GUIDELINES ON UROLITHIASIS

H-G. Tiselius, D. Ackermann, P. Alken, C. Buck, P. Conort, M. Gallucci
1. BACKGROUND

Urolithiasis in its different forms is a frequently encountered urological condition. For many years it has been in the forefront of Urology. This might have changed with the advent of new technological approaches to manage less invasively urinary calculi. Nevertheless, urinary stones continue to occupy an important place in everyday urological practice. Therefore it remains essential and necessary to evaluate the current knowledge with respect to stone disease and to derive from these insights guidelines and recommendations for the diagnosis, medical, and interventional treatment and for prophylaxis and metapyllaxis of urinary tract calculi.

2. CLASSIFICATION

The different categories of stone formers are shown in Table 1. These different categories are useful for decisions on the metabolic evaluation and medical treatment of patients with stone disease (1).

3. RISK FACTORS

Risk factors for stone formation are listed in Table 2.

4. DIAGNOSIS

Diagnostic imaging

Patients with renal stone colic present with typical pain, vomiting, fever, and 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, a solitary kidney or when the stone diagnosis is in doubt. Routine examination involves a plain abdominal film of the kidneys, ureters, and bladder (KUB) plus an ultrasound examination. Alternatively, excretory pyelography (urography) can be performed. Excretory pyelography must not be carried out in patients with:

- An allergy to contrast media
- S-creatinine > 200 mmol/L
- On medication with metformin
- Myelomatosis.

Special examination that can be carried out include:

- Retrograde or antegrade pyelography
- Spiral (helical) unenhanced computed tomography (CT)
- Scintigraphy

When transurethral manipulation is necessary the diagnosis can be improved by retrograde pyelography and by antegrade pyelography when a nephrostomy has been inserted. Treatment with the anti-diabetic drug metformin should be stopped 2-3 days prior to administration of iodine containing contrast medium. There is a risk of impaired renal function due to lactic acidosis particularly in patients with reduced renal function (2,3). Spiral (helical) CT is a new non-invasive technique that might be considered when iodine containing contrast medium cannot be administered. Additional information regarding the renal function might be obtained by combining CT with contrast infusion (1-3).

Laboratory investigations

Routine laboratory investigations include: urinary sediment/dip stick test for diagnosis of red cells, white cells, nitrite and pH; and c-creatinine level. In case of fever, CRP (C-reactive protein), B-white cell count, and urine culture should be carried out. In case of vomiting, S-sodium, S-potassium should be measured. In order to avoid the need for future repeated blood analyses in the search of metabolic risk factors, it might be of value to assess already at this point of time S-calcium, and S-urate.

An analytical programme for patients with stone disease is shown in Table 3. Two collections for each set of analyses are recommended. The urine collections are repeated when necessary (4-6). A number of alternative collection options are feasible.
Option 1: Two 24 h collections:
- Sample 1 collected in a bottle containing 15ml of 6 mol/L hydrochloric acid (HCl)
- Sample 2 collected in a bottle containing 15ml of 0.3 mol/L sodium azide

Option 2: One 24 h collection:
- Sample collected in a bottle containing 15ml of 6 mol/L HCl

One 16 h urine collection and one 8 h urine collection:
- Sample 1 collected between 06.00 and 22.00 h in a bottle containing 10ml of 6 mol/L HCl
- Sample 2 collected between 22.00 and 06.00 in a bottle containing 10 ml of 0.3 mol/L sodium azide

Spot urine sample:
- The excretion of each urine variable is related to creatinine.

HCl prevents the precipitation of calcium oxalate and calcium phosphate in the bottle during storage. It also counters the oxidation of ascorbate to oxalate. In acidified samples, uric acid precipitates and has to be dissolved by alkalinization if the excretion of urate is of interest. Urate can be analysed in bottles where sodium azide is used. A urine collection without HCl is necessary for pH measurement. In this respect a sample collected with sodium azide is useful. A night urine sample in which the pH is measured soon after the collection has been completed is of advantage because pH alters during storage of urine.

