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1. BACKGROUND

The management of patients with urolithiasis is an important part of everyday urological practice. The optimal clinical management of urolithiasis requires knowledge of the diagnostic procedures, the rational treatment of acute stone colic, stone expulsion treatment, and the latest methods of stone removal. A basic understanding of the aetiology of stone formation and of metabolic risk evaluation are also essential, as they provide a sound basis on which to select appropriate measures to prevent stone recurrence.

During the past few decades, the treatment of urolithiasis has been characterized by changes resulting from major technical achievements, improved understanding of the mechanisms of stone formation and advances in pharmacological treatment.

These guidelines are based on published results. Some of the therapeutic principles are based on evidence from randomized or controlled studies; some statements are based on other types of study or on substantial clinical experience. According to the principles of the European Association of Urology (EAU) Guidelines Office, the scientific basis for recommendations or statements has been classified by level of evidence (LE) and grade of recommendation (GR) when appropriate. The criteria for LE and GR are given in Tables 1 and 2.

Table 1: Level of evidence (LE)*

<table>
<thead>
<tr>
<th>Level</th>
<th>Type of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>Evidence obtained from meta-analysis of randomized trials</td>
</tr>
<tr>
<td>1b</td>
<td>Evidence obtained from at least one randomized trial</td>
</tr>
<tr>
<td>2a</td>
<td>Evidence obtained from one well-designed controlled study without randomization</td>
</tr>
<tr>
<td>2b</td>
<td>Evidence obtained from at least one other type of well-designed quasi-experimental study</td>
</tr>
<tr>
<td>3</td>
<td>Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies and case reports</td>
</tr>
<tr>
<td>4</td>
<td>Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities</td>
</tr>
</tbody>
</table>

modified from Sackett et al. (1)

Table 2: Grade of recommendation (GR)*

<table>
<thead>
<tr>
<th>Grade</th>
<th>Nature of recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomized trial</td>
</tr>
<tr>
<td>B</td>
<td>Based on well-conducted clinical studies, but without randomized clinical trials</td>
</tr>
<tr>
<td>C</td>
<td>Made despite the absence of directly applicable clinical studies of good quality</td>
</tr>
</tbody>
</table>

modified from Sackett et al. (1)

In several statements, the methods considered have been assigned preference numbers, 1, 2, 3, etc, to indicate which treatment alternative was considered most appropriate or was preferred, according to the literature or consensus reached. If two procedures were considered equally useful, the same preference number is given. The preferred treatment alternative always has the preference number 1.

For the management of patients with stones in the ureter (see Chapter 9), we refer to the 2007 Guideline for the Management of Ureteral Calculi, a document resulting from collaboration between the American Urological Association (AUA) and the EAU (2, 3; http://www.auanet.org/guidelines and http://www.uroweb.org/professional-resources/guidelines). An ‘index patient’ has been defined to describe the typical individual with a ureteral stone.

The index patient is a non-pregnant adult with a unilateral non-cystine/non-uric acid radiopaque ureteral stone without renal calculi requiring therapy whose contralateral kidney functions normally and whose medical condition, body habitus, and anatomy allow any one of the treatment options to be undertaken.

Whenever possible, statements are graded as ‘standard’, ‘recommendation’ or ‘option’ to reflect the degree of flexibility in application. ‘Standard’ is the most rigid treatment policy; ‘recommendation’ has significantly less rigidity, and ‘option’ allows for the greatest flexibility.

1. **STANDARD**: the health outcomes of the alternative interventions are sufficiently well known to permit meaningful decisions, and there is virtual unanimity about which intervention is preferred.
2. **RECOMMENDATION:** the health outcomes of the alternative interventions are sufficiently well known to permit meaningful decisions, and an appreciable, but not unanimous, majority agrees on which intervention is preferred.

3. **OPTION:** the health outcomes of the interventions are not sufficiently well known to permit meaningful decisions, or preferences are unknown or equivocal.

It is not possible to translate these levels of grading to the grade of recommendations currently used by the EAU. However, the statements made in Chapter 9 will correspond, at least partly, to the preference numbers used in the other fields of urolithiasis discussed in this guideline.

For all clinical problems, the recommendations in this guideline are supported by comments based on the most important publications or, when data from the literature are contradictory or lacking, by panel opinion. However, no attempt was made to perform a structural analysis of the available literature.

Where recommendations are made, the main focus is on medical aspects. A discussion of the associated economic issues is beyond the scope of a European guideline document because of the wide geographical diversity of, and variation between, different financial systems in the European healthcare sector.

The Panel is aware of the different treatment and technical facilities available geographically. Our intention has been to highlight the alternatives that appear most convenient for the patient in terms of low invasiveness and risk of complications; however, this does not mean that other methods are not applicable. When a certain form of therapy is not recommended, this has been specifically stated.

This edition of Guidelines on Urolithiasis is an update of previously published documents (4–6).

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### REFERENCES


---

2. **CLASSIFICATION**

2.1 **Categories of stone-forming patients**

A system for categorizing stone-forming patients according to type of stone and severity of disease is shown in Table 3. These categories are useful when making decisions regarding the need for metabolic evaluation and medical treatment (1–4).
Table 3: Categories of stone-forming patients

<table>
<thead>
<tr>
<th>Definition</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection stone: magnesium ammonium phosphate, carbonate apatite or ammonium urate</td>
<td>INF</td>
</tr>
<tr>
<td>Uric acid/ammonium urate/sodium urate stone</td>
<td>UR</td>
</tr>
<tr>
<td>Cystine stone</td>
<td>CY</td>
</tr>
<tr>
<td>First-time stone former without residual stone or fragments</td>
<td>( S_0 )</td>
</tr>
<tr>
<td>First-time stone former with residual stone or fragments</td>
<td>( S_{res} )</td>
</tr>
<tr>
<td>Recurrent stone former with mild disease and without residual stone(s) or fragments</td>
<td>( R_{m0} )</td>
</tr>
<tr>
<td>Recurrent stone former with mild disease and with residual stone(s) or fragments</td>
<td>( R_{mres} )</td>
</tr>
<tr>
<td>Recurrent stone former with severe disease with or without residual stone(s) or fragments or with specific risk factors irrespective of otherwise defined category (Table 4)</td>
<td>( R_3 )</td>
</tr>
</tbody>
</table>

* Ammonium urate stones form when a urease-producing infection occurs in patients with urine that is supersaturated with uric acid/urate.

2.2 Specific risk factors for stone formation

Risk factors for stone formation are listed in Table 4.

Table 4: Risk factors for recurrent stone formation

- Onset of urolithiasis early in life (i.e. below 25 years of age)
- Stones containing brushite (calcium hydrogen phosphate; CaHPO\(_4\)\(\cdot\)2H\(_2\)O)
- Strong family history of stone formation
- Only one functioning kidney (although only one kidney does not mean an increased risk of stone formation, these patients should be particularly considered for measures to prevent stone recurrence)
- Diseases associated with stone formation
  - hyperparathyroidism
  - renal tubular acidosis (partial/complete)
  - cystinuria
  - primary hyperoxaluria
  - jejun-ileal bypass
  - Crohn's disease
  - intestinal resection
  - malabsorptive conditions
  - sarcoidosis
- Medication associated with stone formation
  - calcium supplements
  - vitamin D supplements
  - acetazolamide
  - ascorbic acid in megadoses (> 4 g/day)
  - sulphonamides
  - triamterene
  - indinavir
- Anatomical abnormalities associated with stone formation
  - tubular ectasia (medullary sponge kidney)
  - pelvo-ureteral junction obstruction
  - caliceal diverticulum, caliceal cyst
  - ureteral stricture
2.3 REFERENCES

3. DIAGNOSTIC PROCEDURES

3.1 Diagnostic imaging
Stone disease often presents as an episode of acute stone colic. Patients with renal stone colic usually have characteristic loin pain, vomiting and mild fever, and possibly a history of stone disease. The clinical diagnosis should be supported by an appropriate imaging procedure, which will immediately inform the decision to take a conservative approach or consider another treatment.

**Imaging is imperative in patients with fever or a solitary kidney, and when the diagnosis of stone is in doubt**

<table>
<thead>
<tr>
<th>LE = level of evidence; GR = grade of recommendation</th>
</tr>
</thead>
</table>

The diagnostic work-up of all patients with symptoms of urinary tract stones requires a reliable imaging technique (Table 5). For an acute stone colic, excretory urography (intravenous pyelography, IVP) has been the gold standard however, in recent years, unenhanced helical computed tomography (CT) has been introduced as a quick and contrast-free alternative (1-3). In randomized prospective studies, for patients with acute flank pain, the specificity and sensitivity of unenhanced helical CT was found to be similar (4, 5–9) or superior (10–11) to that obtained with urography.

In selected cases, additional information regarding renal function may be obtained by combining CT with contrast infusion. Advantages of CT are the demonstration of uric acid and xanthine stones, which are radiolucent on plain films, and the ability to detect alternative diagnoses (7, 12). However, the advantage of a non-contrast imaging modality must be balanced against the higher radiation dose given to the patient during CT investigation (3, 5, 13). Furthermore, CT is less suited for follow-up after treatment of radiopaque stones.

An alternative, commonly used, method for evaluating patients with acute flank pain is a plain film of the kidneys, ureters and bladder (KUB) combined with ultrasonography (US). Extensive experience shows that in a large proportion of patients these methods are sufficient for the diagnosis of a ureteral stone.

Special examinations carried out in selected cases include retrograde pyelography, antegrade pyelography and scintigraphy.

**Table 5: Imaging modalities in the diagnostic work-up of patients with acute flank pain**

<table>
<thead>
<tr>
<th>Preference number</th>
<th>Examination</th>
<th>LE</th>
<th>GR</th>
<th>References</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Non-contrast CT</td>
<td>1</td>
<td>A</td>
<td>1–12</td>
<td>3.1</td>
</tr>
<tr>
<td>1</td>
<td>Excretory urography</td>
<td>Standard procedure</td>
<td></td>
<td>3.1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>KUB + US</td>
<td>2a</td>
<td>B</td>
<td>6</td>
<td>3.1</td>
</tr>
</tbody>
</table>

Although intravascular administration of contrast medium is usually the responsibility of the radiologist, injection of contrast medium is occasionally used as an auxiliary procedure for stone localization during shock-wave lithotripsy. Many urologists also take responsibility for the diagnostic radiological work-up.
of patients with stone problems. A basic understanding of the risks associated with the use of contrast medium and the precautions needed is therefore essential (Table 6).

3.1.1 Allergy to contrast medium
When contrast medium needs to be administered to a patient who has had or who may be at risk of an allergic reaction to the medium, the following precautions must be taken (14, 15):
• always use low-molecular non-ionic contrast medium
• give a corticosteroid (e.g. prednisolone, 30 mg) between 12 hours and 2 hours before the contrast medium is injected.
• combine corticosteroid with an intramuscular injection of an antihistamine agent (e.g. clemastine, 2 mg) given 1 hour prior to administration of the contrast medium.

3.1.2 Metformin
Metformin, which is used to treat diabetes type II, may give rise to lactic acidosis in case of contrast-induced anuria (16–18). This unusual complication is caused by retention of dimethylbiguanide.
Unfortunately, lactic acidosis is associated with high mortality and great care needs to be taken when using contrast medium in patients taking metformin, particularly when renal function is reduced (i.e. serum creatinine level > 130 μmol/L or > 1.50 mg/100 mL).
According to the recommendations given by the European Society of Urogenital Radiology (14, 15), serum creatinine level should be measured in every patient with diabetes being treated with metformin. In addition, the following should be considered.
• In patients who are being treated with metformin and have a normal serum creatinine, contrast medium can be administered, but the intake of metformin should be stopped for 48 hours from the time of the radiological examination and until the serum creatinine remains normal.
• In patients with reduced renal function, metformin should be stopped and administration of contrast medium delayed until 48 hours have passed after the last intake of metformin. Treatment with metformin may resume 48 hours after the examination provided that serum creatinine remains at the pre-examination level.
• When no information on renal function is available, alternative imaging techniques should be used.
• When contrast medium has been given to a patient on metformin, for whom no information on the renal function is available, or who has reduced renal function, metformin must be stopped immediately and the patient hydrated so that diuresis is ≥ 100 ml/h during 24 hours. Serum creatinine, lactic acid and blood pH should be monitored. Symptoms of lactic acidosis are vomiting, somnolence, epigastric pain, anorexia, hyperpnoea, lethargy, diarrhoea and thirst. The investigative findings are a blood pH < 7.25 and serum lactic acid concentration > 5 mmol/L (16,17).

3.1.3 Reduced renal function
Intravenous administration of contrast medium might result in a reduced renal perfusion and toxic effect on tubular cells. Vasocostriction of glomerular afferent arterioles causes a reduced glomerular filtration rate (GFR) and increased renal vascular resistance. Nephrotoxicity caused by contrast medium is diagnosed by an increase of 25%, or at least 44 μmol/L, in the level of serum creatinine during the 3 days following intravascular administration of the agent, when there is no alternative explanation.

Risk factors for development of reduced renal function
The following risk factors should be noted before intravenous contrast medium is used:
• increased serum creatinine
• dehydration
• age over 70 years
• diabetes
• congestive heart failure
• concurrent treatment with nephrotoxic drugs, for example non-steroidal anti-inflammatory agents (NSAIDs)
• aminoglycosides should be stopped for at least 24 hours before contrast medium is injected.
Patients with multiple myeloma should be examined either after adequate hydration or using an alternative method. Avoid repeated injections of contrast medium at intervals less than 48 hours (see Section 3.1.2.) to 72 hours.

Dosage of iodine
Reduced renal function is defined as serum creatinine ≥ 140 μmol/L or GFR ≤ 70 mL/min.
For a patient with GFR 80–120 mL/min, the dose of iodine should not exceed 80–90 g. When the GFR is
reduced to 50–80 mL/min, the dose of iodine should not exceed the same amount as the GFR expressed in mL/min/1.73 m² body surface area (12, 13). Useful formulae for calculating GFR and body surface area are given in Table 7 (19). For further advice regarding the appropriate dose of contrast medium, see the guidelines presented by the Radiological Society (20). In patients with a serum or plasma creatinine ≥ 140 μmol/L (1.6 mg/100 mL), hydration, before and after use of contrast medium, may be beneficial in order to prevent nephropathy. Administration of N-acetylcysteine, 600 mg twice on the day before injection of contrast medium has been recommended to prevent renal failure caused by contrast medium (21).

3.1.4 Untreated hyperthyroidism

For patients in whom hyperthyroidism is suspected, the level of thyroid-stimulating hormone should be assessed before use of contrast medium. Contrast medium should not be given unless these patients are appropriately treated for hyperthyroidism.

Table 6: General considerations regarding the use of contrast medium

<table>
<thead>
<tr>
<th>Contrast medium should not be given, or should be avoided, in the following circumstances</th>
<th>LE</th>
<th>GR</th>
<th>Selected references</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patients with an allergy to contrast media</td>
<td>–</td>
<td>–</td>
<td>14,15</td>
<td>3.1.1</td>
</tr>
<tr>
<td>• Serum or plasma creatinine &gt; 150 μmol/L</td>
<td>4</td>
<td>C</td>
<td>15</td>
<td>3.1.1</td>
</tr>
<tr>
<td>• Patients receiving metformin</td>
<td>3</td>
<td>B</td>
<td>15–18</td>
<td>3.1.2</td>
</tr>
<tr>
<td>• Untreated hyperthyroidism</td>
<td>3</td>
<td>B</td>
<td>–</td>
<td>3.1.4</td>
</tr>
<tr>
<td>• Patients with myelomatosis</td>
<td>3</td>
<td>B</td>
<td>15</td>
<td>3.1.3</td>
</tr>
</tbody>
</table>

LE = level of evidence; GR = grade of recommendation

Table 7: Formulae for calculating glomerular filtration rate (GFR) and body surface area (19)

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>GFR</td>
<td>GFR = (140 – age)· kg/(0.82· serum creatinine)</td>
<td>GFR = (0.85 x (140 – age)· kg/(0.82· serum creatinine)</td>
</tr>
<tr>
<td>For patients &lt; 20 years, the</td>
<td></td>
<td></td>
</tr>
<tr>
<td>following formula should be</td>
<td></td>
<td></td>
</tr>
<tr>
<td>used:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body surface area = kg0.425 ·</td>
<td></td>
<td></td>
</tr>
<tr>
<td>height(cm)0.725 · 0.007184</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine clearance = 1.73m²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine clearance = (42.5 ·</td>
<td></td>
<td></td>
</tr>
<tr>
<td>height(cm)/serum creatinine) ·</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(kg/70)0.07</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3.1.5 References

3.2 Analysis of stone composition

Stones that pass spontaneously, are removed surgically, or excreted as fragments following disintegration, should be analysed to determine their composition (1–5). The preferred analytical procedures are X-ray crystallography and infrared spectroscopy. All patients should have at least one stone analysed. Repeated analysis is indicated when any changes in urine composition, as a result of medical treatment, dietary habits, environment or diseases, might have influenced stone composition.

When stone(s) or stone material have not been retrieved, stone composition may be assessed using the following:

- qualitative cystine tests (e.g. sodium nitroprusside test, Brand’s test (6), or any other cystine test)
bacteriuria/urine culture (in the case of a positive culture, ask for urease-producing micro-organisms)
- microscopic examination of the urinary sediment to detect crystals of struvite or cystine
- serum urate (in cases where a uric acid or urate stone is a possible alternative)
- urine pH (low in patients with uric acid stones, high in patients with infection stones)
- radiographic characteristics of the stone.

An appropriate quantitative or semi-quantitative analysis of stone material should enable the main constituent(s) to be determined.

The following calcium stones, which are not associated with infection, are referred to as radiopaque stones:
- calcium oxalate
  - calcium oxalate monohydrate
  - calcium oxalate dihydrate
- calcium phosphate
  - hydroxyapatite
  - carbonate apatite
  - octacalcium phosphate
  - brushite
  - whitlockite.

The following stones, which are not associated with infection, are referred to as uric acid/urate stones:
- uric acid
- sodium urate.

Infection stones have the following typical constituents:
- magnesium ammonium phosphate
- carbonate apatite.

Less common stone constituents include 2,8-dihydroxyadenine, xanthine and various drug metabolites (e.g. sulphonamide, indinavir). Calcium stones, uric acid/urate stones, cystine stones and ammonium urate stones associated with infection are referred to as ‘stones with infection’.

3.2.1 References

3.3 Biochemical investigations
3.3.1 Analytical work-up in the acute phase (Table 8)

Table 8: Biochemical analyses recommended for patients with an acute stone episode

<table>
<thead>
<tr>
<th>All patients</th>
<th>Urinary sediment/dipstick test for: Red cells, test for bacteriuria (nitrite) and urine culture in case of a positive reaction Serum creatinine to measure renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with fever</td>
<td>C-reactive protein and blood cell count</td>
</tr>
<tr>
<td>Patients who vomit</td>
<td>Serum/plasma sodium Serum/plasma potassium</td>
</tr>
</tbody>
</table>
Optional useful information

Approximate pH level\(^a\)
Serum/plasma calcium\(^b\)
All other examinations that might be necessary in case of intervention

\(^a\) Knowledge of pH might reflect the type of stone.
\(^b\) This might be the only occasion on which patients with hypercalcaemia are identified.

3.3.2 Analysis of urine in search for risk factors for stone formation

For an identification of metabolic risk factors for stone formation, an analytical programme for the different categories of stone formers is available (Table 9).

Table 9: Analytical programme for patients with stone disease

<table>
<thead>
<tr>
<th>Category of stone former(^1)</th>
<th>Blood analysis (serum/plasma)</th>
<th>Urine analysis follow-up</th>
<th>Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>INF</td>
<td>Creatinine</td>
<td>Culture, pH</td>
<td>Yes</td>
</tr>
<tr>
<td>UR</td>
<td>Creatinine, urate</td>
<td>Urate, pH</td>
<td>Yes</td>
</tr>
<tr>
<td>CY</td>
<td>Creatinine(^2)</td>
<td>Cystine, pH</td>
<td>Yes</td>
</tr>
<tr>
<td>S(_o)</td>
<td>Yes (see Table 11)</td>
<td>Limited urine analysis (only fasting spot urine)</td>
<td>No</td>
</tr>
<tr>
<td>S(_{res})</td>
<td>Yes (see Table 11)</td>
<td>Yes (see Table 11)</td>
<td>Yes</td>
</tr>
<tr>
<td>R(_{mo})</td>
<td>Yes (see Table 11)</td>
<td>Limited urine analysis (only fasting spot urine)</td>
<td>No</td>
</tr>
<tr>
<td>R(_{in-res})</td>
<td>Yes (see Table 11)</td>
<td>Yes (see Table 11)</td>
<td>Yes</td>
</tr>
<tr>
<td>R(_s)</td>
<td>Yes (see Table 11)</td>
<td>Yes (see Table 11)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

\(^1\) See Table 3 in Chapter 2 for an explanation of the categories of stone formers.
\(^2\) The type of medical treatment being received by these patients will determine which other blood variables need to be included in the follow-up analysis.

For each set of analyses, two urine collections are recommended. The urine collections are repeated when necessary (1–3). Several alternative collection options are feasible (Table 10).

Table 10: Some alternatives for urine collection

<table>
<thead>
<tr>
<th>Alternative</th>
<th>Timing of collection</th>
<th>Description of collection</th>
</tr>
</thead>
</table>
| 1           | Two 24-hour collections | Sample 1 collected in a bottle containing 30 mL of 6 mol/L hydrochloric acid  
Sample 2 collected in a bottle containing 30 mL of 0.3 mol/L sodium azide |
| 2           | One 24-hour collection | Sample collected in a bottle containing 30 mL of 6 mol/L hydrochloric acid |
| 3           | One 16-hour urine collection and one 8-hour urine collection | Sample 1 collected between 06.00 and 22.00 hours in a bottle containing 20 mL of 6 mol/L hydrochloric acid  
Sample 2 collected between 22.00 and 06.00 hours in a bottle containing 10 mL of 0.3 mol/L sodium azide |
| 4           | Spot urine sample | Excretion of each urine variable is related to creatinine level |

Hydrochloric acid (HCl) prevents precipitation of calcium oxalate and calcium phosphate in the container during storage. In addition, HCl counteracts oxidation of ascorbate to oxalate. In acidified samples, uric acid precipitates and must be dissolved by alkalinization if urate excretion is of interest. Urate can be analysed in samples collected with sodium azide as preservative.

For pH measurement, collection of urine without HCl is needed; a sample collected with sodium azide is useful. As urinary pH may alter during storage, a night-time sample in which pH is measured soon after urine collection is useful.

A patient with uncomplicated stone disease is one who is either stone-free after the first stone episode or who has a history of mild recurrent disease with long intervals between stone episodes (categories So, Rmo; Table 3). The stone, blood (serum or plasma) and urine analyses recommended for these patients are shown in Table 11.
Ideally, a fasting morning urine sample should be analysed. However, as it is not always easy to obtain this sample during routine clinical work, a spot urine sample can provide a rough guide to the need of further analyses.

A patient with complicated stone disease has a history of frequent recurrences, with or without residual fragments or stones in the kidney, or the patient presents specific risk factors. First-time stone formers with residual fragments may also be considered in this category (categories: Rs, Sres, Rm-res; Table 3). The stone, blood and urine analyses recommended for these patients are shown in Table 11 (4–12). Urine collection should be postponed until at least 4 weeks after stone removal or after an episode of obstruction and should never be carried out in the presence of infection or haematuria. For special tests that might be required see Table 12 (13–18).

Table 11. Analyses in patients with uncomplicated and complicated stone disease.

<table>
<thead>
<tr>
<th>Stone</th>
<th>Blood</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>In every patient one stone should be analysed.</td>
<td>Calcium</td>
<td>Fasting morning spot urine or spot urine sample:</td>
</tr>
<tr>
<td></td>
<td>Albumin¹</td>
<td>pH</td>
</tr>
<tr>
<td></td>
<td>Creatinine</td>
<td>Leucocytes / Bacteria</td>
</tr>
<tr>
<td></td>
<td>Urate²</td>
<td>Cystine test (when necessary)</td>
</tr>
</tbody>
</table>

**Additional analyses for patients with complicated calcium stone disease**

<table>
<thead>
<tr>
<th>Preference</th>
<th>Urine variable</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Calcium</td>
</tr>
<tr>
<td>1</td>
<td>Oxalate</td>
</tr>
<tr>
<td>1</td>
<td>Citrate</td>
</tr>
<tr>
<td>1</td>
<td>Creatinine</td>
</tr>
<tr>
<td>1</td>
<td>Volume</td>
</tr>
</tbody>
</table>

| 2         | Urate⁴       |
| 2         | Magnesium⁵   |
| 2         | Phosphate⁵,⁶ |
| 2         | Urea⁵,⁶      |
| 2         | Sodium⁴,⁶    |
| 2         | Potassium⁴,⁶ |

¹ Analysis of calcium + albumin to correct for differences in calcium concentration attributable to albumin binding, or direct analysis of ionized (free) calcium
² Optional
³ 24-hour urine, 16-hour + 8-hour urine or any other collection period can be chosen provided normal excretion data are available (4–7). A spot urine sample can be used with creatinine-related variables (7).
⁴ As uric acid precipitates in acid solutions, urate has to be analysed in a sample that has not been acidified or following alkalinization to dissolve uric acid. When a 16-hour urine sample has been collected in a bottle with an acid preservative, the remaining 8 hours of the 24-hour period can be used to collect urine in a bottle with sodium azide for urate analysis.
⁵ Analysis of magnesium and phosphate is necessary to calculate estimates of supersaturation with calcium oxalate (CaOx) and calcium phosphate (CaP), for example AP(CaOx) index and AP(CaP) index (8–12). Formulae are given below.
⁶ Urea, phosphate, sodium and potassium measurements are useful for assessing the patient’s dietary habits.

3.3.3 Comments on the analytical work-up

The purpose of analysing serum or plasma calcium is to identify patients with hyperparathyroidism or other conditions associated with hypercalcaemia. In the case of a high calcium concentration (> 2.60 mmol/L), the diagnosis of hyperparathyroidism should be established or excluded by repeated calcium analyses and assessment of the parathyroid hormone level (19–24).

When a stone analysis has not been carried out, a high serum urate level together with a radiolucent stone support the suspicion of a uric acid stone. Although a uric acid stone is usually invisible on a plain film (KUB), it is clearly demonstrated with a CT examination.

A spot morning urine sample should be used to measure pH (25). A pH above 5.8 in fasting morning urine raises the suspicion of incomplete or complete renal tubular acidosis (RTA) (26). In the same fasting morning or spot urine sample, bacteriuria and cystinuria can be excluded or confirmed (27).
The aim of adding serum potassium to the analytical programme is to obtain further support for a diagnosis of suspected rTa. Hypokalaemic hypocitraturia might be one reason for therapeutic failures in patients treated with thiazides.

The recommendation to collect two urine samples is based on observations that this approach will increase the likelihood of detecting urine abnormalities. Various collection periods (e.g. 24 hours, 16 hours, 17 hours, 12 hours, 4 hours, or even spot urine samples) are useful for this purpose, provided a set of normal values is available for the collection period (4–7).

The urine sample used for analysis of calcium, oxalate, citrate and phosphate must be acidified, preferably with HCl, to:
- maintain calcium, oxalate and phosphate in solution, during and after the collection period
- prevent bacterial growth and the associated alteration of urine composition
- prevent the in-vitro oxidation of ascorbate to oxalate (28, 29).

The following urine variables can be analysed in the acidified sample: calcium, oxalate, citrate, magnesium, phosphate, urea, sodium, chloride and potassium.

Although the creatinine concentration might be slightly altered, it must be assessed in the same sample when creatinine-related variables are used and also for conclusions on the completeness of the collection. Urate forms uric acid in the acidified urine and must therefore be analysed either following complete dissolution with alkali or in a urine sample that has not been acidified.

