Guidelines on Urolithiasis

H.-G. Tiselius, D. Ackermann, P. Alken, C. Buck, P. Conort, M. Gallucci, T. Knoll

© European Association of Urology 2007
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>1.</th>
<th>Background</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>References</td>
<td>6</td>
</tr>
<tr>
<td>2.</td>
<td>Classification</td>
<td>6</td>
</tr>
<tr>
<td>2.1</td>
<td>Categories of stone formers</td>
<td>6</td>
</tr>
<tr>
<td>2.2</td>
<td>Specific risk factors for stone formation</td>
<td>6</td>
</tr>
<tr>
<td>2.3</td>
<td>References</td>
<td>7</td>
</tr>
<tr>
<td>3.</td>
<td>Diagnostic procedures</td>
<td>8</td>
</tr>
<tr>
<td>3.1</td>
<td>Diagnostic imaging</td>
<td>8</td>
</tr>
<tr>
<td>3.1.1</td>
<td>Allergy to contrast medium</td>
<td>8</td>
</tr>
<tr>
<td>3.1.2</td>
<td>Metformin</td>
<td>8</td>
</tr>
<tr>
<td>3.1.3</td>
<td>Reduced renal function</td>
<td>9</td>
</tr>
<tr>
<td>3.1.4</td>
<td>Risk factors for the development of reduced renal function</td>
<td>9</td>
</tr>
<tr>
<td>3.1.5</td>
<td>Dosage of iodine</td>
<td>9</td>
</tr>
<tr>
<td>3.2</td>
<td>Analysis of stone composition</td>
<td>11</td>
</tr>
<tr>
<td>3.2.1</td>
<td>References</td>
<td>12</td>
</tr>
<tr>
<td>3.3</td>
<td>Biochemical investigations</td>
<td>12</td>
</tr>
<tr>
<td>3.3.1</td>
<td>Analytical work-up in the acute phase</td>
<td>12</td>
</tr>
<tr>
<td>3.3.2</td>
<td>Analysis of urine in search for risk factors of stone formation</td>
<td>13</td>
</tr>
<tr>
<td>3.3.3</td>
<td>Comments on the analytical work-up</td>
<td>15</td>
</tr>
<tr>
<td>3.3.4</td>
<td>References</td>
<td>16</td>
</tr>
<tr>
<td>4.</td>
<td>Stone burden</td>
<td>19</td>
</tr>
<tr>
<td>4.1</td>
<td>References</td>
<td>19</td>
</tr>
<tr>
<td>5.</td>
<td>Treatment of patients with renal colic</td>
<td>19</td>
</tr>
<tr>
<td>5.1</td>
<td>Pain relief</td>
<td>19</td>
</tr>
<tr>
<td>5.1.1</td>
<td>Treatment with non-steroidal anti-inflammatory drugs (NSAIDs)</td>
<td>19</td>
</tr>
<tr>
<td>5.1.2</td>
<td>Prevention of recurrent episodes of renal colic</td>
<td>20</td>
</tr>
<tr>
<td>5.1.3</td>
<td>Effects of diclofenac on renal function</td>
<td>20</td>
</tr>
<tr>
<td>5.2</td>
<td>References</td>
<td>20</td>
</tr>
<tr>
<td>6.</td>
<td>Indications for active stone removal</td>
<td>21</td>
</tr>
<tr>
<td>6.1</td>
<td>References</td>
<td>21</td>
</tr>
<tr>
<td>7.</td>
<td>Active removal of stones in the kidney</td>
<td>22</td>
</tr>
<tr>
<td>7.1</td>
<td>Extracorporeal shock wave lithotripsy (ESWL) for stone removal</td>
<td>22</td>
</tr>
<tr>
<td>7.1.2</td>
<td>ESWL for removal of large renal stones</td>
<td>23</td>
</tr>
<tr>
<td>7.1.2.1</td>
<td>Location of the stone mass</td>
<td>23</td>
</tr>
<tr>
<td>7.1.2.2</td>
<td>Stone burden</td>
<td>24</td>
</tr>
<tr>
<td>7.1.2.3</td>
<td>Composition and hardness of the stone</td>
<td>24</td>
</tr>
<tr>
<td>7.1.2.4</td>
<td>References</td>
<td>25</td>
</tr>
<tr>
<td>7.2</td>
<td>Percutaneous removal of renal stones</td>
<td>30</td>
</tr>
<tr>
<td>7.2.1</td>
<td>Complications</td>
<td>30</td>
</tr>
<tr>
<td>7.2.2</td>
<td>References</td>
<td>30</td>
</tr>
<tr>
<td>7.3</td>
<td>Aspects on staghorn stone treatment and importance of stone burden</td>
<td>31</td>
</tr>
<tr>
<td>7.3.1</td>
<td>ESWL</td>
<td>31</td>
</tr>
<tr>
<td>7.3.2</td>
<td>Percutaneous nephrolithotomy (PNL)</td>
<td>31</td>
</tr>
<tr>
<td>7.3.3</td>
<td>ESWL and PNL</td>
<td>31</td>
</tr>
<tr>
<td>7.3.4</td>
<td>Percutaneous surgery versus ESWL for removal of renal stones</td>
<td>32</td>
</tr>
<tr>
<td>7.3.5</td>
<td>References</td>
<td>32</td>
</tr>
<tr>
<td>7.4</td>
<td>Open surgery for removal of renal stones</td>
<td>33</td>
</tr>
<tr>
<td>7.4.1</td>
<td>Indications for open surgery</td>
<td>33</td>
</tr>
<tr>
<td>7.4.2</td>
<td>Operative procedures</td>
<td>33</td>
</tr>
<tr>
<td>7.4.3</td>
<td>References</td>
<td>34</td>
</tr>
</tbody>
</table>
14.2.6 Cellulose phosphate 66
14.2.7 Pyridoxine 66
14.2.8 Recommendations 66
14.2.9 References 67

14.3 Pharmacological treatment of uric acid stone disease 72
  14.3.1 References 73

14.4 Pharmacological treatment of cystine stone disease 74
  14.4.1 References 74

14.5 Pharmacological treatment of infection stone disease 74
  14.5.1 References 75

15. ACKNOWLEDGEMENTS 75

16. ABBREVIATIONS USED IN THE TEXT 76

17. APPENDICES 77
  A1 Approximate stone surface area with known diameters of the stone 77
  A2 Devices for endoscopic disintegration of stones 78
  A3 References 78
1. BACKGROUND

Patients with urolithiasis constitute an important part of everyday urological practice. The optimal clinical management of this disease requires knowledge of the diagnostic procedures, the rational treatment of acute stone colic and the modern principles of stone removal. It is also essential to have a basic understanding of the aetiological factors of stone formation and how a metabolic risk evaluation should be carried out in order to provide a sound basis for appropriate recurrence preventive measures.

During the past few decades, the whole field of treatment of patients with urolithiasis has been characterized by changes that are attributable to pronounced technical achievements, an increased understanding of the mechanisms of stone formation and advancements in pharmacological treatment of the various aspects of stone disease. The guidelines and recommendations given below are based on results presented in the modern literature. Some of the therapeutic principles are the result of evidence obtained from randomized or controlled studies, whereas other statements rely on a substantial clinical experience. According to the principles set by the European Association of Urology (EAU) Guidelines Office, the scientific basis for the various recommendations or statements has been classified in terms of level of evidence and grade of recommendation when appropriate.

The criteria for level of evidence (LE) (Table 1) and grades of recommendation (GR) (Table 2) are shown below (1). The abbreviations LE and GR are used in the tables and recommendations given in these guidelines.

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>

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>

The various recommendations are supported by comments based on the most important relevant publications. It needs to be emphasized, however, that no attempt has been made to cover the literature completely, as such a step was beyond the possibilities of our work.

When recommendations were formulated, we focused mainly on medical aspects, since discussing associated economic issues may be - due to the extensive geographical diversity and variability between the financial systems in the health care sector - beyond the scope of a European guideline document. We are very well aware of the different treatment and technical facilities available geographically, but our intention has been to highlight the alternatives that appear most convenient for the patient in terms of low invasiveness and risk of complications. This does not mean that other methods are not applicable. However, when a certain form of therapy is not recommended, this has been specifically stated.

A number of tables throughout the text give an overview of the most appropriate methods for stone removal for different stone situations and stone compositions (tables 15, 16, 18, 19, 20, 22, 24 & 26). Numbers (1, 2, 3, 4, 5) have been allocated to the procedures according to the consensus reached. When two procedures were considered equally useful they have been given the same number. The first alternative always has the number 1.

The current edition of Guidelines on Urolithiasis published here is an update of our previously published document (2,3).
1.1 REFERENCES

2. CLASSIFICATION

2.1 Categories of stone formers
A system for subgrouping stone-forming patients into different categories is shown in Table 3. These different categories are useful when making decisions regarding the need for metabolic evaluation and medical treatment (1,2,3).

Table 3: Categories of stone formers

<table>
<thead>
<tr>
<th>Definition</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection stone</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>S₀</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_mo</td>
</tr>
<tr>
<td>Recurrent stone former with mild disease and with residual stone(s) or fragments</td>
<td>R_m-res</td>
</tr>
<tr>
<td>Recurrent stone former with severe disease with or without residual stone(s) or fragments with specific risk factors</td>
<td>R_s</td>
</tr>
<tr>
<td>irrespective of otherwise defined category (Table 4)</td>
<td></td>
</tr>
</tbody>
</table>

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 disease early in life, i.e., below 25 years of age
- Stones containing brushite (calcium hydrogen phosphate; CaHPO$_4$·2H$_2$O)
- Strong family history of stone formation
- Only one functioning kidney (only one kidney does not mean an increased risk of stone formation, but these patients should be particularly considered for measures to prevent stone recurrence)
- **Diseases associated with stone formation**
  - hyperparathyroidism (HPT)
  - renal tubular acidosis (RTA) (partial/complete)
  - cystinuria
  - primary hyperoxaluria
  - jejunoileal bypass
  - Crohn’s disease
  - intestinal resection
  - malabsorptive conditions
  - sarcoidosis
  - hyperthyroidism
- **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
  - vesico-ureteral reflux
  - horseshoe kidney
  - ureterocele

### 2.3 REFERENCES

3. DIAGNOSTIC PROCEDURES

3.1 Diagnostic imaging

Stone disease very often presents as an episode of acute stone colic. Patients with renal stone colic usually have characteristic loin pain, vomiting and mild fever, and they may have a history of stone disease. The clinical diagnosis should be supported by an appropriate imaging procedure. This will immediately help to decide if a conservative approach is justified or if another treatment should be considered. Imaging is imperative in patients with fever or a solitary kidney, and when the diagnosis of stone is in doubt.

The diagnostic work-up of all patients with symptoms of urinary tract stones requires a reliable imaging technique (Table 5). In case of an acute stone colic, excretory urography (intravenous pyelography, IVP) has been established as a gold standard. During recent years, unenhanced helical computed tomography (CT) examinations have been introduced as a quick and contrast-free alternative (1,2,3). In randomized prospective studies, the specificity and sensitivity of this method for patients with acute flank pain was found to be similar to that obtained with urography (4,5-9). In selected cases, additional information regarding renal function may be obtained by combining CT with contrast infusion. One great advantage of CT is the demonstration of uric acid and xanthine stones, which are radiolucent on plain films. Another advantage is the ability of CT to detect alternative diagnoses (7,10). However, the advantage of a non-contrast imaging modality has to be balanced against the higher radiation dose given to the patient during CT investigation (3,5,11).

An alternative and commonly applied method for evaluating patients with acute flank pain is a plain film of kidneys, ureters and bladder (KUB) combined with ultrasonography (US). There is a huge bulk of experience to show that these two methods are sufficient in a large proportion of patients 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>Examination</th>
<th>GR and/or LE</th>
<th>References</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>KUB + US</td>
<td>B/2a</td>
<td>6</td>
<td>3.1</td>
</tr>
<tr>
<td>Excretory urography</td>
<td>Standard</td>
<td></td>
<td>3.1</td>
</tr>
<tr>
<td>Unenhanced helical CT</td>
<td>A/1</td>
<td>1-10</td>
<td>3.1</td>
</tr>
</tbody>
</table>

GR = grade of recommendation; LE = level of evidence; CT = computed tomography; KUB = kidney, ureters and bladder urography; US = ultrasound.

Although the intravascular administration of contrast medium is usually a concern for the radiologist, 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. It is therefore essential to have a basic understanding of the risks associated with the use of contrast medium and the necessary precautions.

3.1.1 Allergy to contrast medium

Where there is a need for administration of contrast medium to patients who have reported allergic reactions (Table 7), or in those who are at such a risk, the following precautions should be taken (12,13):

- Always use low-molecular non-ionic contrast medium.
- Give a corticosteroid (e.g., prednisolone 30 mg) between 12 and 2 hours before the contrast medium is injected.
- This medication might be combined with an intramuscular injection of an anti-histamine agent (e.g., clemastine 2 mg), given 1 hour before contrast administration.

3.1.2 Metformin

Administration of metformin (a drug used to treat diabetes type II) might give rise to lactic acidosis in case of contrast-induced anuria (14-16). This is an unusual complication 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 in the presence of reduced renal function (i.e., serum creatinine > 130 µmol/L).

According to the recommendations given by the European Society of Urogenital Radiology (12,13) the serum creatinine level should be measured in every patient with diabetes being treated with metformin.

- In metformin-treated patients with a normal serum creatinine, contrast medium can be administered, but the intake of metformin should be stopped from the time of the radiological examination until 48 hours have passed and the serum creatinine remains normal.
In patients with reduced renal function, medication with 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.

In a situation where no information on renal function is available, alternative imaging techniques should be used.

In a situation when contrast medium has been administered to a patient on metformin treatment, without information on the renal function, or with a reduced renal function, administration of metformin should be stopped immediately and the patient should be 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 (14,16).

### 3.1.3 Reduced renal function

Intravenous administration of contrast medium can bring about a reduced renal perfusion and toxic effect on tubular cells. The vasoconstriction of glomerular afferent arterioles causes a reduced glomerular filtration rate (GFR) and an increased renal vascular resistance. Nephrotoxicity caused by contrast medium is diagnosed by the demonstration of a 25% or 44 µmol/L increase in serum creatinine during the 3 days that follow intravascular administration of the agent when there is no alternative explanation.

**Risk factors for the 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
- diabetes
- congestive heart failure
- concurrent treatment with nephrotoxic drugs, such as non-steroidal anti-inflammatory agents (NSAIDs) and aminoglycosides (the latter should be stopped for at least 24 hours).

Patients with multiple myeloma should either be examined with an alternative method or after adequate hydration.