Analytical work up of patients with calcium stones
A patient with uncomplicated disease is one who is stone free either after the first stone episode or who has a history of mild recurrent disease with long intervals between the stone episodes (Categories So, Rmo). The stone, blood and urine analyses recommended are shown in Table 4. A patient with a complicated 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 might also be considered in this respect (Categories: Rs, S res, Rm res, Risk). The stone, blood and urine analyses recommended are shown in Table 5. Urine collection should be postponed until at least 4 weeks have passed after stone removal or after an episode of obstruction and never in the presence of infection or hematuria. Special tests that may be required are shown in Table 6.

The purpose of analysing serum or plasma calcium is to identify patients with hyperparathyroidism (HPT) or other conditions associated with hyperkalemia. In case of a high calcium concentration (≥ 2.60 mmol/L) the diagnosis of HPT should be established by repeated calcium analyses and assessment of the parathyroid hormone level (17-22).

In those patients in whom a stone analysis has not been carried out, a high serum urate together with a radiolucent stone support the suspicion of a uric acid stone. A fasting morning urine (or a spot morning urine sample) should be used to measure pH (23). A pH above 5.8 in fasting morning urine raises the suspicion of incomplete or complete renal tubular acidosis (24). In the same fasting morning or spot urine sample bacteriuria and cystinuria can be excluded or confirmed by an appropriate dip-stick test and Brand's test (25), respectively.

The aim of adding serum-potassium to the analytical programme is to get further support for the RTA diagnosis in case this suspicion is raised. It is recommended that two 24 h urine collections are carried out in order to increase the likelihood of detecting urine abnormalities. Other collection periods such as 16 h, 17 h, 12 h, 4 h, or even spot urine samples are useful for this purpose provided a set of normal values are available for the chosen collection period (7-10).

It needs to be emphasized that the urine sample used for analysis of calcium, oxalate, citrate and phosphate has to be acidified preferably with hydrochloric acid (90 mmol/24 h portion). 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 derangement of urine composition.
- To prevent the in vitro oxidation of ascorbate to oxalate (26,27).

The following urine variables can be analysed in the acidified sample: calcium, oxalate, citrate, magnesium, phosphate, urea, sodium, chloride and potassium. Although creatinine might be slightly affected it has to be assessed in the same sample when creatinine related variables are used. Urate forms uric acid in the acidified urine and has to be analysed either following complete dissolution with alkali or in a urine sample that has not been acidified.

The optional analyses include: urea, phosphate and sodium reflect dietary factors of therapeutic significance. The protein intake can be derived from the urea excretion (U urea, mmol/L) and urine volume in litres (V) as follows (140):

\[
\text{protein (g)} = (U_{\text{urea}} \times V \times 0.18) + 13
\]
The net alkali absorption (NAE) in meq/24h can be derived as follows (141):

\[
NAE = (\text{Na} + \text{K} + \text{Ca} + \text{Mg}) - (\text{Cl} + 1.8\text{P})
\]

in which formula the 24 h urinary excretion of each variable is expressed in meq.

Estimates of the ion-activity products of CaOx (AP[CaOx]index) and CaP (AP[CaP] index) are derived as follows (115-121):

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

The urine volume (V) is expressed in litres and the urine variables in mmol excreted during the collection period. The factor 1.9 is specific for the 24 h period. For a 16 h urine sample this factor is 2.3.

The AP[CaOx] index approximately corresponds to \(10^8\text{AP}_{\text{CaOx}}\). The AP[CaP] index for a 24 h urine is calculated in the following way:

\[
\text{AP}[\text{CaP}]\text{index} = 2.7\times10^{-3}\text{Ca}^{1.07}\text{P}^{0.70}(\text{pH}-4.5)^{6.8}\text{Cit}^{-0.20}\text{V}^{-1.31}
\]

AP[CaP] index approximately corresponds to \(10^{15}\text{AP}_{\text{CaP}}\).

Factors for other collection periods can be found in reference 16.

**Stone composition**

Stones that pass spontaneously, are removed surgically or excreted as fragments following disintegration should be subjected to stone analysis to disclose their composition (28-32). The preferred analytical procedures are x-ray crystallography and infrared spectroscopy. All patients should have at least one stone analysed. Repeated analysis is indicated when any changes in urine composition, 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 might be based on the following observations:

- Qualitative cystine test (e.g. sodium nitroprusside test, Brand's test (25), cystine dip stick or any other cystine test)
- Bacteriuria/urine culture (in case of a positive culture: ask for urease producing microorganisms)
- Demonstration of crystals of struvite or cystine at microscopic examination of the urinary sediment
- S-urate (in the case a uric acid or urate stone is suspected)
- Urine pH (low in patients with uric acid stones, high in patients with infection stones)
- Radiographic appearance of the stone or conclusions from the ultrasound examination.