Optional analysis of urea, phosphate and sodium helps to assess dietary factors of therapeutic significance.

The protein intake can be derived from the urea excretion (Uurea, mmol/L) and urine volume in litres (V) as follows (30):

\[
\text{Intake of protein (g) during the 24 h period} = (U_{urea} \, \text{mmol}/24 \, \text{h}) \cdot 0.18 + 13
\]

An estimate of the ion-activity products of calcium oxalate (AP[CaOx] index) and calcium phosphate, known as the AP[CaP] index, can be calculated as follows (31–37):

\[
\text{AP[CaOx] index} = 1.9 \cdot \text{Ca}^{0.84} \cdot \text{Ox}^{0.22} \cdot \text{Mg}^{-0.12} \cdot V^{-1.03}
\]

In this formula, the urine volume (V) is expressed in litres (L). The urine variables Ca (calcium), Ox (oxalate), Cit (citrate), and Mg (magnesium) are expressed in millimoles (mmol) excreted during the collection period. The factor 1.9 is specific for the 24-hour period; for a 16-hour urine sample, this factor is 2.3. For other collection periods, consult reference 5.

The AP[CaOx] index corresponds approximately to \(10^9 \cdot AP_{\text{CaOx}}\) (where APCaOx is the ion-activity product of calcium oxalate).

The AP[CaP] index for a 24-hour urine sample is calculated as follows:

\[
\text{AP[CaP] index} = 2.7 \cdot 10^{-3} \cdot \text{Ca}^{1.07} \cdot \text{P}^{0.70} \cdot (\text{pH} - 4.5)^{6.8} \cdot \text{Cit}^{-0.20} \cdot V^{-1.31}
\]

The AP[CaP] index corresponds approximately to \(10^{15} \cdot AP_{\text{CaP}}\) (where APCaP is the ion-activity product of calcium phosphate). Factors for other collection periods can be found in reference 5. P is used for phosphate. A relationship between abnormalities in urine composition and severity of calcium stone formation has been demonstrated (38–44). Although individual abnormal urine variables might indicate a risk of stone formation, it is the concerted action of the various urine constituents that produces supersaturation and crystallization of the stone.

Occasionally, it may be necessary to measure pH variation during the day or to make an acid loading for identification of disturbances in urine acidification. The principles for such a work-up are summarized in Table 12.

Analytical findings in patients with incomplete and complete rTa are summarized in Table 13.
Table 12: Additional analytical work-up in patients with calcium stone disease

**pH profile** (13)
Repeated measurements of pH during the 24-hour period
• Frequent samples should be collected for immediate measurement of pH with pH paper or a glass electrode
• Sampling every second hour or otherwise as appropriate

**Acid loading** (14–18)
This test is carried out together with blood sampling to show whether or not the patient has a complete or an incomplete acidification defect
• Breakfast + ammonium chloride tablets (0.1 g/kg body weight), drink 150 mL
• 09.00 Collect urine and measure pH, drink 150 mL
• 10.00 Collect urine and measure pH, drink 150 mL
• 11.00 Collect urine and measure pH, drink 150 mL
• 12.00 Collect urine and measure pH, drink 150 mL
• 13.00 Collect urine and measure pH, lunch

**Interpretation**
pH of 5.4 or lower indicates no renal tubular acidosis (RTA)

Table 13: Analytical findings in patients with complete or incomplete distal renal tubular acidosis (RTA) (13)

<table>
<thead>
<tr>
<th>Test</th>
<th>Incomplete RTA</th>
<th>Complete RTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood (pH)</td>
<td>Low</td>
<td>Normal</td>
</tr>
<tr>
<td>Plasma bicarbonate</td>
<td>Low</td>
<td>Normal</td>
</tr>
<tr>
<td>Plasma/serum potassium</td>
<td>Low</td>
<td>Normal</td>
</tr>
<tr>
<td>Plasma/serum chloride</td>
<td>High</td>
<td>Normal</td>
</tr>
<tr>
<td>Urinary calcium</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Urinary phosphate</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Urinary citrate</td>
<td>Low</td>
<td>Low</td>
</tr>
</tbody>
</table>

RTA = renal tubular acidosis

3.3.4 A simplified overview of the principles of analytical work-up in patients
Correct categorization of patients requires both information on the stone composition and an actual imaging procedure. If a reasonable assumption regarding the patient’s category can be made, the principles shown in Figure 1 can be applied to all patients. If this assumption is not possible, an alternative analytical approach must be used until more data have been collected.
3.3.5 References


---

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>STONE</th>
<th>BLOOD</th>
<th>URINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>INF</td>
<td>YES</td>
<td>Creatinine</td>
<td>Culture Urease? pH</td>
</tr>
<tr>
<td>UR</td>
<td>YES</td>
<td>Urate Creatinine</td>
<td>Urate pH Volume</td>
</tr>
<tr>
<td>CY</td>
<td>YES</td>
<td>Creatinine</td>
<td>Cystine pH Volume</td>
</tr>
<tr>
<td>Calcium stone</td>
<td>YES</td>
<td>Calcium Albumin Creatinine (Urate)</td>
<td>Bacteria pH</td>
</tr>
<tr>
<td>So $R_{mo}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium stone</td>
<td>YES</td>
<td>Calcium Albumin Creatinine (Urate)</td>
<td>Calcium Oxalate Citrate Creatinine Volume (Magnesium) (Phosphate) (Urea) (Urate)</td>
</tr>
<tr>
<td>SRES $R_{mRES}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium stone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$R_{s}$</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


STONE BURDEN

The size of a concrement (stone burden or stone size) can be expressed in different ways. In the literature, the largest diameter (i.e. the length of the stone as measured on the plain film) is most commonly used to describe stone size. Using length (l) and width (w), surface area (SA) can be estimated for most stones (1):

\[ SA = l \cdot w \cdot \pi \cdot 0.25 \]
For a quick estimate of the stone SA, see Table A1 (Appendix 2). The SA can also be measured using computerized systems and from CT scans; however these procedures are not necessarily easy and the software not always available. Using SA, stone volume SV can be calculated as follows (2):

\[
SV = 0.6 \cdot SA^{1.27}
\]

In this guideline, we have based our statements on stone SA in addition to largest stone diameter. With the more common use of CT, improved estimates of SV can be obtained using length (l), width (w) and depth (d):

\[
SV = l \cdot w \cdot d \cdot \pi \cdot 0.52
\]

4.1 REFERENCES

5. TREATMENT OF PATIENTS WITH RENAL COLIC

5.1 Pain relief
Pain relief is usually the therapeutic step that needs to be taken most urgently in patients with an acute stone episode (Table 14).

Table 14: Pain relief for patients with acute stone colic

<table>
<thead>
<tr>
<th>Preference</th>
<th>Pharmacological agent</th>
<th>LE</th>
<th>GR</th>
<th>References</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Diclofenac sodium</td>
<td>1b</td>
<td>A</td>
<td>1–4</td>
<td>5.1</td>
</tr>
<tr>
<td>1</td>
<td>Indomethacin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Hydrodromorphine</td>
<td>4</td>
<td>C</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LE = level of evidence; GR = grade of recommendation

5.1.1 Treatment using non-steroidal anti-inflammatory drugs (NSAIDs)
Clinical trials have shown that NSAIDs (e.g. diclofenac) provide effective relief in patients who have acute stone colic (1–5). Moreover, the resistant index was reduced in patients with renal colic when NSAID treatment was given (6).

Is it recommended that pain relief should be initiated with diclofenac whenever possible (Table 15) and an alternative drug used if the pain persists. Hydromorphone and other opiates are associated with an increased risk of vomiting, and should not be given without simultaneous administration of atropine.

5.1.2 Prevention of recurrent episodes of renal colic
In a double-blind, placebo-controlled trial, recurrent pain episodes of stone colic were significantly fewer in patients treated with diclofenac, 50 mg tds, during the first 7 days. The effect was most pronounced in the first 4 treatment days (7). For patients who have ureteral stones that are expected to pass spontaneously, suppositories or tablets of diclofenac sodium, 50 mg bid, over 3–10 days, might be useful in reducing inflammation and the risk of recurrent pain.

Facilitation of Stone passage might be facilitated by administration of alpha-blocking agents or,
possibly, nifedipine (see Chapter 9 for further details). Alpha-receptor antagonists inhibit ureteral basal tone and peristaltic activity and dilate the lumen of the ureter. Calcium channel blocking agents reduce ureteral spasm and inhibit the fast peristaltic activity whereas the slow peristaltic activity remains unaffected.

The patient should be instructed to sieve the urine to retrieve a concrement for analysis. Passage of the stone and restoration of normal renal function should be confirmed using appropriate methods. When pain relief cannot be achieved by medical means, drainage using stenting or percutaneous nephrostomy or by stone removal should be carried out.

5.1.3 Effects of diclofenac on renal function
Diclofenac can affect renal function in patients with an already reduced function; however, there is no effect if the kidney are functioning normally (LE = 1b; GR = A) (8).

Table 15: Recommendations and considerations regarding pain relief for the patient with renal colic

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>LE</th>
<th>GR</th>
<th>Selected references</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment should be started with an NSAID</td>
<td>1b</td>
<td>A</td>
<td>1-4</td>
<td>5.1.1</td>
</tr>
<tr>
<td>Diclofenac sodium affects GFR in patients with reduced renal function, but not in patients with normal renal function</td>
<td>2a</td>
<td>2a</td>
<td>8</td>
<td>5.1.3</td>
</tr>
<tr>
<td>Diclofenac sodium is recommended to counteract recurrent pain after an episode of ureteral colic</td>
<td>1b</td>
<td>A</td>
<td>7</td>
<td>5.1.2</td>
</tr>
</tbody>
</table>

GFR = glomerular filtration rate; GR = grade of recommendation; LE = level of evidence; NSAID = non-steroidal anti-inflammatory drug.

5.2 Spontaneous passage of stones
Most ureteral stones pass spontaneously. For further details, please see Chapter 6 and Chapter 9 (9, 10).

5.3 Medical expulsive treatment (MET)
The facilitation of ureteral stone passage is discussed in detail in Chapter 9 (9, 10).

5.4 REFERENCES
6. INDICATIONS FOR ACTIVE STONE REMOVAL

The size, site and shape of the stone at the initial presentation influence the decision for operative intervention (Table 16). The likelihood of spontaneous passage must also be evaluated. Spontaneous stone passage can be expected in up to 80% in patients with stones ≤ 4 mm in diameter. For stones with increasing diameters, the chance for spontaneous passage is decreased (1–4). In the stone interval 6-10 mm spontaneous passage is seen between 10 and 53% of patients (Chapter 9).

The overall passage rate of ureteral stones is:
• proximal ureteral stones: 25%
• mid-ureteral stones: 45%
• distal ureteral stones: 70%.

For stones with a diameter exceeding 6–7 mm, removal is indicated. Studies have shown that asymptomatic stones in the kidney will eventually cause clinical problems (5).

Small stones (< 6–7 mm) in a calix can cause considerable pain or discomfort (6–12). These stones should be removed using a minimally invasive technique. A narrow caliceal neck may require dilatation.

Table 16: Indications for active stone removal

<table>
<thead>
<tr>
<th>Indications for considering active stone removal</th>
<th>LE</th>
<th>GR</th>
<th>Selected references</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stone diameter ≥ 7 mm (because of the chance of spontaneous passage is very low)</td>
<td>2a</td>
<td>B</td>
<td>1–5</td>
</tr>
<tr>
<td>Adequate pain relief cannot be achieved</td>
<td>4</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Stone obstruction is associated with infection*</td>
<td>4</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Risk of pyonephrosis or urosepsis*</td>
<td>4</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Single kidneys with obstruction*</td>
<td>4</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Bilateral obstruction*</td>
<td>4</td>
<td>B</td>
<td></td>
</tr>
</tbody>
</table>

* Diversion of urine with a percutaneous nephrostomy catheter or bypassing the stone with a stent are minimal requirements in these patients.

LE = level of evidence; GR = grade of recommendation.

6.1 REFERENCES


7. ACTIVE REMOVAL OF STONES IN THE KIDNEY

7.1 Extracorporeal shock-wave lithotripsy (ESWL) for removal of kidney stones

The introduction of ESWL during the early 1980s dramatically changed the management of urinary tract stones. The development of new lithotripters, modified indications and treatment principles have completely changed the treatment of kidney stones. Modern lithotripters are smaller and usually included in uroradiological tables, allowing application of not only ESWL but other diagnostic and ancillary procedures associated with ESWL. The latest-generation lithotripters are at least as effective as the first lithotripters, but are much cheaper and have greater versatility.

Contraindications to the use of ESWL are few, but include:  
- pregnancy  
- severe skeletal malformations  
- severe obesity  
- aortic and/or renal artery aneurysms  
- uncontrolled blood coagulation  
- uncontrolled urinary tract infections (1, 2).

ESWL can remove >90% of stones in adults (3-5). The success rate for ESWL depends on the efficacy of the lithotripter and upon:  
- size (volume), number, location and hardness of the stones  
- patient’s habitus  
- ambition and experience of the operator (6).

Each of these factors has an important influence on retreatment rate and final outcome of ESWL. Techniques other than ESWL, usually involving a percutaneous approach, should be used to treat large, hard stones (see below) (3-5,7-17).

Repeat treatment sessions

The disintegrating power of ESWL is generally very good. There is concern about using ESWL for large stones because residual fragments are common so repeat treatment may be necessary, particularly with later generations of lithotripters, which have smaller focal volumes. It is important to limit the number of shock waves and the power used in repeat treatments to avoid causing renal tissue damage and bleeding complications (see below).

The number of ESWL sessions should not exceed three to five. For more sessions, a percutaneous method might be a more rational option.

In the case of infected stones or bacteriuria, antibiotics should be given before ESWL and continued for at least 4 days after treatment.

LE = 4  
GR = C

LE = level of evidence; GR = grade of recommendation

There are no rules on how frequently ESWL sessions can be repeated. However, the interval between
two successive sessions must be longer for electrohydraulic and electromagnetic lithotripsy than for treatments using piezoelectric equipment. The risk of damaging the renal tissue is greatest with treatments directed towards stones in the kidney.

For stones in the ureter, rather than in the kidney, shorter intervals between treatment sessions are usually acceptable. Clinical experience supports this view.  

A variety of lithotripters are in use, it is not possible to make a general recommendation regarding the interval needed between two treatments. This should be determined by the energy level used and the number of shock waves given (18).

The number of shock waves that can be delivered at each session depends on the type of lithotripter and shock-wave power. There is no consensus on the maximum number of shock waves. However, as the shock-wave frequency increases, tissue damage increases (19). Stone disintegration improves at lower frequencies.

The optimal shock wave frequency is 1.0-1.5 Hz (20).

Anatomical abnormalities
Anatomical abnormalities may affect the outcome of ESWL. Malformations of the renal collecting system can cause stone formation, as they alter the mechanism of urine elimination and thus impair the passage of stone fragments. Auxiliary procedures are often needed, in anatomical abnormalities (21-27).

In 35,100 patients treated for kidney stones using ESWL, satisfactory disintegration was recorded in 32,255 (92%) (40-70). The stone-free rate in these patients was 70% with re-treatments in 10.5% (40-70) When results reported during the past 7 years were considered separately, the stone-free rates of 41- 90% corresponded with those reported for the Dornier HM3-lithotripter and for the second- and third-generation lithotripters. Patient selection, stone location, frequency of repeated treatment sessions, use of auxiliary procedures and the experience of the operator might explain the variable outcome. In a prospective randomised trial comparing the Dornier HM3- and the Lithostar Plus lithotripter, the stone-free rates were 89% and 87%, respectively (32). Although the disintegrating capacity varies considerably between devices, late-generation lithotripters can treat kidney stones effectively.

### 7.1.2 Factors influencing the outcome of ESWL

Studies using ESWL to remove kidney stones have reported stone-free rates of 66-99% inpatients who had stones ≤ 20 mm in diameter and 45-60% for stones > 20 mm in diameter (29-31). Similar results were seen with the Dornier HM3 lithotripter; stone-free rates were 75-89% for stones with a diameter ≤ 20 mm versus 39-63% for stones with a diameter ≥ 20 mm (28).

Complications
When ESWL is used to treat large (diameter >20 mm or SA > 300 mm2) renal stones, common complications can include:

- pain
- hydronephrosis
- fever
- occasional urosepsis, as a result of difficulties in the passage of stone particles, especially when disintegration is not sufficient (71-76).

Stents
A double-J stent reduces the obstructive and infective complications that can follow the use ESWL for large renal stones.

Insertion of an internal stent before ESWL is recommended when stones with a diameter ≥ 20 mm (~300 mm2) are to be treated (77).

A recent randomised study reported that the routine use of internal stents before ESWL does not improve outcome in terms of stone-free rate (LE = 1b, GR = A) (78).
The routine use of internal stents before ESWL does not improve outcome in terms of stone-free rate (78)

**LE = level of evidence; GR = grade of recommendation**

Stone particles may pass easily along stents while urine flows in and around the stent. This usually prevents obstruction and loss of ureteral contraction. Occasionally, stents do not efficiently draining purulent or mucoid material, thus leading to a risk of obstructive pyelonephritis. If fever lasts for a few days, a

The following factors all influence the outcome of treatment:

- location of stone mass (pelvic or caliceal)
- total stone burden (number and size of stones; stone volume)
- state of contralateral kidney (e.g. is the other kidney absent or functionless)
- composition and hardness of the stone.

### 7.1.2.1 Location of stone mass

The clearance rate for lower caliceal stones is less than that for stones located elsewhere in the kidney. The clearance rate for upper pole stones is faster than for stones in the lower pole. Many kidney stones are located in the lower calix. The best way to treat these stones is debatable. Most residual fragments are lodged in the lower caliceal system. These stones either originate in the lower pole calices or gravitate there from other locations. It is still unknown why stones preferentially develop in the lower pole calices, although the accumulation of fragments in this position is most probably due to the effect of gravity.

In up to 35% of patients treated using ESWL, the lower calices are incompletely cleared of disintegrated stone material. Using geometrical observations of the anatomy of the lower calix, attempts have been made to explain the incomplete clearance of fragments and to predict the outcome of ESWL treatments; however, the results are contradictory.

In the absence of a geometrical explanation, the size of the stones has been found to be the most important factor (79-83). Although the geometry of the lower calix system is important in the clearance of fragments, the discriminating power is not sufficiently strong to predict the outcome of ESWL or to selecting alternative methods for stone removal (35). Caliceal physiology is another important factor (84, 85).

Several authors have shown that an increased stone-free rate can be obtained with percutaneous nephrolithotomy (PNL), particularly when the stones are large (diameter >20 mm or SA > 300 mm2). The morbidity associated with PNL undoubtedly need to be taken into account. For stones with a diameter of ≤ 20 mm (surface area ~ 300 mm2), ESWL is recommended, despite the lower clearance rate of fragments.

A multi-centre randomised comparison between ESWL and ureteroscopic removal of stones from the lower calyceal system failed to show a significantly better result with ureteroscopy (86) (LE = 1b; GR = A).

### 7.1.2.2 Total stone burden

Although problems associated with stone removal increase with stone volume, there is no clear critical size. Most consider a stone diameter of 20 mm as the practical upper limit for ESWL, though some centres treat larger stones successfully with ESWL (36, 87).

It is difficult to provide specific guidelines on kidney stone removal, as residual fragments occur with stones less than 20 mm (300 mm²) wide, while very large stones can be disintegrated using only one ESWL session. These guidelines recommend ESWL as the first choice of treatment for stones with a diameter ≤ 20 mm (300 mm²). For stones with a diameter ≥20 mm (300 mm²), PNL could be considered, although ESWL may still be an option.

For stones with an area > 40 x 30 mm (1200 mm²) the combination of PNL and ESWL (sandwich approach) carries success rates of 71-96% with acceptable morbidity and complications. The use of ESWL after PNL seems to be more effective than using PNL after ESWL. The risk of complications for either combined treatment or PNL alone is higher than for ESWL monotherapy. With a solitary kidney, it might be possible to try ESWL monotherapy first, even if the stone has an area > 40 x 30 mm (1200 mm²) (75).

### 7.1.2.3 Composition and hardness of the stone

ESWL monotherapy of large calcium- or struvite-containing stones provides reasonable results for stone removal and complications (76). About 1% of patients treated for urinary tract stones by ESWL have cystine stones. A total of 76% of cystine stones have a maximum diameter > 25 mm (only 29% of all patients with stones have stones of this size). Up to 66% more ESWL sessions and shock waves are needed to achieve satisfactory results with large cystine stones than with other types of stone (88).
Instead of multiple ESWL sessions, PnL (possibly combined with ESWL) is an effective treatment for all other cystine stones (88, 89). Note that smooth cystine stones are much more susceptible than rough stones to shock waves (90).

Stone composition can be important in the disintegration and subsequent elimination of fragments. Stones made of uric acid and calcium oxalate dihydrate have a better coefficient of fragmentation than those made of calcium oxalate monohydrate and cystine; success rates for these two groups of stones were 38-81% and 60-63%, respectively (12). In cystine stones <15 mm, the stone-free rate was approximately 71%; in stones > 20 mm, the stone-free rate dropped to 40% (13). For cystine stones >15 mm, monotherapy ESWL is currently not recommended.

7.1.2.4 References


7.2 Percutaneous removal of renal stones

Most renal stones can be removed using percutaneous surgery. However, if ESWL is available, PNL should be used only when the outcome is likely to be less favourable after ESWL. Although PNL is minimally invasive, it is a surgical procedure and, to avoid complications, the patient’s anatomy must be considered.

Pre-procedural KUB (plain abdominal film of the kidneys, ureters and bladder) and intravenous urography (IVU) or computed tomography (CT) scans can be used to plan access and determine likely success. For example, whether stones will respond poorly to ESWL (e.g. stones made of cystine, calcium oxalate monohydrate, brushite) or if fragments are unlikely to pass (e.g. large stones, stones in caliceal diverticulae or horseshoe kidneys). Pre-procedural sonography and fluoroscopy of the kidney and the surrounding structures are recommended:

- to determine the optimal access site and stone position in the kidney (ventral or dorsal)
- to ensure organs adjacent to the kidney (e.g. spleen, liver, large bowel, pleura, lungs) are not within the planned percutaneous path (1,2).

Percutaneous puncture may be easier if a ureteral balloon catheter is used to dilate and opacify the collecting system. The catheter also prevents fragments falling into the ureter. The puncture can be made under combined ultrasound (US) and X-ray control or under biplanar fluoroscopy. Ultrasound makes it easier to identify, and therefore avoid damage to, neighbouring organs (3). In rare cases, where there are anatomical anomalies, CT-guided renal access may be an option (4).

The access site used most often is the dorsal calix of the lower pole. In the least traumatic access, the puncture site on the skin lies in the extension of the long axis of the target calix and the puncture passes through the papilla. The absence of major blood vessels results in only minimal bleeding. This is the safest access point because it uses the infundibulum as a conduit to the pelvis. A subcostal or supracostal upper pole access has been used frequently with good success for the treatment of staghorn stones.

Renal tract dilatation is possible using the Amplatz system, balloon or metallic dilators, with choice depending on experience, availability and costs. Although standard nephrosopes have shaft calibres of 24-30 F, ‘mini-perc’ instruments have smaller shaft calibres of 12-20 F and may therefore have a lower rate of tract dilation-related complications (e.g. bleeding or renal trauma). As treatment time increases with stone size, this method is recommended only for stones with a diameter < 20 mm (5). The value of mini-perc in adults has not been determined, but mini-perc is the method of choice for percutaneous stone removal in children (6-8).

In lower pole stones, ESWL, PNL and flexible uretero-nephroscopy are competing procedures with different success and complication rates and patient acceptance (9-10) (LE = 1b; GR = A). Stones can be extracted straightaway, or following disintegration by US-, electrohydraulic-, laser- or hydro-pneumatic probes. Continuous removal of small fragments by suction or extraction is preferred to reduce the number of residual fragments. In complicated cases or when a second intervention is necessary, a self-retaining balloon nephrostomy tube tamponading the tract and maintaining access to the collecting system is used at the end of the procedure. In uncomplicated cases, tubeless percutaneous nephrolithotomy, with or without tract fulguration, application of a sealant or double-J stenting, is a safe alternative (8,11) (LE = 1b; GR = A).

### 7.2.1 Complications

Major, but rare, complications are lesions to adjacent organs, which can be avoided by US-guided puncture. Bleeding is generally avoided by an anatomically oriented access, as described above. Sepsis and ‘transurethral resection syndrome’ indicate a poor technique that has resulted in high pressure within the
collecting system during manipulation. These problems can be avoided by using continuous flow instruments
or an Amplatz system (1,8). Major bleeding during the procedure requires termination of the operation,
placement of a nephrostomy tube, and secondary intervention at a later date. In most cases, venous bleeding
stops when the nephrostomy tube is clamped for some hours. Persistent or late secondary bleeding is caused
by an arterial injury and can be managed by angiographic super-selective embolisation.

As with open surgery, percutaneous procedures have different degrees of difficulty. The procedure is
more likely to be difficult when anatomical conditions limit the space available for the initial puncture, dilatation
and instrumentation, such as stones in diverticula, stones completely filling the target calix, or a large stone
burden caused by complete or partial staghorn stones. In these cases, only experienced surgeons should carry
out the procedure.

7.2.2  References

7.3  Retrograde removal of ureteral and renal stones (retrograde intrarenal surgery [RIRS])

During the past 20 years, ureterorenoscopy (URS) has dramatically changed the management of ureteral calculi
and is now used extensively in urology centres worldwide. URS is, however, a more invasive technique than
ESWL, and the treatment of choice for ureteral stones is therefore controversial. For renal calculi, ESWL and
PNL are the recommended primary treatment options. Following the wider availability and improvement of flexible URS, its value in removing renal calculi has to be determined. This latter procedure is termed retrograde intrarenal surgery (RIRS).

7.3.1 Standard endoscopic technique

**Before URS, antibiotic prophylaxis should be administered to ensure sterile urine (4, 5).**

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**Level of evidence; Grade of recommendation**

The basic endoscopic technique has been standardised (1-3).

- Fluoroscopic equipment must be available in the operating room.
- Pre-operative imaging of urinary tract confirms location of stone and identifies anatomical abnormalities.
- Under general anaesthesia, spinal anaesthesia or intravenous sedation, place patient in lithotomy position.
- Begin procedure using rigid or flexible cystoscopy.
- Introduce a safety wire (usually an 0.035-inch, non-hydrophobic, floppy tip) under endoscopic and fluoroscopic control and secure it to drapes.
- The safety guide wire prevents the risk of false passage if there is perforation.
- Intramural ureteral dilatation is not routine, but depends on size of ureteroscope and width of ureter.
- Retrograde access to upper urinary tract is usually obtained under video guidance, with a rigid ureteroscope alongside safety wire.
- Flexible ureteroscopes are most easily introduced via an additional guidewire or through an ureteral access sheath, although last-generation scopes allow bare passage in experienced hands. 
- Endoscopic lithotripsy is based on the use of different devices to break the stone into dust or fragments small enough for extraction. The stone may be fragmented by ultrasonic lithotripsy, electrohydraulic lithotripsy (EHL), laser lithotripsy or ballistic (= pneumatic) lithotripsy. Lithotripsy devices are described in Appendix 1. Small stones and fragments are best retrieved with a basket or a forceps (6-9).

**Stone extraction with a basket without endoscopic visualisation of the stone (blind basketing) should not be performed (see Chapter 9).**

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Irrigation with a piston syringe is needed to ensure good direct vision. Take care to avoid high-pressure irrigation as this is associated with an increased complication rate. Stent placement at the end of the procedure is optional and debatable (10-16). Most urologists leave the stent for about 1 week, although there is no evidence regarding the optimal interval. Patients should be followed up by plain abdominal film (IVU), CT or US.