Avoid repeated injections of contrast medium at intervals less than 48 (see section 3.1.2.) - 72 hours.

### Dosage of iodine

Reduced renal function means that the serum creatinine ≥ 140 µmol/L or that the GFR is ≤ 70 ml/min.

For a patient with a GFR of 80-120 mL/min, the administered dose of iodine should not exceed 80-90 g. When the GFR is reduced to a level between 50-80 mL/min, the dose of iodine should be limited to the same amount as the GFR expressed in mL/min/1.73m² body surface area (12,13). Table 6 lists useful formulae for calculating GFR and body surface area (17).

### Table 6: Formulae for calculating glomerular filtration rate (GFR) and body surface area (17)

| Men: GFR = (140 - age) x kg/(0.82 x serum creatinine) |
| Women: GFR = (0.85 x (140 - age)) x kg/(0.82 x serum creatinine) |

For patients < 20 years, the following formula should be used:

- Creatinine clearance = (42.5 x height(cm)/serum creatinine) x (kg/70)^0.77
- GFR = creatinine clearance x 1.73m²
- Body surface area = kg^{0.425} x height(cm)^{0.725} x 0.007184

In patients with a serum/plasma-creatinine level exceeding 140 µmol/L (1.6 mg/100 mL) hydration before and after the use of contrast medium may be beneficial in order to prevent nephropathy. The administration of N-acetylcysteine 600 mg twice on the day before contrast injection has been recommended to prevent renal failure caused by contrast medium (18).
3.1.4 Untreated hyperthyroidism

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

<table>
<thead>
<tr>
<th>Table 7: Considerations regarding excretory urography</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Contrast medium should not be given to, or avoided</strong></td>
</tr>
<tr>
<td><strong>in the following circumstances</strong></td>
</tr>
<tr>
<td>Patients with an allergy to contrast media</td>
</tr>
<tr>
<td>When the serum or plasma creatinine level is &gt; 150 µmol/L</td>
</tr>
<tr>
<td>To patients on medication with metformin</td>
</tr>
<tr>
<td>To patients with myelomatosis</td>
</tr>
<tr>
<td><strong>LE = level of evidence</strong></td>
</tr>
</tbody>
</table>

3.1.5 REFERENCES


UPDATE JUNE 2005


3.2 Analysis of stone composition

Stones that pass spontaneously, are removed surgically, or excreted as fragments following disintegration, should be subjected to stone analysis 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 analyzed. Repeated analysis is indicated when any changes in urine composition, due to medical treatment, dietary habits, environment or diseases, can be expected to have influenced the stone composition.

When stone(s) or stone material have not been retrieved, conclusions on stone composition may be based on the following observations:

- Qualitative cystine test (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 microorganisms).
- Demonstration of crystals of struvite or cystine upon microscopic examination of the urinary sediment.
- 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).
- Radiographical characteristics of the stone.

An appropriate quantitative or semi-quantitative analysis of the stone material should enable conclusions to be drawn regarding the main constituent or constituents.
The following calcium stones not associated with infection are referred to as radio-opaque stones:
- Calcium oxalate
  - calcium oxalate monohydrate
  - calcium oxalate dihydrate
- Calcium phosphate
  - hydroxyapatite
  - carbonate apatite
  - octacalcium phosphate
  - brushite
  - whitlockite.

The following stones not associated with infection are referred to as uric acid/urate stones:
- Uric acid
- Ammonium urate
- 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., sulphamamide, indinavir). Calcium stones, uric acid/urate stones and cystine 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
For patients with an acute stone episode, the routine laboratory investigations should include:
- Urinary sediment/dipstick test for demonstration of red cells.
- White cells and bacteria (nitrite).
- Approximate pH level.
- Serum creatinine should be analyzed as a measure of the renal function.

In cases of fever, C-reactive protein (CRP) should be assessed, and a blood white cell count and urine culture carried out.
In cases of vomiting, serum sodium and serum potassium levels should be measured. In order to avoid the need for future repeated blood analyses in the search for metabolic risk factors, it might be helpful to assess levels of serum calcium and serum urate at this point in time.

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

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

Two urine collections for each set of analyses are recommended. The urine collections are repeated when necessary (1-3). A number of alternative collection options are feasible, with a few examples listed in Table 8.

Table 8: Options for urine collection

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

The presence of hydrochloric acid (HCl) prevents the precipitation of calcium oxalate and calcium phosphate in the container during storage. HCl also counteracts the oxidation of ascorbate to oxalate. In acidified samples, uric acid precipitates and has to be dissolved by alkalinization if urate excretion is of interest. Urate can be analyzed in samples collected with sodium azide. A collection of urine without HCl is necessary for pH measurement. In this respect, a sample collected with sodium azide is useful. A night-time urine sample in which pH is measured soon after the urine has been collected is useful because the pH may be altered when urine is stored.

Table 9: Analytical programme for patients with stone disease

<table>
<thead>
<tr>
<th>Category</th>
<th>Blood analysis (serum / plasma)</th>
<th>Urine analysis</th>
<th>Prevention Follow-up</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</td>
<td>Cystine, pH</td>
<td>Yes</td>
</tr>
<tr>
<td>So</td>
<td>Yes (see Table 10)</td>
<td>Limited urine analysis (only fasting spot urine)</td>
<td>No</td>
</tr>
<tr>
<td>Šres</td>
<td>Yes (see Table 11)</td>
<td>Yes (see Table 11)</td>
<td>Yes</td>
</tr>
<tr>
<td>Rmo</td>
<td>Yes (see Table 10)</td>
<td>Limited urine analysis (only fasting spot urine)</td>
<td>No</td>
</tr>
<tr>
<td>Rm-res</td>
<td>Yes (see Table 11)</td>
<td>Yes (see Table 11)</td>
<td>Yes</td>
</tr>
<tr>
<td>Rs</td>
<td>Yes (see Table 11)</td>
<td>Yes (see Table 11)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

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, plasma) and urine analyses recommended for such patients are shown in Table 10.
Table 10: Blood and urine investigations required for analysis of risk factors in patients with uncomplicated stone disease

<table>
<thead>
<tr>
<th>Stone analysis</th>
<th>Blood analysis</th>
<th>Urine analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>In every patient one stone should be analyzed</td>
<td>Calcium</td>
<td>Fasting morning spot urine sample, dipstick test for:</td>
</tr>
<tr>
<td>Albumin(^1)</td>
<td></td>
<td>• pH</td>
</tr>
<tr>
<td>Creatinine</td>
<td></td>
<td>• Leucocytes/bacteria(^2)</td>
</tr>
<tr>
<td>Urate(^3)</td>
<td></td>
<td>• Cystine test(^4)</td>
</tr>
</tbody>
</table>

\(^1\) Either analysis of calcium + albumin to correct for differences in calcium concentration attributable to the albumin binding or direct analysis of ionized (free) calcium.
\(^2\) Optional analysis, helpful in suspected uric acid/urate stone disease.
\(^3\) Urine culture in case of bacteriuria.
\(^4\) Cystine test if cystinuria cannot be, or has not been, excluded by other means.

A patient with complicated stone disease has a history of frequent recurrences, with or without residual fragments or stones in the kidney or specific risk factors. First-time stone formers with residual fragments may also be considered in this respect (categories: Rs, S\(_{res}\), R\(_m\)-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 have passed after stone removal or after an episode of obstruction and should never be carried out in the presence of infection or haematuria. Special tests that may be required are shown in Table 12 (13-18).

Table 11: Analysis in patients with complicated stone disease

<table>
<thead>
<tr>
<th>Stone analysis</th>
<th>Blood analysis</th>
<th>Urine analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>In every patient one stone should be analyzed</td>
<td>Calcium</td>
<td>Fasting morning spot urine sample:</td>
</tr>
<tr>
<td>Albumin(^1)</td>
<td></td>
<td>Dipstick test</td>
</tr>
<tr>
<td>Creatinine</td>
<td></td>
<td>pH</td>
</tr>
<tr>
<td>Urate(^2)</td>
<td></td>
<td>Leucocytes/bacteria(^3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cystine test(^4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Urine collection during a defined period of time:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Calcium</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oxalate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Citrate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Urate(^5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Magnesium(^2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phosphate(^4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Urea(^5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sodium(^5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Potassium(^5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Creatinine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Volume</td>
</tr>
</tbody>
</table>

\(^1\) Either analysis of calcium + albumin to correct for differences in calcium concentration attributable to the albumin binding, or direct analysis of ionized (free) calcium.
\(^2\) Optional analysis.
\(^3\) 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).
\(^4\) Analysis of magnesium and phosphate is necessary to calculate estimates of supersaturation with calcium oxalate (CaOx) and calcium phosphate (CaP), such as AP(CaOx) index and AP(CaP) index (8-12).
\(^5\) Urea, phosphate, sodium and potassium measurements are used to assess the dietary habits of the patient.
\(^6\) As uric acid precipitates in acid solutions, urate has to be analyzed 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 with sodium azide for analysis of urate.
3.3.3 Comments on the analytical work-up

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

In those patients in whom 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. In this regard it needs to be emphasized that whereas a uric acid stone is usually invisible on a plain film (KUB), it is clearly demonstrated with a CT examination.

A fasting morning urine sample (or 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 by an appropriate test (27).

The aim of adding serum potassium to the analytical programme is to obtain further support for a diagnosis of suspected RTA. Hypokalaemic hypocitraturia may be one reason for therapeutic failures in patients treated with thiazides.

The recommendation to collect two urine samples is based on observations that such an approach will increase the likelihood of detecting urine abnormalities. Various collection periods, such as for 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).

It must be emphasized that the urine sample used for analysis of calcium, oxalate, citrate and phosphate has to be acidified, preferably with HCl. The reasons for this acidification are:

- To maintain calcium, oxalate and phosphate in solution, during and after the collection period.
- To prevent bacterial growth and the associated alteration of urine composition.
- To prevent the in-vitro oxidation of ascorbate to oxalate (28,29).

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

Although the creatinine concentration might be slightly affected, it has to 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 has to be analyzed either following complete dissolution with alkali or in a urine sample that has not been acidified.

The optional analysis of urea, phosphate and sodium helps to reflect dietary factors of therapeutic significance. The protein intake can be derived from the urea excretion ($U_{\text{urea}}$, mmol/L) and urine volume in litres ($V$) as follows (30):

\[
\text{Intake of protein (gram) during the 24h period} = (U_{\text{urea}} \times 0.18) + 13
\]

Estimates of the ion-activity products of calcium oxalate ($\text{AP}[\text{CaOx}]$ index) and calcium phosphate ($\text{AP}[\text{CaP}]$ index) can be calculated as follows (31-37):

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

In this formula, the urine volume ($V$) is expressed in litres and the urine variables (Ca, calcium; Ox, oxalate; Cit, citrate; Mg, magnesium) in 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, the reader should consult reference 5.

The $\text{AP}[\text{CaOx}]$ index approximately corresponds to $10^5 \times \text{AP}_{\text{CaOx}}$ (where $\text{AP}_{\text{CaOx}}$ is the ion-activity product of calcium oxalate). The $\text{AP}[\text{CaP}]$ index for a 24-hour urine sample is calculated in the following way:

\[
\text{AP}[\text{CaP}] \text{ index} = 2.7 \times 10^5 \times \text{Ca}^{1.07} \times \text{P}^{0.75} \times (\text{pH} - 4.5)^{0.6} \times \text{Cit}^{-0.24} \times V^{-1.31}
\]

The $\text{AP}[\text{CaP}]$ index approximately corresponds to $10^{15} \times \text{AP}_{\text{CaP}}$ (where $\text{AP}_{\text{CaP}}$ is the ion-activity product of calcium phosphate). Factors for other collection periods can be found in reference 5.

A relationship between abnormalities in urine composition and severity of calcium stone formation has been demonstrated (38-44). It should be noted that although individual abnormal urine variables might indicate a risk of stone formation, it is the concerted action of the various urine constituents which result in supersaturation and crystallization of the stone.

The additional analytical work-up in patients with calcium stone disease is summarized in Table 12. It might occasionally be useful to carry out a calcium loading test, but this test is not often used clinically today (13).
Table 12: Additional analytical work-up in patients with calcium stone disease

<table>
<thead>
<tr>
<th>pH profile (13)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Repeated measurements of pH during the 24-hour period</td>
<td></td>
</tr>
<tr>
<td>Frequent samples should be collected for immediate measurement of pH with pH paper or a glass electrode.</td>
<td></td>
</tr>
<tr>
<td>Sampling every second hour or otherwise as appropriate.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Acid loading (14-18)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>This test is carried out together with blood sampling to show whether or not the patient has a complete or an incomplete acidification defect:</td>
<td></td>
</tr>
<tr>
<td>08.00 Breakfast + NH$_4$Cl tablets (0.1 g/kg body weight), drink 150 mL</td>
<td></td>
</tr>
<tr>
<td>09.00 Collect urine and measure pH, drink 150 mL</td>
<td></td>
</tr>
<tr>
<td>10.00 Collect urine and measure pH, drink 150 mL</td>
<td></td>
</tr>
<tr>
<td>11.00 Collect urine and measure pH, drink 150 mL</td>
<td></td>
</tr>
<tr>
<td>12.00 Collect urine and measure pH, drink 150 mL</td>
<td></td>
</tr>
<tr>
<td>13.00 Collect urine and measure pH, lunch</td>
<td></td>
</tr>
<tr>
<td>Interpretation: a pH of 5.4 or lower indicates no RTA</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Findings in blood</th>
<th>Complete RTA</th>
<th>Incomplete RTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>Low</td>
<td>Normal</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>Low</td>
<td>Normal</td>
</tr>
<tr>
<td>Potassium</td>
<td>Low</td>
<td>Normal</td>
</tr>
<tr>
<td>Chloride</td>
<td>High</td>
<td>Normal</td>
</tr>
</tbody>
</table>

NH$_4$Cl = ammonium chloride; RTA = renal tubular acidosis.

3.3.4 REFERENCES

UPDATE JUNE 2005


UPDATE JUNE 2005


4. STONE BURDEN

The size of a concrement (stone burden) can be expressed in different ways. A notation of the largest diameter is the most common way of expressing size in the literature, i.e., the length of the stone as measured on the plain film. With knowledge of the length (l) and the width (w), an appropriate estimate of the stone surface area (SA) can be obtained for most stones (1):

\[ SA = l \times w \times \pi \times 0.25 \]

For a quick estimate of the stone surface area, please refer to Table A1 (Appendix).

The surface area can also be measured using computerized systems and from CT scans, but these are not always easy procedures. With knowledge of the surface area, the stone volume can be calculated by the formula below (2):

\[ Volume = 0.6 \times SA^{1.27} \]

In this guideline document, we have based our recommendations on the stone surface area as well as on the largest stone diameter.