An appropriate quantitative or semi-quantitative analysis of the stone material should enable conclusions regarding the main constituent of constituents. The following calcium stones not associated with infection are referred to as radio-opaque stones:

- Calcium oxalate:
  - calcium oxalate monohydrate (COM)
  - calcium oxalate dihydrate (COD)
- Calcium phosphate
  - hydroxyapatite
  - carbonate apatite
  - octacalcium phosphate
  - brushite.

The following stones not associated with infection are referred to as uric acid/urate stones:

- Uric acid
- Sodium urate
- Ammonium urate.

Infection stones include:

- Magnesium ammonium phosphate
- Carbonate apatite.

Less common stone constituents include dihydroxyadenine, xantine and various other drug metabolites (e.g. sulphonamide, indinavir).

Calcium stones, uric acid/urate stones and cystine stones associated with infection are referred to as 'stones with infection'.
5. **TREATMENT**

**Pain relief**
Pain relief involves the administration by various routes of the following agents:
- Diclofenac sodium (Voltaren®)
- Indomethacin
- Hydromorphone hydrochloride + atropine sulphate (Dilaudin-Atropin®)
- Methamizol
- Pentazocin
- Tramadol

Treatment should be started with non-steroidal anti-inflammatory drugs, and changed 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. Diclofenac sodium affects GFR (Glomerular filtration rate) in patients with reduced renal function, but not in patients with normal GFR (33).

For patients with ureteral stones expected to pass spontaneously, suppositories or tablets of diclophenac sodium 50 mg administered twice daily during 3-10 days, might be useful in reducing the ureteral oedema 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 evaluation of the renal function should be confirmed with appropriate methods.

Where spontaneous passage is expected, the patient should be followed with appropriate methods until the stone has passed.

When pain relief cannot be obtained by medical means, drainage by stenting or percutaneous nephrostomy or stone removal should be carried out.

**Stone removal**

*General recommendations for stone removal*
A test for bacteriuria should be carried out in all patients in whom stone removal is planned. Screening with dip sticks might be sufficient in the uncomplicated case. In others, a urine culture is necessary. In all patients with a positive test for bacteriuria, with a positive urine culture or when there is a suspicion of an infective component, treatment with antibiotics should be started before the stone-removing procedure.

Bleeding disorders and anticoagulation treatment should be considered. These patients should be referred to an internist for appropriate therapeutic measures during the stone removing procedure. Treatment with salicylates should be stopped 10 days before the planned stone removal.

In patients with coagulation disorders, the following treatments are contra-indicated: ESWL, PNL, URS and open surgery. 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 needs to 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 (34-39). For patients with pacemaker it is wise to consult a cardiologist before undertaking an ESWL-treatment.

*Indications for active stone removal*
The size, site and shape of the stone at the initial presentation influence the decision to remove the stone. Also, the likelihood of spontaneous passage has to be evaluated. Spontaneous stone passage can be expected in up to 80% of patients with stones not larger than 4 mm. For stones with a diameter exceeding 7 mm the chance of spontaneous passage is very low (40-43). The overall passage rate of ureteral stones is:
- Proximal ureteral stones: 25%
- Mid ureteral stones: 45%
- Distal ureteral stones: 70%.

Stone removal usually is indicated for stones with a diameter exceeding 6-7 mm. Active stone removal is strongly recommended in patients with the following criteria:
- Persistent pain despite adequate medication
- Persistent obstruction with risk of impaired renal function
- Stone with urinary tract infection
- Risk of pyonephrosis or urosepsis
- Bilateral obstruction.
Principles for active stone removal: all sizes

For different stone situations and stone compositions the most appropriate methods for stone removal are given in Tables 7-9. Numbers (1, 2, 3...) have been designated 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 number 1.