7.3.2 Anaesthesia

Improvement of ureteroscopes and stone retrieval instruments has enabled ureteroscopic procedures for ureteral calculi to be carried out using sedation analgesia with similar success rates (88-97%) to those using general anaesthesia (17-19). URS is particularly useful for removal of distal ureteral stones in women (20). For treatment of renal calculi with flexible URS, general anaesthesia may help minimise movements of the kidney.

7.3.3 Assessment of different devices

7.3.3.1 Ureteroscopes

Rigid and flexible ureteroscopes are available. In most cases, miniaturisation (and regular pre-stenting of the ureter) avoid the need to dilate the intramural ureter and associated complications (21-23). The small tip diameters (5.0-7.5 F) allow easier and safer progression of rigid ureteroscopes up to the proximal ureter.

Flexible ureteroscopes (5-7.5 F) are suitable for access to the upper part of the ureter and renal collecting system, without dilatation of the intramural ureter in most cases (3, 24-27). In the lower ureter, a flexible ureteroscope is less suitable because of its tendency to fall back into the bladder. Current scopes provide higher tip deflections and are more durable than the older generation (28-30).

7.3.3.2 Disintegration devices

Disintegration devices are discussed in Appendix 1. Holmium:yttrium aluminium garnet (Ho:YAG) laser lithotripsy is a reliable method for treating urinary calculi, regardless of hardness (31-34) and is the preferred method when carrying out flexible URS (3, 34-37).

**Ho:YAG laser lithotripsy is the preferred method when carrying out flexible URS (3, 34-37).**

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**Level of evidence; Grade of recommendation**

UPDATE MARCH 2008
A 365 μm laser fibre is the best choice for ureteral stones. The 200 μm fibre preserves tip deflection of flexible ureterorenoscopes and allows fragmentation of intracalceal calculi (38). If manipulated with care, laser lithotripsy is safe; however, significant side-effects may be more common with EHL (39-43). For distal ureteral stones, Ho:YAG lithotripsy give better stone-free results at 3 months than EHL (87% versus 87%, respectively) (39).

Ballistic lithotripters (pneumatic or electropneumatic), using a 2.4 F probe in a semi-rigid ureteroscope, provide excellent fragmentation rates (90-96%). Low cost with simple and safe handling are major advantages of this type of device (44-46). Nevertheless, stone migration towards the renal pelvis from the mid- or proximal ureter may limit the use of ballistic lithotripsy (47,48).

7.3.3.3 Baskets and forceps
Ureteroscopic removal of small ureteral stones with a basket or forceps is a relatively quick procedure with a lower morbidity rate than that associated with lithotripsy (8,9). Several new endoscopic stone retrieval baskets are available.

| Nitinol baskets preserve tip deflection of flexible ureterorenoscopes and the tipless design reduces the risk of mucosa injury (38). Nitinol baskets are most suitable for use in flexible URS. | LE = 2b/3  
GR = B |
|---|---|

Nitinol baskets are more vulnerable than a stainless steel basket, and laser or EHL might break the wires of the basket (49,50).

7.3.3.4 Dilatation, ureteral access sheaths and stenting
Attempts to modify the standard technique of dilatation and stenting have been carried out during recent years. The use of thin ureteroscopes has resulted in reduced dilatation (0-40%), operating time and post-operative ureteral stenting.

Today, ureteral access sheaths are used widely to facilitate retrograde manipulation in the proximal ureter and the kidney. Available access sheaths (9-16 F) have a hydrophilic surface and are introduced via a guide wire with the tip placed in the proximal ureter. Operating time might be reduced for higher stone burdens where multiple ureter passages are necessary (51-53). Another advantage is the maintenance of a low-pressure irrigation system by continuous outflow through the sheath (54-55). First follow-up series indicate a low rate of ureteral strictures, comparable to sheathless URS (56).

| Stenting following uncomplicated URS is optional (see also Chapter 9. | LE = 1a  
GR = A |
|---|---|

Several randomised prospective trials have found that routine stenting after uncomplicated URS may not be necessary (10-16,57-60). Ureteric stenting is associated with lower urinary tract symptoms and pain that can, even if only temporary, reduce quality of life (58-64). In addition, complications associated with ureteral stenting, include:

- stent migration
- urinary tract infection
- breakage
- encrustation
- obstruction.

Moreover, ureteral stents increase the overall cost of URS. Unless a pull-string is attached to the distal end of the stent, secondary cystoscopy is required for stent removal (13). Indications for stenting after the completion of URS, including:

- ureteral injury
- stricture
- solitary kidney
- renal insufficiency
- a large residual stone burden.

7.3.4 Clinical results
7.3.4.1 Renal calculi
Current guidelines suggest ESWL is the therapy of first choice for intrarenal calculi ≤ 20 mm, with PNL used to treat larger stones (69,70). However, as the results using ESWL for lower pole stones are poor, the use of
primary PNL might be justified for smaller calculi starting from ≥ 15 mm in this location (69-73).

Flexible URS may offer an alternative to ESWL or PNL, but to date, this procedure has not been mentioned by most guidelines. Unfortunately, few comparative data are available on the use of flexible URS for renal calculi. The latest-generation ureteroscopes allow access to almost all calices. Together with laser lithotripsy, ureteral access sheaths and nitional retrieval tools, enable the removal of most calculi. Stone-free rates for calculi ≤ 1.5 cm are 50-80% (51,74-78); larger stones can also be treated successfully.

Flexible URS has been demonstrated to be an effective treatment for ESWL-refractory calculi (79-80).

Flexible URS has not been recommended as a first-line treatment for renal calculi, and there are no valid data to support such a recommendation. However, because using ESWL for lower pole stones has poor results, flexible URS could become a reliable first-line treatment for lower pole stones ≤ 1.5 cm.

Some authors have reported the combination of flexible URS with ESWL or PNL to improve stone-free rates (81-82). The simultaneous use of flexible URS and PNL may offer an attractive approach to achieve complete stone-free states after one procedure and to avoid multiple percutaneous tracts. However, such an approach requires significant experience and equipment and is therefore not used routinely.

7.3.5. Complications

A meta-analysis published by the EAU-AUA Guidelines panel has evaluated the most relevant complications of sepsis, Steinstrasse, stricture, ureteral injury and urinary tract infection (UTI). URS for ureteral calculi had minimal side-effects (65-66). Serious complications, including death and loss of kidney, were rare, and data from which to estimate their rates of occurrence were not available. Complication rates for the overall population, by treatment, size, and location are shown in Table 5, Chapter 9.

Significant acute complication rates of 11% and 9% have been reported for the proximal and distal ureters, respectively (65, 66). Ureteral strictures were the only long-term complication (estimated rate 1%). There is a pronounced relationship between the complication rate, equipment used, and/or expertise of the urologist (83). The overall complication rates reported in the recent literature are 5–9%, with a 1% rate of significant complications (7, 44, 46, 83-86). The major acute complication remains ureteral avulsion (44,87); autologous transplantation or uretero-ileoplasty are the methods of choice in these cases. Ureteral perforation at the site of the stone is the primary risk factor for stricture. Most perforations seen during the procedure are successfully treated with approximately 2 weeks of stenting (46,83,85).

URS can also be applied when ESWL might be contraindicated or ill-advised.

URS can be carried out safely in patients for whom stopping anticoagulants is unsafe (42). In addition, the success of URS is not affected by patient habitus. Morbidly obese patients can be treated with success rates and complication rates similar to those in the general population (88, 89) and has been used safely during pregnancy (90-91). However, URS should be limited to carefully selected patients. Finally, in selected cases, URS can be used safely to treat bilateral ureteral stones simultaneously (92, 93).

7.3.6 Conclusions

Improvements in the design of ureteroscopes, accessories and URS have significantly improved the successful removal of ureteral stones along with a decrease in morbidity (65,66). In experienced hands, the new generation of ureteroscopes can treat of proximal and distal ureteric stones. Flexible URS is an effective treatment for ESWL-refractory renal calculi.

Further studies are needed to determine whether flexible URS can be a first-line treatment of renal calculi where, depending on size and location, ESWL or PNL are currently procedures of first choice. For ureteric calculi, both ESWL and URS are acceptable alternatives. Although ESWL is less invasive and has the lowest complication rates, a stone-free state can be achieved faster using URS. For larger calculi, the stone-free rates achieved using URS might be advantageous.

Randomised and prospective studies to compare all forms of stone removal for renal and ureteric calculi are needed.
7.3.7 References


7.4 Open surgery for removal of renal stones

With advances in ESWL and endourological surgery (i.e. URS and PNL), the indications for open stone surgery have decreased markedly. Centres with the equipment, expertise and experience in surgical treatment of renal tract stones report that open surgery is needed in 1.0-5.4% of cases (1-5).

Most cases requiring open surgery involve difficult stone situations, and urologists must therefore maintain their proficiency, skills and expertise in open renal and ureteral surgical techniques. However, with different treatment modalities now available for surgical management of stones, it can be debated whether or not open operation is appropriate in a particular case. These guidelines provide general principles for open surgery based on a consensus of opinion drawn from experience and bearing in mind the technical limitations of less invasive alternative approaches.

An open surgical procedure may be preferred when the major stone volume is located peripherally in the calices, especially if several percutaneous accesses and several, probably unsuccessful, shock-wave sessions are likely to be needed for complete stone removal. However, many hospitals now have limited experience with open stone surgery and it may be advisable to send patients to a centre experienced in the use of extended pyelocalicotomy (6), anatrophic nephrolithotomy (7-10), multiple radial nephrotomy (11, 12) and renal surgery under hypothermia.

Recently, intra-operative B-mode scanning and Doppler sonography (13, 14) have been used to identify avascular areas in the renal parenchyma close to the stone or dilated calices. This allows removal of large staghorn stones by multiple small radial nephrotopectomies without loss of kidney function.

7.4.1 Indications for open and laparoscopic surgery

Indications for open stone surgery include:

- complex stone burden
- treatment failure of ESWL and/or PNL, or failed ureteroscopic procedure
- intrarenal anatomical abnormalities: infundibular stenosis, stone in the caliceal diverticulum (particularly in an anterior calix), obstruction of the ureteropelvic junction, stricture
- morbid obesity
- skeletal deformity, contractures and fixed deformities of hips and legs
- co-morbid medical disease
- concomitant open surgery
- non-functioning lower pole (partial nephrectomy), non-functioning kidney (nephrectomy)
- patient choice following failed minimally invasive procedures; the patient may prefer a single procedure and avoid the risk of needing more than one PNL procedure
- stone in an ectopic kidney where percutaneous access and ESWL may be difficult or impossible
- cystolithotomy for giant bladder calculus
- large stone burden in children; open stone surgery will provide easy access and requires only one anaesthetic procedure.

7.4.2 Operative procedures

Operative procedures that can be carried out include:

- simple and extended pyelolithotomy
- pyelonephrolithotomy
- anatrophic nephrolithotomy
- ureterolithotomy
- radial nephrolithotomy
- pyeloplasty
• partial nephrectomy and nephrectomy
• removal of calculus with re-implantation of the ureter (i.e. ureteroneocystotomy).

The superiority of open surgery over less invasive therapy, in terms of stone-free rates, is based on historical experience, but no comparative studies are available yet (15, 16) (LE 4).

Open surgery for renal tract stones has become almost obsolete, with laparoscopic surgery increasingly replacing open surgery, in situations such as complex stone burden, failed previous ESWL and / or endourological procedures, anatomical abnormalities, or morbid obesity. Laparoscopic surgery was initially used for ablative surgery in renal cancer and correction of pelviureteric junction obstruction, but is now being used to remove both renal and ureteric stones. Many patients with impacted ureteric stones have been treated successfully using laparoscopic ureterolithotomy, with less than 2% being converted to open surgery. Laparoscopic ureterolithotomy can be carried out using either retroperitoneal or transperitoneal access (17-22). Laparoscopic ureterolithotomy should be considered when other non-invasive or low-invasive procedures have failed (23-39). Laparoscopic (video-endoscopic) surgery may be useful, particularly for stones located in a ventral caliceal diverticulum (33).

Laparoscopic surgery should be carried out only by surgeons trained in this technique and in well-equipped, dedicated centres. The advantages of laparoscopic surgery are low post-operative morbidity, reduced hospital stay and minimal blood loss. However, the procedure takes considerably longer than conventional surgery.

When expertise is available, laparoscopic surgery should be considered before proceeding to open surgery (40).


http://www.ncbi.nlm.nih.gov/pubmed/17263607


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7.5 Chemolytic dissolution of stones using percutaneous irrigation

Chemolytic dissolution of stones or stone fragments is a useful adjunct to ESWL, PNL, URS or open surgery to achieve more complete elimination of small residual stones or fragments. The combined treatment of ESWL and chemolysis is a particularly low-invasive option for patients who have partial or complete infection staghorn stones. Oral chemolytic treatment is an alternative for removing uric acid stones.

In percutaneous chemolysis, at least two nephrostomy catheters should be used to allow irrigation of the renal collecting system, while preventing chemolytic fluid draining into the bladder and reducing the risk of increased intrarenal pressure. For a large stone burden, use a double-J stent to protect the ureter during the procedure (1,2).

7.5.1 Infection stones
Stones composed of magnesium ammonium phosphate and carbonate apatite can be dissolved using a 10% solution of hemiacidrin (Renacidin) (pH 3.5-4) or Suby’s G solution. Under antibiotic prophylaxis, the chemolytic solution is allowed to flow in through one nephrostomy catheter and out through another. The contact surface area between the stone or the stone remnants and the chemolytic agent is increased using ESWL. The time required for dissolution depends on stone burden and chemical composition, but several weeks of chemolysis combined with ESWL are needed to dissolve a complete staghorn stone. The major advantage of this approach is that it can be carried out without anaesthesia and may therefore be an option for high-risk patients or for patients in whom anaesthesia or other surgical procedures must be avoided (3-13).

Hemiacidrin and Suby’s G solution carry a risk of cardiac arrest due to hypermagnesaemia if there is leakage and magnesium is absorbed. These solutions should be used only when there is good evidence that the renal tract has healed following surgery. They should never be infused in the immediate post-operative stage.

7.5.2 Brushite stones
Brushite is also soluble in the acid solutions hemiacidrin and Suby’s G solution. Chemolytic dissolution should be considered in patients who have residual brushite fragments after other stone-removing procedures.

7.5.3 Cystine stones
Cystine is soluble in an alkaline environment, e.g. 0.3 or 0.6 mol/L trihydroxymethyl aminomethan (THAM) solution (pH range 8.5-9.0), or N-acetylcysteine (200 mg/L). These solutions can be used to improve elimination of fragments and stone residuals from the collecting system. Percutaneous chemolysis is a useful method for complete stone clearance together with other stone-removing techniques (14-18).

7.5.4 Uric acid stones
A high concentration of urate and a low pH are the determinants of uric acid stone formation. Percutaneous chemolysis can be achieved using THAM solutions. Oral chemolysis is, however, the preferred option. It involves lowering the urate concentration using allopurinol and a high fluid intake and increasing the pH to alkali (19-21).
Uric acid stones can also be removed using oral chemolysis involving an alkali and allopurinol. Further details of this regimen are given in Section 17.2.

7.5.5  Calcium oxalate and ammonium urate stones

No physiologically useful chemolytic agents are available for dissolving calcium oxalate or ammonium urate stones (22). The presence of calcium oxalate in an infection stone markedly reduces the stone’s solubility in hemiacidrin (6).

7.5.6  References


   [Local chemolysis of urinary stones]


   [Percutaneous chemolyses of struvite stones in renal-pelvic and caliceal obstruction]


    [Dissolution of cystine calculi with N-acetylcysteine following percutaneous nephrosonomy]


UPDATE MARCH 2008
7.6 Recommendations for removal of renal stones

The options for kidney stone removal are ESWL, PnL, rIrS with a flexible ureteroscope, video-endoscopic laparoscopic or open surgery. For any given stone situation, a method offering low invasiveness and morbidity should be selected.

More than 20 years of experience with low-invasive methods have shown that open surgery is necessary only in exceptional cases, mainly for patients in whom anatomical reconstruction is needed. Video-endoscopic retroperitoneal or laparoscopic surgery is not a standard procedure for removing kidney stones. However, this technique should be considered as an alternative before choosing open surgery, and has advantages in some types of reconstructive surgery.

For small stones (maximum diameter ≤ 20 mm or a surface area of ~300 mm²), ESWL is the standard procedure because it is non-invasive, has a low rate of complications, and (at least in adults) avoids the need for regional or general anaesthesia.

Debate continues about whether large renal stones are best treated with ESWL or with PnL. Although large stones can be treated successfully with ESWL, ESWL has sometimes to be repeated and residual fragments are relatively common. Although PnL is faster at debulking stone than ESWL, it must be emphasised that considerable expertise and experience is required to clear stones completely from the caliceal system. Unless a meticulous technique is used, residual fragments may remain.

There is a low risk that residual fragments can develop into new stones. However, a follow-up programme is needed because patients with stone disease have an inherent tendency to new stone formation.

Residual fragments of infection stones, which are associated with the most pronounced risk of recurrent stone formation, can be eliminated with PnL, with or without percutaneous chemolysis. Such a step might also be used as an auxiliary procedure for cystine stones.

For uric acid stones, oral chemolysis is the treatment of choice. However, the combination of stone disintegration and chemolysis can increase the rate of dissolution and may be considered for removal of large uric acid stones.

An overview of treatment recommendations according to size and stone type is shown in Tables 17-22.

Table 17: Active removal of radiopaque (calcium) renal stones with a largest diameter ≤ 20 mm (surface area ~ ≤ 300 mm²)

<table>
<thead>
<tr>
<th>Preference (decreasing order)</th>
<th>Procedure</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ESWL, also including piezolithotripsy</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>2</td>
<td>PnL</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>3</td>
<td>rIrS</td>
<td>2a</td>
<td>C</td>
</tr>
<tr>
<td>4</td>
<td>Laparoscopic surgery</td>
<td>2a</td>
<td>C</td>
</tr>
<tr>
<td>5</td>
<td>Open surgery</td>
<td>4</td>
<td>C</td>
</tr>
</tbody>
</table>

LE = level of evidence; GR = grade of recommendation

Infection stones are also radiopaque and usually contain calcium in the form of carbonate apatite and hydroxyapatite. These stones should be treated in the same way as sterile calcium stones, provided there is no obstruction and that a symptomatic infection has been adequately treated.

For all patients with infection stones, recent history of urinary tract infection or bacteriuria, antibiotic prophylaxis should be started before the stone-removing procedure and continued least 4 days afterwards.

LE = level of evidence; GR = grade of recommendation
Table 18: Active removal of uric acid renal stones with a largest diameter ≤ 20 mm (surface area ~ ≤ 300 mm²)

<table>
<thead>
<tr>
<th>Preference</th>
<th>Procedure</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Oral chemolysis</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td>2</td>
<td>ESWL (including piezolithotripsy) + oral chemolysis</td>
<td>2a</td>
<td>B</td>
</tr>
</tbody>
</table>

LE = level of evidence; GR = grade of recommendation; ESWL = extracorporeal shock-wave lithotripsy

For patients with uric acid stones and a percutaneous nephrostomy catheter in place, stone disintegration with ESWL can advantageously be combined with percutaneous chemolysis (see Section 7.5).

Table 19: Active removal of cystine stones with a largest diameter ≤ 20 mm (surface area ~ ≤ 300 mm²)

<table>
<thead>
<tr>
<th>Preference</th>
<th>Procedure</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ESWL (including piezolithotripsy)</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td>1</td>
<td>PNL</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td>2</td>
<td>RIRS</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td>3</td>
<td>Laparoscopic surgery</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td>4</td>
<td>Open surgery</td>
<td>4</td>
<td>C</td>
</tr>
</tbody>
</table>

LE = level of evidence; GR = grade of recommendation; ESWL = extracorporeal shock-wave lithotripsy

Table 20: Active removal of radiopaque (calcium) renal stones with a largest diameter > 20 mm (surface area > 300 mm²)

<table>
<thead>
<tr>
<th>Preference</th>
<th>Procedure</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PNL</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>2</td>
<td>ESWL (including piezolithotripsy)</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>3</td>
<td>PNL + ESWL (including piezolithotripsy)</td>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td>4</td>
<td>Laparoscopic surgery</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td>4</td>
<td>Open surgery</td>
<td>4</td>
<td>C</td>
</tr>
</tbody>
</table>

LE = level of evidence; GR = grade of recommendation; ESWL = extracorporeal shock-wave lithotripsy

Table 21: Active removal of uric acid renal stones with a largest diameter > 20 mm (surface area ~ > 300 mm²)

<table>
<thead>
<tr>
<th>Preference</th>
<th>Procedure</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Oral chemolysis</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td>2</td>
<td>ESWL (including piezolithotripsy) + oral chemolysis</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td>3</td>
<td>PNL</td>
<td>3</td>
<td>C</td>
</tr>
<tr>
<td>3</td>
<td>Percutaneous + chemolysis</td>
<td>3</td>
<td>C</td>
</tr>
</tbody>
</table>

LE = level of evidence; GR = grade of recommendation; ESWL = extracorporeal shock-wave lithotripsy

For patients with uric acid stones and a percutaneous nephrostomy catheter in place, stone disintegration with ESWL combined with percutaneous chemolysis is a good alternative to quickly dissolve the stone material (see Section 7.5).
Table 22: Active removal of cystine stones with a largest diameter > 20 mm (surface area > 300 mm²)

<table>
<thead>
<tr>
<th>Preference</th>
<th>Procedure</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Percutaneous nephrolithotomy</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td>1</td>
<td>PNL+ ESWL (including piezolithotripsy)</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td>1</td>
<td>PNL+ chemolysis</td>
<td>3</td>
<td>C</td>
</tr>
<tr>
<td>2</td>
<td>ESWL (including piezolithotripsy) + chemolysis</td>
<td>3</td>
<td>C</td>
</tr>
<tr>
<td>3</td>
<td>Laparoscopic surgery</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td>3</td>
<td>Open surgery</td>
<td>4</td>
<td>C</td>
</tr>
</tbody>
</table>

LE = level of evidence; GR = grade of recommendation; ESWL = extracorporeal shock-wave lithotripsy

Patients for whom ESWL-treatment of stones (with a diameter exceeding 20 mm ~300 mm²) is scheduled should have an internal stent to avoid problems related to Steinstrasse. GR = B

LE = level of evidence; GR = grade of recommendation

8. STAGHORN STONES

A staghorn stone is defined as a stone with a central body and at least one caliceal branch. A partial staghorn stone fills only part of the collecting system. A complete staghorn stone fills all the calices and the renal pelvis.

Patients with staghorn stones can usually be treated according to the principles given for large stones (diameter > 20 mm / 300 mm²) (see Chapter 7). GR = A/B

LE = level of evidence; GR = grade of recommendation

In patients with small staghorn stones and a non-dilated system, repeated ESWL sessions with a stent can be a reasonable treatment alternative. Nephrectomy should be considered in the case of a non-functioning kidney. In selected cases with infection, cystine, uric acid and calcium phosphate stones, the combined use of ESWL or other stone-removing procedures, with chemolysis may be useful. The principles of chemolytic treatment are discussed in Chapter 7.
9. MANAGEMENT OF PATIENTS WITH STONES IN THE URETER.

2007 GUIDELINE FOR THE MANAGEMENT OF URETERAL CALCULI

European Association of Urology and American Urological Association Education and Research, Inc.

EAU/AUA Nephrolithiasis Guideline Panel

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DIAGNOSIS AND TREATMENT

RECOMMENDATIONS

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UPDATE MARCH 2008
9.1 Introduction
The American Urological Association (AUA) Nephrolithiasis Clinical Guideline Panel was established in 1991. Since that time, the Panel has developed three guidelines on the management of nephrolithiasis, the most recent being a 2005 update of the original 1994 Report on the Management of Staghorn Calculi (1). The European Association of Urology (EAU) began their nephrolithiasis guideline project in 2000, yielding the publication of Guidelines on Urolithiasis, with updates in 2001 and 2006 (2). While both documents provide useful recommendations on the management of ureteral calculi, changes in shock-wave lithotripsy (SWL) technology, endoscope design, intracorporeal lithotripsy techniques, and laparoscopic expertise have burgeoned over the past five to ten years.

Under the sage leadership of the late Dr. Joseph W. Segura, the AUA Practice Guidelines Committee suggested to both the AUA and the EAU that they join efforts in developing the first set of internationally endorsed guidelines focusing on the changes introduced in ureteral stone management over the last decade. We therefore dedicate this report to the memory of Dr. Joseph W. Segura whose vision, integrity, and perseverance led to the establishment of the first international guideline project.

This joint EAU/AUA Nephrolithiasis Guideline Panel (hereinafter the Panel) performed a systematic review of the English language literature published since 1997 and a comprehensively analyzed outcomes data from the identified studies.

Based on their findings, the Panel concluded that when removal becomes necessary, SWL and ureteroscopy (URS) remain the two primary treatment modalities for the management of symptomatic ureteral calculi. Other treatments were reviewed, including medical expulsion therapy (MET) to facilitate spontaneous stone passage, percutaneous antegrade ureteroscopy, and laparoscopic and open surgical ureterolithotomy. In concurrence with the previously published guidelines of both organizations, open stone surgery is still considered a secondary treatment option. Blind basketing of ureteral calculi is not recommended. In addition, the Panel was able to provide some guidance regarding the management of pediatric patients with ureteral calculi. The Panel recognizes that some of the treatment modalities or procedures recommended in this document require access to modern equipment or presupposes a level of training and expertise not available to practitioners in many clinical centers. Those situations may require physicians and patients to resort to treatment alternatives.

This article will be published simultaneously in European Urology and The Journal of Urology. The Panel believes that future collaboration between the EAU and the AUA will serve to establish other internationally approved guidelines, offering physician and patient guidance worldwide.

9.2 Methodology
The Panel initially discussed the scope of the guideline and the methodology, which would be similar to that used in developing the previous AUA guideline. All treatments commonly employed in the United States and/or Europe were included in this report except for those that were explicitly excluded in the previous guideline or newer treatments for which insufficient literature existed. In the analysis, patient data were stratified by age (adult versus child), stone size, stone location, and stone composition. Later, however, the data were found to be insufficient to allow analysis by composition. The outcomes deemed by the Panel to be of particular interest to the patient included the following: stone-free rate, number of procedures performed, stone-passage rate or probability of spontaneous passage, and complications of treatment. The Panel did not examine economic effects, including treatment costs.

Outcomes were stratified by stone location (proximal, mid, and distal ureter) and by stone size (dichotomized as ≤10 mm and >10 mm for surgical interventions, and ≤5 mm and >5 mm for medical interventions and observation where possible; exceptions were made when data were reported, for example as <10 mm and ≥10 mm). The mid ureter is the part of the ureter that overlies the bony pelvis, i.e., the position of the ureter that corresponds to the sacroiliac joint; the proximal ureter is above and the distal ureter is below. Treatments were divided into three broad groups:

1. Observation and medical therapy
2. Shock-wave lithotripsy and ureteroscopy
3. Open surgery, laparoscopic stone removal, or percutaneous antegrade ureteroscopy.

The review of the evidence began with a literature search and data extraction. Articles were selected from a database of papers derived from MEDLINE searches dealing with all forms of urinary tract stones. This database was maintained by a Panel chair. The abstract of each paper was independently reviewed by an American and a European Panel member, and articles were selected for data extraction if any panel member felt it might have useful data. Additional articles were suggested by Panel members or found as references in review articles. In total, 348 citations entered the extraction process. An American and a European Panel member each independently extracted data from each article onto a standardized form. The team members reconciled the extractions, and the data were entered into a Microsoft Access® (Microsoft, Redmond, WA)
database. The Panel scrutinized the entries, reconciled the inconsistencies in recording, corrected the extraction errors, and excluded some articles from further analysis for the following reasons:

1. The article was included in the previous guideline.
2. The article did not provide usable data on the outcomes of interest.
3. Results for patients with ureteral stones could not be separated from results for those with renal stones.
4. The treatments used were not current or were not the focus of the analysis.
5. The article was a review article of data reported elsewhere.
6. The article dealt only with salvage therapy.