4.1 REFERENCES


5. TREATMENT OF PATIENTS WITH RENAL COLIC

5.1 Pain relief

The relief of pain is usually the most urgent therapeutic step in patients with an acute stone episode. Pain relief involves the administration of the following agents by various routes:

- Diclofenac sodium (LE: 1b)
- Indomethacin
- Ibuprophen
- Hydromorphone hydrochloride + atropine sulphate
- Methamizol
- Pentazocine
- Tramadol.

5.1.1 Treatment with non-steroidal anti-inflammatory drugs (NSAIDs)
A double-blind study comparing diclofenac and spasmofen (a narcotic analgesic) (1) demonstrated a better effect with diclofenac and fewer side effects. In another double-blind, placebo-controlled study, the efficacy of diclofenac (2) was clearly demonstrated.
When diclofenac was compared with ketoprofen in a randomized, double-blind, comparative study, no differences were recorded between the two substances (3). Moreover, the resistant index was reduced in patients with renal colic when NSAID treatment was given (4).

The recommendation is to start with diclofenac whenever possible (Table 13) and change to an alternative drug if the pain persists. Hydromorphone and other opiates without simultaneous administration of atropine should be avoided because of the increased risk of vomiting.

Comment: In France, ketoprofen is the only drug approved for the treatment of renal colic. In case of contra-indication (pregnancy) or allergy to non-steroidal anti-inflammatory drugs, morphine chlorhydrate (with titration) is indicated, taking account of the side-effects.

5.1.2 Prevention of recurrent episodes of renal colic
In a double-blind, placebo-controlled trial, it was shown that recurrent pain episodes of stone colic were significantly fewer in patients treated with 50 mg of diclofenac three times daily during the first 7 days. The effect was most pronounced in the first 4 treatment days (5). For patients with ureteral stones that are expected to pass spontaneously, suppositories or tablets of diclofenac sodium, 50 mg administered twice daily over 3-10 days, might therefore be useful in reducing the inflammatory process and the risk of recurrent pain. The patient should be instructed to sieve the urine in order to retrieve a concrement for analysis. Passage of the stone and normalization of renal function should be confirmed using appropriate methods. When pain relief cannot be obtained by medical means, drainage by stenting or percutaneous nephrostomy (PN) or by stone removal should be carried out.

5.1.3 Effects of diclofenac on renal function
Although the renal function can be affected in patients with an already reduced function, this is not the case for normally functioning kidneys (6).

Table 13: Recommendations and considerations regarding treatment of the patient with renal colic

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>LE/GR</th>
<th>Selected references</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment should be started with an NSAID</td>
<td>1b/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>6</td>
<td>5.1.3</td>
</tr>
<tr>
<td>Diclofenac sodium is recommended as a method to counteract recurrent pain after an episode of ureteral colic</td>
<td>1b/A</td>
<td>5</td>
<td>5.1.2</td>
</tr>
</tbody>
</table>

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

5.2 REFERENCES
6. INDICATIONS FOR ACTIVE STONE REMOVAL

The size, site and shape of the stone at the initial presentation are factors that influence the decision to remove the stone (Table 14). 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 a diameter ≥7 mm, the chance of spontaneous passage is very low (1-4).

The overall passage rate of ureteral stones is:

- Proximal ureteral stones: 25%.
- Mid-ureteral stones: 45%.
- Distal ureteral stones: 70%.

Stone removal is accordingly indicated for stones with a diameter exceeding 6-7 mm. Studies have shown that asymptomatic stones in the kidney sooner or later give rise to clinical problems (5).

It should also be observed that small stones (< 6-7 mm) residing in a calix can cause considerable pain or discomfort (6-12). Such stones should be removed with a technique that is as little invasive as possible. A narrow caliceal neck may require dilatation.

<table>
<thead>
<tr>
<th>Table 14: Indications for active stone removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>LE/GR Selected references</td>
</tr>
<tr>
<td>Active stone removal should be considered when the stone diameter is ≥ 7 mm because of a low rate of spontaneous passage</td>
</tr>
<tr>
<td>When adequate pain relief cannot be achieved</td>
</tr>
<tr>
<td>When stone obstruction is associated with infection*</td>
</tr>
<tr>
<td>When there is a risk of pyonephrosis or urosepsis*</td>
</tr>
<tr>
<td>In single kidneys with obstruction*</td>
</tr>
<tr>
<td>Bilateral obstruction*</td>
</tr>
</tbody>
</table>

*Diversion of urine with a PN 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 stone removal

Twenty years after the worldwide dissemination of ESWL technology, the development of lithotripters, as well as modified indications and principles for treatment, have changed the type and rate of complications. Modern lithotripters are smaller and, in the vast majority of cases, part of a uroradiological table which allows the application of not only ESWL treatment, but also of all the diagnostic and ancillary procedures associated with ESWL treatment. All these factors give an efficacy that is the same as, or superior to, that of the first lithotripters on the market, but at a lower cost and with greater versatility. Even the indications for stone removal were modified when shock wave lithotripsy was introduced. Currently, the contraindications to ESWL treatment are restricted to pregnancy, severe skeletal malformations, severe obesity and aortic and/or renal artery aneurysms (1,2). Moreover, ESWL should not be carried out in patients with uncontrolled blood coagulation or uncontrolled urinary tract infection. A pacemaker is, however, not a contraindication.

Accumulated experience has clearly shown that the success rate of ESWL is directly related to the size (volume) of the concrement and that an increased stone burden is associated with an increase in the re-treatment rate. This has led to the conclusion that large stones are better treated with a percutaneous approach (see below). In addition to the size of the stone, the intrarenal position and chemical composition of the stone are determinants of the treatment results. Numerous authors have addressed this issue in recent years (3-12). Generally, the disintegrating power of ESWL is very good and the concerns about ESWL treatment of large stones are mainly related to the common occurrence of residual fragments and the need for repeated sessions. The latter factor probably has become more important with later generations of lithotripters, because of their smaller focal volumes, for example, in comparison with the Dornier HM3-lithotripter. When repeated treatments are necessary, it is recommended that the number of shock waves and the power used should be restricted in order to avoid damage to the renal tissue and bleeding complications (see below).

It is recommended that the number of ESWL sessions should not exceed three to five (dependent on the lithotripter used), otherwise a percutaneous lithotripsy might be considered as a more rational option. In the case of infected stones or bacteriuria, antibiotic therapy should be given before ESWL treatment and continued for at least 4 days after the treatment. There are no clearly established rules on how often ESWL sessions can be repeated. It is reasonable to assume, however, that the interval between two successive sessions must be longer for electrohydraulic and electromagnetic lithotripsy than for treatments with piezoelectric equipment.
Moreover, the risk of damage is most pronounced with treatments directed towards stones in the kidney, and shorter intervals between treatment sessions are usually acceptable for stones in the ureter. Clinical experience supports this view.

It stands to reason, however, that the interval should be determined by the energy level used and the number of shock waves given. In view of the numerous lithotripters presently in use it is not possible to give a general recommendation in this regard. It might, however, be helpful to note that the time required for resolution of contusions in the renal tissue is in the range of about 2 weeks (13) and it might accordingly be wise to allow 10-14 days to pass between two successive ESWL sessions for stones in the kidney.

There is no consensus on the maximum number of shock waves that can be delivered at each session. This number again depends on the type of lithotripter and the shock wave power used.

One factor that might affect the result of ESWL treatment is the presence of anatomical abnormalities. Malformations of the renal collecting system can be the reason for stone formation due to an altered mechanism of urine elimination and thus to an impaired stone fragment passage. The need of auxiliary procedures in these patients is high, with one study showing that only 50% of the patients were stone-free at 3-months follow-up (14). In the horseshoe kidney, the incidence of stones is around 20%. The success rate depends mainly on the lithotripter used and varies between 53% and 60%. In one treatment series the incidence of auxiliary procedures was reported to be 24% and the re-treatment rate 27% (15).

Some authors claim that percutaneous surgery is the treatment of choice for these patients (16,17), but in view of the greater morbidity and complication rate of this technique percutaneous lithotripsy can only be recommended when previous ESWL treatment has failed. There are some reports indicating that ESWL is also useful in patients with medullary sponge kidneys (tubular ectasia) and nephrocalcinosis (18,19). In ectopic kidneys, the efficacy of ESWL is strictly related to the position of the kidney. In transplanted kidneys, the efficacy of ESWL is similar to that in normal kidneys and well tolerated, without any particular side-effects (20). In a series of 35,100 patients treated for kidney stones with ESWL, satisfactory disintegration was recorded in 32,255 cases, which is 92%. The stone-free rate in these patients was 70% with re-treatments in 10.5% (21-52).

7.1.2 ESWL for removal of large renal stones

ESWL for the treatment of large renal stones often causes problems. Frequent complications are pain, hydronephrosis, fever, and occasional urosepsis due to difficulties in passage of stone particles especially in case of insufficient disintegration (53-58).

By using a double-J stent, the obstructive and infective complications after ESWL due to large renal stones are reduced. Insertion of the stent before ESWL is advocated for stones with a diameter > 20 mm (54,55). Stone particles may pass easily along stents while urine flows in and around the stent. This usually prevents obstruction with loss of ureteral contraction. Sometimes, stents are not efficient in draining purulent or mucoid material, leading to a risk of obstructive pyelonephritis. In case of fever lasting for a few days, a PN tube is necessary, even when ultrasonography does not reveal any dilatation.

The following factors are crucial with respect to treatment success:

- Location of the stone mass (pelvic or caliceal).
- Total stone burden.
- State of contralateral kidney: nephrectomy or functionless kidney on the other side.
- Composition and hardness of the stone (53).

7.1.2.1 Location of the stone mass

Lower caliceal stones are considered to have a lower successful clearance rate than stones located elsewhere in the kidney. A faster clearance of upper pole stones has been observed.

Almost since the introduction of ESWL, there has been a continuous debate on the best way to treat stones in the lower calix. This is an important issue because a large number of kidney stones are located in this part of the kidney. Moreover, it is well recognized that most residual fragments are lodged in the lower caliceal system. Such fragments either emerge from stones originally found in this part of the kidney or from stones at 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.

It has been observed that the lower calices are insufficiently cleared of disintegrated stone material in up to 35% of ESWL-treated patients. Attempts have been made to explain the insufficient clearance of fragments and to predict the outcome of ESWL-treatments from geometrical observations of the lower calix anatomy.
By taking measurements of the infundibulopelvic angle, as well as the infundibulum length and width, several authors have concluded that an acute infundibulum angle (59-63), a long infundibulum (59,63) and/or a narrow infundibulum (59-61,63) have a negative influence on fragment clearance. In other studies, however, no such relationship has been demonstrated (64-69), and in one report the authors even noted that the clearance of fragments was better with an infundibulopelvic angle below, rather than above, 70° (68). In the absence of a geometrical explanation, the size of the stones has been found to be the most important determining factor (64,66,67,69). This conclusion was based both on observations in a randomised prospective study comparing ESWL and PNL (66) and in a multivariate analysis (64). Another factor that most certainly is of great importance is the less well-understood caliceal physiology (63,69).

Several authors have shown that a better stone-free rate can be obtained with PNL, particularly when the stones become larger. The invariance and morbidity of PNL undoubtedly needs to be taken into account. At least for stones with a largest diameter of 20 mm (surface area ~ 300 mm²), ESWL is the recommended treatment, despite the lower clearance of fragments. It might be relevant to note that a previous percutaneous procedure in one study (69) was considered as a negative determinant of fragment clearance.

Although an acute angle, a long calix neck or a narrow calix can undoubtedly counteract elimination of fragments, the results are contradictory and there is no strong evidence that these variables can be used to predict the outcome of ESWL.

7.1.2.2 Stone burden
Although the problems associated with removal of stones from the kidney increases with the volume of the stone, there is no clear cut-off for a critical stone size. Today most authors consider a largest stone diameter of 20 mm as a practical upper limit for ESWL, but larger stones are also successfully treated with ESWL in some centres.

Since residual fragments are found in patients with stones smaller than 20 mm (300 mm²) and since very large stones can be successfully disintegrated with only one ESWL session, it is difficult to formulate specific guidelines on how to remove stones from the kidney. The recommended upper size limit for ESWL in this document is 20 mm (300 mm²). Below this size, ESWL should be considered to be the first choice for treatment. For larger stones, the problem might be more rationally solved using PNL. However, ESWL can still be considered an option for treatment, provided the pros and cons are clear.

It appears that an area of 40 x 30 mm (940 mm²) could represent an upper limit for ESWL alone. With ESWL monotherapy (only stent), a success rate of 86% (stone-free or residual material likely to undergo spontaneous discharge) after 3 months was described for stones with an area smaller than that. The success rate for larger stones was only 43% after 3 months with ESWL monotherapy.

In the treatment of stones with an area larger than 40 x 30 mm, the combination of PNL and ESWL (sandwich approach) has emerged as a solution, with success rates of 71-96% and acceptable morbidity and complications. ESWL after PNL seems to be more effective than PNL after ESWL. The indication for open stone surgery has become extremely rare because of the invasiveness of this approach (55,56).

It is of note, however, that the risk of complications of the combined treatment or PNL alone is higher than for ESWL monotherapy. In the case of a solitary kidney, it might be feasible to try ESWL monotherapy first, even if the stone has an area larger than 40 x 30 mm (57).

7.1.2.3 Composition and hardness of the stone
ESWL monotherapy of large calcium- or struvite-containing stones provides reasonable results in terms of stone removal and complications (58). About 1% of all patients treated for urinary tract stones by ESWL have cystine stones. A total of 76% of cystine stones have a maximum diameter larger than 25 mm (while only 29% of all stone patients have stones of this size). Patients with large cystine stones need up to 66% more ESWL sessions and shock waves to reach satisfactory results in comparison with other stone patients (70). ESWL monotherapy provided satisfactory results only in patients with pelvic stones smaller than 1 cm.

Instead of multiple ESWL sessions, PNL, possibly combined with ESWL, is an effective treatment for all other patients with cystine stones (70,71). It is important to note that there are two types of cystine stone morphology: smooth and rough. The latter is much more susceptible to shockwaves than the first one (72).

