for the majority of urinary stones, endourology, in particular ureterorenoscopy (URS) has become more important during the past few years. Flexible URS is mainly used for caliceal stones, in most cases after unsuccessful SWL treatment.<sup>(107)</sup> As the stone-free rate of SWL is unsatisfactorily poor for the lower calyx, primary flexible URS offers an attractive procedure for this localization.<sup>(108)</sup> Increased experience and recent technological improvements such as active tip deflection, better lithotripsy probes and laser technology have led to a worldwide rising frequency of ureterorenoscopic procedures and an enlargement of indications.<sup>(109,110)</sup>

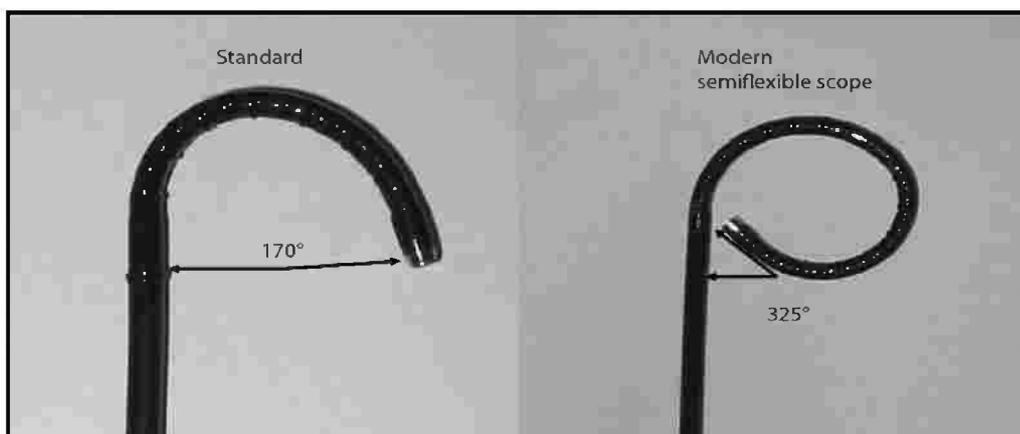
The infundibular length, infundibular width, pelvicaliceal height, and infundibulopelvic angle were measured by intraoperative retrograde urogram, as previously described by Elbahnasy et al (Fig. 5). IL was measured from the most distal point at the bottom of the infundibulum to a mid-point at the lower lip of the renal pelvis. IW was measured at the narrowest point along the infundibular axis. PCH was the distance between the lower lip of the renal pelvis and bottom of the calyx. The IPA of the lower calyces was measured as an inner angle formed at the intersection of the ureteropelvic axis defined by Elbahnasy et al and the central axis of the lower pole infundibulum.<sup>(111)</sup>



**Fig 5:** Infundibulopelvic angle for preoperative planning of lower pole access.<sup>(111)</sup>

Flexible ureterorenoscopy is rapidly becoming a major part of the urologist's therapeutic armamentarium. As with any sophisticated new technique, the operator must have a detailed knowledge of the features of the equipment, and perfect control of the instruments used. Over the past 2 decades flexible ureterorenoscopes (F-URS) continue to evolve and improve significantly including F-URS design, deflection capabilities, irrigation flow, imaging equipment, and durability. Due to the recent developments, endourologists have expanded the clinical indications for flexible ureterorenoscopy.<sup>(112-119)</sup>

Most flexible scopes have an active, bilateral deflection mechanism at the tip and a passive deflection mechanism proximally of the tip. Recently, a scope with two separate active deflection mechanisms has been introduced. While most standard flexible scopes have maximal deflection angles of 120°–180° (Fig. 6), a new generation of flexible ureterorenoscopes have bilateral deflections >270° (Fig. 6). A second advantage of such new-generation endoscopes is a stiffer shaft, that improves durability and controllability.<sup>(120)</sup>



**Fig 6:** Maximal tip deflection of standard and new generation flexible ureterorenoscopes.<sup>(121)</sup>

Different lithotripsy techniques, including ultrasonic, pneumatic and laser lithotripsy, have all been shown to be safe and effective. Because of the smaller size of the probes, laser energy is easier to use in smaller instruments and is more useful for pediatric cases.<sup>(122-126)</sup>

The holmium-YAG laser is a solid state laser made from a rare element, holmium, and an yttrium-aluminum-garnet (YAG) crystal. It delivers pulsatile energy and operates at a wave length of 2.100 nm (in the infrared part of the spectrum, which is invisible to the human eye). The laser allows intracorporeal lithotripsy to be performed, ureteral strictures to be managed, and urothelial tumors to be removed. This is a contact laser: For the system to work, the laser fiber must be placed right against the target (tissue or stone). A flexible ureterorenoscope requires two types of laser fibers: a small-diameter (150–200  $\mu\text{m}$ ) fiber and a large-diameter (365–600  $\mu\text{m}$ ) fiber. The large-diameter fibers will deliver more energy, but restrict the deflection of the scope. The reverse is true of the small-diameter fibers: they deliver less energy, but leave the scope free to deflect.<sup>(127)</sup>