A total of 244 of the 348 articles initially selected had extractable data. Articles excluded from evidence combination remained candidates for discussion in the text of the guideline.

The goal was to generate outcomes tables comparing estimates of outcomes across treatment modalities. To generate an outcomes table, estimates of the probabilities and/or magnitudes of the outcomes are required for each intervention. Ideally, these are derived from a synthesis or combination of the evidence. Such a combination can be performed in a variety of ways depending on the nature and quality of the evidence. For this report, the Panel elected to use the Confidence Profile Method (3), which provides methods for analyzing data from studies that are not randomized controlled trials (RCTs). The Fast*Pro computer software was used in the analysis. This program provides posterior distributions from meta-analyses from which the median can be used as a best estimate, and the central 95% of the distribution serves as a confidence interval (CI). Statistical significance at the p<0.05 level (two-tailed) was inferred when zero was not included in the CI.

Because of the paucity of controlled trials found on literature review, however, the outcome for each intervention was estimated by combining single arms from various clinical series. These clinical series frequently had very different outcomes, likely due to a combination of site-to-site variations in patient populations, in the performance of the intervention, in the skill of those performing the intervention, and different methods of determining stone-free status. Given these differences, a random-effects, or hierarchical, model was used to combine the studies.

Evidence from the studies meeting the inclusion criteria and reporting a given outcome was combined within each treatment modality. Graphs showing the results for each modality were developed to demonstrate similarities and differences between treatments.

The available data for procedures per patient would not permit a statistical analysis using these techniques. Unlike the binary outcome of stone-free status (the patient either is or is not stone free), the number of procedures per patient is a discrete rate. In some cases discrete rates can be approximated with a continuous rate, but in order to meta-analyze continuous rates, a measure of variance (e.g., standard deviation, standard error) is needed in addition to the mean. Unfortunately, measures of variance were rarely reported in the studies reviewed. As a result, numbers of procedures per patient were evaluated by calculating the average across studies weighted by the number of patients in each study. Procedures per patient were counted in three totals: primary procedures, secondary procedures, and adjunctive procedures. Primary procedures were all consecutive procedures of the same type aimed at removing the stone. Secondary procedures were all other procedures used to remove the stone. Adjunctive procedures were defined as additional procedures that do not involve active stone removal. One difficulty in estimating the total number of procedures per patient is that secondary and adjunctive procedures were not reported consistently. Since the Panel had decided to analyze primary, secondary, and adjunctive procedures separately, only studies that specifically reported data on a type of procedure were included in estimates for that procedure type. This approach may have overestimated numbers of secondary and adjunctive procedures because some articles may not have reported that procedures were not performed.

It is important to note that, for certain outcomes, more data were reported for one or another treatment modality. While resulting CIs reflect available data, the probabilities for certain outcomes can vary widely within one treatment modality. In addition, the fact that data from only a few RCTs could be evaluated may have somewhat biased results. For example, differences in patient selection may have had more weight in analyses than differing treatment effects. Nevertheless, the results obtained reflect the best outcome estimates presently available.

Studies that reported numbers of patients who were stone free after primary procedures were included in the stone-free analysis. Studies that reported only the combined number of patients who either were stone free or had “clinically insignificant fragments” were excluded. Many studies did not indicate how or when stone-free status was determined. The stone-free rate was considered at three time points: after the first procedure, after all consecutive procedures using the primary treatment, and after the total treatments.

Initially, the Panel divided complications into three broad categories: acute, long-term, and medical; however, after examining the available evidence, the Panel determined that this breakdown was not useful.
Several factors caused inaccuracy in the estimates, but did so in opposite directions, thereby reducing the magnitude of inaccuracy. For example, including studies that did not specifically mention that there were no occurrences of a specific complication may have led to overestimates of complication rates when meta-analyzed. By combining similar complications, the Panel also potentially mitigated the overestimate by making it more likely that a complication in the class was reported. The probability that a patient will have a complication may still be overstated slightly because some patients experienced multiple complications. Since the grouping of complications varies by study, the result of the meta-analysis is best interpreted as the mean number of complications that a patient may experience rather than as the probability of having a complication. Moreover, since reporting of complications is not consistent, the estimated rates given here are probably less accurate than the CIs would indicate. There were insufficient data to permit meaningful meta-analyses of patient deaths.

Data analyses were conducted for two age groups. One analysis included studies of patients ages 18 or younger (or identified as pediatric patients in the article without specifying age ranges). The adult analysis included all other studies even if children were included.

After the evidence was combined and outcome tables were produced, the Panel met to review the results and identify anomalies. From the evidence in the outcome tables and expert opinion, the Panel drafted the treatment guidelines.

In this guideline the standard, recommendations, and options given were rated according to the levels of evidence published from the U.S. Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research (5):

Ia. Evidence obtained from meta-analysis of randomized trials

Ib. Evidence obtained from at least one randomized trial

IIa. Evidence obtained from at least one well-designed controlled study without randomization

IIb. Evidence obtained from at least one other type of well-designed quasi-experimental study

III. Evidence obtained from well-designed nonexperimental studies, such as comparative studies, correlation studies, and case reports

IV. Evidence obtained from expert committee reports, or opinions, or clinical experience of respected authorities

As in the previous AUA guideline, the present statements are graded with respect to the degree of flexibility in application. Although the terminology has changed slightly, from the original AUA reports, the current three levels are essentially the same. A “standard” is the most rigid treatment policy. A “recommendation” has significantly less rigidity, and an “option” has the largest amount of flexibility. These terms are defined as follows:

1. **Standard**: A guideline statement is a standard if: (1) the health outcomes of the alternative interventions are sufficiently well known to permit meaningful decisions, and (2) there is virtual unanimity about which intervention is preferred.

2. **Recommendation**: A guideline statement is a recommendation if: (1) the health outcomes of the alternative interventions are sufficiently well known to permit meaningful decisions, and (2) an appreciable, but not unanimous majority agrees on which intervention is preferred.

3. **Option**: A guideline statement is an option if: (1) the health outcomes of the interventions are not sufficiently well known to permit meaningful decisions, or (2) preferences are unknown or equivocal.

The draft was sent to 81 peer reviewers of whom 26 provided comments; the Panel revised the document based on the comments received. The guideline was submitted first for approval to the Practice Guidelines Committee of the AUA and the Guidelines Office of the EAU and then forwarded to the AUA Board of Directors and the EAU Board for final approval.


### 9.3 Results of the Outcomes Analysis

The results of the analysis described in this chapter provide most of the evidentiary basis for the guideline statements. Further details and tables corresponding to the figures in this section are found in Chapter 3 and the Appendices.

The panel’s attempt to differentiate results for pediatric patients from those for adults was not completely successful as most studies included both adults and children. Where possible, the panel performed two analyses, one including all studies regardless of patient age, and a second including only those studies or groups of patients that were comprised entirely of pediatric patients.
9.3.1 Observation and Medical Therapies

Stone-passage rates

Only limited data were found on the topic of spontaneous passage by stone size. For stones \( \leq 5 \) mm, meta-analysis of five patient groups (224 patients) yielded an estimate that 68% would pass spontaneously (95% CI: 46% to 85%). For stones >5 mm and \( \leq 10 \) mm, analysis of three groups (104 patients) yielded an estimate that 47% would pass spontaneously (95% CI: 36% to 59%). Details of the meta-analysis are presented in Appendixes 8 and 9.

Two medical therapies had sufficient analyzable data: the calcium channel blocker nifedipine and alpha-receptor antagonists. Analyses of stone-passage rates were done in three ways. The first combined all single arms evaluating the therapies. Using this approach, meta-analysis of four studies of nifedipine (160 patients) yielded an estimate of a 75% passage rate (95% CI: 63% to 84%). Six studies examined alpha blockers (280 patients); the meta-analysis yielded a stone-passage rate of 81% (95% CI: 72% to 88%).

The second method was a standard Bayesian hierarchical meta-analysis of the available RCTs that compared either nifedipine or alpha blockers to control therapies. The results for nifedipine showed an absolute increase of 9% in stone-passage rates (95% CI: -7% to 25%), which was not statistically significant. Meta-analysis of alpha blockers versus control showed an absolute increase of 29% in the stone-passage rate (95% CI: 20% to 37%), which was statistically significant.

The Panel also attempted to determine whether alpha blockers provide superior stone passage when compared to nifedipine. Two randomized controlled trials were identified. When hierarchical meta-analysis was performed on these two studies, tamsulosin provided an absolute increase in stone-passage rate of 14% (95% CI: -4% to 32%) which was not statistically significant. When nonhierarchical methods were used, the stone-passage improvement increased to 16% (95% CI: 7% to 26%) which was statistically significant. Finally, the Panel used the results of the meta-analyses versus controls (second method above) to determine the difference between alpha blockers and calcium channel blockers. This method allows the use of more data but is risky since it depends on the control groups having comparable results. The analysis yielded a 20% improvement in stone-passage rates with alpha blockers, and the 95% CI of 1% to 37% just reached statistical significance.

9.3.1.1 Shock-wave Lithotripsy and Ureteroscopy

Stone-free rates were analyzed for a number of variant methods of performing SWL and URS. The Panel attempted to differentiate between bypass, pushback, and in situ SWL as well as differences between lithotripters. Most differences were minimal and did not reach statistical significance. For that reason, the data presented in this Chapter compare the meta-analysis of all forms of SWL to the meta-analysis of all forms of URS. The Panel also attempted to differentiate between flexible and rigid ureteroscopes. Details of the breakdowns by type of SWL and URS are given in Chapter 3. Data were analyzed for both efficacy and complications. Two efficacy outcomes were analyzed: stone-free rate and procedure counts. Complications were grouped into classes. The most important classes are reported herein. The full complication results are in Appendix 10.

Analyses were performed for the following patient groups where data were available.

1. Proximal stones \( \leq 10 \) mm
2. Proximal stones >10 mm
3. Proximal stones regardless of size
4. Mid-ureteral stones \( \leq 10 \) mm
5. Mid-ureteral stones >10 mm
6. Mid-ureteral stones regardless of size
7. Distal stones \( \leq 10 \) mm
8. Distal stones >10 mm
9. Distal stones regardless of size

Analyses of pediatric groups were attempted for the same nine groups, although data were lacking for many groups.

9.3.1.2 Efficacy Outcomes

Stone-free rates

The Panel decided to analyze a single stone-free rate. If the study reported the stone-free rate after all primary procedures, that number was used. If not and the study reported the stone-free rate after the first procedure, then that number was used. The intention of the Panel was to provide an estimate of the number of primary procedures and the stone-free rate after those procedures. There is a lack of uniformity in the literature in reporting the time to stone-free status, thereby limiting the ability to comment on the timing of this parameter.

The results of the meta-analysis of stone-free data are presented for the overall group in Table
1 and Figure 1. The results are presented as medians of the posterior distribution (best central estimate) with 95% Bayesian CIs (credible intervals [CIs])

### Overall Population

<table>
<thead>
<tr>
<th>Stone Free Rate - Primary Treatments or First Treatment</th>
<th>SWL</th>
<th>URS</th>
</tr>
</thead>
<tbody>
<tr>
<td>G/P</td>
<td>Med / 95% CI</td>
<td>G/P</td>
</tr>
<tr>
<td>Distal Ureter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>74% (73-75)%*</td>
<td>59</td>
</tr>
<tr>
<td>6981</td>
<td>(73-75)%*</td>
<td>5952</td>
</tr>
<tr>
<td>Distal ureter &lt; 10 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>86% (80-91)%</td>
<td>13</td>
</tr>
<tr>
<td>1684</td>
<td>(80-91)%</td>
<td>1622</td>
</tr>
<tr>
<td>Distal ureter &gt; 10 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>74% (57-87)%</td>
<td>8</td>
</tr>
<tr>
<td>966</td>
<td>(57-87)%</td>
<td>412</td>
</tr>
<tr>
<td>Mid Ureter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>73% (66-79)%</td>
<td>30</td>
</tr>
<tr>
<td>1607</td>
<td>(66-79)%</td>
<td>1024</td>
</tr>
<tr>
<td>Mid ureter &lt; 10 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>84% (65-95)%</td>
<td>5</td>
</tr>
<tr>
<td>44</td>
<td>(65-95)%</td>
<td>80</td>
</tr>
<tr>
<td>Mid ureter &gt; 10 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>76% (36-97)%</td>
<td>5</td>
</tr>
<tr>
<td>15</td>
<td>(36-97)%</td>
<td>73</td>
</tr>
<tr>
<td>Proximal Ureter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>41</td>
<td>82% (79-85)%</td>
<td>16</td>
</tr>
<tr>
<td>6428</td>
<td>(79-85)%</td>
<td>2242</td>
</tr>
<tr>
<td>Proximal ureter &lt; 10 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>90% (85-93)%</td>
<td>9</td>
</tr>
<tr>
<td>886</td>
<td>(85-93)%</td>
<td>243</td>
</tr>
<tr>
<td>Proximal ureter &gt; 10 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>68% (55-79)%</td>
<td>8</td>
</tr>
<tr>
<td>293</td>
<td>(55-79)%</td>
<td>230</td>
</tr>
</tbody>
</table>

G = Number of Groups/Treatment arms extracted; P = Number of Patients in those groups

### Table 1. Stone-Free Rates for SWL and URS in the Overall Population

![Stone Free Rates after Primary/First Treatment](image)

**Figure 1. Stone-Free Rates for SWL and URS in the Overall Population**

Estimated Occurrence Rate with 95% CI

CI = confidence interval
This analysis shows that overall, for stones in the proximal ureter (n=8,670), there was no difference in stone-free rates between SWL and URS. However, for proximal ureteral stones <10 mm (n=1,129), SWL had a higher stone-free rate than URS, and for stones >10 mm (n=523), URS had superior stone-free rates. This difference arises because the stone-free rate for proximal ureteral stones treated with URS did not vary significantly with size, whereas the stone-free rate following SWL negatively correlated with stone size. For all distal stones, URS yields better stone-free rates overall and in both size categories. For all mid-ureteral stones, URS appears superior, but the small number of patients may have prevented results from reaching statistical significance.

Unfortunately, RCTs comparing these treatments were generally lacking, making an accurate assessment impossible. However, the posterior distributions resulting from the meta-analysis can be subtracted, yielding a distribution for the difference between the treatments. If the CI of this result does not include zero, then the results may be considered to be statistically significantly different. This operation is mathematically justifiable but operationally risky: if the patients receiving different treatments are different or if outcome measures are different, results may be meaningless. Nonetheless, the Panel performed the comparison and found that URS stone-free rates were significantly better than SWL rates for distal ureteral stones <10 mm and >10 mm and for proximal ureteral stones >10 mm. The stone-free rate for mid-ureteral stones was not statistically significantly different between URS and SWL. The results with URS using a flexible ureteroscope for proximal ureteral stones appear better than those achieved with a rigid device, but not at a statistically significant level.

Stone-free results for pediatric patients are shown in Table 2 and Figure 2. The very small number of patients in most groups, particularly for URS, makes comparisons among treatments difficult. However, it does appear that SWL may be more effective in the pediatric subset than in the overall population, particularly in the mid and lower ureter.

Table 2. Stone-Free Rates for SWL and URS, Pediatric Population

<table>
<thead>
<tr>
<th>Pediatric Population</th>
<th>AUA / EAU Ureteral Stones Guideline Panel Stone Free Rate - Primary Treatments or First Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SWL</td>
</tr>
<tr>
<td>Distal Ureter</td>
<td>G/P</td>
</tr>
<tr>
<td>Distal ureter &lt; 10 mm</td>
<td>5</td>
</tr>
<tr>
<td>Distal ureter &gt; 10 mm</td>
<td>2</td>
</tr>
<tr>
<td>Mid Ureter</td>
<td>6</td>
</tr>
<tr>
<td>Mid ureter &lt; 10 mm</td>
<td>4</td>
</tr>
<tr>
<td>Mid ureter &gt; 10 mm</td>
<td>1</td>
</tr>
<tr>
<td>Proximal Ureter</td>
<td>7</td>
</tr>
<tr>
<td>Proximal ureter &lt; 10 mm</td>
<td>5</td>
</tr>
<tr>
<td>Proximal ureter &gt; 10 mm</td>
<td>3</td>
</tr>
</tbody>
</table>

G = Number of Groups/Treatment arms extracted; P = Number of Patients in those groups
Figure 2. Stone-Free Rates for SWL and URS, Pediatric Population

<table>
<thead>
<tr>
<th>Procedure Type</th>
<th>Procedure Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal Ureter - SWL</td>
<td></td>
</tr>
<tr>
<td>Distal Ureter - URS</td>
<td></td>
</tr>
<tr>
<td>Distal Ureter &lt; 10 mm - SWL</td>
<td></td>
</tr>
<tr>
<td>Distal Ureter &lt; 10 mm - URS</td>
<td></td>
</tr>
<tr>
<td>Distal Ureter &gt; 10 mm - SWL</td>
<td></td>
</tr>
<tr>
<td>Mid Ureter - SWL</td>
<td></td>
</tr>
<tr>
<td>Mid Ureter - URS</td>
<td></td>
</tr>
<tr>
<td>Mid Ureter &lt; 10 mm - SWL</td>
<td></td>
</tr>
<tr>
<td>Mid Ureter &lt; 10 mm - URS</td>
<td></td>
</tr>
<tr>
<td>Mid Ureter &gt; 10 mm - SWL</td>
<td></td>
</tr>
<tr>
<td>Mid Ureter &gt; 10 mm - URS</td>
<td></td>
</tr>
<tr>
<td>Proximal Ureter - SWL</td>
<td></td>
</tr>
<tr>
<td>Proximal Ureter - URS</td>
<td></td>
</tr>
<tr>
<td>Proximal Ureter &lt; 10 mm - SWL</td>
<td></td>
</tr>
<tr>
<td>Proximal Ureter &gt; 10 mm - SWL</td>
<td></td>
</tr>
</tbody>
</table>

As mentioned in Chapter 2, it was not possible to perform a meta-analysis or to test for statistically significant differences between treatments due to the lack of variance data, and only weighted averages could be computed. The procedure count results for the overall population are shown in Table 3 and Figure 3. Figure 3 results are presented as stacked bars.
Table 3. Procedure Counts for SWL and URS in the Overall Population

<table>
<thead>
<tr>
<th>Procedure Counts</th>
<th>Overall Population</th>
<th>Procedure Counts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grps/Pts</td>
<td># Procs</td>
</tr>
<tr>
<td>SWL Distal Ureter</td>
<td>48/7117</td>
<td>1.22</td>
</tr>
<tr>
<td>Distal Ureter &lt; 10 mm</td>
<td>16/1618</td>
<td>1.34</td>
</tr>
<tr>
<td>Distal Ureter &gt; 10 mm</td>
<td>11/1051</td>
<td>1.44</td>
</tr>
<tr>
<td>Mid Ureter</td>
<td>10/2091</td>
<td>1.11</td>
</tr>
<tr>
<td>Mid Ureter &lt; 10 mm</td>
<td>20/121</td>
<td>1.29</td>
</tr>
<tr>
<td>Mid Ureter &gt; 10 mm</td>
<td>3/53</td>
<td>1.76</td>
</tr>
<tr>
<td>Proximal Ureter</td>
<td>37/502</td>
<td>1.31</td>
</tr>
<tr>
<td>Proximal Ureter &lt; 10 mm</td>
<td>16/1243</td>
<td>1.26</td>
</tr>
<tr>
<td>Proximal Ureter &gt; 10 mm</td>
<td>10/409</td>
<td>1.49</td>
</tr>
<tr>
<td>URS Distal Ureter</td>
<td>56/5308</td>
<td>1.04</td>
</tr>
<tr>
<td>Distal Ureter &lt; 10 mm</td>
<td>12/1117</td>
<td>1.01</td>
</tr>
<tr>
<td>Distal Ureter &gt; 10 mm</td>
<td>5/231</td>
<td>1.02</td>
</tr>
<tr>
<td>Mid Ureter</td>
<td>25/686</td>
<td>1.04</td>
</tr>
<tr>
<td>Mid Ureter &lt; 10 mm</td>
<td>4/52</td>
<td>1.00</td>
</tr>
<tr>
<td>Mid Ureter &gt; 10 mm</td>
<td>2/18</td>
<td>1.00</td>
</tr>
<tr>
<td>Proximal Ureter</td>
<td>42/7634</td>
<td>1.02</td>
</tr>
<tr>
<td>Proximal Ureter &lt; 10 mm</td>
<td>6/68</td>
<td>1.00</td>
</tr>
<tr>
<td>Proximal Ureter &gt; 10 mm</td>
<td>5/137</td>
<td>1.07</td>
</tr>
</tbody>
</table>

Figure 3. Procedure Counts for SWL and URS in the Overall Population

Procedures per Patient

Weighted Mean Procedures per Patient

Primary Procedures
Secondary Procedures
Adjunctive Procedures

Procedure count results for pediatric patients are shown in Table 4 and Figure 4. Again, the numbers of patients with available data were small and did not support meaningful comparisons among treatments.
9.3.1.4 Complications

The articles were extracted for various complications; however, the Panel believes the following are the most relevant:

1. Sepsis
2. Steinstrasse
3. Stricture
4. Ureteral injury
5. Urinary tract infection (UTI)

Serious complications, including death and loss of kidney, were sufficiently rare that data were not available to estimate their rates of occurrence. Other complications are listed in Chapter 3.

The complication rates for the overall population by treatment, size, and location are shown in Table 5.
Table 5. Complications Occurrence Rates with SWL and URS, Overall Population

<table>
<thead>
<tr>
<th></th>
<th>SWL Med/95% CI</th>
<th>URS Med/95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Groups/Patients</td>
<td></td>
</tr>
<tr>
<td>Distal Ureter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>2019</td>
<td>(2 - 5)%</td>
<td>(1 - 4)%</td>
</tr>
<tr>
<td>Steinstrasse</td>
<td>1%</td>
<td>4%</td>
</tr>
<tr>
<td>26</td>
<td>(0 - 17)%</td>
<td></td>
</tr>
<tr>
<td>Stricture</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>609</td>
<td>(0 - 1)%</td>
<td>(1 - 2)%</td>
</tr>
<tr>
<td>Ureteral Injury</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>45</td>
<td>(0 - 5)%</td>
<td>(3 - 4)%</td>
</tr>
<tr>
<td>UTI</td>
<td>2%</td>
<td>4%</td>
</tr>
<tr>
<td>87</td>
<td>(1 - 12)%</td>
<td>(2 - 7)%</td>
</tr>
<tr>
<td>Mid Ureter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>398</td>
<td>(0 - 20)%</td>
<td>(1 - 11)%</td>
</tr>
<tr>
<td>Steinstrasse</td>
<td>8%</td>
<td>1%</td>
</tr>
<tr>
<td>37</td>
<td>(2 - 20)%</td>
<td>(3 - 8)%</td>
</tr>
<tr>
<td>Stricture</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>43</td>
<td>(0 - 6)%</td>
<td>(2 - 7)%</td>
</tr>
<tr>
<td>Ureteral Injury</td>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>514</td>
<td>(1 - 16)%</td>
<td>(2 - 7)%</td>
</tr>
<tr>
<td>UTI</td>
<td>6%</td>
<td>4%</td>
</tr>
<tr>
<td>37</td>
<td>(1 - 16)%</td>
<td>(0 - 7)%</td>
</tr>
<tr>
<td>Proximal Ureter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>704</td>
<td>(2 - 4)%</td>
<td>(2 - 6)%</td>
</tr>
<tr>
<td>Steinstrasse</td>
<td>5%</td>
<td>0%</td>
</tr>
<tr>
<td>235</td>
<td>(2 - 10)%</td>
<td>(0 - 2)%</td>
</tr>
<tr>
<td>Stricture</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>124</td>
<td>(0 - 8)%</td>
<td>(1 - 5)%</td>
</tr>
<tr>
<td>Ureteral Injury</td>
<td>2%</td>
<td>6%</td>
</tr>
<tr>
<td>124</td>
<td>(0 - 8)%</td>
<td>(3 - 9)%</td>
</tr>
<tr>
<td>UTI</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>360</td>
<td>(2 - 7)%</td>
<td>(1 - 8)%</td>
</tr>
</tbody>
</table>
Table 6 summarizes complications for all pediatric groups. Since there are few groups and patients, it was not possible to stratify data by stone size or location. The reported frequencies of pain may be inaccurate because of inconsistent reporting.

### Table 6. Complication Occurrence Rates - Overall, Pediatric Population

<table>
<thead>
<tr>
<th>Complications</th>
<th>SWL</th>
<th>URS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Groups/Patient</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bleeding</strong></td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>Overall Significant complications</strong></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Pain</strong></td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td><strong>Retention</strong></td>
<td>63</td>
<td>26</td>
</tr>
<tr>
<td><strong>Sepsis</strong></td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>Skin</strong></td>
<td>168</td>
<td>73</td>
</tr>
<tr>
<td><strong>Stricture</strong></td>
<td>25</td>
<td></td>
</tr>
<tr>
<td><strong>Ureteral Obstruction</strong></td>
<td>283</td>
<td></td>
</tr>
<tr>
<td><strong>UTI</strong></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>Infection</strong></td>
<td>63</td>
<td></td>
</tr>
<tr>
<td><strong>Stent Migration</strong></td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>Ureteral Injury</strong></td>
<td>25</td>
<td>6</td>
</tr>
<tr>
<td><strong>Ureteral Obstruction</strong></td>
<td>26</td>
<td>1</td>
</tr>
<tr>
<td><strong>UTI</strong></td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td><strong>Stricture</strong></td>
<td>5</td>
<td>106</td>
</tr>
<tr>
<td><strong>Other Long Term CX</strong></td>
<td>1</td>
<td>43</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Med / 95% CI</strong></th>
<th><strong>Med / 95% CI</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bleeding</strong></td>
<td>(0-24)%</td>
</tr>
<tr>
<td><strong>Overall Significant complications</strong></td>
<td>1%</td>
</tr>
<tr>
<td><strong>Pain</strong></td>
<td>(9-30)%</td>
</tr>
<tr>
<td><strong>Retention</strong></td>
<td>(0-7)%</td>
</tr>
<tr>
<td><strong>Sepsis</strong></td>
<td>(1-12)%</td>
</tr>
<tr>
<td><strong>Skin</strong></td>
<td>(0-1)%</td>
</tr>
<tr>
<td><strong>Stricture</strong></td>
<td>(0-9)%</td>
</tr>
<tr>
<td><strong>Ureteral Obstruction</strong></td>
<td>(1-6)%</td>
</tr>
<tr>
<td><strong>UTI</strong></td>
<td>(0-9)%</td>
</tr>
<tr>
<td><strong>Infection</strong></td>
<td>(2-13)%</td>
</tr>
<tr>
<td><strong>Stent Migration</strong></td>
<td>5%</td>
</tr>
<tr>
<td><strong>Ureteral Injury</strong></td>
<td>(0-17)%</td>
</tr>
<tr>
<td><strong>Ureteral Obstruction</strong></td>
<td>(0-9)%</td>
</tr>
<tr>
<td><strong>UTI</strong></td>
<td>(0-19)%</td>
</tr>
<tr>
<td><strong>Stricture</strong></td>
<td>(2-11)%</td>
</tr>
<tr>
<td><strong>Other Long Term CX</strong></td>
<td>12%</td>
</tr>
</tbody>
</table>

**G** = number of groups/treatment arms extracted; **P** = number of patients in those groups.

### 9.3.1.5 Other Surgical Interventions

Small numbers of studies reported on open surgery, laparoscopic stone removal, and percutaneous antegrade ureteroscopy. Because these procedures are usually reserved for special cases, the reported data should not be used to compare procedures with each other or with SWL or URS. As expected, these more invasive procedures yielded high stone-free rates when used.