Stone composition can be an important factor in the disintegration and subsequent elimination of fragments. Stones composed of uric acid and calcium oxalate dihydrate have a better coefficient of fragmentation than those composed of calcium oxalate monohydrate and cystine. Success rates for these two groups of stones were shown to be 38-81% and 60-63%, respectively (8). For cystine stones with a diameter less than 15 mm, a stone-free rate of about 71% was reported, a figure that dropped to 40% when the diameter exceeded 20 mm (9). Thus, for cystine stones with a diameter greater than 15 mm, ESWL as monotherapy is currently not recommended.
7.1.2.4 REFERENCES


UPDATE JUNE 2005


26 UPDATE JUNE 2005


7.2 Percutaneous removal of renal stones

Principally, the majority of renal stones can be removed by percutaneous surgery. However, if ESWL is available, the indications for PNL should be limited to cases in which a less favourable outcome is expected after ESWL. Although PNL is minimally invasive, it is still a surgical procedure and thus it is necessary to carefully consider the patient's anatomy in order to avoid complications.

Pre-procedural KUB and intravenous urography or uroCTscan are used to plan access. These images will also give some indication as to whether the stones will respond poorly to ESWL (such as stones composed of cystine, calcium oxalate, calcium monohydrate, brushite) or if fragments are unlikely to pass (large stones, caliceal diverticula). Pre-procedural sonography of the kidney and the surrounding structures is recommended to determine the optimal access site and the position of the stone in the kidney (ventral or dorsal), and to ensure that organs adjacent to the kidney (such as the spleen, liver, large bowel, pleura and lungs) are not within the planned percutaneous path (1,2).

The percutaneous puncture may be facilitated by the preliminary placement of a balloon ureteral catheter to dilate and opacify the collecting system. Furthermore, such a catheter will prevent fragments from falling into the ureter. The puncture can be performed under combined ultrasound and X-ray control or under biplanar fluoroscopy. The use of ultrasound allows easy identification of neighbouring organs and therefore lowers the risk of injuries to adjacent organs. In selected cases with anatomical anomalies, CT-guided renal access may be an option (3).

The most frequently used access site 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 goes through the papilla. There are no major vessels in this region and there is only minimal bleeding. It is also the safest point of access because it uses the infundibulum as a conduit to the pelvis.

Dilatation of the tract is possible with the Amplatz system, balloon dilators or metallic dilators. The choice is a matter of experience, availability and costs. While standard nephroscopes have shaft calibres of 24-30 F, so-called ‘mini-perc’ instruments have smaller dimensions with 12-20 F. These small-calibre instruments possibly have a lower rate of tract dilation-related complications such as bleeding or renal trauma. However, treatment time increases with stone size, which is why this method is recommended only for stones with a diameter < 20 mm (4). While the value of mini-perc in adults has not been determined, it is the method of choice for percutaneous stone removal in children (5-7).

Stones can be extracted straightaway or following disintegration by ultrasound, electrohydraulic, laser or hydropneumatic probes. To reduce the number of residual fragments, continuous removal of small fragments by suction or extraction is preferred. After completion of the procedure, a self-retaining balloon nephrostomy tube is the best choice to secure tamponading of the tract and access to the collecting system. However, in selected patients, tubeless percutaneous nephrolithotomy may be a safe alternative (7).

7.2.1 Complications

Major complications are lesions to adjacent organs. This can be avoided by puncture under ultrasound guidance. Bleeding is generally avoided by an anatomically oriented access, as described above. Sepsis and ‘transurethral resection syndrome’ indicate a poor technique with high pressure within the collecting system during manipulation. These problems can be avoided by using continuous flow instruments or an Amplatz sheath (1,8). Major bleeding during the procedure requires termination of the operation, placement of a nephrostomy tube and secondary intervention at a later date. Venous bleeding stops in most cases when the nephrostomy tube is clamped for some hours. Persistent, clinically significant, bleeding results from an arterial injury and can be managed by angiographic superselective embolization.

As with open surgery, percutaneous procedures have different degrees of difficulty. A difficult procedure is indicated by anatomical conditions that offer only limited space for the initial puncture, dilatation and instrumentation, such as stones in diverticulae or stones completely filling the target calix. The procedure should only be carried out by experienced surgeons in these cases.

7.2.2 REFERENCES


7.3 Aspects on staghorn stone treatment and importance of stone burden
Staghorn stones may significantly vary in size, composition and distribution within the collecting system, as well as in their secondary effects on renal anatomy and function. There is no generally accepted classification system that allows for determination of success and complication rates of single or combined procedures. Thus, all techniques - ESWL, PNL, surgery and partial or complete nephrectomy - are included in the treatment strategy (1). If the global kidney function is reduced or if there is bilateral stone disease, every effort must be made to preserve functioning nephrons.

7.3.1 ESWL
Staged ESWL in combination with a double-J stent may be used in cases where the stone image mimics a normal contrast-filled collecting system, i.e., there is no dilatation of the collecting system and the stone has a small volume (2).

7.3.2 PNL
Percutaneous nephrolithotomy (PNL) may be used for stones of larger volume that expand and obstruct the collecting system and in which the majority of the stone volume lies within the renal pelvis and the target calix. These are stones with a large, centrally located, stone volume. The use of two or more percutaneous accesses should follow the same rules (3). Although multi-tract PNL only moderately increases morbidity, the use of flexible nephroscopes can reduce the need for multiple accesses (4).

7.3.3 ESWL and PNL
A combined procedure should be planned in such a way that each single step is successful in itself. Staghorn stones with a large central stone volume in the access calix and the renal pelvis and one or two small extensions in the middle and upper caliceal group, without obstruction of these calices, are good indications for a combined procedure. Stones with large volume extensions into the calices, with obstruction of the collecting system, are not suitable for this approach.
7.3.4 Percutaneous surgery versus ESWL for removal of renal stones

PNL and ESWL are complementary rather than competing procedures. Principally, the indication for PNL can also be extended to include so-called ‘easy cases’ when ESWL is not available. Stones ≥ 2 cm in diameter in the renal pelvis or the upper and middle caliceal group without obstruction and dilatation of the collecting system are generally accepted as ideal indications for ESWL.

The clearance of stone fragments from the lower pole calices varies between different studies but is generally considered as poor, with overall stone-free rates between 37% and 67% (see section 7.1.2.1) while percutaneous procedures result in a stone-free rate of up to 97% (4-11). A percutaneous approach might therefore be preferable, particularly for patients with an obstructed lower calix or when the stone burden is considerable (i.e., diameter exceeding 20 mm or stone surface area more than 300 mm²). Numerous studies have addressed the problem of lower pole clearance for stones measuring 10-20 mm (75-300 mm²) and attempts have been made to predict the outcome from analysis of the spatial anatomy of the lower calices. Currently, there is no consensus on the usefulness of measuring the infundibulopelvic angle and the length and width of the calix (see above section 7.1.2.1 Location of the stone mass), and the best treatment for stones in the lower calices is still controversial. However, it can be stated that, although PNL has a higher, initial, stone-free rate, PNL is associated with more severe complications than ESWL.

7.3.5 REFERENCES


7.4 Open surgery for removal of renal stones

With the advances in ESWL and endourological surgery (ureteroscopy [URS] and PNL) over the past 15-20 years, the indications for open stone surgery have markedly diminished. Centres with the equipment, expertise and experience in the surgical treatment of renal tract stones report a need for open surgery in 1-5.4% of cases (1-5). It is now accepted that, in some circumstances, there is a place for open surgical removal of calculi. Since most of these cases will usually involve difficult stone situations, it is important that urologists maintain proficiency, skills and expertise in open renal and ureteral surgical techniques. However, with the various modalities of treatment that are now available for the surgical management of stones, there will inevitably be some controversy as to when open operation in a particular case is, or is not, appropriate. Thus, it is only possible to propose general principles for open surgery based on consensus of opinion from experience and the technical limitations of the less invasive alternative approaches.

Whenever the major stone volume is located peripherally in the calices, especially if these calices are obstructed so that either several percutaneous accesses and several, probably unsuccessful, shockwave sessions will be necessary for complete stone removal, an open surgical procedure should be preferred. With today’s limited experience with open stone surgery in many hospitals, it may be advisable to send patients to a centre where the urologists still know how to properly perform the techniques of extended pyelocalicotomy (6), anatrophic nephrolithotomy (7-10), multiple radial nephrolithotomy (11,12) and renal surgery under hypothermia. The latest progress in this area has been the introduction of intra-operative B-mode scanning and Doppler sonography (13,14) to identify avascular areas in the renal parenchyma close to the stone or dilated calices to enable removal of large staghorn stones by multiple small radial nephrotoomies without loss of kidney function.

7.4.1 Indications for open surgery

Indications for open surgery for stone removal include:

- Complex stone burden.
- Treatment failure with 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 - single procedure in preference to possibly more than one PNL procedure.
- Stone in a transplanted kidney where there may be a risk of damage to the overlying bowel.
- Stone in an ectopic kidney where percutaneous access and ESWL may be difficult or impossible.
- Cystolithotomy for giant bladder calculus.
- A large stone burden in children because of easy surgical access and the need for 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 reimplantation of the ureter - ureteroneocystotomy.
The superiority of open surgery over less invasive therapy in terms of stone-free rates is based on considerable historical experience, but (as yet) there are no comparative studies available (LE:4).

In one recent report reasons given to perform open surgery were a complex stone burden in 55%, failed low invasive surgery in 29%, anatomical abnormalities in 24%, morbid obesity in 10% and co-morbid medical diseases in 7% of cases (5). Another report mentions 25 open surgical procedures in 799 treatments for renal stones, while a large stone burden in association with abnormal anatomy limiting endoscopic access in 31% of the cases, concurrent surgical procedures in 24% and previously failed endourologic procedures as the reason for open surgery in another 17% of cases is listed in a retrospective study (15). A 2% need for open surgery was recorded in 2,651 stone procedures carried out in Singapore (16).

Laparoscopic surgery is also an option, particularly for stones located in a ventral caliceal diverticulum (17).

7.4.3 REFERENCES


7.5 Chemolytic possibilities
Chemolytic dissolution of stones or stone fragments is a useful adjunct to ESWL, PNL, URS or open surgery for a more complete elimination of stone fragments or residual fragments. The combined treatment of ESWL and chemolysis is a particularly low-invasive option for selected patients with partially or completely infected staghorn stones. Oral chemolytic treatment is also a very attractive therapeutic alternative for the removal of uric acid stones. This section provides a summary of chemolytic treatment options.

For percutaneous chemolysis, the patient should have at least two nephrostomy catheters. This enables irrigation of the renal collecting system while preventing chemolytic fluid from draining into the bladder and reducing the risk of increased intrarenal pressure. In the case of a large stone burden, the ureter should be protected by a double-J stent during the procedure (1,2).

7.5.1 Infection stones
Stones composed of magnesium ammonium phosphate and carbonate apatite can be dissolved with a 10% solution of hemiacidrin, which is an acid solution with a pH between 3.5 and 4. Another useful agent is Suby's solution. During appropriate antibiotic treatment the chemolytic solution is allowed to flow in through one nephrostomy catheter and out through another. The surface area of the stone or the stone remnants is increased by ESWL. The time required for dissolution depends on the stone burden, but several weeks will be necessary to dissolve a complete staghorn stone using chemolysis combined with ESWL. The major advantage of this therapeutic approach is that it can be carried out without anaesthesia and might thus be an option for high-risk patients or for any other patients in whom anaesthesia or other surgical procedures must be avoided (3-13). It should be noted that Hemiacidirin and Suby G solutions carry a serious risk of mortality (cardiac arrest) from hypermagnesemia. This form of treatment must only be used when there is good evidence that the renal tract has healed following surgery and never infused in the immediate post-operative stage.

7.5.2 Brushite stones
Brushite is also soluble in the acid solutions mentioned above in section 7.5.1. This option should be considered in patients with residual brushite fragments after other stone-removing procedures. This is a particularly interesting treatment approach in view of the very high recurrence rate of brushite stones.

7.5.3 Cystine stones
Cystine is soluble in an alkaline environment. For this purpose, 0.3 or 0.6 mol/L trihydroxymethyl aminomethan (THAM) solution can be used. The pH of these solutions is in the range 8.5-9.0. Another option is acetylcysteine. The two solutions can also be used in combination. Percutaneous chemolysis is a useful method for complete stone clearance in combination with other stone-removing techniques (14-18).

7.5.4 Uric acid stones
A high concentration of urate and a low (acidic) pH are the determinants of uric acid stone formation. Percutaneous dissolution can be accomplished with THAM solutions. Oral chemolysis is, however, the most attractive alternative. This method involves lowering urate concentration using allopurinol and a high fluid intake, and increasing the pH to alkali (19-21).
7.5.5 Calcium oxalate and ammonium urate stones

There is currently no physiologically useful chemolytic agents for dissolving stones composed of calcium oxalate or ammonium urate (22). The presence of calcium oxalate in an infection stone markedly reduces the solubility in hemiacidrin (6).

7.5.6 REFERENCES


7.6 Recommendations for removal of renal stones

Recommendations on the most appropriate method for removal of stones from the kidney are based on several important considerations. The available options are ESWL, PNL, flexible URS, as well as video-endoscopic retroperitoneal and open surgery. All these methods are applicable, but for any given stone situation, it is logical to select a method with low invasiveness and low morbidity.

More than two decades of experience with low invasive methods have clearly shown that open surgery is necessary only in exceptional cases and mainly for those patients in whom anatomical reconstruction is necessary. Video-endoscopic retroperitoneal surgery has no place as standard procedure for removal of stones from the kidney, though it is advantageous in some types of reconstructive surgery.

For small stones (up to a maximum diameter of 20 mm or a surface area of 300 mm²), ESWL has been established as the standard procedure because it is non-invasive, has a low rate of complications and there is no need for regional or general anaesthesia. Although larger stones can also be treated successfully with ESWL, percutaneous stone removal might be preferable for faster debulking of the stone. It needs to be emphasized, however, that complete clearance of stones from the caliceal system by a percutaneous technique requires considerable expertise and experience.

For large renal stones, there is an ongoing debate as to whether large renal stones are best treated with ESWL or with PNL. The drawbacks of ESWL are a frequent need for repeated treatments and the relatively common occurrence of residual fragments. However, it is important to note that unless percutaneous surgery is carried out with a meticulous technique, residual fragments of stone may be left behind in these patients.

Although residual fragments can develop into new stones, several reports have shown that risk to be reasonably low. A follow-up programme for patients with residual fragments appears necessary, but such a routine is indicated also because of the inherent tendency to new stone formation that characterizes patients with stone disease.

Residual fragments of infection stones, associated with the most pronounced risk of recurrences can be eliminated with percutaneous chemolysis. Such a step might also be used as an auxiliary procedure in the treatment of cystine stones.

For uric acid stones, oral chemolysis is the first choice of treatment for stone disintegration. However, an increased rate of dissolution can be obtained following stone disintegration and treatment in this order may be considered for removing large uric acid stones.

The approximate estimates of surface area corresponding to oval stone projections with certain diameters are given in Appendix A.