Repeated sessions are frequently necessary for in situ extracorporeal shock wave lithotripsy (ESWL)-treatment of stones in the ureter. Large and impacted stones will demand the highest retreatment rate. In some situations, a ureteral catheter to push the stones up to the kidney or just to bypass the stones might improve the success rate in difficult cases (see APPENDIX 3). Uric acid stones can be localized with ultrasound, intravenous or retrograde contrast medium. In terms of distal uric acid ureteral stones, only those with an intramural position can be localized with ultrasound.

It is of note that only uric acid stones, not sodium urate or ammonium urate, can be dissolved by oral chemolytic treatment (44). For stones with a low radiodensity, the localisation 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 fragment. The principles for chemolytic treatment are outlined in the APPENDIX 11.

Blind basketing without radiographic or endoscopic control is not recommended.

In case of failure with the minimally invasive techniques an open surgical procedure might be required to remove the stone (see APPENDIX 10). Videoendoscopic retroperitoneal surgery is a minimally invasive alternative to open surgery. These techniques also have to be applied in case of contraindications for ESWL and ureteroscopy (URS), for example, 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. The advantages and disadvantages with these two procedures are discussed in the APPENDIX 2.

Principles for active stone removal: ≤ 20 mm and > 20 mm

The success rate of ESWL is directly related to the size (volume) of the concrement; the larger the stone the higher is the required retreatment rate (45-48). There is a debate as to whether large renal stones are best treated with ESWL or with PNL. The advantages and disadvantages of the two procedures are discussed in APPENDIX 6. An overview of treatment according to size and stone type is shown in Table 10.

Residual fragments, so called clinically insignificant fragments (CIRF) are common after ESWL treatment of stones in the kidney. Residual fragments usually accumulate in the lower calix and are more commonly seen in patients with an acute (< 90°) infundibulopelvic angle. For determination of the infunibulopelvic angle the reader is referred to APPENDIX 1.

For a kidney with stones or fragments in the lower caliceal system and with no functioning parenchyma in that part of the kidney, a lower pole resection is an alternative treatment that should be considered (49). 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. The principles for chemolytic treatment are given in APPENDIX 11. Double-J stenting before ESWL is recommended for stones with a largest diameter of more than 20 mm in order to avoid problem with an accumulation of stones obstructing the ureter: a Steinstrasse (50-62).

Stones composed of brushite or calcium oxalate monohydrate are characterized by particular hardness. This might mitigate in favour of a 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.

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, can be dissolved by oral chemolytic treatment.

Cystine stones are of two types, those responding well to ESWL and those responding badly (63). For the large ESWL-resistant stone, percutaneous nephrolithotomy with or without lithotripsy (PNL) will be the best alternative for efficient removal, thereby avoiding too much shock wave energy to the renal tissue.

It should be observed that also small stones residing in a calix can cause considerable pain or discomfort (64-70). In such cases, a narrow caliceal neck might require dilatation.

Complete or partial staghorn stones

A staghorn stone is defined as a stone with a central body and at least one caliceal branch. Whereas the partial staghorn stone fills up only a part of the collecting system the complete staghorn stone fills all calices and the renal pelvis. Treatment of both types is detailed in Table 11.
In patients with small staghorn stones and a non-dilated system, repeated ESWL-sessions with a stent can be a reasonable treatment alternative. The importance of stone size and anatomy of the renal collecting system is discussed in APPENDIX 9. Nephrectomy should be considered in 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 might be useful. The principles for chemolytic treatment are discussed in APPENDIX 11.

Managing special problems
Calix diverticulum stones are treated using ESWL, PNL (if possible) or retrograde ureteroscopy (URS). An optional method for removal of diverticular stones is video-endoscopic retroperitoneal surgery. The principles for video-endoscopic surgery is outlined elsewhere (71-75). In 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 might become asymptomatic as a result of the stone disintegration only. Horseshoe kidneys may be treated according to the principles for stone treatment presented above (76). It needs to be emphasised, however, that according to the anterior position of the kidney it is commonly necessary to carry out the ESWL treatment in prone position.

Recommendations for the removal of stones in transplanted kidneys are ESWL or PNL. For pelvic kidney, ESWL or video endoscopic laparoscopic surgery are recommended. ESWL, PNL or open surgery are the options in obese patients. The stones formed in a continent reservoir constitute a varied and often difficult problem (77-84). General directions for the management of this problem cannot be given. Each stone problem has to be considered and treated individually.