A single pediatric report provided procedure counts for two patients who had one open procedure each. Two studies reported stone-free rates for children with open procedures (n=five patients); the computed stone-free rate was 82% (95% CI: 43% to 99%).

### 9.4 The Index Patient

In constructing these guidelines, an “index patient” was defined to reflect the typical individual with a ureteral stone whom a urologist treats. The following definition was created.
The index patient is a nonpregnant adult with a unilateral noncystine/nonuric acid radiopaque ureteral stone without renal calculi requiring therapy whose contralateral kidney functions normally and whose medical condition, body habitus, and anatomy allow any one of the treatment options to be undertaken.

### 9.5 Treatment Guidelines for the Index Patient

#### 9.5.1 For All Index Patients

**Standard:** Patients with bacteriuria should be treated with appropriate antibiotics.

[Based on Panel consensus/Level IV]

Untreated bacteriuria can lead to infectious complications and possible urosepsis if combined with urinary tract obstruction, endourologic manipulation, or SWL. Urine culture prior to intervention is recommended; screening with dipsticks might be sufficient in uncomplicated cases (2). In case of suspected or proven infection, appropriate antibiotic therapy should be administered before intervention (6).

**Standard:** Stone extraction with a basket without endoscopic visualization of the stone (blind basketing) should not be performed.

[Based on Panel consensus/Level IV]

Before the availability of modern ureteroscopes, extraction of distal ureteral stones with a basket with or without fluoroscopy was common. This procedure is, however, associated with an obvious risk of injury to the ureter. It is the expert opinion of the Panel that blind stone extraction with a basket should not be performed, and that intraureteral manipulations with a stone basket should always be performed under direct ureteroscopic vision. Fluoroscopic imaging of the stone alone is not sufficient.

#### 9.5.2 For Ureteral Stones <10 mm

**Option:** In a patient who has a newly diagnosed ureteral stone <10 mm and whose symptoms are controlled, observation with periodic evaluation is an option for initial treatment. Such patients may be offered an appropriate medical therapy to facilitate stone passage during the observation period.

[Based on review of the data and panel opinion/Level 1A]

The Panel performed a meta-analysis of studies in which spontaneous ureteral stone passage was assessed. The median probability of stone passage was 68% for stones ≤5 mm (n=224) and 47% for those >5 and ≤10 mm (n=104) in size (details previously discussed and provided in the appendices). The Panel recognized that these studies had certain limitations including nonstandardization of the stone size measurement methods and lack of analysis of stone position, stone-passage history, and time to stone passage in some. A meta-analysis of MET was also performed which demonstrated that alpha blockers facilitate stone passage and that the positive impact of nifedipine is marginal. This analysis also indicates that alpha blockers are superior to nifedipine and, hence, may be the preferred agents for MET (details provided in the Appendixes). A similar benefit of MET was demonstrated in a recently published meta-analytic study (7). The methods of analysis used in this study were somewhat different as the absolute improvement in stone passage was calculated in our study and the relative improvement in the latter. The vast majority of the trials analyzed in this and our analysis were limited to patients with distal ureteral stones. The majority of stones pass spontaneously within four to six weeks. This was demonstrated by Miller and Kane (8), who reported that of stones ≤2 mm, 2 to 4 mm and 4 to 6 mm in size, 95% of those which passed did so by 31, 40, and 39 days, respectively. In a choice between active stone removal and conservative treatment with MET, it is important to take into account all individual circumstances that may affect treatment decisions. A prerequisite for MET is that the patient is reasonably comfortable with that therapeutic approach and that there is no obvious advantage of immediate active stone removal.

**Standard:** Patients should be counseled on the attendant risks of MET including associated drug side effects and should be informed that it is administered for an “off label” use.

[Based on Panel consensus/Level IV]

**Standard:** Patients who elect for an attempt at spontaneous passage or MET should have well-controlled pain, no clinical evidence of sepsis, and adequate renal functional reserve.

[Based on Panel consensus/Level IV]
**Standard**: Patients should be followed with periodic imaging studies to monitor stone position and to assess for hydronephrosis.

[Based on Panel consensus/Level IV]

**Standard**: Stone removal is indicated in the presence of persistent obstruction, failure of stone progression, or in the presence of increasing or unremitting colic.

[Based on Panel consensus/Level IV]

9.5.3 **For Ureteral Stones >10 mm**
Although patients with ureteral stones >10 mm could be observed or treated with MET, in most cases such stones will require surgical treatment. No recommendation can be made for spontaneous passage (with or without medical therapy) for patients with large stones.

9.5.4 **For Patients Requiring Stone Removal**

**Standard**: A patient must be informed about the existing active treatment modalities, including the relative benefits and risks associated with each modality.

[Based on Panel consensus/Level IV]

Specifically, both SWL and URS should be discussed as initial treatment options for the majority of cases. Regardless of the availability of this equipment and physician experience, this discussion should include stone-free rates, anesthesia requirements, need for additional procedures, and associated complications. Patients should be informed that URS is associated with a better chance of becoming stone free with a single procedure, but has higher complication rates.

**Recommendation**: For patients requiring stone removal, both SWL and URS are acceptable first-line treatments.

[Based on review of the data and Panel consensus/Level 1A-IV (details provided in Chapter 3)]

The meta-analysis demonstrated that URS yields significantly greater stone-free rates for the majority of stone stratifications.

**Recommendation**: Routine stenting is not recommended as part of SWL.

[Based on Panel consensus/Level III]

The 1997 AUA guideline, *Report on the Management of Ureteral Calculi*, stated that “Routine stenting is not recommended as part of SWL (9).” The 1997 guideline Panel noted that it had become common practice to place a ureteral stent for more efficient fragmentation of ureteral stones when using SWL. However, the data analyzed showed no improved fragmentation with stenting (9). The current analysis demonstrates similar findings. In addition, studies assessing the efficacy of SWL treatment with or without internal stent placement have consistently noted frequent symptoms related to stents (10-13).

**Option**: Stenting following uncomplicated URS is optional.

[Based on Panel consensus/Level 1A]

Several randomized prospective studies published since the 1997 AUA guideline document have demonstrated that routine stenting after uncomplicated URS may not be necessary (10,14-19). It is well documented that ureteral stenting is associated with bothersome lower urinary tract symptoms and pain that can, albeit temporarily, alter quality of life (15-17,20-26). In addition, there are complications associated with ureteral stenting, including stent migration, urinary tract infection, breakage, encrustation, and obstruction. Moreover, ureteral stents add some expense to the overall ureteroscopic procedure and unless a pull string is attached to the distal end of the stent, secondary cystoscopy is required for stent removal (27). There are clear indications for stenting after the completion of URS. These include ureteral injury, stricture, solitary kidney, renal insufficiency, or a large residual stone burden.

**Option**: Percutaneous antegrade ureteroscopy is an acceptable first-line treatment in select cases.

[Based on Panel consensus/Level III]

Instead of a retrograde endoscopic approach to the ureteral stone, percutaneous antegrade access can be substituted (28). This treatment option is indicated:
• in select cases with large impacted stones in the upper ureter
• in combination with renal stone removal
• in cases of ureteral stones after urinary diversion (29)
• in select cases resulting from failure of retrograde ureteral access to large, impacted upper ureteral stones (30).

**Option: Laparoscopic or open surgical stone removal may be considered in rare cases where SWL, URS, and percutaneous URS fail or are unlikely to be successful.**

[Based on Panel consensus/Level III]

The 1997 AUA guideline stated that “Open surgery should not be the first-line treatment (9).” The invasiveness and morbidity of open surgery can be avoided. In very difficult situations, however, such as with very large, impacted stones and/or multiple ureteral stones, or in cases of concurrent conditions requiring surgery, an alternative procedure might be desired as primary or salvage therapy. Laparoscopic ureterolithotomy is a less invasive alternative to open surgery in this setting. Comparative series indicate that open surgical ureterolithotomy can be replaced by laparoscopic ureterolithotomy in most situations (31,32). From the 15 case series of laparoscopic ureterolithotomy included in the Panel’s literature review, the median stone-free rate was 88% for the primary treatment. It is notable that this success was achieved when virtually all of the procedures were for large and/or impacted calculi.

9.6 **Recommendations for the Pediatric Patient**

**Option: Both SWL and URS are effective in this population. Treatment choices should be based on the child’s size and urinary tract anatomy. The small size of the pediatric ureter and urethra favors the less invasive approach of SWL.**

[Based on review of data and Panel consensus/Level III]

9.7 **Recommendations for the Nonindex Patient**

**Standard: For septic patients with obstructing stones, urgent decompression of the collecting system with either percutaneous drainage or ureteral stenting is indicated. Definitive treatment of the stone should be delayed until sepsis is resolved.**

[Based on Panel consensus/Level III]

The compromised delivery of antibiotics into the obstructed kidney mandates that the collecting system be drained to promote resolution of the infection. The choice of drainage modality, whether percutaneous nephrostomy or ureteral stent, is left to the discretion of the urologist, as both have been shown in a randomized trial to be equally effective in the setting of presumed obstructive pyelonephritis/pyonephrosis (33). Definitive treatment of the stone should be delayed until sepsis has resolved and the infection is cleared following a complete course of appropriate antimicrobial therapy.

9.8 **Discussion**

There are two significant changes in treatment approach that distinguish the present document from the guideline published by the AUA in 1997. The most significant change is the use of retrograde URS as first-line treatment for middle and upper ureteral stones with a low probability of spontaneous passage. This change reflects both the vast technological improvements that have been made during the last decade and the experience and facility that surgeons now have with the procedure. The other change is the establishment of effective MET to facilitate spontaneous stone passage. These advances, the current status of other technologies and procedures, issues related to nonindex patients, and future directions and research germane to this condition will be subsequently discussed.

9.8.1 **Medical Expulsive Therapy**

There is growing evidence that MET, the administration of drugs to facilitate stone passage, can be efficacious. Studies have demonstrated that this approach may facilitate and accelerate the spontaneous passage of ureteral stones as well as stone fragments generated with SWL (34-38). Our meta-analysis demonstrated the effectiveness of MET. Nine percent (CI: -7% to 25%) more patients receiving nifedipine passed their stones than did controls in our meta-analysis, a difference that was not statistically significant. In contrast, a statistically significant 29% (CI: 20% to 37%) more patients passed their stones with alpha blocker therapy than did control patients. These findings indicate that alpha blockers facilitate ureteral stone passage while nifedipine may provide a marginal benefit. Therefore, the Panel feels that alpha blockers are the preferred
agents for MET at this time. Similar findings have been reported by Hollingsworth and associates (7), who recently performed a meta-analysis of studies involving alpha blockers or nifedipine in patients with ureteral stones. The differences in methodology from our study have been previously mentioned. Patients given either one of these agents had a greater likelihood of stone passage than those not receiving such therapy. The pooled-risk ratios and 95% CIs for alpha blockers and calcium channel blockers were 1.54 (1.29 to 1.85) and 1.90 (1.51 to 2.40) (7). The benefit of adding corticosteroids was reported to be small (7,37). Tamsulosin has been the most common alpha blocker utilized in these studies. However, one small study demonstrated tamsulosin, terazosin, and doxazosin as equally effective in this setting (39). These studies also demonstrated that MET reduces the stone-passage time and limits pain. The beneficial effects of these drugs are likely attributed to ureteral smooth muscle relaxation mediated through either inhibition of calcium channel pumps or alpha-1 receptor blockade. Further prospective and randomized studies are warranted to determine the patients who best respond to MET. A large, multicenter, randomized, placebo-controlled study has recently been funded in the United States for this purpose. Patients with ureteral stones in all segments of the ureter will be randomized to tamsulosin or placebo.

9.8.2 Shock-wave Lithotripsy
Shock-wave lithotripsy was introduced to clinical practice as a treatment for ureteral stones in the early 1980s. Today, even with the refinement of endourologic methods for stone removal such as URS and PNL, SWL remains the primary treatment for most uncomplicated upper urinary tract calculi. The meta-analysis published by the AUA Nephrolithiasis Guideline Panel in 1997 documented that the stone-free rate for SWL for proximal ureteral stones overall was 83% (78 studies, 17,742 patients). To achieve this result, 1.40 procedures were necessary per patient. The results were very similar in the distal ureter, with a stone-free rate of 85% (66 studies, 9,422 patients) necessitating 1.29 primary and secondary procedures per patient. There was no significant difference between various SWL techniques (SWL with pushback, SWL with stent or catheter bypass, or SWL in situ). Consequently, the Panel suggested that the use of a ureteral stent to improve stone-free rates was not warranted. This observation is also confirmed by the present analysis. However, there may be circumstances such as when the stone is small or of low radiographic density where a stent or ureteral catheter (sometimes using a contrast agent) may help facilitate localization during SWL. The Panel considered complications of SWL for ureteral stones to be infrequent.

The current meta-analysis analyzed SWL stone-free results for three locations in the ureter (proximal, mid, distal). The SWL stone-free results are 82% in the proximal ureter (41 studies, 6,428 patients), 73% in the mid ureter (31 studies, 1,607 patients), and 74% in the distal ureter (50 studies, 6,981 patients). The results in the 1997 guideline, which divided the ureter into proximal and distal only, reported SWL stone-free results of 83% and 85%, respectively. The CIs for the distal ureter do not overlap and indicate a statistically significant worsening of results in the distal ureter from the earlier results. No change is shown for the proximal ureter. The cause of this difference is not clear. Additional procedures also were infrequently necessary (0.62 procedures per patient for proximal ureteral stones, 0.52 for mid-ureteral stones, and 0.37 for distal ureteral stones). Serious complications were again infrequent. As expected, stone-free rates were lower and the number of procedures necessary were higher for ureteral stones >10 mm in diameter managed with SWL.

The outcomes for SWL for ureteral calculi in pediatric patients were similar to those for adults, making this a useful option, particularly in patients where the size of the patient (and ureter/urethra) may make URS a less attractive option.

The newer generation lithotritors with higher peak pressures and smaller focal zones should, in theory, be ideal for the treatment of stones in the ureter but instead have not been associated with an improvement in stone-free rates or a reduction in the number of procedures needed when this treatment approach is chosen. In fact, the SWL stone-free rates for stones in the distal ureter have declined significantly when compared with the 1997 AUA analysis. The explanation for the lack of improvement in SWL outcomes is unknown.

Although ureteroscopic stone removal is possible with intravenous sedation, one clear advantage of SWL over URS is that the procedure is more easily and routinely performed with intravenous sedation or other minimal anesthetic techniques. Therefore, for the patient who desires treatment with minimal anesthesia, SWL is an attractive approach.

Shock-wave lithotripsy can be performed with the aid of either fluoroscopy or ultrasound (US). While some stones in the proximal and distal ureter can be imaged with US, this imaging modality clearly limits SWL application in the ureter when compared to fluoroscopy. However, a combination of both fluoroscopy and US can facilitate stone location and minimize radiation exposure.

As documented in the 1997 AUA report, there appears to be little, if any, advantage to routine stenting when performing SWL for ureteral stones.

Concerns have been raised, too, regarding the use of SWL to treat distal ureteral calculi in women of childbearing age because of the theoretical possibility that unfertilized eggs and/or ovaries may be damaged.
To date, no objective evidence has been discovered to support such concerns, but many centers require that women age 40 or younger be fully informed of the possibility and give their consent before treatment with SWL (40-44).

9.8.3 Ureteroscopy

Ureteroscopy has traditionally constituted the favored approach for the surgical treatment of mid and distal ureteral stones while SWL has been preferred for the less accessible proximal ureteral stones. With the development of smaller caliber semirigid and flexible ureteroscopes and the introduction of improved instrumentation, including the holmium:YAG laser, URS has evolved into a safer and more efficacious modality for treatment of stones in all locations in the ureter with increasing experience worldwide (45,46). Complication rates, most notably ureteral perforation rates, have been reduced to less than 5%, and long-term complications such as stricture formation occur with an incidence of 2% or less (47). Overall stone-free rates are remarkably high at 81% to 94% depending on stone location, with the vast majority of patients rendered stone free in a single procedure (Figure 1 and Chapter 3).

In 1997, the AUA Nephrolithiasis Clinical Guideline Panel recommended SWL for <1 cm stones in the proximal ureter and either SWL or URS for >1 cm proximal ureteral stones. With improved efficacy and reduced morbidity currently associated with ureteroscopic management of proximal ureteral stones, this modality is now deemed appropriate for stones of any size in the proximal ureter. Indeed, the current analysis revealed a stone-free rate of 81% for ureteroscopic treatment of proximal ureteral stones, with surprisingly little difference in stone-free rates according to stone size (93% for stones <10 mm and 87% for stones >10 mm). The flexible ureteroscope is largely responsible for improved access to the proximal ureter; superior stone-free rates are achieved using flexible URS (87%) compared with rigid or semirigid URS (77%). These stone-free rates are comparable to those achieved with SWL.

The middle ureter poses challenges for all surgical stone treatments; the location over the iliac vessels may hinder access with a semirigid ureteroscope, and identification and targeting of mid-ureteral stones for SWL has proved problematic due to the underlying bone. Despite the limitations, ureteroscopic management is still highly successful; a stone-free rate of 86% was demonstrated in the current analysis, although success rates declined substantially when treating larger stones (>10 mm) compared with smaller stones (78% versus 91%, respectively).

Ureteroscopic treatment of distal ureteral stones is uniformly associated with high success rates and low complication rates. An overall stone-free rate of 94% was achieved with either a rigid or semirigid ureteroscope, with little drop off in stone-free rates when treating larger stones. On the other hand, flexible URS was less successful than rigid or semirigid URS for distal ureteral stones, particularly those >10 mm, likely due to difficulty maintaining access within the distal ureter with a flexible ureteroscope.

A number of adjunctive measures have contributed to the enhanced success of ureteroscopic management of ureteral calculi. Historically, stones in the proximal ureter have been associated with lower success rates than those in the mid and distal ureter, in part because the proximal ureter is more difficult to access and stone fragments often become displaced into the kidney where they may be difficult to treat. Improved flexible ureteroscopes and greater technical skill, along with the introduction of devices to prevent stone migration (48,49) have improved the success of treating proximal ureteral stones.

Although the efficacy of URS for the treatment of ureteral calculi has been amply shown, the need for a ureteral stent with its attendant morbidity has biased opinion towards SWL in some cases. Clearly, SWL is associated with fewer postoperative symptoms and better patient acceptance than URS. However, a number of recent prospective, randomized trials have shown that for uncomplicated URS, the ureter may be left unstented without undue risk of obstruction or colic requiring emergent medical attention (10,14-19).

Ureteroscopy can also be applied when SWL might be contraindicated or ill-advised. Ureteroscopy can be performed safely in select patients in whom cessation of anticoagulants is considered unsafe (50). In addition, URS has been shown to be effective regardless of patient body habitus. Several studies have shown that morbidly obese patients can be treated with success rates and complication rates comparable to the general population (51,52). Finally, URS can be used to safely simultaneously treat bilateral ureteral stones in select cases (53-55).

9.8.4 Percutaneous Antegrade Ureteroscopy

Percutaneous antegrade removal of ureteral stones is a consideration in selected cases, for example, for the treatment of very large (>15 mm diameter) impacted stones in the proximal ureter between the ureteropelvic junction and the lower border of the fourth lumbar vertebra (30,56). In these cases with stone-free rates between 85% and 100%, its superiority to standard techniques has been evaluated in one prospective randomized (57) and in two prospective studies (28,30). In a total number of 204 patients, the complication rate was low, acceptable, and not specifically different from any other percutaneous procedure.

Percutaneous antegrade removal of ureteral stones is an alternative when SWL is not indicated or
has failed (58) and when the upper urinary tract is not amenable to retrograde URS; for example, in those with urinary diversion (29) or renal transplants (59).

9.8.5 Laparoscopic and Open Stone Surgery
Shock-wave lithotripsy, URS, and percutaneous antegrade URS can achieve success for the vast majority of stone cases. In extreme situations or in cases of simultaneous open surgery for another purpose, open surgical ureterolithotomy might rarely be considered (60,61). For most cases with very large, impacted, and/or multiple ureteral stones in which SWL and URS have either failed or are unlikely to succeed, laparoscopic ureterolithotomy is a better alternative than open surgery if expertise in laparoscopic techniques is available. Both retroperitoneal and transperitoneal laparoscopic access to all portions of the ureter have been reported. Laparoscopic ureterolithotomy in the distal ureter is somewhat less successful than in the middle and proximal ureter, but the size of the stone does not appear to influence outcome.

Although highly effective, laparoscopic ureterolithotomy is not a first-line therapy in most cases because of its invasiveness, attendant longer recovery time, and the greater risk of associated complications compared to SWL and URS.

9.8.6 Special Considerations
9.8.6.1 Pregnancy
Renal colic is the most common nonobstetrical cause of abdominal pain in pregnant patients requiring hospitalization. The evaluation of pregnant patients suspected of having renal colic begins with ultrasonography, as ionizing radiation should be limited in this setting. If the US examination is unrevealing and the patient remains severely symptomatic, a limited intravenous pyelogram may be considered. A typical regimen includes a preliminary plain radiograph (KUB) and two films, 15 minutes and 60 minutes following contrast administration. Noncontrast computed tomography is uncommonly performed in this setting because of the higher dose of radiation exposure. Magnetic resonance imaging can define the level of obstruction, and a stone may be seen as a filling defect. However, these findings are nonspecific. In addition, there is a paucity of experience with using this imaging modality during pregnancy (62).

Once the diagnosis has been established, these patients have traditionally been managed with temporizing therapies (ureteral stenting, percutaneous nephrostomy), an approach often associated with poor patient tolerance. Further, the temporizing approach typically requires multiple exchanges of stents or nephrostomy tubes during the remainder of the patient’s pregnancy due to the potential for rapid encrustation of these devices.

A number of groups have now reported successful outcomes with URS in pregnant patients harboring ureteral stones. The first substantial report was by Ulvik, et al (63) who reported on the performance of URS in 24 pregnant women. Most patients had stones or edema, and there were no adverse sequelae associated with ureteroscopic stone removal. Similar results have been reported by Lifshitz and Lingeman (64) and Watterson et al (65) who found that the ureteroscopic approach was both diagnostic and therapeutic in pregnant patients with very low morbidity and the need for only short-term ureteral stenting, if at all, afterwards. When intracorporeal lithotripsy is necessary during ureteroscopic treatment of calculi in pregnant patients, the holmium laser has the advantage of minimal tissue penetration, thereby theoretically limiting risk of fetal injury.

9.8.6.2 Pediatrics
Both SWL and URS are effective treatment alternatives for stone removal in children. Selection of the most appropriate treatment has to be based on the individual stone problem, the available equipment and the urologist’s expertise in treating children. Children appear to pass stone fragments after SWL more readily than adults (66-71).

Ureteroscopy may be used as a primary treatment or as a secondary treatment after SWL in case of poor stone disintegration. Less efficient SWL disintegration might be seen in children with stones composed of cystine, brushite and calcium oxalate monohydrate or when anatomic abnormalities result in difficulties in fluoroscopic or ultrasonographic visualization of the stone (72-74).

One of the main problems with pediatric URS is the size of the ureteroscope relative to the narrow intramural ureter and the urethral diameter. This problem has lately been circumvented by the use of smaller ureteroscopes, for example, mini or needle instruments as well as small flexible semirigid or rigid ureteroscopes and pediatric (6.9 Fr) cystoscopes. With the availability of 4.5 and 6.0 Fr semirigid ureteroscopes, a 5.3 Fr flexible ureteroscope and a holmium:YAG laser energy source, instrument-related complications have become uncommon (73-75). However, the utilization of proper technique remains the most important factor for generating successful outcomes in this population. Percutaneous stone removal is also possible in pediatric patients with comparable indications to those in adults. Such an approach might be considered for stone removal in children with a malformation of the lower urinary tract.
9.8.6.3 Cystine Stones

Individuals with cystinuria are considered nonindex patients by the Panel for a variety of reasons. There are limited data regarding treatment outcomes in this group (76-83). In vitro studies also show that these stones are commonly resistant to SWL, although the degree of resistance may be variable (77,78). The structural characteristics of these stones are thought to contribute to their decreased SWL fragility. In addition, some of these stones may be barely opaque on standard imaging or fluoroscopy, potentially compromising shock-wave focusing. In contrast to SWL, technology currently utilized for intracorporeal lithotripsy during URS, including the holmium laser, ultrasonic and pneumatic devices, can readily fragment cystine stones (81).

Certain imaging characteristics may predict SWL outcomes for this patient group. Bhatta and colleagues reported that cystine stones having a rough-appearing external surface on plain film imaging were more apt to be fragmented with shock-wave energy than those with a smooth contour (82). Kim and associates reported that the computed tomography attenuation coefficients of the latter were significantly higher than the rough-type stones (83). Other types of stones with higher attenuation values have also been demonstrated to be resistant to shock-wave fragmentation (84).

Patients with this rare genetic disorder typically have their first stone event early in life, are prone to recurrent stones, and are consequently subject to repetitive removal procedures. In addition, patients with cystinuria are at risk for developing renal insufficiency over time (85,86). Prophylactic medical therapy and close follow-up can limit recurrence.

9.8.6.4 Uric acid Stones

Uric acid calculi are typically radiolucent, thus limiting the ability to treat such patients using in situ SWL. However, this approach may be possible with devices that use US if the stone can indeed be localized. When properly targeted, these stones fragment readily with SWL. Uric acid stones have lower computed tomography attenuation values, and can usually be distinguished from calcium, cystine, and struvite calculi (87). The presence of a low attenuation or a radiolucent stone, particularly in a patient with a low urinary pH, should lead the clinician to suspect this diagnosis. Manipulation of the urinary pH with oral potassium citrate, sodium citrate, or sodium bicarbonate to a level ranging from 6.0 to 7.0 may obviate the need for surgical intervention. Moreover, this medical treatment may allow stone dissolution in patients whose symptoms are controllable, should prevent the development of future uric acid stones, and has also been shown to enhance stone clearance with SWL (88). Medical expulsive therapy may be administered concomitantly. Ureteroscopy is a very effective method of treating patients who are not candidates for observation (89).

9.9 Research and Future Directions

Ten years have elapsed since the last publication of the AUA guidelines, and one year since the EAU recommendations on ureteral stones. Extensive cooperation between AUA and EAU Panel members has produced this unique collaborative report. This venture should provide the foundation for future collaborative efforts in guideline development.

The Panel encountered a number of deficits in the literature. While the management of ureteral stones remains commonly needed, few RCTs were available for data extraction. The data were inconsistent, starting from the definition of stone sizes and ending with variable definitions of a stone-free state. These limitations hinder the development of evidence-based recommendations.

To improve the quality of research, the Panel strongly recommends the following:

- conducting RCTs comparing interventional techniques like URS and SWL
- conducting pharmacological studies of stone-expulsion therapies as double-blinded RCTs
- reporting stone-free data without inclusion of residual fragments
- using consistent nomenclature to report stone size, stone location, stone-free rates, time point when stone-free rate is determined, or method of imaging to determine stone-free rate
- reporting data stratified by patient/stone characteristics, such as patient age, stone size, stone location, stone composition, gender, body mass index, and treatment modality
- reporting all associated treatments including placement of ureteral stents or nephrostomies
- using standardized methods to report acute and long-term outcomes
- developing methods to predict outcomes for SWL, URS, and MET
- providing measures of variability such as standard deviation, standard error, CI, or variance with corresponding average patient numbers
- reporting raw data to facilitate meta-analyses

The Panel suggests focusing on the following issues in future investigations:

- investigating the proposed current efficacy problems of second and third generation shock-wave machines and developing approaches to improve SWL.
• determining the safety of each technique with respect to acute and long-term effects
• investigating the promising medical stone expulsion in basic research studies and in clinical trials to unravel the underlying mechanisms and to optimize the treatment regimens
• addressing issues such as patient preferences, quality of life, and time until the patient completed therapy when evaluating treatment strategies. To date, only a few studies have addressed patient preference.90-92
• although largely dependent on different health systems, addressing cost-effectiveness

9.10 Acknowledgements and Disclaimers
The supporting systematic literature review and data analysis, and the drafting of this document were conducted by the EAU/AUA Nephrolithiasis Guideline Panel (hereinafter the Panel). Each association selected a Panel chair who in turn appointed the Panel members, urologists with specific expertise in this disease.