An overview of treatment recommendations according to size and stone type is shown in Tables 15 and 16.
Table 15: Recommendations for active removal of renal stones with a diameter ≤ 20 mm* (surface area ≤ 300 mm²)

<table>
<thead>
<tr>
<th>Type of stone</th>
<th>Procedure</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radio-opaque stones</td>
<td>1. ESWL</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>2. PNL</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>Infection stones and stones with infection</td>
<td>These stones should be managed like any other stones provided there is no obstruction and that a symptomatic infection has been adequately treated.</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td>Uric acid/urate stones</td>
<td>1. Oral chemolysis</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>2. Stent + ESWL + oral chemolysis</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td>Cystine stones</td>
<td>1. ESWL</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>2. PNL</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>3. Open or video-endoscopic retroperitoneal surgery</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LE = level of evidence; GR = grade of recommendation; ESWL = extracorporeal shock wave lithotripsy, also including piezolithotripsy; PNL = percutaneous nephrolithotomy.

* Numbers (1, 2, 3) have been allocated to the procedures according to the consensus reached. When two procedures were considered equally useful they have been given the same number. The first alternative always has the number 1.

Table 16: Recommendations for active removal of renal stones with a diameter > 20 mm* (surface area > 300 mm²)

<table>
<thead>
<tr>
<th>Type of stone</th>
<th>Procedure</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radio-opaque stones</td>
<td>1. PNL</td>
<td>1b</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>2. ESWL with or without stenting</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>3. PNL + ESWL</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td>Infection stones and stones with infection</td>
<td>These stones should be managed like any other stones provided there is no obstruction and that a symptomatic infection has been adequately treated.</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td>Uric acid/urate stones</td>
<td>1. Oral chemolysis</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>2. Stent + ESWL + oral chemolysis</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td>Cystine stones</td>
<td>1. PNL</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>2. PNL + ESWL</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>3. PNL + flexible nephroscopy</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>4. Open or video-endoscopic retroperitoneal surgery</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LE = level of evidence; GR = grade of recommendation; ESWL = extracorporeal shock wave lithotripsy, also including piezolithotripsy; PNL = percutaneous nephrolithotomy.

* Numbers (1, 2, 3, 4) have been allocated to the procedures according to the consensus reached. When two procedures were considered equally useful they have been given the same number. The first alternative always has the number 1.

8. ACTIVE REMOVAL OF STONES IN THE URETER

8.1 ESWL for removal of ureteral stones

Following an initially sceptical attitude to the use of ESWL for disintegrating stones in the ureter, this technique has been extensively used and a considerable experience has demonstrated that ESWL is very useful for stone removal from the ureter. It has been shown clearly that, in most cases, it is possible to remove a ureteral stone using ESWL without regional or general anaesthesia and with a very low rate of complications and side effects. It is, however, assumed that ureteral stones generally require higher shock wave energy and a greater number of shock waves. Improved results in complicated cases can be achieved by combining ESWL with low-invasive auxiliary procedures (e.g., by stenting or urethral catheters). The literature comprises numerous reports with a variable success rate. This lack of consistency is obviously related to the type of lithotripter, size and composition of the stone, degree of impaction and extent to which repeated shock waves sessions are
acceptable. Another important and probably neglected factor is the experience and ambition of the operator. Stones in the ureters can be treated in situ with or without a catheter or stent, by passing the stone with the catheter or by placing a catheter below the stone. Stone treatment can also be completed following retrograde manipulation of the stone to the kidney (‘push and bang’ procedure). Today, the vast majority of ureteral stones are successfully treated in situ without auxiliary procedures and using only analgesics and sedation.

Out of approximately 20,000 patients with ureteral stones a stone-free state was achieved in 81% (1-40). The re-treatment rate in these patients was 12%. Auxiliary procedures were used in 17% and regional or general anaesthesia in 26%. In a report comprising 18,825 patients treated with ESWL for ureteral stones in the United States, 84% became stone free. The re-treatment rate in the latter series of patients was 11% (41).

Stones at different levels of the ureter present with different degrees of difficulty. The results of ESWL-treatment of stones in the proximal-, mid-, and distal ureter, as presented in a number of reports, are summarized in Table 17.

<table>
<thead>
<tr>
<th>Level of stone in the ureter</th>
<th>No. of patients</th>
<th>Stone free % (range)</th>
<th>Auxiliary procedures %</th>
<th>Anaesthesia %</th>
<th>Re-ESWL %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal (30 reports)</td>
<td>8,825</td>
<td>77.4 (63-100)</td>
<td>13.0</td>
<td>11.3</td>
<td>10.0</td>
</tr>
<tr>
<td>Mid (24 reports)</td>
<td>429</td>
<td>80.3 (60-98)</td>
<td>4.3</td>
<td>4.3</td>
<td>8.2</td>
</tr>
<tr>
<td>Distal (38 reports)</td>
<td>6,896</td>
<td>77.9 (59-100)</td>
<td>12.9</td>
<td>11.1</td>
<td>9.4</td>
</tr>
</tbody>
</table>

8.1.1 REFERENCES


8.2 Retrograde manipulation of stones

The push-back technique has been applied in order to avoid problems with insufficient disintegration of ureteral stones. When compared with stone-free rates of 62-97% following in situ treatment (1-10), retrograde manipulation resulted in stone-free rates of 73-100% (5,7,9,11). It needs to be emphasized, however, that the success rate associated with pushing the stone up to the kidney varied considerably and it can be extremely difficult or impossible to manipulate large or impacted stones.

8.2.1 Stenting

The value of an expanding fluid chamber around the stone is the rationale for using a ureteral catheter that either bypasses the stone or is placed just below the stone. Although slightly better results have been reported with this procedure, the retreatment rate was usually not significantly lower (3,8-14). It might, however, be of some help to use a ureteral catheter when treating large and impacted ureteral stones, but it is difficult to find definite evidence for this assumption in the literature. Another reason for stenting might be to aid in the location of small and less radio-opaque stones, as well as to fill the collecting system with contrast medium for detecting radiolucent stones.

8.2.2 REFERENCES


During the past two decades, URS has dramatically changed the management of ureteral calculi. Nowadays, URS is extensively used in many urological centres all over the world. However, it is an invasive technique compared to ESWL, and the treatment of choice for ureteral stones with diameters of 1 mm or larger is still controversial.

New ureteroscopes (semi-rigid and flexible) and lithotripsy devices have recently become available.

### 8.3 Endoscopic technique

The basic endoscopic technique has been well standardized for many years (1, 2). Antibiotic prophylaxis should be administered before the procedure to ensure sterile urine. A pre-operative plain film of the urinary tract is obtained to confirm the location of the stone. The operating room must have fluoroscopic equipment. Under general spinal anaesthesia or intravenous sedation, the patient is placed in the lithotomy position. The procedure starts with rigid or flexible cystoscopy. A guide wire is introduced under endoscopic and fluoroscopic control, and secured to the drapes. Intramural ureteral dilatation is not indicated routinely, but
depends on the size of the ureteroscope and width of the ureter. Retrograde access to the upper urinary tract is usually obtained under video-guidance with a rigid ureteroscope (9.5-11 F), a semi-rigid ureteroscope (6.0-8.5 F). A flexible ureteroscope is inserted either alongside a second 0.035-inch safety guide wire with a floppy tip or in a 10-13 F sheath.

Endoscopic lithotripsy is based on the use of different devices in order to break the stone into dust or fragments with diameters ≤ 2 mm. The stone may be fragmented by ultrasonic lithotripsy, electrohydraulic lithotripsy, laser lithotripsy or ballistic (or pneumatic) lithotripsy. Small stones and fragments ≤ 5 mm in diameter are best retrieved with a basket or a grasper (3,4).

Irrigation facilitated with a piston syringe or a flow control unit is needed to ensure good direct vision. Flushing of large fragments or the stone itself up to the renal pelvis or calices or perforation of the ureteral wall may occur. The safety guide wire prevents the risk of false passage in case of perforation.

Stent placement at the end of the procedure is optional and a matter of debate (2). It is dependent on the injury to the ureteral mucosa due to the stone or the ureteroscope. Dilatation of the intramural ureter and use of a laser usually requires the insertion of a single/double pigtail stent under fluoroscopic guidance. The stent will usually remain in place for about 1 week. The operating time is generally between 10 and 60 minutes, but may be substantially longer for flexible URS. If the stone is impacted, the best approach is to insert a ureteral stent for several days prior to the URS (2). Patients should be followed up by plain abdominal film, ultrasonography or intravenous urography after 2-12 weeks (2,5).

8.3.2 Anaesthesia
The improvement of ureteroscopes and stone retrieval instruments allows ureteroscopic procedures to be carried out under sedation analgesia with a similar success rate (88-97%) to general anaesthesia. This technique is particularly useful for removal of distal ureteral stones in women (2,6,7).

8.3.3 Assessment of different devices
8.3.3.1 Ureteroscopes
Semi-rigid and thin ureteroscopes are available. Miniaturization avoids dilatation of the intramural ureter (with associated complications) in more than 50% of cases (8-10). The small diameter (6.0-7.5 F) allows easier progression of the ureteroscope up to the proximal ureter.

The use of flexible ureteroscopes (7-7.5 F) has been evaluated (1,2,11-15). They are suitable for access to the upper part of the ureter and renal collecting system, without dilating the intramural ureter in over 75% of cases. In the lower ureter, a flexible ureteroscope, because of its tendency to fall back into the bladder, is not recommended (1,3). The recently developed (semi-)flexible ureterorenoscopes (Storz) with enhanced maximal deflection provide particular advantages for ureteroscopic surgery (36-39).

8.3.3.2 Disintegration devices
Laser lithotripsy is a reliable method for the treatment of ureteral stones, regardless of the hardness of the stone (16). It is the only applicable method when performing flexible URS (12,17,18). A 365 µm holmium:yttrium aluminium garnet (Ho:YAG) laser fibre is the best choice for ureteral stones, as minimal deflection is required to access the stone. The 200 µm fibre is more expensive but it is the only fibre that minimally impairs maximal tip deflection and is therefore recommended for fragmentation of intrarenal calculi (12,19). The Nd:YAG (frequency-doubled) laser has a lower efficacy than the Ho:YAG system and is not suitable for very hard stones or cystine stones, but provides a sufficiently efficient alternative for most stone compositions. This device offers an excellent cost-performance ratio (40).

The ideal energy and frequency settings are less than 1.0 J and 5-10 Hz. If manipulated with care, the laser does not damage the ureteral mucosa (16,18,20). An operating time for laser lithotripsy of between 7 minutes and 45 minutes is acceptable (18).

Laser lithotripsy using pulsed dye laser has shown similar results to those obtained using the Ho:YAG laser (21). Ho:YAG lithotripsy seems to give better stone-free results at 3 months than electrohydraulic lithotripsy (97% versus 87%) for distal ureteral stones (5). However, for ureteral calculi ≤ 15 mm in diameter, laser lithotripsy will require a longer operating time than the electrohydraulic technique (5) but because of the greater risk of tissue damage, electrohydraulic devices should not be used as a standard procedure.

Ballistic lithotriptors (pneumatic or electropneumatic) using a 2.4 F probe in a semi-rigid ureteroscope provide excellent fragmentation rates (90-96%). A low capital cost and simple and safe handling are major advantages of this type of device. Its cost-effectiveness is three times that of laser lithotripsy (9,14,22-24). Nevertheless, migration of stones towards the renal pelvis from the mid- or proximal ureter might be a limiting factor of ballistic lithotripsy (25).
8.3.3.3 Baskets
Ureteroscopic removal of small ureteral stones with a basket is a relatively quick procedure with a lower morbidity rate than lithotripsy (3,4). The basket technique should be attempted first for small distal ureteral calculi. Several new designs of endoscopic stone retrieval baskets are available. The nitinol tipless basket is more effective than a flat-wire basket because of its greater flexibility (4,13, 23). The tipless nitinol basket is non-traumatic and allows excellent control inside calices. Laser or electrohydraulic lithotripsy may break the wires of the basket (16). Small ureteral stones or fragments can be removed fast and safely with forceps which can be better controlled than a basket.

8.3.3.4 Dilatation and stenting
Over recent years it has been attempted to modify the standard technique of dilatation and stenting. An access sheath may facilitate URS, particularly when the ureter has to be re-entered several times, such as for instance in case of a great stone burden (41) and when it is desirable to maintain low pressure inside the upper urinary tract. An access sheath of a suitable dimension can be introduced over a guide wire. Most procedures can, however, be carried out without an access sheath (42).

Reduced need for dilatation (0-40%), operating time and post-operative ureteral stenting have resulted from the use of thin ureteroscopes Routine stent placement following uncomplicated URS may be unnecessary. Patient discomfort is modest and satisfactorily controlled by oral analgesics (21,26).

8.3.3.5 Clinical results
The Ureteral Clinical Guidelines Panel of the American Urological Association have conducted a meta-analysis of relevant studies between 1966 and 1996. Members produced a report for guidelines in August 1997, which was published in the Journal of Urology (27). When the material was stratified into results for proximal and distal ureteral stones, the overall stone-free rates were 72% and 90%, respectively. For ureteral stones with a diameter ≤ 10 mm, the stone-free rates were 56% and 89% for proximal and distal stones, respectively.

Analysis of the literature for the past 3 years indicates an improvement in stone-free rates. Semi-rigid and/or flexible ureteroscopes provide 90-100% stone-free rates for distal ureteral calculi and only a 74% stone-free rate in the proximal ureter. This last result is considerably better than the results reviewed before 1997 (25,28,29). Similar results were observed in children and in obese patients (11,30). A total of 95% of patients were successfully treated with only one endoscopic procedure. The best results were reported with Ho:YAG laser lithotripsy, especially in the proximal ureter (5). This latter technique might be a good alternative to ESWL, for example, in obese patients or in those with less visible stones (9,11).

8.3.3.6 Complications
Significant acute complication rates of 11% and 9% have been reported for the proximal and distal ureters, respectively (27). Ureteral strictures were the only long-term complication reported, with the estimated rate being 1%.

There is a strong relationship between the complication rate and the equipment used and/or the expertise of the urologist (31,32). The overall complication rates reported in recent literature are 5-9%, with a 1% rate of significant complications (3,8-10,12,20,29,32-35).

The major acute complication remains ureteral avulsion (9,33). Autologous transplantation or uretero-ileoplasty are the methods of choice in cases of avulsion (33).

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 (8).

8.3.3.7 Conclusion
Improvements in the design of ureteroscopes, accessories and the URS technique have led to a significant increase in the success rate for the removal of ureteral stones and a decreased morbidity (3). This means that in experienced hands the new generation of ureteroscopes can be used for the treatment of proximal as well as distal ureteral stones, particularly when the stone diameter ≤ 10 mm. Thus, both ESWL and URS can be considered acceptable treatment alternatives for stones in these positions.