In patients with PUJ (Pelvo-Ureteral Junction) -obstruction, the stones can be removed at the same time as the outflow abnormality is corrected either by percutaneous endopyelotomy (85-99) or by open reconstructive surgery. Transureteral endopyelotomy (Acucise) is another alternative that might be considered provided the stones can be prevented from falling down in the pelvo-ureteral incision (100-110).

Residual fragments
The importance of so called clinically insignificant fragments (CIRF) is a matter of debate (111-123). Although some residual fragments will be the nidus of new stone formation this is not the case for all. Patients with residual fragments or stones should be regularly followed to monitor the course of the disease. Identification of biochemical risk factors and an appropriate stone prevention might be particularly indicated in patients with residual fragments or stones. In symptomatic patients, it is important to rule out obstruction and deal with 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 corresponding stone situation.

Steinstrabe
A Steinstrabe or a 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 (124). 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 percutaneous nephrostomy catheter (PN) usually results in passage of the fragments (125). For distally located accumulations of fragments, URS might be useful to remove the leading stone fragment by contact disintegration. Recommendations for treatment are given in Table12.

Preventive treatment in calcium stone disease
The 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 (126). This advice is valid irrespective of stone composition. For a normal adult the 24 h urine volume thereby should exceed 2000 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 the 24 h period and particular attention should be paid to situations with an unusual loss of fluid.

Diet should be of a common sense type, a mixed balanced diet with contributions from all food groups but without excesses of any kind (127). The intake of fruits and vegetables should be encouraged because of the beneficial effects of fibres (128). Care must be taken, however, to avoid fruits and vegetables rich in oxalate. Wheat bran is rich in oxalate and should be avoided. 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 those patients in whom a high excretion of oxalate has been demonstrated. The following products have a high content of oxalate (129):
Vitamin C in doses up to 4 g per day can be taken without increasing the risk of stone formation (130-132). Animal protein should not be ingested in excessive amounts (133-140). It is recommended that the animal protein intake is limited to approximately 150 g/day. Calcium intake should not be restricted unless there are very strong reasons for such an advice (141). The minimum daily requirement of calcium is 800 mg and the general recommendation is 1000 mg/day. Supplements of calcium are not recommended except in enteric hyperoxaluria, in which additional calcium should be ingested with meals.

The intake of food stiffs particularly rich in urate should be restricted in patients with hyperuricosuric calcium oxalate stone disease (142-147), as well as in patients with uric acid stone disease. The intake of urate should not be more than 500 mg/day. Below follows examples of food rich in urate (148):

<table>
<thead>
<tr>
<th>Food</th>
<th>mg urate/100 g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calf thymus</td>
<td>900</td>
</tr>
<tr>
<td>Liver</td>
<td>260-360</td>
</tr>
<tr>
<td>Kidneys</td>
<td>210-255</td>
</tr>
<tr>
<td>Poultry skin</td>
<td>300</td>
</tr>
<tr>
<td>Herring with skin, sardines, anchovies, sprats</td>
<td>260-500</td>
</tr>
</tbody>
</table>

**Pharmacological treatment of calcium stone disease**
Recommended pharmacological agents are shown in Table 13. The following forms of treatment are discouraged: magnesium oxide and magnesium hydroxide as monotherapy. Magnesium salts might, however, be useful in combination with thiazides (149). Cellulose phosphate and sodium cellulose phosphate have no place in the recurrence prevention of patients with calcium stone disease. Neither is there a place for synthetic or semisynthetic glycosaminoglycans (e.g. SPP).

The evidence and scientific basis for recommendations on the recurrence preventive treatment are summarized in APPENDIX 13.

**Pharmacological treatment of uric stone disease**
The pharmacologic treatment of a patient with uric stone disease is outlined in Table 14.

**Pharmacological treatment of cystine stone disease**
The pharmacologic treatment of a patient with cystine stone disease is outlined in Table 15.

**Pharmacological treatment of infection stone disease**
The pharmacologic treatment of a patient with infection stone disease is outlined in Table 16.