The mission of the Panel was to develop either analysis- or consensus-based recommendations, depending on the type of evidence available and Panel processes to support optimal clinical practices in the management of ureteral calculi. This document was submitted to 81 urologists and other health care professionals for peer review. After revision of the document based upon the peer review comments, the guideline was submitted for approval to the Practice Guidelines Committee of the AUA and the Guidelines Office of the EAU. Then it was forwarded to the AUA Board of Directors and the EAU Board for final approval. Funding of the Panel and of the PGC was provided by the AUA and the EAU, although Panel members received no remuneration for their work. Each member of the PGC and of the Panel furnished a current conflict of interest disclosure to the AUA.

The final report is intended to provide medical practitioners with a current understanding of the principles and strategies for the management of ureteral calculi. The report is based on an extensive review of available professional literature as well as clinical experience and expert opinion. Some of the medical therapies currently employed in the management of ureteral calculi have not been approved by the US Food and Drug Administration for this specific indication. Thus, doses and dosing regimens may deviate from that employed for the Food and Drug Administration-approved indications, and this difference should be considered in the risk-versus-benefit assessment.

This document provides guidance only, and does not establish a fixed set of rules or define the legal standard of care. As medical knowledge expands and technology advances, this guideline will change. Today it represents not absolute mandates but provisional proposals or recommendations for treatment under the specific conditions described. For all these reasons, the guideline does not preempt physician judgment in individual cases. Also, treating physicians must take into account variations in resources, and in patient tolerances, needs and preferences. Conformance with the guideline reflected in this document cannot guarantee a successful outcome.

9.11 REFERENCES


10. GENERAL RECOMMENDATIONS AND PRECAUTIONS FOR STONE REMOVAL

10.1 Infections
A test should be carried out in all patients in whom stone removal is planned, should be tested for bacteriuria. For uncomplicated cases, dipsticks might be sufficient for screening, in others, urine culture is necessary. Where there is clinically significant infection and obstruction, several days of drainage, via a stent or a percutaneous nephrostomy, should precede active intervention for stone removal.

10.2 Anticoagulation and stone treatment
Patients with bleeding diathesis or who are receiving anticoagulations should be referred to an internist for appropriate therapeutic measures before, and during, the stone-removing procedure. In patients with an uncorrected bleeding diathesis, the following are generally contraindicated:
- extracorporeal shock-wave lithotripsy (ESWL)
- percutaneous nephrolithotomy with or without lithotripsy (PNL)
- open surgery (1, 2).

Although ESWL is feasible and safe after correction of the underlying coagulopathy (3–5), ureterorenoscopy might offer an alternative approach, which is associated with less morbidity. The used of the holmium (Ho:YAG) laser, in combination with contemporary small-calibre ureteroscopes, is safe in these patients. Furthermore, ureteroscopic Ho:YAG laser lithotripsy, without the need for pre-operative correction of the haemostatic parameters, limits the risk of thromboembolic complications and avoids the costs associated with an extended hospital stay.
To decrease bleeding complications, electrohydraulic lithotripsy must be avoided (6, 7).

**LE = level of evidence; GR = grade of recommendation**

10.3 Pacemaker
Patients who have a pacemaker can be treated with ESWL; however, it is recommended that the patient’s cardiologist is consulted before ESWL is undertaken. Patients with implanted cardioverter defibrillators must be managed with special care, as some devices need to be deactivated during ESWL; however, this might not be necessary with the use of new-generation lithotripters (8).

10.4 Hard stones
Stones composed of brushite or calcium oxalate monohydrate are particularly hard. Percutaneous removal of these stones might be appropriate, particularly if they are large. Chemolytic treatment of brushite stone fragments is possible; this is important as a this type of stone is associated with a high recurrence rate.

There are two types of cystine stone: those that respond well to ESWL and those that respond poorly (9). PNL, which avoids subjecting the renal tissue to too much shock-wave energy, is the best alternative for efficient removal of large ESWL-resistant stones.

10.5 Radiolucent stones
Uric acid concrements can be localized using US, or intravenous or retrograde administration of contrast medium. Only uric acid stones, not sodium urate or ammonium urate stones, can be dissolved by oral chemolysis.

10.6 Recommendations for special considerations in the removal of stones
Table 23 summarizes recommendations for special considerations.

<table>
<thead>
<tr>
<th>Special considerations</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the presence of a positive urine culture, positive dip-stick test or suspicion of an infective component, treatment with antibiotics should precede stone removal</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td>Salicylates should be stopped 10 days before planned stone removal</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td>ESWL and PNL are contraindicated in pregnant women</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td>ESWL is possible in patients with a pacemaker</td>
<td>4</td>
<td>C</td>
</tr>
</tbody>
</table>

**GR = grade of recommendation; ESWL = extracorporeal shock-wave lithotripsy; LE = level of evidence; PNL = percutaneous nephrolithotomy.**

10.7 REFERENCES


11. MANAGING SPECIAL PROBLEMS IN STONE REMOVAL

Caliceal diverticulum stones are treated using ESWL, PNL (if possible) or RIRS. Diverticular stones can also be removed using video-endoscopic retroperitoneal surgery. The principles of video-endoscopic surgery are outlined elsewhere (1-5). If there is a narrow communication between the diverticulum and the renal collecting system, well-disintegrated stone material will remain in the original position. These patients may become asymptomatic as a result of stone disintegration only.

Horseshoe kidneys can be treated in line with the stone treatment options described above (6). However, as the kidney lies anteriorly, ESWL is commonly carried out with the patient in the prone position (i.e. with shock-wave entrance from the abdominal side).

Stones in transplanted kidneys: ESWL and PNL are recommended for the removal of stones in transplanted kidneys. For pelvic kidneys, ESWL or video-endoscopic laparoscopic surgery is recommended. For obese patients, the options are ESWL, PNL or open surgery.

Stones formed in a continent reservoir present a varied and often difficult problem (7–14). Each stone problem must be considered and treated individually.

Patients with obstruction of the ureteropelvic junction: when the outflow abnormality is corrected, stones can be removed with either percutaneous endopyelotomy (15–35) or open reconstructive surgery. Transureteral endopyelotomy with Ho:YAG laser endopyelotomy can also be used to correct this abnormality. Incision with an Acucise balloon catheter might also be considered, provided the stones can be prevented from falling into the pelvo-ureteral incision (36–39).

11.1 REFERENCES


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12. MANAGEMENT OF STONE PROBLEMS DURING PREGNANCY

Urolithiasis during pregnancy, though rare, presents diagnostic and therapeutic challenges. The incidence of urolithiasis has been reported to be 0.026 – 0.53%. When compared to non-pregnant age-matched controls, pregnant women do not have an elevated incidence of urolithiasis. No major differences in stone composition have been found when comparing pregnant women to the general population (1–6).

Stones may be present in both kidneys with an equal frequency, and ureteral stones are twice as common as renal calculi. Symptomatic stone disease presents in the second or third trimester in 80–90% of women. Stones affect the two kidneys with equal frequency, although physiological hydronephrosis of pregnancy more commonly affects the right side (7).

Management of these patients can pose significant and multiple challenges to the patient, obstetrician and urologist, but fortunately a considerable number of the symptomatic stones (70–80%) pass spontaneously. Obstetricians should be aware of the symptoms, the practical diagnosis and the risks associated with urolithiasis (8).

12.1 Symptoms

Generally, pregnant women present with symptoms of urolithiasis in the second or third trimesters. If signs such as flank pain with tenderness, haematuria and/or unresolved bacteriuria are present, urinary calculi must
be considered. This is important because the obstetric complications associated with urolithiasis potentially include preterm labour and premature rupture of membranes. Failure to diagnose and manage urinary stones promptly during pregnancy might have adverse consequences for mother and child (9).

12.2 Diagnostic evaluation

As a consequence of the normal physiological changes occurring during pregnancy, the diagnosis of urolithiasis is often difficult as... In addition to maternal renal functional status and stone-related factors (number, size, location and configuration), imaging is essential for diagnosis and appropriate treatment planning. The most important factor complicating the radiological evaluation of stone disease in pregnancy is the potential damage that can be caused by exposing the fetus to radiation, including teratogenesis, carcinogenesis, and mutagenesis. The risk of damage depends on gestational age and the amount of radiation delivered.

<table>
<thead>
<tr>
<th>Ultrasonography (US) (using the change in resistive index and transvaginal US when necessary) has become the primary radiological diagnostic tool.</th>
<th>LE = 1a</th>
</tr>
</thead>
<tbody>
<tr>
<td>GR = A</td>
<td></td>
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</tbody>
</table>

*LE = level of evidence; GR = grade of recommendation*

The value of US is limited value in cases of acute obstruction because of poor sound transmission through gas and bone and the, operator-dependent, ability of US to differentiate between physiological dilatation of pregnancy and ureteral. A limited excretory urogram or magnetic resonance imaging may be carried out in particularly complicated cases. Other diagnostic modalities used to diagnose the presence of the stone(s) and assess the degree of obstruction in pregnant women include:

- transvaginal/endoluminal US (evaluation of possible stones at the vesicoureteral junction)
- magnetic resonance urography (MRU), avoiding ionizing radiation and administration of iodinated contrast medium, which should be reserved for complex cases when US fails to provide a diagnosis
- more recently, gadolinium-enhanced breath-hold gradient-echo MR excretory urography (MREU).

12.3 Management of the stone problem

Following a correct diagnosis:

<table>
<thead>
<tr>
<th>Preference</th>
<th>Conservative management with bed rest, appropriate hydration and analgesia should be the first-line treatment for all pregnant women with non-complicated urolithiasis.</th>
<th>LE = 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>GR = C</td>
<td></td>
</tr>
</tbody>
</table>

If spontaneous passage of the stones does not occur or if complications develop (commonly the induction of premature labour), established treatment options should be considered.

<table>
<thead>
<tr>
<th>Preference</th>
<th>An internal stent or percutaneous nephrostomy catheter are suggested first-line treatment alternatives.</th>
<th>LE = 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>GR = C</td>
<td></td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Preference</th>
<th>URS, although more invasive, has been accepted as a minimally invasive treatment alternative (9–13).</th>
<th>LE = 1b</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>GR = A</td>
<td></td>
</tr>
</tbody>
</table>

*LE = level of evidence; GR = grade of recommendation*

Stone-related pain during pregnancy has been managed using acetaminophen and narcotic analgesics with no known teratogenic effects. Although no drug is absolutely free of risk during pregnancy, these drugs appear to be associated with minimal risk when used judiciously under medical supervision. Aspirin and NSAIDs can be used, while being aware of their non-teratogenic adverse effects (14, 15).

In recent years, epidural blocks have been commonly used to reduce maternal pain, and their safety for mother and foetus are well accepted, provided maternal hypotension is avoided. Although this approach is used infrequently, it may be helpful for selected patients who fail more conservative expectant management and when operative intervention is not possible (e.g. because of patient refusal, absence of equipment or lack of endourological expertise) (16).
12.3.1 Surgical management

Despite the commonly accepted success of conservative management, surgical intervention might be needed in certain situations such as for instance when there is febrile urinary tract infection, pyonephrosis, sepsis, obstruction of a solitary kidney, intractable pain, nausea or vomiting. A team including a urologist, obstetrician and anaesthesiologist should make a develop an appropriate management plan based on the patient’s wishes and her comfort level.

12.3.2 Temporary urinary diversion

Decompression of the renal collecting system using a percutaneous nephrostomy tube or an internal ureteral stent was first suggested by Meares in 1978. The efficacy of these procedures is established, however, each has its own advantages and disadvantages.

12.3.2.1 Percutaneous nephrostomy catheter

This widely accepted approach is routinely carried out with local anaesthesia under US guidance. Increasing experience has shown that the percutaneous approach has certain advantages over retrograde stent placement:

- In most cases, only local anaesthesia is needed to place the tube under US guidance in acutely ill or septic patients, providing immediate urine drainage and culture to determine organism-specific antibiotic therapy.
- This approach may provide access PNL, which might be required post partum and at the same time manipulation of the obstructed ureter. The potential risks of perforation and infection are avoided.
- The percutaneous approach enables immediate confirmation and continuous supervision of drainage. Failure to drain is easily identified and appropriately managed.
- Subsequent percutaneous chemolytic irrigation of the renal collecting system might be useful for dissolution of uric acid, cystine, or struvite stones (17).

The disadvantages of external tubes are the inconvenience of dealing with a collection device, the risk for accidental dislodgement and bacterial colonization. Also, insertion of a percutaneous nephrostomy catheter might be complicated by significant bleeding as as result of tract creation and dilatation.

12.3.2.2 Internal ureteral stent

Drainage of the obstructed renal collecting system can be accomplished using an internal ureteral stent inserted under local or general anaesthesia with transabdominal US guidance or limited fluoroscopy, or without imaging procedures. Stent insertion is routinely carried out by most urologists and the equipment should be readily available at most centres (18).

However, stent-related irritative lower urinary tract symptoms and rapid encrustation, which may be attributed to hypercalciuria, hyperuricosuria or infection that occur during pregnancy, are well-known problems associated with this approach. Internal stents may also be associated with increased analgesic requirements and decreased overall quality of life.

Some investigators therefore recommend hydration, dietary calcium restriction and antibiotics as well as frequent stent replacement at intervals of 4–8 weeks. Infection and migration are other complications of internal stents and it has therefore been advocated that ureteral stent placement is reserved for the later stages (> 22 weeks) of pregnancy.

The choice between these methods is based on the factors discussed above (21–23).

When conservative management fails and urinary diversion is needed, both nephrostomy tube placement and internal ureteral insertion are appropriate alternatives.

LE = level of evidence; GR = grade of recommendation

12.3.2.3 Ureteroscopy (URS)

The use of flexible and thin ureteroscopes for diagnostic and therapeutic purposes in a less invasive and traumatic manner has led several urologists to consider this method as first-line treatment for pregnant women who have failed conservative management. However, ureteroscopic management during pregnancy should be planned and performed at an experienced urological centre under close obstetric and anaesthetic surveillance.

General anaesthesia might be needed for URS, and it is important to always be aware of the potential risk of ureteral perforation and sepsis. The intervention should be carried out by an experienced urologist. The anatomical distortion of the bladder and distal ureter, particularly during the third trimester, can make semi-rigid URS more difficult. Stone manipulation at or near term should therefore be discouraged. Most distal-ureteral stones can be retrieved with a stone basket, but some may require fragmentation, which can be accomplished safely with a pulsed-dye laser, Ho:YAG laser or pneumatic lithotripsy (24, 25).
The most important contraindications to URS during pregnancy are:
- inexperience
- inadequate endoscopic instruments
- stones with a diameter > 1 cm
- multiple calculi
- transplanted kidney
- sepsis (because of the higher risk of complications).

Caution must be exercised when performing URS during pregnancy with a solitary kidney.

Ureteroscopy in experienced hands can be an effective treatment alternative to removal of ureteral stones during pregnancy (LE = 1b; GR = B).

ESWL and percutaneous nephrolithotripsy (PNL) are contraindicated in pregnancy, as there are established and obvious risks associated with exposing the foetus to radiation as well as shock waves.

\[ \text{LE} = \text{level of evidence}; \text{GR} = \text{grade of recommendation} \]

12.4 Conclusions

Urolithiasis in pregnancy remains a diagnostic and therapeutic challenge. Although US is the method of choice for the practical and safe evaluation of a pregnant woman, a limited intravenous urography, isotope renography or MREU is useful for delineating the level and grade of obstruction in case of hydronephrosis.

Depending on the stage of the pregnancy, degree of pain and presence of certain complications (e.g., obstruction, urosepsis and renal functional deterioration), conservative management with bed rest, hydration and analgesia will result in spontaneous passage of the stone in two-thirds of patients. If conservative treatment fails, temporary urinary diversion with percutaneous nephrostomy or an internal stent may be appropriate.

However, developments in diagnostic technology and endoscopic instrumentation during the last 5 years, have made it possible to use high-quality imaging and small-calibre ureteroscopes. Endoscopy is therefore a feasible and safe approach both for diagnostic and therapeutic purposes, but should be carried out only in centres with sufficient experience. ESWL in pregnancy remains an absolute contraindication.

12.5 REFERENCES

13. MANAGEMENT OF STONE PROBLEMS IN CHILDREN

In addition to the global increase in the rates of urolithiasis in developed countries, there has been a shift in the age group experiencing a first stone episode (1–3). More than 1% of all urinary stones have been registered in patients <18 years. As a result of malnutrition and racial factors, paediatric urolithiasis remains an endemic disease in some areas (e.g. Turkey, the Far East); in other regions the rates are similar to those observed in developed countries (4–7).
13.1 Investigations
Paediatric patients with urinary stones are considered to be a high-risk group for developing recurrent stones.

In paediatric patients, investigations for stone diagnosis, as well as metabolic abnormalities, are essential, as this group is at high risk for developing recurrent stones (6).

LE = level of evidence; GR = grade of recommendation

Investigations can be divided into the following categories:
• those related to the diagnosis of stones, including anatomic and functional information about the urinary tract ("imaging")
• those related to metabolism.

Infants and children may present with a wide range of uncharacteristic symptoms in the presence of urinary stones. All investigations start with an evaluation of the patient’s personal and family history, including nutritional habits and fluid intake, physical investigation, and laboratory tests of blood and urine.

For the investigation of stones in infants and children, urine culture is mandatory (8).

LE = level of evidence; GR = grade of recommendation

13.1.1 Imaging
When selecting diagnostic procedures to identify urolithiasis in paediatric patients, remember that these patients may be uncooperative, require anaesthesia, or be sensitive to ionizing rays. Ultrasound (US) is therefore very useful because it is an easy and gentle procedure.

More than one imaging study or combinations of various procedures will be required in most cases (9). Besides US, several optional procedures, including plain films (KUB), intravenous urography (IVU), helical CT, magnetic resonance urography (MRU), or nuclear imaging may be used.

13.1.1.1 Ultrasound
US is the most popular imaging study. For paediatric patients, its advantages are absence of irradiation and that there is no need for anaesthesia.

US evaluation should include the kidney, the filled bladder, and adjoining portions of the ureter (10).

LE = level of evidence; GR = grade of recommendation

In addition, colour-Doppler US showing differences in the ureteric jet (11) (LE = 4; GR = C) and in the resistive index of the arciform arteries of both kidneys are indicative of the grade of obstruction (12) (LE = 4; GR = C).

US can be used to obtain information about the presence, size and location of a stone, and the grade of dilatation and obstruction. It will also indicate signs of abnormalities that facilitate the formation of stones. US is part of the metaphylactic work-up.

Nevertheless, US fails to identify stones in more than 40% of paediatric patients (13, 14) (LE = 4) and provides no information about renal function.

13.1.1.2 Plain films (KUB)
In combination with US or MRU, KUB may help to identify stones and their radiopacity and to facilitate follow-up.

13.1.1.3. Intravenous urography (IVU)
IVU is an important diagnostic tool with which nearly all stones in the collecting system can be identified and which will provide anatomical and functional information. Post-interventional KUB can be easily compared with previous IVPs in cases of radiopaque stones. However, the injection of contrast dye is needed for IVU. The radiation dose for IVU is comparable to that used for a voiding cystourethrogram (dose range, 49.06 to 83.33 cGy/cm²).

Recently developed CT protocols may further reduce the exposure to radiation (18) (LE = 4; GR = C). However, the radiation dose and the extent of information about renal function must be considered when using non-enhanced helical CT.
Conventional imaging models are indispensable in some cases (15, 16).

**LE = 4**

**GR = C**

13.1.1.4 Helical computed tomography (CT)

Non-enhanced helical CT is a well-established procedure for diagnosing urolithiasis in adults. It has the highest sensitivity and specificity of all diagnostic procedures.

In paediatric patients, only 5% of stones escape detection by non-enhanced helical CT (4, 14, 17).

**LE = 4**

**GR = C**

Sedation or anaesthesia is rarely needed when a modern high-speed CT apparatus is used (10) **LE = 4**.

13.1.1.5 Magnetic resonance urography (MRU)

MRU cannot be used to detect a urinary stone. However, it might provide detailed information about the anatomy of the urinary collecting system, the location of an obstruction or stenosis in the ureter, and the morphology of renal parenchyma (19) **(LE = 4)**.

13.1.1.6 Nuclear imaging

The DMSA scan (99mTc-dimercaptosuccinyl acid) provides information about cortical abnormalities such as scarring, but does not help in the primary diagnosis of urolithiasis. A diuretic renogram with injection of a radiotracer (MAG3 or DPTA) and furosemide can be used to demonstrate renal function, identify obstruction in the kidney after injection of furosemide, and indicate the anatomical level of the obstruction (10) **(LE = 4; GR = C or B)**.

13.1.2 Metaphylactic investigations

Paediatric patients who have urinary stones are a high-risk group for developing recurrent urinary stones and therefore require specific metaphylaxis for effective stone prevention. The risk may arise from anatomical or functional disorders of the urinary collecting system, or metabolic failures, including genetic disorders.

In paediatric patients, the most common non-metabolic disorders are vesico-ureteral reflux, ureteropelvic junction obstruction, a neurogenic bladder, or other voiding difficulties (9).

**LE = 4**

If urinary stones are suspected, suitable investigations must be performed (see appropriate chapter quantify...)

Metabolic investigations are based on an appropriate or thorough stone analysis. According to the current standard, infrared spectroscopy or X-ray diffraction are mandatory for adult patients. A wet chemistry analysis is insufficient (20).

**LE = 2b**

**GR = B**

Based on the composition of stones (see also Chapter 16).

Additional serum chemistry and 24-hour urine collections may be required (8).

**LE = 2**

**GR = A**

13.2 Stone removal

In principle, the same treatment modalities are used for adult and paediatric patients; however, the specific circumstances of treating children must be taken into account.

Spontaneous passage of a stone is more likely to occur in children than in adults (21).

**LE = 4**

**GR = C**

Although the use of nifedipine or alpha-blockers is very common in adults, there is no evidence to demonstrate the safety and efficacy of these agents in paediatric patients.

In paediatric patients, both ESWL and endourologic are effective procedures for stone removal.

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Several factors must be considered when selecting the procedure to be used in children:
• compared to adults, children pass fragments more rapidly after ESWL
• for endourological procedures, the smaller organ size in children must be considered when selecting instruments for PNL or ureteroscopy (URS)
• to eliminate radiation exposure, US can be used for localization during ESWL. in order to
• anticipated stone composition (cystine stones are more resistant to ESWL)
• co-morbidity and any concomitant treatment
• the need for general anaesthesia for ESWL; this will depend on the patient’s age and the lithotripter used.

13.2.1 Endourological procedures
The improvement of intracorporal lithotripsy devices and the development of smaller instruments facilitate both PNL and URS in children. For PNL, nephroscopes that are 15F or less are available (LE = 4; GR = C). Smaller ‘needle ureteroscopes’ and flexible scopes are also available.

During URS, dilatation of the ureteral orifice is rarely needed (24).

LE = level of evidence; GR = grade of recommendation

As in adults (see Chapters 7 and 9).

The holmium:yttrium aluminium garnet (Ho:YAg) laser is the preferred device for intracorporal lithotripsy (25).

LE = level of evidence; GR = grade of recommendation

For PNL or URS with larger instruments, US or pneumatic lithotripsy are appropriate alternatives (26).

LE = level of evidence; GR = grade of recommendation

13.2.2 ESWL
The literature regarding the use of SWL in the paediatric population, emphasizing the efficiency and safety of ESWL in paediatric urolithiasis, has grown considerably since 1986. ESWL, a minimally invasive procedure, with satisfactory stone-free rates, has been found to render the patients stone-free over a short period, using a reasonable number of shockwaves and only limited auxiliary procedures. Despite the increasing application of PNL, the development of smaller-diameter flexible ureteroscopes and ancillary instruments, ESWL is still the least invasive procedure (23, 27, 29).

Remember, however, that the higher incidence of metabolic and anatomical abnormalities in paediatric patients, compared with the adult population, is a major concern in stone formation and can influence the management options and ultimate effectiveness of the selected treatment. Despite a successful disintegration, residual fragments after ESWL should be followed closely by regular examinations. Residuals may predispose to recurrent urolithiasis (28, 29).

For paediatric patients the indications for ESWL are similar to those in adults. Children with renal pelvic stones or caliceal stones with a diameter up to 20 mm (~ 300 mm²) are ideal cases for this form of stone removal. The success rates tend to decrease as the stone burden increases.

LE = level of evidence; GR = grade of recommendation

Stone-free rates of 67–93% in short-term and 57– 92% in long-term follow-up studies have been reported. More effective disintegration of even larger stones, together with swifter and uncomplicated discharge of larger fragments, can be achieved with ESWL in children than in adults (29-31). Stones located in calices, as well as in abnormal kidneys, and larger stones, are more difficult to disintegrate and clear. Additionally, the likelihood of urinary obstruction is higher in such cases, and children should be followed closely for the prolonged risk of urinary tract obstruction. Depending on the stone-related factors, the re-treatment rate ranges from 13.9% to 53.9% and the need for ancillary procedures and/or additional interventions ranged from 7% to 33% (27, 28, 32).

A general anaesthetic is needed for 30–100% of children treated by ESWL. However, this need and the method of anaesthesia used vary widely, depending on the age of the child and type of lithotripter. General anaesthesia is generally used, except possibly for older children , for whom sedation is usually needed to relieve the discomfort caused by ESWL (23, 28). Despite its effectiveness and minimally invasive character,
theoretical concerns have been raised regarding the safety and bioeffects that ESWL might have in children on the immature, growing kidney and surrounding organs. However, during both short- and long-term follow-up, no irreversible functional or morphological side effects of high-energy shockwave have been demonstrated. In addition, when the potential deterioration of renal function is taken into account (although it is transient), restriction of the number of shockwaves and the energy used during each treatment session will help to protect the kidneys (33, 34).

Ureteral stones with a diameter < 5 mm are likely to pass spontaneously in up to 98% of paediatric patients. Intervention will be required for large, as well as for impacted, stones. ESWL is the treatment of choice for most stones located in the upper urinary tract in children; however, the success rate of ESWL decreases as the stone passes to the more distal parts of the ureter. Overall stone-free rates have ranged from 80% to 97% in different series, and the success rates for proximal and distal ureteral stones range from 75% to 100%, respectively (23, 27, 35, 36).

Although endoscopic procedures can be used to definitively remove ureteral stones, acceptable success rates have made ESWL a favourable first-line treatment for most proximal ureteral stones. Currently, ESWL is unlikely to be successful for the treatment of stones with a diameter >10 mm or for impacted stones, calcium oxalate monohydrate and cystine stones, or stones in children with unfavourable anatomy and in whom localization difficulties exist. Compared to adults, children pass stone fragments easily and the need for a stent is rare. If the stone burden is so large, that a ureteral stent is required, alternative procedures should be considered. Although internal stents are seldom needed following ESWL-treatment of upper tract stones, ureteral pre-stenting appeared to have decreased the stone-free rate after the initial treatment and retreatments of 12–14% were recorded (23, 31, 37).

13.2.3 Conclusions
Among the available treatment strategies of paediatric urinary calculi, ESWL is the method of choice for smaller stones (diameters < 20 mm, surface area ~ < 300 mm2). The successful stone-free rates emphasize the efficacy of this treatment modality when combined with judicious use of auxiliary procedures. Where appropriate, ESWL is a safe and highly effective treatment alternative for the management of stones in children. However, satisfactory outcomes with reasonable low complication rates can be achieved only with adequate experience. Particular attention should be paid to residual fragments, especially in children with predisposing metabolic, as well as anatomical, disorders.