The cost-effectiveness of ureteroscopic treatment has not been assessed. New requirements for endoscopic sterilization could dramatically increase the cost of the procedures, even with a parallel decrease in operating time and complication rate. Randomized and prospective studies are needed in order to compare all forms of stone removal from the ureter.
8.3.4 REFERENCES


8.4 Should ESWL or URS be used for stone removal?
This is indeed a controversial issue for which there is a lack of consensus. Arguments have been presented for and against both these procedures. Although the need for re-treatment is definitely greater with ESWL than with URS, the advantages of ESWL are non-invasiveness and no need for regional or general anaesthesia. Even with the addition of auxiliary procedures, ESWL can be considered a low-invasive and gentle procedure.

On the other hand, URS is considered to be a one-step procedure that in the majority of studies has been carried out under anaesthesia. Several comparative studies between URS and ESWL can be found in the literature, but most focus on stones in the distal ureter (1-10). Although these studies demonstrate what has been mentioned above, several groups concluded that ESWL is preferable in view of its lower degree of invasiveness.

Although the access to flexible ureteroscopes and efficient laser devices has made it more attractive to treat stones in the mid- and distal ureter ureteroscopically, little information is available on how the ureter reacts to repeated ureteroscopic procedures. Furthermore, the need for anaesthesia is unchanged.

It can be assumed that the production and marketing of lithotripters, which obviously were inferior to the initial HM3-device, have contributed to a less favourable attitude to ESWL from urologists. However, a remarkable improvement has been noticed in recent years with lithotripters that have the capacity to disintegrate ureteral stones as efficiently as, or even more so, than the HM3 machine.

The size of ureteral stones has also been considered a limiting factor for ESWL, but URS-disintegrated stones also require elimination of residual fragments.

In conclusion, it is difficult or impossible to give priority to either of these procedures. The urologist’s experience, access to adequate equipment and specific circumstances are probably the best determinants of which method will be most appropriate for a particular patient.

8.4.1 REFERENCES
8.5 Recommendations for active removal of ureteral stones: all sizes

In case of failure with minimally invasive techniques, an open surgical procedure might be required to remove the stone. Video-endoscopic retroperitoneal surgery is a minimally invasive alternative to open surgery. These techniques also have to be applied when there are contraindications for ESWL and URS, e.g., in patients with a stone proximal to a ureteral stricture.

There is controversy as to whether ESWL or URS is the best method for removal of ureteral stones, particularly for those situated in the lower ureter. There are advantages and disadvantages of both these procedures, but ESWL usually can be carried out without anaesthesia and has a low morbidity. Although retreatments are necessary in a substantial fraction of ESWL-treated patients, in our opinion they are considered equally useful for the removal of distal ureteral stones.

It is of note that only uric acid stones, not those composed of ammonium urate or sodium urate, can be dissolved by oral chemolytic treatment. For stones with a low radiodensity, the location can be facilitated by means of a ureteral catheter or a double-J stent. In selected cases with infection stones, uric acid stones, cystine stones and pure calcium phosphate stones, percutaneous chemolytic irrigation can be used to increase the clearance rate of stone fragments. The principles of chemolytic treatment are outlined above (see section 7.5).
### Table 18: Principles of active stone removal (all sizes) in the proximal ureter*

<table>
<thead>
<tr>
<th>Type of stone</th>
<th>Procedure</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radio-opaque stones</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. ESWL <em>in situ</em></td>
<td></td>
<td>1a</td>
<td>A</td>
</tr>
<tr>
<td>2. ESWL following retrograde manipulation of the stone (‘push up’)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. URS + contact disintegration:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- semi-rigid or flexible URS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. PNL + URS in antegrade direction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Infection stones and stones with infection</strong></td>
<td>These stones should be managed like any other stones provided there is no obstruction and that a symptomatic infection has been adequately treated</td>
<td>1a</td>
<td>A</td>
</tr>
<tr>
<td><strong>Uric acid/urate stones</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Stent + oral chemolysis</td>
<td></td>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td>2. ESWL <em>in situ</em> (with i.v. or retrograde contrast) + oral chemolysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. URS + contact disintegration:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- semi-rigid or flexible URS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Percutaneous URS in antegrade direction</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**LE = level of evidence; GR = grade of recommendation; ESWL = extracorporeal shock wave lithotripsy, also including piezolithotripsy; PNL = percutaneous nephrolithotomy with or without lithotripsy; URS = ureteroscopy. Whether proximal ureteral stones should be ESWL-treated in supine or prone position is directed by the type of lithotriptor in use and its geometrical properties.**

* Numbers (1, 2, 3, 4) have been allocated to the procedures according to the consensus reached. When two procedures were considered equally useful they have been given the same number. The first alternative always has the number 1.

### Table 19: Principles of active stone removal (all sizes) in the mid ureter*

<table>
<thead>
<tr>
<th>Type of stone</th>
<th>Procedure</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radio-opaque stones</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. ESWL <em>in situ</em>, prone position*</td>
<td></td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td>2. URS + contact disintegration:</td>
<td></td>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td>- semi-rigid or flexible URS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Ureteral catheter or intravenous contrast + ESWL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Percutaneous antegrade URS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Infection stones and stones with infection</strong></td>
<td>These stones should be managed like any other stones provided there is no obstruction and that a symptomatic infection has been adequately treated</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td><strong>Uric acid/urate stones</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. ESWL <em>in situ</em>, prone position*</td>
<td></td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td>2. URS + contact disintegration:</td>
<td></td>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td>- semi-rigid or flexible URS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Ureteral catheter or intravenous contrast + ESWL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Percutaneous antegrade URS</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Cystine stones
1. ESWL in situ, prone position\textsuperscript{a}  2a B
1. URS with lithotripsy:
   - semi-rigid or flexible ureteroscopy  2a B
2. Ureteral catheter + ESWL
2. Ureteral catheter with retrograde manipulation
   ('push up') + ESWL
3. Percutaneous antegrade URS

\textit{LE} = level of evidence; \textit{GR} = grade of recommendation; \textit{ESWL} = extracorporeal shock wave lithotripsy, also including piezolithotripsy; \textit{URS} = ureteroscopy.
\textsuperscript{a} For lithotripters with the shock wave source below the patient.

\* Numbers (1, 2, 3) have been allocated to the procedures according to the consensus reached. When two procedures were considered equally useful they have been given the same number. The first alternative always has the number 1.

Table 20: Principles of active stone removal (all sizes) in the distal ureter\*  

<table>
<thead>
<tr>
<th>Type of stone</th>
<th>Procedure</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radio-opaque stones</td>
<td>1. ESWL in situ</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>1. URS + contact disintegration:</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>- rigid URS + US, laser or ballistic/pneumatic disintegration</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- semi-rigid URS</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. Ureteral catheter + ESWL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection stones and stones</td>
<td>These stones should be managed like any other stones provided there is no obstruction and that a symptomatic infection has been adequately treated</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>with infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uric acid/urate stones</td>
<td>1. ESWL in situ (i.v. contrast medium)</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>1. URS + contact disintegration</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>2. Ureteral catheter (+ contrast medium) + ESWL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. PN + antegrade contrast + ESWL in situ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystine stones</td>
<td>1. ESWL in situ</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>1. URS + contact disintegration</td>
<td>3</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>- rigid URS + US, laser or electrohydraulic disintegration</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- semi-rigid URS</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. Ureteral catheter + ESWL</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\* Numbers (1, 2, 3) have been allocated to the procedures according to the consensus reached. When two procedures were considered equally useful they have been given the same number. The first alternative always has the number 1.

9. GENERAL RECOMMENDATIONS AND PRECAUTIONS FOR STONE REMOVAL

9.1 Infections
A test for bacteriuria should be carried out in all patients in whom stone removal is planned. Screening with dipsticks might be sufficient in uncomplicated cases. In others, urine culture is necessary.

In cases with clinically significant infection and obstruction, several days of drainage procedures by a stent or a percutaneous nephrostomy should precede the active intervention for stone removal.
9.2 Bleeding
Bleeding disorders and anticoagulant treatment should be considered. These patients should be referred to an internist for appropriate therapeutic measures during the stone-removing procedure. In patients with coagulation disorders, the following treatments are contraindicated: extracorporeal shock wave lithotripsy (ESWL), percutaneous nephrolithotomy (PNL) with or without lithotripsy, ureteroscopy (URS) and open surgery.

9.3 Pregnancy
In pregnant women, ESWL, PNL and URS are contraindicated. In expert hands, URS has been successfully used to remove ureteral stones during pregnancy, but it must be emphasized that complications of this procedure might be difficult to manage. In such women, the preferred treatment is drainage, either with a percutaneous nephrostomy catheter, a double-J stent or a ureteral catheter (1-7).

9.4 Pacemaker
Although the rule is that patients with a pacemaker can be treated with ESWL, it is recommended that the patient’s cardiologist is consulted before undertaking ESWL treatment.

9.5 Hard stones
Stones composed of brushite or calcium oxalate monohydrate are characterized by particular hardness. This may mitigate in favour of percutaneous removal of such stones, particularly if they are large. The possibility of chemolytic treatment of brushite stone fragments is noteworthy in view of the high recurrence rate seen with this type of stone.

Cystine stones are of two types - those responding well to ESWL and those responding poorly (8). For large ESWL-resistant stones, PNL is the best alternative for efficient removal, thereby avoiding too much shock wave energy to the renal tissue.

9.6 Radiolucent stones
Uric acid concrements can be localized with ultrasound, or with intravenous or retrograde administration of contrast medium. It is of note that only uric acid stones, not sodium urate or ammonium urate stones, can be dissolved by oral chemolytic treatment.

Table 21: Special considerations

<table>
<thead>
<tr>
<th>Treatment with antibiotics should precede stone-removing procedures in case of a positive urine culture, positive dip-stick test or suspicion of an infective component</th>
<th>GR</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>9.1</td>
</tr>
</tbody>
</table>

| Treatment with salicylates should be stopped 10 days before the planned stone removal | B | 9.2 |
| ESWL and PCNL are contraindicated in pregnant women | C | 9.3 |
| ESWL is possible in patients with a pacemaker | C | 9.4 |

GR = grade of recommendation; ESWL = extracorporeal shock wave lithotripsy; PCNL = percutaneous nephrolithotripsy.

9.7 REFERENCES


10. COMPLETE OR PARTIAL STAGHORN STONES

A staghorn stone is defined as a stone with a central body and at least one caliceal branch. Whereas a partial staghorn stone fills up only part of the collecting system, a complete staghorn stone fills all calices and the renal pelvis. Treatment of both types of staghorn stone is detailed in Table 22.

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 and chemolysis may be useful. The principles of chemolytic treatment are discussed in Section 7.5.

<table>
<thead>
<tr>
<th>Type of stone</th>
<th>Procedure</th>
<th>LE</th>
<th>GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radio-opaque stones</td>
<td>1. PNL</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>2. PNL + ESWL</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>3. ESWL + PNL</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>4. Open surgery standard</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection stones and</td>
<td>1. Antibiotics + PNL</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>stones with infection</td>
<td>2. Antibiotics + PNL + ESWL</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>3. Antibiotics + ESWL + PNL</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>4. Antibiotics + ESWL + local chemolysis</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>5. Antibiotics + open surgery</td>
<td>standard</td>
<td></td>
</tr>
<tr>
<td>Uric acid/urate stones</td>
<td>1. PNL</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>2. PNL + ESWL</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>3. PNL/ESWL + oral chemolysis</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>4. ESWL + PNL</td>
<td>1b</td>
<td>B</td>
</tr>
<tr>
<td>Cystine stones</td>
<td>1. PNL</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>2. PNL + ESWL</td>
<td>2a</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>3. ESWL + PNL</td>
<td>2a</td>
<td>B</td>
</tr>
</tbody>
</table>

*Numbers (1, 2, 3, 4, 5) have been allocated to the procedures according to the consensus reached. When two procedures were considered equally useful they have been given the same number. The first alternative always has the number 1.
11. MANAGING SPECIAL PROBLEMS

Caliceal diverticulum stones are treated using ESWL, PNL (if possible) or retrograde URS. An optional method for removal of diverticular stones is video-endoscopic retroperitoneal surgery. The principles of video-endoscopic surgery are outlined elsewhere (1-5). In the case of 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 may be treated according to the principles of stone treatment presented above (6). It needs to be emphasized, however, that according to the anterior position of the kidney, it is commonly necessary to carry out ESWL treatment with the patient in the prone position (i.e., with shock wave entrance from the abdominal side).

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

The stones formed in a continent reservoir present a varied and often difficult problem (7-14). General directions for the management of this problem cannot be given. Each stone problem has to be considered and treated individually.

In patients with obstruction of the ureteropelvic junction, stones can be removed at the same time as the outflow abnormality is corrected either with percutaneous endopyelotomy (15-35) or with open reconstructive surgery. Transureteral endopyelotomy with Ho:YAG laser endopyelotomy is another alternative to correct such an abnormality. Incision with an Acucise balloon catheter may also be considered provided the stones can be prevented from falling down into the pelvo-ureteral incision (36-39).

11.1 REFERENCES


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

Different imaging techniques have variable degrees of sensitivity. Thus, a CT or topographic examination both demonstrate small fragments better than a standard film (KUB). A CT scan also has the capacity to demonstrate uric acid concrements, which are otherwise radiolucent. Reports on residual fragments therefore vary from one institution to another depending on which imaging method is used. However, there is no data in the literature demonstrating the clinical value of being able to detect small tiny concretions visible only on CT scan. Moreover, CT scans cannot be carried out everywhere.

It is our recommendation that the results of a stone-removing procedure are based on the findings of a good-quality KUB and that CT examination is only necessary for uric acid stones.

Stone residuals with a largest diameter of 4 mm should be termed residual fragments. Residuals with a diameter of 5 mm or more should be termed 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 regularly followed up to monitor the course of their disease. Identification of biochemical risk factors and appropriate stone prevention may be particularly indicated in patients with residual fragments or stones. In symptomatic patients, it is important to rule out obstruction and to treat this problem if present. In other cases, necessary therapeutic steps need to be taken to eliminate symptoms. In asymptomatic patients where the stone is unlikely to pass, treatment should be applied according to the relevant stone situation.

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 the patients with stone fragments 3 months after treatment experienced stone progression. The corresponding stone-free rate was 20% (1).