A red or green aiming beam shows where the fiber is in relation to the target. The holmium-YAG laser may cut through guide wires and nitinol instruments. This property may be put to good use when it comes to freeing a stone that has become blocked into a nitinol extraction basket. The holmium-YAG laser's penetrative power is very weak (<0.4 mm); so there is no risk of tissue perforation if the laser fiber comes into contact with the tissue. To perforate the ureteral mucous membrane, the surgeon must push the laser fiber through to the ureteral wall. One of the dangers of the holmium-YAG laser is the risk of damaging the ureterorenoscope due to the photo-thermal effects of the laser. Generally, this type of damage happens when the surgeon starts the fragmentation and simultaneously withdraws the laser fiber. To avoid this, a perfect synergy between the ureterorenoscope and the laser fiber is mandatory.<sup>(127)</sup>

Multiple studies showed a growing number of case series on the use of flexible ureteroscopic interventions in children. Both intrarenal and ureteric stones can be treated using this approach.<sup>(128-132)</sup> In these studies, the authors generally did not use active orifice dilation, but attempted to use a ureteral sheath whenever possible. However, an important problem was the inability to obtain retrograde access to the ureter in approximately half of the cases.<sup>(131)</sup> This problem can be overcome by stenting and leaving the stent indwelling for passive dilation of the orifice, and performing the procedure in a second session. The success rates varied between 60 and 100%, with a negligible number of complications.<sup>(132)</sup> The need for additional procedures was related to stone size, although the use of flexible instruments seems feasible for the present time, more data are needed for comparison with other endourological modalities in children.<sup>(128)</sup>

The overall rate of ureteral injuries reported in the literature is 5%, with open repair reserved for the rare case of ureteral avulsion.<sup>(75)</sup>

Intraoperative complications are stone migration, inability to access the stone and ureteral perforation. Early postoperative complications include hematuria, pyelonephritis, stent migration, and fever, whereas ureteral stricture and vesicoureteral reflux constitutes the delayed postoperative complications. Appropriate sized pediatric instruments allow easy access to the stone and lessen the possibility of ureteral trauma. Stone migration can be prevented by cautious use of irrigation fluid and new cone baskets, which can be placed proximal to the stone.<sup>(133)</sup>

Schuster et al identified a ureteral perforation rate of 1.4% and a stricture rate of 0.9% in pediatric patients undergoing ureteroscopy for calculus disease.<sup>(105)</sup> Ureteral perforation and stone migration may be experienced regardless of the type of the energy source. Squeezing the stone gently between the probe and ureteric wall prevents this complication. Use of laser seems to be beneficial with its lower pushing effect than the electrohydraulic or pneumatic lithotripters. Besides this, as the depth of thermal effect is 0.5 mm to 1.0 mm, being cautious on this effect is important to prevent complications.<sup>(134)</sup>

Minor ureteral traumas or perforation are easily managed with a properly indwelled ureteric stent without any complication. Postoperative infectious complications can be prevented by having sterile urine preoperatively. Perioperative use of single-shot antibiotic prophylaxis has been shown to be effective in adults and should be used in children as well.<sup>(135)</sup>

Relative contraindications are: anatomical situations aggravating the retrograde access such as phimosis, urethral stricture, ureterocele, ureteral strictures and also arteriosclerosis or former urological surgery such as ureteral reimplantation or urinary diversion.<sup>(121)</sup>

## **Open stone surgery**

Most stones in children can be managed by SWL and endoscopic techniques. However, in some situations, open surgery is inevitable. Good candidates for open stone surgery include very young children with large stones and/or a congenitally obstructed system, which also requires surgical correction. Open surgery is also necessary in children with severe orthopedic deformities that limit positioning for endoscopic procedures.<sup>(136)</sup>

In centers with a well-established experience, a laparoscopic approach may be a good alternative for some cases as a last resort before open surgery. Suitable candidates include patients who have a history of previous failed endoscopic procedures, complex renal anatomy (ectopic or retro renal colon), concomitant ureteropelvic junction obstruction or caliceal diverticula, mega-ureter, or large impacted stones. Laparoscopic stone surgery via conventional or a robot-assisted trans-peritoneal or retroperitoneal approach can be attempted. However, there is very limited experience with these techniques and they are not routine therapeutic modalities.<sup>(136,137)</sup>