13.2.4 Open or laparoscopic surgery
The rate of open procedures in stone patients has dropped significantly in all age groups, including children. Open surgery, if required, may be replaced by laparoscopic procedures. Indications for surgery include failure of primary therapy for stone removal (38), abnormal position of the kidney (39), or an additional target of therapy apart from stone removal (e.g. treatment of stones in a primary obstructive megaueter) (40) (LE = 4; GR = C).

13.3 REFERENCES


14. RESIDUAL FRAGMENTS

Residual fragments are commonly seen after ESWL, and most frequently present in the lower calix, following the disintegration of large stones. However, residual fragments may occur following ESWL for all sizes of stones.

Different imaging techniques have variable degrees of sensitivity. Computed tomography CT or tomographic examinations demonstrate small fragments better than a standard plain abdominal film of the
kidneys, ureters and bladder (KUB). A CT scan can also demonstrate uric acid concrements, which are otherwise radiolucent. Reports on residual fragments therefore vary between institutions, depending on which imaging method has been used. However, there are no data in the literature demonstrating the clinical value of being able to detect very small concretions, visible only on CT scan. Moreover, CT examinations are not universally available.

The Panel recommends that the selection of a stone-removing procedure should be based on the findings of a good-quality KUB and that CT examination is necessary only for uric acid stones.

- Stone residuals with a diameter ≤ 4 mm should be called residual fragments.
- Residuals with a diameter ≥ 5 mm should be called residual stones.

The clinical problem of asymptomatic stone residuals in the kidney is related to the risk of developing new stones from such nidi.

Patients with residual fragments or stones should be followed up regularly to monitor the course of their disease. LE = 4 GR = C

Identification of biochemical risk factors and appropriate stone prevention is particularly indicated in patients with residual fragments or stones (35). LE = 1b GR = A

In symptomatic patients, it is important to rule out obstruction, or to treat this problem if it is present, and to take the therapeutic steps necessary to eliminate symptoms. In asymptomatic patients where the stone is unlikely to pass, treat according to the relevant stone situation.

For well-disintegrated stone material residing in the lower calix, consider inversion therapy during high diuresis and mechanical percussion (38). LE = 1a GR = A

The risk of recurrence in patients with residual fragments after treatment of infection stones is well recognized. In a 2.2 year follow-up of 53 patients, 78% of patients with stone fragments 3 months after treatment experienced stone progression. The stone-free rate was 20%, the remaining 2% had stable disease (1). The term ‘clinically insignificant residual fragments’ (CIRF) was introduced for calcium stone residual fragments. The role of CIRF has been a matter of concern and debate (2–13). Most studies on the long-term course of the disease in patients with residual fragments are restricted to 1–6 years; the longest follow-up period was reported by Yu et al. (14). After 6.3 years, stone growth was observed in 26% of patients and recurrent stone formation in 15%. During a follow-up of 7–96 months (average 3.4 years), the residual fragments had increased in size in 37% of patients; a new stone-removing procedure was undertaken in 22% of patients (15). Data from 104 patients with residual fragments showed that, in 40%, the size of the residual fragments had decreased or remained stable, while in 5% stone growth was seen during a mean follow-up of 1.2 years (16); by 2 years of follow-up, further intervention was needed in 9.3% of patients. In a 4-year follow-up of patients with residual fragments < 4 mm, there was obvious increase in size in 37% and a need for retreatment in 12% (17).

It is assumed that the percentage of stone-free patients is overestimated. The potential for new stone formation should therefore be considered in patients who have been treated with ESWL.

- Reported stone recurrences were 8.4% after 1 year, 6.2% after 1.6 years, 9.7% after 3.3 years, 20% after 3.5 years and 7% after 3.6 years (18).
- In a Japanese report, the recurrence rates were 6.7%, 28.0% and 41.8% after 1, 3 and 5 years, respectively (19).
- For a group of Swedish patients with calcium stones, a 20% risk of recurrent stone formation was recorded during the first 4 years after ESWL. Twenty-five per cent of patients with infection stones had formed new stones after 2 years. The greatest risk was seen in patients with stones containing a high content of calcium phosphate (20).
- In a neural network analysis, an increased stone size was noted in 48% of patients with residual fragments followed up for 3.5 years; however, none of the identified risk factors for stone growth was found to be individually predictive for continuing stone formation (37).

For a kidney with stones or fragments in the lower caliceal system and with no functioning parenchyma in that part, lower pole resection is an alternative to ESWL (21). For stones in the upper and middle calyces, URS with contact disintegration is another option. Percutaneous chemolysis can be used for stone fragments composed of magnesium ammonium phosphate, carbonate apatite, uric acid, cystine and brushite. For stones with a largest diameter ≤ 20 mm (~300 mm²), internal ureteral stenting before ESWL is recommended to avoid problems with an accumulation of stones obstructing the ureter, known as
a Steinstrasse (see Chapter 15) (22–34). The risk of developing a Steinstrasse is particularly high for stones located in the renal pelvis (36). Table 24 summarizes the recommendations for the treatment of residual fragments.

Table 24: Recommendations for the treatment of residual fragments

<table>
<thead>
<tr>
<th>Residual fragments, stones (largest diameter)</th>
<th>Symptomatic residuals</th>
<th>Asymptomatic residuals</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 4–5 mm</td>
<td>Stone removal</td>
<td>Reasonable follow-up</td>
</tr>
<tr>
<td>&gt; 6–7 mm</td>
<td>Stone removal</td>
<td>Consider appropriate method for stone removal</td>
</tr>
</tbody>
</table>

14.1 REFERENCES


15. **STEINSTRASSE**

A Steinstrasse or fragment column in the ureter is an accumulation of gravel that does not pass within a reasonable period of time and that interferes with the passage of urine (1). As internal ureteral stents are now commonly inserted before ESWL for large renal stones, the frequency of Steinstrasse has decreased.

In all patients with signs of infection, antibiotics must be given and adequate drainage provided as soon as possible.

Insertion of a percutaneous nephrostomy catheter usually results in passage of the fragments (2). For distally located accumulations of fragments, ureteroscopy (URS) might be useful to remove the leading stone fragment by contact disintegration.

Treatment recommendations are summarized in Table 25.

**Table 25: Recommended treatment of Steinstrasse**

<table>
<thead>
<tr>
<th>Position</th>
<th>Unobstructed</th>
<th>Obstructed and/or of stone symptomatic</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal ureter</td>
<td>1. ESWL</td>
<td>1. PN</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>2. URS</td>
<td>1. Stent</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. URS</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. ESWL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mid-ureter</td>
<td>1. ESWL</td>
<td>1. PN</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>2. URS</td>
<td>1. Stent</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. URS</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. ESWL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal ureter</td>
<td>1. ESWL</td>
<td>1. PN</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>1. URS</td>
<td>1. Stent</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. URS</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. ESWL</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LE = level of evidence; GR = grade of recommendation; ESWL = extracorporeal shockwave lithotripsy; PN = percutaneous nephrostomy catheter; URS = ureteroscopy

15.1 **REFERENCES**


16. **INTERNAL STENTING – WHEN AND WHY**

16.1 **Introduction**

Stents were introduced into clinical urological practice in the 1970s (1, 2). The internal ureteral stent is made of flexible, synthetic polymers and constructed and designed to be retained in situ. The stent has become an important device in the urologist’s armamentarium to assist and maintain drainage of the upper urinary tract in
the face of obstruction or anticipated obstruction (3).

As the renal calculus is the most commonest cause of upper urinary tract obstruction, the ureteric stent has become almost a sine qua non in the surgical management of upper tract renal and ureteral calculi in conjunction with extra- and intra-corporeal stone removal/disintegration. Although stent insertion for the immediate relief of significant and serious obstruction caused by a calculus is unquestionable, and placement of a stent in the ureter following ureteroscopic procedures was considered to be mandatory, a revised approach in some circumstances is now being considered on the basis of experience.

No stent is ideal and the surgeon must be to be familiar with indications for usage, selection, modes of insertion and potential complications. Even though retrograde insertion of the stent is the usual method, a percutaneous antegrade approach through the loin under X-ray or ultrasound (US) control might, in some circumstances, be undertaken. Although both techniques are within the expertise of a competent, trained urological surgeon, the percutaneous antegrade method is often and most commonly performed by radiologists.

16.2 Stents in the management of kidney stones

Extra-corporeal shock-wave lithotripsy (ESWL) or percutaneous nephrolithotomy (PNL) is the treatment of choice for renal calculi (see Chapter 7 for principles of active removal). Most simple renal calculi (80–85%) can be treated with SWL, while PNL is the treatment of choice for complex renal calculi (4, 5). With stones > 20 mm in diameter, the placement of a stent before ESWL was recommended to obviate the possible obstruction by a Steinstrasse. It was reported that the peri-operative placement of double-J stents can significantly reduce post ESWL morbidity and does not impede passage of the disintegrated stone fragments (6). In any case, this becomes almost obligatory when treating stones in a solitary kidney, where the avoidance of risk of obstruction by even small fragments is particularly relevant.

There is little or no reason to leave a stent in situ after PNL because all disintegrated stone material is captured and removed at operation and the kidney drained by a nephrostomy tube. However, with bimodal therapy for staghorn stones, where PNL is followed by ESWL for residual fragments, internalized stenting prevents obstruction if stone fragments fall into the ureter before ESWL and prevents subsequent formation of an obstructing Steinstrasse.

Technological advances of flexible, miniaturized ureteroscopes facilitates the treatment of simple renal calculi, with stone-free rates similar to those obtained using SWL and without the morbidity that accompanies PNL. The placement of a stent might be indicated in this situation; the decision to stent is a matter of clinical judgement and individual circumstances.

16.3 The use of stents in the ureter

The size, character and location of stones in the ureter determine management. The criteria that apply to the spontaneous passage of a stone are well documented and form the basis of expectant treatment. Likewise, ureteral obstruction by a stone, unlikely to pass, requires intervention to remove the stone and relieve obstruction. The two competing approaches to the interventional management of stones in the ureter are ESWL and/or ureteroscopic (URS) stone removal/disintegration. The relative advantages, benefits and results of the two are discussed elsewhere (7). Indications for the insertion of a stent together with SWL or URS and the relief of obstruction need to be defined (8).

16.3.1 Indications for stenting for urgent relief of obstruction

The indications for stenting for urgent relief of obstruction are:

- infection with urinary tract obstruction
- urosepsis
- intractable pain and/or vomiting
- obstruction in a solitary or transplanted kidney
- bilateral obstructing stones
- ureteral calculus obstruction in pregnancy, pending definitive therapy in the post-partum period.

A randomized controlled trial showed that ureteral catheters, ureteral stents and percutaneous nephrostomy tubes were equally effective for decompressing the urinary tract (9; Chapter 9).

For decompression of the renal collecting system ureteral catheters, stents and percutaneous nephrostomy catheters are apparently equally effective

LE = level of evidence; GR = grade of recommendation

16.4 Stents in conjunction with ESWL therapy for ureteral stones

The assumption that a stent in the ureter contributed to more efficient fragmentation of the stone with ESWL led to the routine pre-treatment placement of an internal stent. Several studies, including randomized
controlled trials, in large numbers of patients have now shown that there was no difference in stone-free rates between stented and non-stented patients (10). In fact, stenting was seen to be significantly associated with a decreased stone-free rate (11).

Indeed, stenting has several disadvantages. It makes a non-invasive procedure into an invasive one, causes undesirable side effects, and increases the cost of treatment. The recommendation, therefore, is that stent insertion before SWL for obstructing ureteral stones ≤2 cm provides no advantage and is unnecessary.

16.5 Stents in conjunction with URS
Routine placement of a stent has been considered to be an integral adjunct to URS, and was undertaken to prevent:
- obstruction
- renal pain caused by oedema as a result of balloon dilatation
- trauma of instrumentation
- stone manipulation and disintegration.

Several prospective, randomized, controlled trials comparing non-stented versus stented ureteroscopic lithotripsy have shown significantly more morbidity with regard to haematuria, flank and abdominal pain, dysuria and hospital stay in the stented patients (12–14). In a non-randomized study, up to 80% of participants experienced urinary symptoms and pain associated with indwelling ureteral stents, which interfered with daily activities and resulted in a reduced quality of life (15). A recent study has also reported that an indwelling ureteral stent can impair the quality of sexual life in both male and female patients (16). In a meta-analysis of nine randomized controlled trials of stenting versus non-stenting after URS in 831 patients, Nabi et al. (17) reported that the incidence of irritative lower urinary tract symptoms was significantly higher in the stented patients, while there were no differences in stone-free rates, urinary tract infection rates, requirements for analgesia or long-term ureteric stricture formation.

It is therefore recommended that ureteric stents are not necessary following uncomplicated URS for stones.

16.6 REFERENCES
7. Tiselius HG. Removal of ureteral stones with extracorporeal shock wave lithotripsy and ureteroscopic procedures. What can we learn from the literature in terms of results and treatment efforts?. Urological Reseach 2005;33:185-90

UPDATE March 2008


17. RECURRENCE PREVENTIVE TREATMENT

17.1 Recurrence preventive treatment of patients with calcium stone disease

Table 24 summarizes various therapeutic tools, which aim to reduce the risk of recurrent calcium stone formation. The levels of evidence (LE) and the grades of recommendation (GR) refer to the effects on stone formation reported in the literature. The description of biochemical effects enables the most appropriate treatment to be selected in patients with known abnormalities in urine composition.

### Table 24: Dietary and pharmacological treatment regimens for prevention of recurrent calcium stone formation

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Biochemical effects</th>
<th>References</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased fluid intake</td>
<td>Dilution of urine</td>
<td>6, 7</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>Reduced intake of oxalate</td>
<td>Reduced excretion of oxalate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduced intake of animal protein</td>
<td>Reduced excretion of:</td>
<td>28</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>Reduced intake of animal protein</td>
<td>• Calcium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduced intake of animal protein</td>
<td>• Oxalate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduced intake of animal protein</td>
<td>• Urate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduced intake of animal protein</td>
<td>Increased excretion of:</td>
<td></td>
<td>1b</td>
<td></td>
</tr>
<tr>
<td>Reduced intake of animal protein</td>
<td>• Citrate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduced intake of animal protein</td>
<td>• Increased pH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduced intake of sodium</td>
<td>Reduced excretion of calcium</td>
<td>28</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>Increased intake of fibres</td>
<td>Increased excretion of citrate</td>
<td>12, 13</td>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td>Increased intake of vegetables, provided there is a simultaneous adequate intake of calcium</td>
<td>Increased excretion of citrate</td>
<td>36</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td>Avoid excessive intake of vitamin C</td>
<td>Reduced urinary oxalate</td>
<td>18</td>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td>Thiazide</td>
<td>Reduced excretion of calcium</td>
<td>52-63, 67</td>
<td>1a</td>
<td>A</td>
</tr>
<tr>
<td>Potassium citrate</td>
<td>Increased excretion of citrate</td>
<td>70, 71</td>
<td>1b</td>
<td>A</td>
</tr>
</tbody>
</table>
Abnormal crystalluria is a common finding in patients with recurrent calcium stone disease. Compared to non-stone formers, stone-forming patients have been shown to have more, larger, and aggregated crystals (1). Moreover, crystalluria found in early morning urine samples seems to predict the risk of recurrent stone formation (2). The abnormal crystalluria can cause:

- A small urine volume
- Increased excretion of urine variables important for increasing the ion-activity products of calcium oxalate/calcium phosphate, or,
- Reduced activity of inhibitors of crystal growth and crystal agglomeration.

These factors have been extensively reported in a large number of articles and the issue has been previously comprehensively summarized (3-5).

It is axiomatic that without sufficiently supersaturated urine there can be no crystal formation and accordingly no stone formation. It therefore seems essential to make the relevant corrections of urine composition in order to counteract critical supersaturation and pathological crystallization. The treatment recommendations, which are based on assumed or demonstrated abnormalities, should be adapted to the severity of the disease to avoid overtreatment and obtain reasonable patient compliance.

### 17.1.1 Drinking recommendations

An inverse relationship between high fluid intake and stone formation has been demonstrated (6, 7). The general recommendation for calcium stone formers is to maintain a high urine flow by a generous intake of fluids. The aim should be to obtain a 24-hour urine volume of at least 2 L (LE 1b; GR A).

Although most beverages can be drunk to increase fluid intake and help prevent stone formation, grapefruit juice has been shown to be associated with an increased risk of stone formation (8) (LE 3; GR C). The presence of citrate appears to be the important determinant of the effect of fruit juices. In the presence of hydrogen ions, the net result is neutralization. However, with potassium, pH and citrate are increased. For this reason, orange juice is beneficial but not cranberry juice (9,10). Although grapefruit juice has a high potassium content, its effect on calcium oxalate supersaturation is counteracted by a high supply of oxalate (11).

### 17.1.2 Dietary recommendations

Diet should be of a ‘common sense’ type, i.e. a mixed balanced diet with contributions from all food groups, but without excesses of any kind (12).

**Fruits, vegetables and fibres:** Fruit and vegetable intake should be encouraged because of the beneficial effects of fibre (13). The alkaline content of a vegetarian diet also gives rise to a desirable increase in urinary pH (12).

**Oxalate:** An excessive intake of oxalate-rich products, should be limited or avoided to prevent an oxalate load. This includes fruit and vegetable rich in oxalate such as wheat bran. This is particularly important in patients in whom an high oxalate excretion has been demonstrated. The following products have a high content of oxalate (14):

- Rhubarb, 530 mg oxalate/100 g
- Spinach, 570 mg oxalate/100 g
- Cocoa, 625 mg oxalate/100 g
- Tea leaves, 375-1450 mg oxalate/100 g
- Nuts, 200-600 mg oxalate/100 g.

**Potassium magnesium citrate**

- Increased urine pH
- Increased excretion of citrate
- Increased inhibition of crystal growth and crystal agglomeration
- Reduced supersaturation with CaOx as a result of increased urinary magnesium
- Increased inhibition of CaP crystal growth and aggregation

**Allopurinol (in patients with hyperuricuric calcium oxalate stone formation)**

- Reduces urinary urate
- Decreased risk of calcium oxalate crystal formation

**Pyridoxine**

- In patients with primary hyperoxaluria: reduced excretion of oxalate

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**Update March 2008**
Vitamin C is a precursor of oxalate, but its role as a risk factor in calcium oxalate stone formation remains controversial. Some studies have shown that a daily intake of up to 4 g might be allowed without risk (15-17). However, a recent study demonstrated a significantly increased risk in stone formation for men taking 1 g/day or more of vitamin C compared to men taking less than 90 mg (18). It therefore seems justified to advise calcium oxalate stone formers to avoid excessive intake of vitamin C. The allowed amount is not obvious but a daily intake of more than 500 mg (11) to 1 g (18) should probably be avoided.

Animal protein should not be ingested in excessive amounts (19-25), and it is recommended that animal protein intake is limited to 0,8-1 g/kg body weight. An excessive consumption of animal protein gives rise to several unfavourable effects on stone formation, such as hypocitraturia, low pH, hyperoxaluria and hyperuricosuria. Moreover, an increased resorption of bone increases urinary calcium (26).

Calcium intake should not be restricted unless there are very strong reasons because of the inverse relationship between dietary calcium and calcium stone formation (27). The minimum daily requirement for calcium is 800 mg and the general recommendation is 1,000 mg/day. Calcium supplements are not recommended except in cases of renal hyperoxaluria, when additional calcium should be ingested with meals to bind intestinal oxalate.

Sodium: A high consumption of sodium brings about several changes in urine composition. Calcium excretion is increased by reduced tubular reabsorption. Urinary citrate is reduced due to loss of bicarbonate. The risk of forming sodium urate crystals is increased and the effect of thiazide in reducing urinary calcium is counteracted by a high sodium intake. The combined restriction of sodium and animal protein in a randomized study resulted in a reduced rate of calcium stone formation (28). The daily sodium intake should not exceed 3 g.

Urate: The intake of food particularly rich in urate should be restricted in patients with hyperuricosuric calcium oxalate stone disease (29-34), as well as in patients with uric acid stone disease. The intake of urate should not exceed 500 mg/day. Examples of food rich in urate (21) include:

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

In patients with an expected low risk of recurrent stone formation (S or Rm), advice on fluid intake and diet may be sufficient to prevent stone recurrence. The positive effect of such a regimen has been referred to as the ‘stone clinic effect’.

17.1.3  Pharmacological treatment
The general opinion is that any treatment aiming at correction of abnormalities in urine composition and elimination of risk factors of pathological crystallization should always start by giving patients advice regarding dietary and drinking habits. In case pharmacological treatment is considered (following prior unsuccessful therapeutic approaches) adequate patient education regarding drinking and dietary recommendations is even more imminent since treatment outcome will largely depend on patient compliance. In this respect, it is essential to choose the most appropriate form of treatment. The ideal pharmacological agent should halt the formation of calcium stones, be free of side effects and be easy to administer. These aspects are all of utmost importance in order to achieve a reasonably good compliance.

The recommendations given in this guideline document are based on what has been published in this field. An extensive review and interpretation of literature results were carried out by the European Urolithiasis Research group at a Consensus Conference in Mannheim, Germany in 1996, and have subsequently been referred to in several publications (37-41). The ensuing recommendations are to a large extent still highly relevant. It seems logical and theoretically most attractive to administer pharmacological agents in a selective way with the aim of correcting one or several biochemical abnormalities. It needs to be emphasized, however, that there is no absolute consensus on such a view (42, 43, 11).

The pharmacological agents most commonly used for patients with recurrent calcium stone formation are thiazides, potassium citrate, orthophosphate, magnesium and allopurinol. The scientific basis of these forms of treatment is briefly summarized below.

17.1.3.1 Thiazides and thiazide-like agents
Hydrochlorothiazide, bendroflumethiazide, trichlorothiazide and the non-thiazide indapamide have been used for recurrence prevention in patients with calcium stone disease. The purpose of thiazide treatment is to reduce
the excretion of calcium in hypercalciuric patients, but it has been stated that calcium reduction is also seen in patients with normocalciuria (20). The hypocalciuric action of thiazides is thought to be mediated by increased reabsorption of calcium in the proximal as well as in the distal parts of the nephron (20,44). It has, moreover, been suggested that thiazides might decrease the excretion of oxalate, possibly by a reduced intestinal absorption of calcium (45-47), but recent studies have shown that such an effect is unlikely to occur. However, a thiazide-induced reduction in urinary oxalate is not a consistent finding in the clinical studies. There is more than 35 years of clinical experience with thiazides as a method for stone prevention. Following the initial report by Yendt in 1970 (48), a large number of reports have been published, most of which support a reduced rate of recurrent stone formation.

The clinical effect of thiazide treatment has accordingly been evaluated in 10 randomized studies, four of which included placebo-treated patients. Although two short-term placebo-controlled studies (49,50) failed to confirm a positive effect of thiazides, a significantly reduced recurrence rate was recorded in three 3-year follow-up studies (51-55). A similar result was also obtained in three groups of patients treated with thiazides between 2.3 and 4.3 years, in comparison with conservatively treated patients (56,57). A significantly reduced rate of stone formation was also noted when a thiazide was given intermittently to recurrent stoneformers (58).

A reduced rate of recurrence was also observed in several other studies which compared treated patients with those not given any pharmacological agent (58-62). In some other studies, the results were less convincing (63,64).

The convincing positive effect of thiazide treatment was further supported by a meta-analysis based on randomized trials. This analysis showed significantly better results with active treatment than with placebo or no treatment (p < 0.02) (65).

The major drawback of thiazide treatment is the occurrence of side effects. The unmasking of normocalcaemic hyperparathyroidism, development of diabetes and gout, as well as erectile dysfunction, contribute to a limited tolerance and a high drop-out rate. Compliance is usually in the range of only 50-70%.

Whether or not thiazide treatment should be reserved only for patients with hypercalciuria, or used also in patients without this abnormality, cannot be definitely concluded from the various studies. Suffice it to mention that of the randomized studies, three studies selected hypercalciuric patients (55-57) and all three showed a significantly positive effect of thiazides.

In the other seven randomized trials, in which no selection was made, a significant effect was reported in five. Due to the frequent occurrence of hypercalciuria also in an unselected group of stone formers, there is no strong scientific basis for a recommendation in this regard. It is our opinion, however, that the major indication for choosing a thiazide or a thiazide-like agent should be hypercalciuria. In the absence of high calcium excretion, other forms of treatment may be better first-choice alternatives. As in all situations when pharmacological treatment is considered, a judgment must be made between the benefits and risks of the medication. According to these considerations, treatment with thiazide is usually reserved for patients with a high excretion of calcium (i.e. more than 6.5-7 mmol/24 hours or more than 4.5-5 mmol/16 hours).

Hydrochlorothiazide is usually administered at a dosage of 25-50 mg once or twice daily. The thiazide-induced loss of potassium should be substituted by giving either potassium citrate 3.5-7 mmol twice daily or another potassium salt. It has been shown, however, that potassium citrate was superior to potassium chloride in this regard (66). Hypocitraturia associated with hypokalaemia is thought to explain therapeutic failures in thiazide-treated patients.

17.1.3.2 Alkaline citrate
Treatment with alkaline citrate is commonly used as a method to increase urinary citrate in patients with hypocitraturia. A low citrate excretion is a well-recognized and common finding in patients with calcium stone disease. The role of citrate is important because of its complex formation with calcium. This chelation reduces the ion-activity products of both calcium oxalate and calcium phosphate. Moreover, citrate is an inhibitor of growth and aggregation/agglomeration of these crystals (67). Administration of an alkaline salt brings about an increased pH and an increased excretion of citrate. There are also reports of favourable clearance of residual fragments during treatment with alkaline citrate (see below).

Although the general principle is to give citrate preparations, it is the alkalinization of the tubular cells that is the most important factor that results in an increased citrate excretion, with only a small fraction of the administered citrate being excreted in urine.

The alkalinizing agents used to prevent recurrent calcium stone formation are sodium potassium citrate, potassium citrate, sodium magnesium citrate, potassium bicarbonate and sodium bicarbonate.

Alkaline citrate has been used in four randomized studies. Potassium citrate was used in two studies (68,69), sodium potassium in one study (70) and sodium magnesium citrate in another study (71). In the two studies of potassium citrate, a significantly reduced recurrence rate was recorded. A favourable effect was also reported with potassium magnesium citrate, whereas no effect was noted with sodium potassium citrate.
compared with an untreated group.

Other non-randomized studies with alkaline citrate have shown a variable outcome. However, the general impression is that potassium citrate (68, 69, 72-77) has a greater potential for preventing recurrence than sodium potassium citrate (39, 70, 78, 79). This observation is also supported by the different effects of potassium citrate and sodium citrate on urine composition (80).

Although potassium magnesium citrate appears efficient in prevention of recurrent stone formation, this agent is not yet generally available. Further studies are necessary to show whether this preparation is superior to potassium citrate.

Whether or not alkaline citrate preparations should be reserved for patients with hypocitraturia or used in a non-selective way has not been appropriately addressed in any study. An attempt to compare literature data has suggested a trend towards selective treatment (81). In a meta-analysis of randomized trials, it was not possible to adequately analyse the therapeutic outcome (65).

The usefulness of alkaline citrate as a way of increasing stone clearance after SWL has been studied by several groups. It was accordingly shown that sodium potassium citrate (82), as well as potassium citrate (77, 83), increased the clearance of stone fragments. According to preliminary and unpublished data from a European multicentre investigation, this effect has not been confirmed.

The frequency of side effects is fairly high and compliance with alkaline citrate administration was shown to be no better than approximately 50%.