For calcium stones, the term ‘clinically insignificant residual fragments’ (CIRF) was introduced. The role of CIRF has been a matter of debate and concern for some time (2-13). Most studies on the long-term course of the disease in patients with residual fragments are restricted to periods between 1 and 6 years. The longest follow-up period was reported by Yu and co-workers (14). After 6.3 years, stone growth was observed in 26% of patients and recurrent stone formation in 15%. During a follow-up of between 7 and 96 months, with an average follow-up of 3.4 years, the residual fragments increased in size in 37% of patients. A new stone-removing procedure was undertaken in 22% of patients (15). In data on 104 patients with residual fragments, 40% showed decreased disease or remained stable, while 5% progressed during a mean follow-up of 1.2 years (16), with further intervention necessary in 9.3% of patients by 2 years of follow-up. In a follow-up of patients with < 4 mm residual fragments during a 4-year period, there was obvious increase in size in 37% and a need for retreatment in 12% (17).

New stone formation is another aspect to consider in ESWL-treated patients because of the assumption that the fraction of stone-free patients is overestimated. Stone recurrences were thus reported to be 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. 25% 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).

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 treatment to be considered (21). For stones in the upper and middle calices, URS with contact disintegration is another treatment option. Percutaneous chemolysis is an alternative treatment for stone fragments composed of magnesium ammonium phosphate, carbonate apatite, uric acid, cystine and brushite.

Double-J stenting before ESWL is recommended for stones with a largest diameter of more than 20 mm (300 mm²) in order to avoid problems with an accumulation of stones obstructing the ureter, known as a Steinstrasse (see Section 13) (22-34). Table 23 summarizes the 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>
12.1 REFERENCES


13. 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 urine passage (1). The frequency of this complication has decreased with the liberal insertion of double-J stents before ESWL of large renal stones. In all patients with signs of infection, it is necessary to give antibiotics and to provide adequate drainage as soon as possible. Insertion of a PN catheter usually results in passage of the fragments (2). For distally located accumulations of fragments, URS might be useful to remove the leading stone fragment by contact disintegration. Recommendations for treatment are summarized in Table 24.

Table 24: Recommendations for treatment of Steinstrasse*

<table>
<thead>
<tr>
<th>Position of stone</th>
<th>Unobstructed</th>
<th>Obstructed and/or symptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal ureter</td>
<td>1. ESWL</td>
<td>1. PN</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. Stent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4. ESWL ESWL</td>
</tr>
<tr>
<td>Mid ureter</td>
<td>1. ESWL</td>
<td>1. PN</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Stent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. ESWL ESWL</td>
</tr>
<tr>
<td>Distal Ureter</td>
<td>1. ESWL</td>
<td>1. PN</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. ESWL ESWL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. URS URS</td>
</tr>
</tbody>
</table>

ESWL = extracorporeal shock wave lithotripsy, also including piezolithotripsy; PN = percutaneous nephrotomy; URS = ureteroscopy.

*Numbers (1, 2, 3, 4) have been allocated to the procedures according to the consensus reached. When two procedures were considered equally useful they have been given the same number. The first alternative always has the number 1.

13.1 REFERENCES

14. PREVENTIVE TREATMENT IN CALCIUM STONE DISEASE

14.1 General recommendations
Preventive treatment in patients with calcium stone disease should be started with conservative measures. Pharmacological treatment should be instituted only when the conservative regimen fails. Patients should be encouraged to have a high fluid intake (1). This advice is valid, irrespective of stone composition. For a normal adult, the 24-h urine volume should exceed 2,000 mL, but the supersaturation level should be used as a guide to the necessary degree of urine dilution. The fluid intake should be evenly distributed over a 24-hour period, and particular attention should be paid to situations in which an unusual loss of fluid occurs.

Diet should be of a ‘commonsense’ type - a mixed balanced diet with contributions from all food groups, but without excesses of any kind (2). The intake of fruits and vegetables should be encouraged because of the beneficial effects of fibre (3). Care must be taken, however, to avoid fruits and vegetables that are rich in oxalate. Wheat bran, for instance, is rich in oxalate and in order to avoid an oxalate load, the
excessive intake of products rich in oxalate should be limited or avoided. This is of particular importance in
patients in whom high excretion of oxalate has been demonstrated. The following products have a high content
of oxalate (4):
• Rhubarb 530 mg oxalate/100 g.
• Spinach 570 mg oxalate/100 g.
• Cocoa 625 mg oxalate/100 g.
• Tea leaves 375-1450 mg oxalate/100 g.
• Nuts 200-600 mg oxalate/100 g.

Vitamin C in doses up to 4 g/day can be taken without increasing the risk of stone formation (5-7).
Animal protein should not be ingested in excessive amounts (8-14), and it is recommended that animal protein
intake is limited to approximately 150 g/day. Calcium intake should not be restricted unless there are very
strong reasons for such advice. The minimum daily requirement for calcium is 800 mg and the general
recommendation is 1000 mg/day. Supplements of calcium are not recommended except in cases of enteric
hyperoxaluria, in which additional calcium should be ingested with meals.

The intake of food particularly rich in urate should be restricted in patients with hyperuricosuric
calcium oxalate stone disease (15-20), as well as in patients with uric acid stone disease. The intake of urate
should not exceed more than 500 mg/day. Below are examples of food rich in urate (21):
• 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.

14.1.1 REFERENCES
Abstract
=Abstract
3. Ebisuno S, Morimoto S, Yasukawa S, Ohkawa T. Results of long-term rice bran treatment on stone
Abstract
4. Hesse A, Tiselius HG, Jahnen A. In: Urinary stones - Diagnosis, treatment and prevention of
5. Wandzlak TR, D’André SD, Davis PA, Williams HE. Effect of high dose vitamin C on urinary oxalate
Abstract
Abstract
7. Auer BL, Auer D, Rodger AL. The effects of ascorbic acid ingestion on the biochemical and physico-
1998;36:143-147.
Abstract
Abstract
Abstract


14.2 Pharmacological agents in prevention of recurrent calcium stone formation

The general opinion is that attempts should always be made to correct abnormalities in urine composition and to eliminate risk factors of pathological crystallization by advice regarding drinking and dietary habits. Only when such treatment turns out to be unsuccessful, should a pharmacological approach be considered in addition to the drinking and dietary recommendations. 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 easy to administer. All these aspects are 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 form the basis for the above-mentioned recommendations (1). The conclusions of the Consensus Conference have been published separately (2,3,4). In the present edition of the Urolithiasis guideline document, information has been added on recent studies with special emphasis on data from randomized studies.

We have given our recommendations for the various agents both for when they are given in a non-selected way (Table 25) and when given for a specific urine abnormality (Table 26). We believe that the latter approach is theoretically most attractive but it needs to be emphasized, however, that there is no absolute consensus on such a view (5,6).

The pharmacological agents most commonly used in patients with recurrent calcium stone formation are thiazides, orthophosphate, magnesium, cellulose phosphate, sodium cellulose phosphate, allopurinol, and in some situations pyridoxine and oxabsorb. The scientific basis of these forms of treatment is briefly summarized below.
14.2.1 Thiazides and thiazide-like agents

Hydrochlorothiazide, bendroflumethiazide, trichlorothiazide and 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 (7). The hypocalciuric action of thiazides is thought to be mediated by an increased reabsorption of calcium in the proximal as well as in the distal parts of the nephron (7,8). It has, moreover, been suggested that thiazides might decrease the excretion of oxalate, possibly by a reduced intestinal absorption of calcium (9-11). However, a thiazide-induced reduction in urinary oxalate is not a consistent finding in the clinical studies.

There is more than 30 years’ clinical experience with thiazides as a method for stone prevention. Following the initial report by Yendt in 1970 (12), a large number of reports have been published, most of which support a positive effect of recurrence prevention. 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 (13,14) failed to confirm a positive effect of thiazides, a significantly reduced recurrence rate was recorded in three 3-year follow-up studies (15-18). A similar result was also obtained in three groups of patients treated with thiazides for 2.3 and 4.3 years in comparison with conservatively treated patients (19-21). A significantly reduced rate of stone formation was also noted when a thiazide was given intermittently to recurrent stoneformers (22).

A reduced rate of recurrence was also observed in a number of other studies in which the treated patients were compared with patients not given any pharmacological agent (23-26). In several other studies, the results were less convincing (27,28).

A positive effect of thiazide treatment was further supported by a meta-analysis of randomized trials which showed significantly better results with active treatment than with placebo or no treatment (p < 0.02) (29).

The major drawback of thiazide treatment is the occurrence of side-effects. The unmasking of normocalcaemic HPT, development of diabetes and gout, as well as erectile dysfunction, contribute to a low 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 (19-21) 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 stoneformers, 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 a high calcium excretion, other forms of treatment may be more appropriate first-choice alternatives. As in all situations when pharmacological treatment is considered, a judgment must be made between the positive and the negative effects of the medication.

14.2.2 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 frequent finding in patients with calcium stone disease. The role of calcium is important because citrate chelates calcium and thereby reduces the ion-activity products of both calcium oxalate and calcium phosphate. Moreover, citrate is an inhibitor of growth and aggregation of these crystals (30). 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 affecting 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 citrate, potassium magnesium citrate, potassium bicarbonate and sodium bicarbonate.

Alkaline citrate has been used in four randomized studies. Potassium citrate was used in two (31,32), sodium potassium in one (33) and sodium magnesium citrate in another (34). In the two studies with 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 overall impression is that potassium citrate (31,32,35-40) has a greater potential for preventing recurrence than sodium potassium citrate (2,33,41,42). This observation is also supported by the different effects of potassium citrate and sodium citrate on urine composition (43).
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 (44). In a meta-analysis of randomized trials it was not possible to adequately analyze the therapeutic outcome (29).

The usefulness of alkaline citrate as a means to increase the stone clearance after shock wave lithotripsy has been studied by several groups and has recently been the subject of a European multicentre investigation (not yet finally analyzed). It was accordingly shown that sodium potassium citrate (45), as well as potassium citrate (40, 46), increased clearance of stone fragments.

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 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 no reports of this problem in the literature.

14.2.3 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 (47).

The rate of stone formation during 3 years of treatment with phosphate was also studied in two randomized studies (16,17). 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 (48,49), it was also not possible to confirm a reliable effect of phosphate treatment. A reduced rate of stone formation was, however, noted by others (50,51). In reviews of literature results, there is a lack of scientific evidence that phosphate is effective in preventing calcium stone formation (29,52).

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 PTH (parathyroid hormone) needs consideration. It is possible that the pattern of side effects is favourably affected by slow-release potassium phosphate (53). The effect of phosphate administration on calcium stone phosphate 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.

14.2.4 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 (54). 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 under Section 14.2.2 on alkaline citrate and will not be further discussed here.

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 (55) and one with magnesium oxide and untreated controls (16). None of them showed a statistically significant effect on stone formation despite follow-up periods of four and three years, respectively.

The positive effects of magnesium administration that have been reported previously (56, 57) have not been confirmed by recent controlled studies (52,29). Thus, there is insufficient evidence to recommend magnesium as monotherapy in calcium stone prevention.
14.2.5 Allopurinol

Treatment with allopurinol in order to counteract the formation of calcium oxalate stones was introduced following demonstration of a relationship between hyperuricosuria and calcium oxalate stone formation (58). The effect of allopurinol on calcium oxalate stone formation may be mediated through a reduced salting-out effect, a decreased risk of uric acid or urate crystals as promoters of calcium oxalate precipitation, complex formation between colloidal urate and macromolecular inhibitors, and/or possibly by a reduced excretion of oxalate. It also needs to 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. This effect was statistically significant. Three other randomized studies compared treatment with allopurinol and placebo or no treatment (16,17,59) 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 (60). A similar result was recorded in another Swedish study (61). These results are in contrast to those obtained in patients treated for hyperuricosuria (62,63).

The tolerance to allopurinol 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, but it cannot be recommended as treatment for patients with other biochemical abnormalities.

14.2.6 Cellulose phosphate

Cellulose phosphate and sodium cellulose phosphate have been used to reduce calcium absorption in patients with absorptive hypercalciuria. Unfortunately, this complex formation may result in hyperoxaluria. Binding of magnesium causes hypomagnesuria and other ions may also be negatively affected by this form of treatment. Of nine studies in the literature, none were randomized (64-71). The overall results showed that 40% of the patients formed new stones.

Cellulose phosphate and sodium cellulose phosphate cannot be recommended for prophylactic treatment against stone recurrence.

14.2.7 Pyridoxine

Theoretically, administration of pyridoxine (vitamin B₆) might favourably influence the endogenous production of oxalate. Such an effect can be explained by an increased transamination of glyoxylate due to the action of pyridoxal phosphate.

Pyridoxine has successfully been used together with orthophosphate in the treatment of patients with primary hyperoxaluria (72), as well as patients with idiopathic hyperoxaluria (73,74). There are no controlled studies that presently 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 giving a therapeutic trial of pyridoxine in order to reduce the excretion of oxalate in patients with primary hyperoxaluria Type I.

14.2.8 Recommendations

The following forms of treatment are discouraged: magnesium oxide and magnesium hydroxide as monotherapy. Magnesium salts might, however, be useful in combination with thiazides (74). Cellulose phosphate and sodium cellulose phosphate have no place in the prevention of stone recurrence in patients with calcium stone disease. Neither is there a place for synthetic or semisynthetic glycosaminoglycans (GAGs) (e.g., sodium pentosan polysulphate).

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 (6). Recommendations for a selective therapeutic approach are given in Table 25.
Table 25: Level of evidence and grade of recommendation for various forms of pharmacological treatment of patients with recurrent calcium stone disease

<table>
<thead>
<tr>
<th>Pharmacological agent</th>
<th>LE</th>
<th>GR</th>
<th>Selected references</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiazides/thiazide-like agents</td>
<td>1a</td>
<td>A</td>
<td>7-29</td>
<td>14.2.1</td>
</tr>
<tr>
<td>Alkaline citrate</td>
<td>1b</td>
<td>A</td>
<td>2, 30-46</td>
<td>14.2.2</td>
</tr>
<tr>
<td>Allopurinol</td>
<td>1b</td>
<td>A*</td>
<td>16,17, 58-63</td>
<td>14.2.5</td>
</tr>
<tr>
<td>Orthophosphate</td>
<td>3</td>
<td>-</td>
<td>16,17,29,47-53</td>
<td>14.2.3</td>
</tr>
<tr>
<td>Magnesium</td>
<td>3</td>
<td>-</td>
<td>16, 29, 54-57</td>
<td>14.2.4</td>
</tr>
<tr>
<td>Pyridoxine</td>
<td>2b</td>
<td>B**</td>
<td>72-73</td>
<td>14.2.7</td>
</tr>
<tr>
<td>Cellulose phosphate</td>
<td>-</td>
<td>Not recommended</td>
<td>64-71</td>
<td></td>
</tr>
<tr>
<td>Sodium cellulose phosphate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* only for patients with hyperuricosuria; ** only for patients with hyperoxaluria.