Because of the many effects on calcium oxalate and calcium phosphate crystallization and stone formation, treatment with alkaline citrate, nevertheless, can be recommended as a treatment for preventing recurrent stones. The recommended agent is potassium citrate. Although it is likely that this form of treatment is most beneficial for patients with a low citrate excretion, so far there is no solid evidence in the literature to support this assumption and further studies are necessary. The risk of forming calcium phosphate stones as a result of the increased pH is theoretical, but there are only occasional reports of such an outcome.

17.1.3.3 Orthophosphate
The theoretical rationale for giving orthophosphate to patients with recurrent calcium oxalate stone formation is to reduce the excretion of calcium and increase the excretion of pyrophosphate. Pyrophosphate is an inhibitor of both calcium oxalate and calcium phosphate crystal growth. The effect on urinary calcium is assumed to be mediated by formation of 1,25 (OH)2-vitamin D with an associated decreased absorption of calcium and reduced bone resorption. Administration of orthophosphate (neutral) has been reported to also increase urinary citrate.

There are only a few studies in the literature that deal with the effect of orthophosphate on stone formation. In a randomized, placebo-controlled study on potassium acid phosphate given during a period of 3 years, stone formation increased in the orthophosphate-treated group (84).

The rate of stone formation during 3 years of treatment with phosphate was also studied in two randomized studies (52, 53). The number of patients in each of these studies was small and there were no statistically significant differences between treated and untreated patients. In some, less well-controlled, studies (85, 86), it was also not possible to confirm a reliable effect of phosphate treatment. A reduced rate of stone formation was, however, noted by others (87, 88). In reviews of the literature results, there is a lack of scientific evidence that phosphate is effective in preventing calcium stone formation (65, 89).

Although patient compliance with treatment is reported as good, side effects such as diarrhoea, abdominal cramps, nausea and vomiting are common. Moreover, a possible effect on parathyroid hormone must be considered. It is possible that the pattern of side effects is favourably affected by slow-release potassium phosphate (90). The effect of phosphate administration on calcium phosphate stone formation has not been elucidated.

In conclusion, there is only very weak evidence that orthophosphate significantly reduces calcium oxalate stone formation. Although this form of treatment may be a possible option in patients with absorptive hypercalciuria, so far there is insufficient evidence to recommend its use.

17.1.3.4 Magnesium
An increased excretion of magnesium might reduce the ion-activity product of calcium oxalate and inhibit the growth of calcium phosphate crystals. There are also observations of an increased excretion of citrate following administration of magnesium (91). Magnesium is also considered important for the transformation between various calcium phosphate crystal phases. A high urinary concentration of magnesium is thus thought to decrease the risk of brushite formation.

Magnesium oxide, magnesium hydroxide, potassium magnesium citrate and magnesium aspartate have been used. The effect of potassium magnesium citrate is discussed above regarding alkaline citrate.

There are two randomized studies on the clinical effects of magnesium, one in which treatment with magnesium hydroxide was compared with a placebo control group (92) and one with magnesium oxide and
untreated controls (52). None of them showed a statistically significant effect on stone formation despite follow-up periods of 4 and 3 years, respectively.

The positive effects of magnesium administration reported previously (93, 94) have not been confirmed by recent controlled studies (65, 89). Thus, there is insufficient evidence to recommend magnesium as monotherapy in calcium stone prevention.

17.1.3.5 Allopurinol

Treatment with allopurinol to counteract the formation of calcium oxalate stones was introduced following demonstration of a relationship between hyperuricosuria and calcium oxalate stone formation (95). The effect of allopurinol on calcium oxalate stone formation may be mediated through:

- Reduced salting-out effect
- Decreased risk of uric acid or urate crystals as promoters of calcium oxalate precipitation
- Complex formation between colloidal urate and macromolecular inhibitors, and/or
- Reduced excretion of oxalate.

It should also be mentioned that allopurinol may influence crystallization by its antioxidative properties.

Allopurinol has been used clinically to treat patients both with, and without, hyperuricosuria. In a placebo-controlled randomized study of allopurinol-treated, hyperuricosuric, calcium-oxalate stone formers, 75% of patients given allopurinol were free of recurrent stone formation compared with 45% in the placebo group (96). This effect was statistically significant. Three other randomized studies compared treatment with allopurinol and placebo or no treatment (96-98) in patients not selected because of hyperuricosuria. No significant difference was found between treated and untreated patients in any of these studies.

In a long-term follow-up of non-selected, calcium oxalate stone formers treated with 300 mg of allopurinol daily, no effect was found on stone formation (97). A similar result was recorded in another Swedish study (98). These results are in contrast to those obtained in patients treated for hyperuricosuria (99,100).

Allopurinol tolerance is usually good, but severe side effects have been reported with high doses.

There is no information on compliance. The results indicate that allopurinol might be useful for treating patients with hyperuricosuric calcium oxalate stone formation. However, it cannot be recommended for patients with other biochemical abnormalities.

17.1.3.6 Pyridoxine

Theoretically, administration of pyridoxine (vitamin B6) might favourably influence the endogenous production of oxalate. This may be explained by an increased transamination of glyoxylate due to the action of the co-enzyme pyridoxal phosphate.

Pyridoxine has successfully been used together with orthophosphate in the treatment of patients with primary hyperoxaluria (101), as well as patients with idiopathic hyperoxaluria (102). There are no controlled studies to support the use of pyridoxine in patients with idiopathic calcium oxalate stone disease.

Due to the rarity, and severity, of primary hyperoxaluria, there are no randomized studies on the efficacy of pyridoxine. Several reports confirm, however, that a fraction of patients with Type 1 hyperoxaluria responds favourably to large doses of pyridoxine. Because of the lack of other effective forms of treatment, it is definitely worthwhile trying pyridoxine therapeutically, with the aim of reducing oxalate excretion in patients with primary hyperoxaluria Type I.

17.1.3.7 Management of patients with enteric hyperoxaluria

Enteric hyperoxaluria is a particularly problematic condition encountered in patients with intestinal malabsorption of fat. This abnormality, which is associated with a high risk of stone formation is for example seen after intestinal resection, following jejunoileal bypass for treatment of obesity, in Crohn’s disease and in pancreas insufficiency. The intestinal loss of fatty acids is combined with a loss of calcium. The normal complex formation between oxalate and calcium is therefore disturbed and oxalate absorption is dramatically increased. In addition to the ensuing hyperoxaluria, these patients usually present with hypocitraturia because of loss of alkali. Urine pH is usually low and so are urinary calcium and the urine volume. All these abnormalities contribute to particularly high levels of supersaturation with calcium oxalate, crystalluria and stone formation.

To prevent recurrence, it is essential to reduce the hyperabsorption of oxalate and correct any other urine abnormalities. A restricted intake of oxalate-rich foods should be combined with calcium supplements to enable calcium oxalate complex formation in the intestine (103). Calcium should therefore be given at meal times. Other oxalate-binding agents might also be useful, such as the marine colloid, Oxabsorb (104). An increased fluid intake is of course desirable, but its efficacy is often low because of the intestinal loss of water and increased diarrhoea. Administration of alkaline citrate is recommended to raise urinary pH and citrate (105).

The diet should be restricted with regard to fat (106).
17.1.4. Recommendations

Although there is no place for monotherapy with magnesium salts, a combination with thiazides might prove useful, but there is so far insufficient scientific evidence for this approach (107). Nevertheless, this alternative is mentioned because of its possible role in prevention of brushite stones.

It has been assumed that oxalate is more powerful than calcium in affecting supersaturation with calcium oxalate, but recent observations have indicated that calcium and oxalate influence the supersaturation with approximately equal power (108). It is therefore essential to correct abnormalities of both variables.

In patients with incomplete distal renal tubular acidosis, the treatment of choice appears to be potassium citrate, a regimen that has a positive effect on the acidosis, citrate excretion and stone formation (109).

There is no absolute consensus that a selective treatment is better than a non-selective treatment for recurrence prevention in idiopathic calcium stone disease. An analysis of data from the literature, however, has suggested a slight difference in favour of treatment directed towards individual biochemical abnormalities (43). Recommendations for a selective therapeutic approach are given in Table 27. In the absence of any common biochemical risk factors, it was shown that a water load had a positive effect on supersaturation and crystallization (110).

It is generally considered that dietary and drinking advice should always be considered first and that pharmacological alternatives should be added only if the first step fails or if there are specific reasons for starting pharmacological treatment from the beginning. It is essential to note, however, that pharmacological treatment always should be combined with appropriate changes in dietary and drinking habits.

For patients with mild recurrent calcium stone disease and without residual stones or fragments (So, Rmo), it seems sufficient to give the patient general advice regarding dietary and fluid intake. For patients with a similar history of stone formation but with residual stones or fragments in the kidneys (Sres, Rres), it might be worthwhile applying a more aggressive treatment based on urinary findings as this approach has resulted in effective counteraction of active stone formation and growth of residuals (106). For patients in category R, it is logical to take appropriate steps to stop or efficiently counteract recurrent stone formation, irrespective of whether or not the patient has residual stone-fragments (Table 28).

<table>
<thead>
<tr>
<th>Urinary risk factor</th>
<th>Suggested treatment</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypercalciuria</td>
<td>Thiazide + potassium citrate</td>
<td>1a</td>
<td>A</td>
</tr>
<tr>
<td>Hyperoxaluria</td>
<td>Oxalate restriction</td>
<td>2b</td>
<td>A</td>
</tr>
<tr>
<td>Hypocitraturia</td>
<td>Potassium citrate</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>Enteric hyperoxaluria</td>
<td>Potassium citrate</td>
<td>3-4</td>
<td>C</td>
</tr>
<tr>
<td>Calcium supplement</td>
<td>2 B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxalate absorption</td>
<td>3 B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High excretion of sodium</td>
<td>Restricted intake of salt</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>Small urine volume</td>
<td>Increased fluid intake</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>Urea level indicating a high intake of animal protein</td>
<td>Avoid excessive intake of animal protein</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>Distal renal tubular acidosis</td>
<td>Potassium citrate</td>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td>Primary hyperoxaluria</td>
<td>Pyridoxine</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td>No abnormality identified</td>
<td>High fluid intake</td>
<td>2b</td>
<td>B</td>
</tr>
</tbody>
</table>

LE = Level of evidence; GR = grade of recommendation

Table 27: Suggested treatment for patients with specific abnormalities in urine composition

Table 28: When should calcium stone formers be offered recurrence preventive treatment and how?

<table>
<thead>
<tr>
<th>Category</th>
<th>Analysis of urinary risk factors</th>
<th>Recurrence prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>S&lt;sub&gt;s&lt;/sub&gt;</td>
<td>No</td>
<td>General advice</td>
</tr>
<tr>
<td>S&lt;sub&gt;res&lt;/sub&gt;</td>
<td>Yes (r)</td>
<td>Specific advice, with or without a pharmacological agent</td>
</tr>
<tr>
<td>R&lt;sub&gt;mo&lt;/sub&gt;</td>
<td>No</td>
<td>General advice</td>
</tr>
<tr>
<td>R&lt;sub&gt;res&lt;/sub&gt;</td>
<td>Yes (r)</td>
<td>Specific advice, with or without a pharmacological agent</td>
</tr>
</tbody>
</table>

* Optional procedure that is recommended if it is likely that the information obtained can be useful for designing the subsequent treatment.
17.1.5 References


17.2 Medical treatment of patients with uric acid stone disease

Uric acid stones form in urine highly supersaturated with uric acid. The most common abnormality is a low urine pH often occurring with a small urine volume. These two abnormalities provide the basis for precipitation of uric acid, even in patients with a normal urate excretion. A typical example is the patient with ileostomy with loss of both alkali and fluid. The high excretion of urate seen in patients with disturbed purine metabolism can result in a critical supersaturation with reasonably normal pH and volume (1).

17.2.1 Drinking and dietary recommendations

Fluid intake should be adjusted to allow for a 24-hour urine flow of approximately 2-2.5 L (2-5). The intake of animal protein should not exceed 0.8 g/kg/day (6-7).

17.2.2 Pharmacological treatment

Alkalization of urine is mandatory and should preferably be carried out with potassium citrate. The pH should be increased to a level above 6.5 and the general recommendation is to obtain a pH in the range 6.5-7.2 (2,3,5). The dose should be adjusted to obtain a pH in the range between 6.1 and 7.0 (3). There might be a risk of calcium phosphate stone formation if the pH is raised to higher levels, although such a complication seems
to be less common than expected.

Although both sodium bicarbonate and sodium citrate can be used to obtain an alkaline pH (1 g of sodium bicarbonate corresponds to 12 mmol and the recommended dose is 1 g x 3) the preferred agent is potassium citrate. This is because the solubility of potassium urate is greater than that of sodium urate (10, 11) and potassium does not increase the excretion of calcium. For further alkalinization, it has been suggested that acetazolamide or topiramate might be considered (8, 9), but with this therapy the risk of calcium phosphate stones is more pronounced because of the simultaneous decrease in citrate excretion. A reduced excretion of urate is accomplished with allopurinol and this agent should be used when the 24-hour urate excretion exceeds 4 mmol (12). It is interesting to know that a combination of alkali, allopurinol and a high fluid intake can be used to dissolve uric acid stones.

The pharmacological treatment of patients with uric stone disease is outlined in Table 29.

Table 29: Pharmacological treatment of uric acid stone disease

<table>
<thead>
<tr>
<th>Objective</th>
<th>Therapeutic measures</th>
<th>Ref</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevention</td>
<td>Urine dilution: A high fluid intake; 24-hour urine volume exceeding 2-2.5 L</td>
<td>2-5</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td><strong>Alkalization</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Potassium citrate 3-7 mmol x 2-3</td>
<td>8-11</td>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>In patients with a high serum or urine level of urate</td>
<td>12</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td>Medical dissolution of uric acid stones</td>
<td>Urine dilution: A high fluid intake; 24-hour urine volume exceeding 2-2.5L</td>
<td>4</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Alkalization</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Potassium citrate 6-10 mmol x 2-3</td>
<td>13,14</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>Always reduce urate excretion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Allopurinol 300 mg x 1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LE = level of evidence; GR = grade of recommendation

17.2.3 References


17.3 Medical treatment of cystine stone disease

17.3.1 Dietary recommendations

Although a diet low in methionine theoretically might be of value for reducing urinary excretion of cystine, such a step is unlikely to result in reasonable compliance by the patient and this regimen is not usually used or recommended.

A restricted intake of sodium is, however, probably more effective in reducing urinary cystine. The recommendation given is to avoid a daily consumption of sodium above 2 g (1).

17.3.2 Drinking advice

A high diuresis is of fundamental importance. The aim is to dilute the urine so that supersaturation with cystine is decreased below the solubility product of cystine, or at least below its formation product. In general, the goal is a 24-hour urine volume of at least 3 L (2, 3). To reach this goal, a considerable fluid intake evenly distributed during the day is necessary. A more accurate recommendation of the size of urine volume needed can be obtained by knowing the ion-activity product of cystine, which can be calculated from the cystine concentration and the pH (4).

17.3.3 Pharmacological treatment

The solubility of cystine increases in alkaline urine, but a substantial increment in solubility does not occur unless the pH is above 7.5. The rule of thumb is that the solubility of cystine is approximately 250 mg/L (1 mmol/L) at pH 7, 500 mg (2 mmol/L) at pH 7.5 and 750 mg (3 mmol/L) at pH 8 (2). To alkalinize the urine, potassium citrate is the best alternative. Sodium bicarbonate, sodium citrate or sodium potassium citrate should not be given because of the undesirable effect of sodium on the excretion of cystine (1).

A typical dose of potassium citrate is 20-25 mmol per day given three times a day, but the required dose has to be determined by the effect this regimen has on urinary pH. The administration of acetazolamide can be used to improve the alkalinization (5).

When the combined effects of a high diuresis and alkalinization are not enough to prevent stone formation, complex formation by chelating agents is necessary (2, 6, 7). Thiol compounds, such as D-penicillamine (8,9) and α-mercaptopropionyl glycine (tiopronin) (8-10), are most commonly used. The latter compound seems to be associated with fewer side effects than penicillamine. The recommended daily dosage is 10-15 mg/kg (or 750 mg/day), but the daily required dose might be in the range 250-2000 mg. For penicillamine, the daily dose is 1-2 g. A third alternative is captopril (an angiotensin-converting enzyme inhibitor). Positive effects on urinary cystine and stone formation have been reported with a daily dose of 75-100 mg (1, 11, 12). Administration of thiols always should be accompanied by pyridoxine to avoid vitamin B_6-deficiency. The recommended dose is 50 mg/day.

Patients who are treated with thiols should regularly be examined with analysis of blood haemoglobin, white blood cells and thromocytes. Moreover, the urine should be checked for proteinuria.

The treatment of patients with cystine stone disease is outlined in Table 30.

Table 30: Pharmacological treatment of patients with cystine stone disease

<table>
<thead>
<tr>
<th>Therapeutic measures</th>
<th>References</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine dilution</td>
<td>1-3</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td>Alkalization</td>
<td>1-3</td>
<td>3</td>
<td>B</td>
</tr>
</tbody>
</table>

For patients with a cystine excretion below 3 mmol/24h:
Potassium citrate 3-10 mmol x 2-3 should be given to achieve a pH > 7.5

Complex formation with cystine

For patients with a cystine excretion above 3 mmol/24 or when other measures are insufficient

| Tiopronin (α-mercapto-propionyl glycine), 250-2000 mg/day or |
| Captopril, 75-150 mg |

LE = level of evidence; GR = grade of recommendation

17.3.4 References


   http://journals.elsevierhealth.com/periodicals/eeus/issues/contents


17.4 Management of patients with infection stones

17.4.1 Pharmacological treatment of infection stone disease

The pharmacological treatment of patients with infection stone disease is outlined in Table 31. The definition of infection stones is stones composed of magnesium ammonium phosphate and carbonate apatite. These stones are caused by urease-producing micro-organisms. It is fundamental that the renal collecting system is cleared of stone material to prevent recurrence in patients with infection stone disease.

| It is fundamental that the renal collecting system is cleared from stone material. |
| LE = 3 |
| GR = C |
### Table 31: Pharmacological treatment of infection stone disease

<table>
<thead>
<tr>
<th>Therapeutic measures</th>
<th>References</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stone removal</strong></td>
<td>1</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td>Surgical removal of the stone material as completely as possible</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antibiotic treatment</strong></td>
<td>2</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td>Short-term antibiotic course</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long-term antibiotic course</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Acidification</strong></td>
<td>4</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td>Ammonium chloride 1 g x 2-3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methionine 500 mg 1-2 x 3</td>
<td>3</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td><strong>Urease inhibition</strong></td>
<td>5, 6</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>In very selected cases with severe infections, treatment with acetohydroxamic acid (Lithostat) might be a therapeutic option</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**LE** = level of evidence; **GR** = grade of recommendation

#### 17.4.2 References


### 18. Abbreviations Used in the Text

This list is not comprehensive for the most common abbreviations.

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AP&lt;sub&gt;CaOx&lt;/sub&gt;</td>
<td>ion-activity product of calcium oxalate</td>
</tr>
<tr>
<td>AP&lt;sub&gt;CaP&lt;/sub&gt;</td>
<td>ion-activity product of calcium phosphate</td>
</tr>
<tr>
<td>AP(CaOx) index</td>
<td>approximate estimate of AP&lt;sub&gt;CaOx&lt;/sub&gt;</td>
</tr>
<tr>
<td>AP(CaP) index</td>
<td>approximate estimate of AP&lt;sub&gt;CaP&lt;/sub&gt;</td>
</tr>
<tr>
<td>AUA</td>
<td>American Urological Association</td>
</tr>
<tr>
<td>Ca</td>
<td>calcium</td>
</tr>
<tr>
<td>CaHPO&lt;sub&gt;4&lt;/sub&gt;·2H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>calcium hydrogen phosphate</td>
</tr>
<tr>
<td>CaOx</td>
<td>calcium oxalate</td>
</tr>
<tr>
<td>CaP</td>
<td>calcium phosphate</td>
</tr>
<tr>
<td>CI</td>
<td>confidence interval</td>
</tr>
<tr>
<td>CI&lt;sub&gt;s&lt;/sub&gt;</td>
<td>credible intervals</td>
</tr>
<tr>
<td>CI&lt;sub&gt;RF&lt;/sub&gt;</td>
<td>clinically insignificant residual fragments</td>
</tr>
<tr>
<td>Cit</td>
<td>citrate</td>
</tr>
<tr>
<td>CT</td>
<td>computed tomography</td>
</tr>
<tr>
<td>CY</td>
<td>cystine stone</td>
</tr>
<tr>
<td>EAU</td>
<td>European Association of Urology</td>
</tr>
<tr>
<td>EHL</td>
<td>electrohydraulic lithotripsy</td>
</tr>
<tr>
<td>ESWL</td>
<td>extracorporeal shock-wave lithotripsy, also including piezolithotripsy</td>
</tr>
<tr>
<td>GFR</td>
<td>glomerular filtration rate</td>
</tr>
<tr>
<td>GR</td>
<td>grade of recommendation</td>
</tr>
<tr>
<td>HCl</td>
<td>hydrochloric acid</td>
</tr>
<tr>
<td>Ho·:YAG</td>
<td>holmium:yttrium aluminium garnet</td>
</tr>
<tr>
<td>INF</td>
<td>infection stone</td>
</tr>
<tr>
<td>IVP</td>
<td>intravenous pyelography</td>
</tr>
<tr>
<td>IVU</td>
<td>Intravenous urography</td>
</tr>
<tr>
<td>KUB</td>
<td>plain abdominal film of the kidneys, ureters and bladder</td>
</tr>
<tr>
<td>LE</td>
<td>level of evidence</td>
</tr>
<tr>
<td>L</td>
<td>length (of stone)</td>
</tr>
<tr>
<td>MET</td>
<td>medical expulsive therapy</td>
</tr>
<tr>
<td>Mg</td>
<td>magnesium</td>
</tr>
<tr>
<td>MREU</td>
<td>MR excretory urography</td>
</tr>
<tr>
<td>MRU</td>
<td>Magnetic resonance urography</td>
</tr>
<tr>
<td>Nd·:Yag</td>
<td>Nd:YAG frequency doubled laser</td>
</tr>
<tr>
<td>NH&lt;sub&gt;4&lt;/sub&gt;Cl</td>
<td>ammonium chloride</td>
</tr>
<tr>
<td>NSAID</td>
<td>non-steroidal anti-inflammatory drug</td>
</tr>
<tr>
<td>Ox</td>
<td>oxalate</td>
</tr>
<tr>
<td>PNL</td>
<td>percutaneous nephrolithotomy with or without lithotripsy</td>
</tr>
<tr>
<td>R&lt;sub&gt;r&lt;/sub&gt;</td>
<td>recurrent stone former with severe disease with or without residual stone(s) or fragments or with specific risk factors irrespective of otherwise defined category</td>
</tr>
<tr>
<td>R&lt;sub&gt;r&lt;/sub&gt;</td>
<td>recurrent stone former with mild disease with residual stone(s) or stone fragments</td>
</tr>
<tr>
<td>R&lt;sub&gt;r&lt;/sub&gt;</td>
<td>recurrent stone former with mild disease with residual stone(s) or stone fragments</td>
</tr>
<tr>
<td>R&lt;sub&gt;r&lt;/sub&gt;</td>
<td>&lt;sub&gt;res&lt;/sub&gt;</td>
</tr>
<tr>
<td>RTA</td>
<td>renal tubular acidosis</td>
</tr>
<tr>
<td>SA</td>
<td>stone surface area</td>
</tr>
<tr>
<td>S&lt;sub&gt;r&lt;/sub&gt;</td>
<td>first time stone former with residual stone or stone fragments</td>
</tr>
<tr>
<td>S&lt;sub&gt;res&lt;/sub&gt;</td>
<td>first time stone former with residual stone or stone fragments</td>
</tr>
<tr>
<td>SWL</td>
<td>shock-wave lithotripsy</td>
</tr>
<tr>
<td>THAM</td>
<td>trihydroxymethyl aminomethan</td>
</tr>
<tr>
<td>UR</td>
<td>uric acid/sodium urate/ammonium urate stone</td>
</tr>
<tr>
<td>URS</td>
<td>ureteroscopy</td>
</tr>
<tr>
<td>US</td>
<td>ultrasonography</td>
</tr>
<tr>
<td>UTI</td>
<td>urinary tract infection</td>
</tr>
<tr>
<td>V</td>
<td>urine volume</td>
</tr>
<tr>
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APPENDICES

APPENDIX 1: Devices for endoscopic disintegration of stones

BALLISTIC LITHOTRIPSY
Ballistic lithotripsy involves a device in which alternating compression caused by air or electromechanical forces is transmitted to a metal rod. Pulses drive a metallic bullet that bumps the end of the rod against the stone. Rods are 2.4-6 F in diameter and can be used through a semi-rigid ureteroscope and all rigid endoscopes. A similar effect is obtained by alternating mechanical displacement.

ULTRASONIC LITHOTRIPSY
These commercially available units consist of a power generator, an US transducer and a probe, forming the sonotrode. A piezoceramic element in the handle of the sonotrode is stimulated to resonate, and this converts electrical energy into US waves (at a frequency of 23,000-27,000 Hz). The US waves are transmitted along the hollow metal probe to create a vibrating action at its tip. When the vibrating tip is brought into contact with the surface of a stone, the calculus can be disintegrated. The probes, which are available in sizes 10 F and 12 F, are passed through the straight working channel of a rigid ureteroscope or nephroscope. Suction tubing can be connected to the end of the sonotrode.

ELECTROHYDRAULIC LITHOTRIPSY
The electrohydraulic lithotripsy (EHL) unit has a probe, a power generator and a foot pedal. The probe consists of a central metal core and two layers of insulation with another metal layer between them. Probes are flexible and available in many sizes for use in rigid and flexible nephroscopes. The electrical discharge is transmitted to the probe where it generates a spark at the tip. The intense heat produced in the immediate area surrounding the tip results in a cavitation bubble, which produces a shock wave that radiates spherically in all directions. EHL will effectively fragment all kinds of urinary stones, including very hard stones composed of cystine, uric acid and calcium oxalate monohydrate. Recently, a 1.6 F EHL probe was developed. It has been quite successful in fragmenting ureteral and intrarenal stones. It has superior flexibility compared to the laser fibre.

LASER LITHOTRIPSY
Today, neodymium:yttrium-aluminium-garnet (Nd:YAG) or holmium:YAG (Ho:YAG) lasers are used as sources for laser lithotripsy units. The reported results indicate that the Ho:YAG efficacy is superior to the Nd:YAG and does effectively fragment all types of urinary stones, wherever they are located and whatever their composition, including cystine stones. The Ho:YAG system produces light of 2100 nm, with a tissue penetration of less than 0.5 mm and complete absorption in water. The Nd:YAG is used frequency-doubled and produces light of 1064 nm, with a tissue penetration of 4 mm. Fibres for ureteroscopy are available for both lasers at 200 and 365 μm in diameter.

In combination with the actively deflectable, flexible ureteroscope, the Ho:YAG laser has proven to be ideally suited for fragmenting stones in the upper ureter. Potential complications of the Ho:YAG laser when used to fragment ureteral stones include possible perforation of the ureteral wall and consequential formation of strictures.
APPENDIX 2: Approximate stone surface area with known diameters of the stone

An approximate estimate of the stone surface area (mm²) can be extracted from the length and width on the KUB. The calculated surface area for any combination of stone diameters up to 25 mm is shown in Table A1.

### Table A1: Approximate stone surface area (mm²) calculated from the length and width of the stone

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Conflict of interest
All members of the Urolithiasis Guidelines writing panel have provided disclosure statements on all relationships that they have and that might be perceived to be a potential source of conflict of interest. This information is kept on file in the European Association of Urology Central Office database. This guidelines document was developed with the financial support of the European Association of Urology. No external sources of funding and support have been involved. The EAU is a non-profit organisation and funding is limited to administrative assistance and travel and meeting expenses. No honoraria or other reimbursements have been provided.