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

Table 26: Suggested selective treatment of calcium stone formers with known abnormalities in urine composition*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Treatment groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiazides</td>
<td>1) Hypercalciuria</td>
</tr>
<tr>
<td>Thiazides + magnesium</td>
<td>2) Brushite stone formation</td>
</tr>
<tr>
<td>Thiazides + magnesium</td>
<td>3) Other abnormalities</td>
</tr>
<tr>
<td>Alkaline citrate</td>
<td>1) Hypocitraturia</td>
</tr>
<tr>
<td>Alkaline citrate</td>
<td>1) RTA</td>
</tr>
<tr>
<td>Alkaline citrate</td>
<td>2) Enteric hyperoxaluria</td>
</tr>
<tr>
<td>Alkaline citrate</td>
<td>3) Low inhibitory activity</td>
</tr>
<tr>
<td>Alkaline citrate</td>
<td>4) Other abnormalities</td>
</tr>
<tr>
<td>Allopurinol</td>
<td>1) Hyperuricosuria</td>
</tr>
<tr>
<td>Pyridoxine</td>
<td>1) Primary hyperoxaluria type 1</td>
</tr>
<tr>
<td>Pyridoxine</td>
<td>2) Mild hyperoxaluria</td>
</tr>
<tr>
<td>Calcium supplements</td>
<td>1) Enteric hyperoxaluria</td>
</tr>
<tr>
<td>Orthophosphate</td>
<td>1) Hypercalciuria</td>
</tr>
</tbody>
</table>

1. Potassium supplements are necessary to avoid hypokalaemia and hypocitraturia caused by hypokalaemic intracellular acidosis.
2. In case the inhibition of crystal growth or crystal aggregation has been assessed.
3. Orthophosphate is not a first-line alternative, but it can be used in patients with hypercalciuria who do not tolerate thiazides.

* Numbers (1, 2, 3, 4) have been allocated to the procedures according to the consensus reached. When two procedures were considered equally useful they have been given the same number. The first alternative always has the number 1.

14.2.9 REFERENCES


UPDATE JUNE 2005 67


70 UPDATE JUNE 2005


14.3 Pharmacological treatment of uric acid stone disease
The principles for prevention or dissolution of uric acid stones all aim at eliminating one, or all, of the three risk factors: a low urine pH, a high excretion of urate and a small urine volume (1-4). The pH should be increased to a level above 6.5 and the general recommendation is to get a pH in the range 6.5-7.2 (1,2,4). The 24-hour urine volume should be at least 2.0-2.5 litres (1-4) and the 24-hour excretion of urate below 4 mmol (5).

General recommendation nowadays is to use potassium citrate for the alkalinization of urine. The clinical effect of potassium alkali was shown to be superior to that of sodium alkali (5). The solubility of potassium urate is greater than that of sodium urate (6,7) and potassium does not increase the excretion of calcium. The pharmacological treatment of patients with uric stone disease is outlined in Table 27.
### Table 27: Pharmacological treatment of uric acid stone disease

<table>
<thead>
<tr>
<th>Objective</th>
<th>Therapeutic measures</th>
<th>GR</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prevention</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Urine dilution</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>A high fluid intake; 24-hour urine volume</td>
<td>B</td>
<td>1-4</td>
</tr>
<tr>
<td></td>
<td>exceeding 2,000 mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Alkalization</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Potassium citrate 3-7 mmol x 2-3</td>
<td>B</td>
<td>3-5</td>
</tr>
<tr>
<td></td>
<td>Sodium potassium citrate 9 mmol x 2-3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>In patients with a high serum or urine</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>level of urate</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Allopurinol 300 mg x 1</td>
<td>B</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Medical dissolution</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Urine dilution</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>A high fluid intake; 24-hour urine volume</td>
<td>B</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>exceeding 2,000 mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Medical dissolution</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Urine dilution</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>A high fluid intake; 24-hour urine volume</td>
<td>B</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>exceeding 2,000 mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Alkalization</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Potassium citrate 6-10 mmol x 2-3</td>
<td>B</td>
<td>1-4</td>
</tr>
<tr>
<td></td>
<td>Sodium potassium citrate 9-18 mmol x 2-3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Always reduce urate excretion</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Allopurinol 300 mg x 1</td>
<td>B</td>
<td>1-4</td>
</tr>
</tbody>
</table>

**GR** = grade of recommendation

### 14.3.1 REFERENCES


14.4 Pharmacological treatment of cystine stone disease

The pharmacological treatment of patients with cystine stone disease is outlined in Table 28.

Table 28: Pharmacological treatment of cystine stone disease

<table>
<thead>
<tr>
<th>Therapeutic measures</th>
<th>GR</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Urine dilution</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A high fluid intake should be recommended so that the 24-h urine volume exceeds 3,000 mL. To achieve this goal, the intake should be at least 150 ml/h</td>
<td>B</td>
<td>1-3</td>
</tr>
<tr>
<td><strong>Alkalization</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>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 &gt; 7.5.</td>
<td>B</td>
<td>1-3</td>
</tr>
<tr>
<td><strong>Complex formation with cystine</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>For patients with a cystine excretion above 3 mmol/24h: Tiopronin (α-mercapto-propionyl glycine) (250-2,000 mg/day) or Captopril (75-150 mg)</td>
<td>B</td>
<td>1-7</td>
</tr>
</tbody>
</table>

14.4.1 REFERENCES


14.5 Pharmacological treatment of infection stone disease

The pharmacological treatment of patients with infection stone disease is outlined in Table 29. The definition of infection stones is stones composed of magnesium ammonium phosphate and carbonate apatite and caused by urease producing micro-organisms.

Table 29: Pharmacological treatment of infection stone disease

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

GR = grade of recommendation
14.5.1 REFERENCES

15. ACKNOWLEDGEMENTS

Members of the Advisory Board of European Urolithiasis Research contributed to the section on metabolic evaluation and preventive treatment. They include:

16. 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>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>CIRF</td>
<td>clinically insignificant residual fragments</td>
</tr>
<tr>
<td>Cit</td>
<td>citrate</td>
</tr>
<tr>
<td>CRP</td>
<td>C-reactive protein</td>
</tr>
<tr>
<td>CT</td>
<td>computed tomography</td>
</tr>
<tr>
<td>CY</td>
<td>cystine stone</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>GAG</td>
<td>glycosaminoglycan</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:ytrrium aluminium garnet</td>
</tr>
<tr>
<td>HPT</td>
<td>hyperparathyroidism</td>
</tr>
<tr>
<td>INF</td>
<td>infection stone</td>
</tr>
<tr>
<td>IVP</td>
<td>intravenous pyelography</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>Mg</td>
<td>magnesium</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>PCNL</td>
<td>percutaneous nephrolithotripsy</td>
</tr>
<tr>
<td>PN</td>
<td>percutaneous nephrostomy</td>
</tr>
<tr>
<td>PNL</td>
<td>percutaneous nephrolithotomy with or without lithotripsy</td>
</tr>
<tr>
<td>PTH</td>
<td>parathyroid hormone</td>
</tr>
<tr>
<td>R&lt;sub&gt;mo&lt;/sub&gt;</td>
<td>recurrent stone former with mild disease and without residual stone(s) or stone fragments</td>
</tr>
<tr>
<td>R&lt;sub&gt;mo-res&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;s&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>RTA</td>
<td>renal tubular acidosis</td>
</tr>
<tr>
<td>SA</td>
<td>stone surface area</td>
</tr>
<tr>
<td>S&lt;sub&gt;1&lt;/sub&gt;</td>
<td>first time stone former without 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>THAM</td>
<td>trihydroxymethyl aminomethan</td>
</tr>
<tr>
<td>TSH</td>
<td>thyroid stimulating hormone</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>V</td>
<td>urine volume</td>
</tr>
<tr>
<td>w</td>
<td>width (of stone)</td>
</tr>
</tbody>
</table>
### A1. 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.

<table>
<thead>
<tr>
<th>Length mm</th>
<th>Width mm</th>
<th>Surface Area (mm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>0.8</td>
<td>0.8</td>
</tr>
<tr>
<td>1.6</td>
<td>1.6</td>
<td>2.56</td>
</tr>
<tr>
<td>2.2</td>
<td>2.2</td>
<td>5.04</td>
</tr>
<tr>
<td>2.8</td>
<td>2.8</td>
<td>7.84</td>
</tr>
<tr>
<td>3.4</td>
<td>3.4</td>
<td>11.56</td>
</tr>
<tr>
<td>4.0</td>
<td>4.0</td>
<td>15.36</td>
</tr>
<tr>
<td>4.6</td>
<td>4.6</td>
<td>19.36</td>
</tr>
<tr>
<td>5.2</td>
<td>5.2</td>
<td>23.52</td>
</tr>
<tr>
<td>5.8</td>
<td>5.8</td>
<td>27.84</td>
</tr>
<tr>
<td>6.4</td>
<td>6.4</td>
<td>32.16</td>
</tr>
<tr>
<td>7.0</td>
<td>7.0</td>
<td>36.49</td>
</tr>
<tr>
<td>7.6</td>
<td>7.6</td>
<td>40.84</td>
</tr>
<tr>
<td>8.2</td>
<td>8.2</td>
<td>45.22</td>
</tr>
<tr>
<td>8.8</td>
<td>8.8</td>
<td>49.64</td>
</tr>
<tr>
<td>9.4</td>
<td>9.4</td>
<td>54.08</td>
</tr>
<tr>
<td>10.0</td>
<td>10.0</td>
<td>58.56</td>
</tr>
<tr>
<td>10.6</td>
<td>10.6</td>
<td>63.04</td>
</tr>
<tr>
<td>11.2</td>
<td>11.2</td>
<td>67.52</td>
</tr>
<tr>
<td>11.8</td>
<td>11.8</td>
<td>72.00</td>
</tr>
<tr>
<td>12.4</td>
<td>12.4</td>
<td>76.56</td>
</tr>
<tr>
<td>13.0</td>
<td>13.0</td>
<td>81.12</td>
</tr>
<tr>
<td>13.6</td>
<td>13.6</td>
<td>85.68</td>
</tr>
<tr>
<td>14.2</td>
<td>14.2</td>
<td>90.24</td>
</tr>
<tr>
<td>14.8</td>
<td>14.8</td>
<td>94.80</td>
</tr>
<tr>
<td>15.4</td>
<td>15.4</td>
<td>99.36</td>
</tr>
<tr>
<td>16.0</td>
<td>16.0</td>
<td>103.92</td>
</tr>
<tr>
<td>16.6</td>
<td>16.6</td>
<td>108.50</td>
</tr>
<tr>
<td>17.2</td>
<td>17.2</td>
<td>113.08</td>
</tr>
<tr>
<td>17.8</td>
<td>17.8</td>
<td>117.64</td>
</tr>
<tr>
<td>18.4</td>
<td>18.4</td>
<td>122.20</td>
</tr>
<tr>
<td>19.0</td>
<td>19.0</td>
<td>126.76</td>
</tr>
<tr>
<td>19.6</td>
<td>19.6</td>
<td>131.32</td>
</tr>
<tr>
<td>20.2</td>
<td>20.2</td>
<td>135.88</td>
</tr>
<tr>
<td>20.8</td>
<td>20.8</td>
<td>140.44</td>
</tr>
<tr>
<td>21.4</td>
<td>21.4</td>
<td>145.00</td>
</tr>
<tr>
<td>22.0</td>
<td>22.0</td>
<td>149.56</td>
</tr>
<tr>
<td>22.6</td>
<td>22.6</td>
<td>154.12</td>
</tr>
<tr>
<td>23.2</td>
<td>23.2</td>
<td>158.68</td>
</tr>
<tr>
<td>23.8</td>
<td>23.8</td>
<td>163.24</td>
</tr>
<tr>
<td>24.4</td>
<td>24.4</td>
<td>167.80</td>
</tr>
<tr>
<td>25.0</td>
<td>25.0</td>
<td>172.36</td>
</tr>
</tbody>
</table>
A2. Devices for endoscopic disintegration of stones

ELECTROHYDRAULIC LITHOTRIPSY (EHL)
- Principle: electric current generates a flash at the tip of the probe; the resulting heat produces a cavitation bubble leading to a spheric shock wave.
- EHL is able to disintegrate stones of all chemical compositions.
- The undirected transmission of heat comes with a frequent risk of tissue injury, which accounts for the fact that EHL is not used as a standard procedure any more.
- Flexible electrohydraulic probes (EHL) are available in different sizes for use in semirigid or flexible scopes.

PNEUMATIC LITHOTRIPSY
- Pneumatic or ballistic lithotripsy probes with 2.4 F probes are frequently used in semirigid URS with disintegration rates of more than 90%.
- Safe usage and excellent cost effectiveness are advantages of these systems (1).
- The resulting mobilization of fragments into more proximal parts of the urinary tract may decrease the stone-free rate (1). The insertion of stone baskets or special collecting tools like the ‘stone cone’ can prevent this loss of fragments (1).
- Flexible probes are available but they potentially impair the maximal tip deflection of the scope (2).

ULTRASOUND LITHOTRIPSY
- Principle: ultrasound-based lithotripsy probes induce high-frequency oscillation which produces ultrasound waves (23,000-27,000 Hz). The ultrasound is transmitted to the tip of the probe, leading to a vibration that disintegrates the calculi upon contact.
- Combined ultrasound/pneumatic probes are available and can be used for semirigid URS and PNL (3,4).

LASER-BASED LITHOTRIPSY
- The neodymium:yttrium-aluminium-garnet (Nd:YAG) and the holmium:YAG (Ho:YAG) laser are mostly used for intracorporeal laser lithotripsy.
- Several fibres are available for both lasers, 365 µm fibres are typically used in semirigid, 220µm fibres in flexible scopes (2).
- Nd:YAG: frequency-doubled lasers (FREDDY, 532 and 1064 nm) are used for lithotripsy.
- Efficiency is low for hard stones like calcium oxalate-monohydrate stones.
- Cystine stones cannot be disintegrated with the Nd:YAG laser.
- Low cost of the Nd:YAG laser compared to the Ho:YAG laser makes this laser an interesting alternative.
- Ho:YAG: This laser type (2100 nm) can disintegrate stones of all chemical compositions.
- Currently the method of choice for stone treatment by flexible URS (5).
- In comparison with the Nd:YAG low tissue penetration of less than 0.5 mm results in reduced thermal injuries.
- The risk of stone migration is less than with ballistic probes.
- Laser probe must be in contact with the stone surface.
- Perforation of the ureter or the pelvic wall is possible. An increased incidence of strictures could, however, not be demonstrated (6).

A3. REFERENCES