**Table 1: Categories of stone formers**

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-calcium stones</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection stone</td>
<td></td>
<td>INF</td>
</tr>
<tr>
<td>Uric acid / sodium urate / ammonium urate</td>
<td></td>
<td>UR</td>
</tr>
<tr>
<td>Cystine stone</td>
<td></td>
<td>CY</td>
</tr>
<tr>
<td>Calcium stones</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First time stone former without residual stone or fragments</td>
<td></td>
<td>So</td>
</tr>
<tr>
<td>First time stone former with residual stone or fragments</td>
<td></td>
<td>Sres</td>
</tr>
<tr>
<td>Recurrent stone former with a mild disease and without residual stone(s) or fragments</td>
<td></td>
<td>Rmo</td>
</tr>
<tr>
<td>Recurrent stone former with a mild disease and with residual stone(s) or fragments</td>
<td></td>
<td>Rres</td>
</tr>
<tr>
<td>Recurrent stone former with a severe disease and with or without residual stone(s) or fragments</td>
<td></td>
<td>Rs</td>
</tr>
<tr>
<td>Stone former with specific risk factors, irrespective of otherwise defined category</td>
<td></td>
<td>Risk</td>
</tr>
</tbody>
</table>
Table 2: Risk factors for stone formation

- Start of disease early in life: < 25 years
- Stone containing brushite
- Only one functioning kidney
- Diseases associated with stone formation:
  - hyperparathyreoidism
  - renal tubular acidosis (partial / complete)
  - jejunoileal bypass
  - Mb Crohn
  - intestinal resection
  - malabsorptive conditions
  - sarcoidosis
  - hyperthyreoidism
- Medication associated with stone formation:
  - calcium supplements
  - vitamin D supplements
  - acetazolamide
  - ascorbic acid in megadoses (> 4 g per day)
  - sulphonamides
  - triamterene
  - indinavir
- Anatomical abnormalities associated with stone formation:
  - tubular ectasia (MSK)
  - PUJ obstruction
  - calix diverticulum, calix cyst
  - ureteral stricture
  - vesico-ureteral reflux
  - horseshoe kidney
  - ureterocele

Table 3: Analytical programme for patients with stone disease

<table>
<thead>
<tr>
<th>Category</th>
<th>Blood analysis</th>
<th>Urine analysis</th>
<th>Prevention/follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>INF</td>
<td>S-creatinine</td>
<td>U-culture U-pH</td>
<td>YES</td>
</tr>
<tr>
<td>UR</td>
<td>S-creatinine S-urate</td>
<td>U-urate U-pH</td>
<td>YES</td>
</tr>
<tr>
<td>CY</td>
<td>S-creatinine</td>
<td>U-cystine U-pH</td>
<td>YES</td>
</tr>
<tr>
<td>S_0</td>
<td>YES (see Table 4)</td>
<td>Limited urine analysis (only fasting spot urine)</td>
<td>NO</td>
</tr>
<tr>
<td>S_res</td>
<td>YES (see Table 5)</td>
<td>YES (see Table 4)</td>
<td>YES</td>
</tr>
<tr>
<td>R_mo</td>
<td>YES (see Table 4)</td>
<td>Limited urine analysis (only fasting spot urine)</td>
<td>NO</td>
</tr>
<tr>
<td>R_m-res</td>
<td>YES (see Table 5)</td>
<td>YES (see Table 5)</td>
<td>YES</td>
</tr>
<tr>
<td>R_s</td>
<td>YES (see Table 5)</td>
<td>YES (see Table 5)</td>
<td>YES</td>
</tr>
<tr>
<td>RISK</td>
<td>YES (see Table 5)</td>
<td>YES (see Table 5)</td>
<td>YES</td>
</tr>
</tbody>
</table>
### Table 4: Analysis in patients with uncomplicated 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 analysed</td>
<td>Calcium</td>
<td>Fasting morning spot urine sample</td>
</tr>
<tr>
<td></td>
<td>Albumin$^1$</td>
<td>Dip-stick test</td>
</tr>
<tr>
<td></td>
<td>Creatinine</td>
<td>pH</td>
</tr>
<tr>
<td></td>
<td>Urate$^2$</td>
<td>Leucocytes / Bacteria$^4$</td>
</tr>
<tr>
<td></td>
<td>Cystine test$^3$</td>
<td></td>
</tr>
</tbody>
</table>

1. Either analysis of calcium + albumin to correct for differences in calcium concentration attributable to the albumin concentration, or direct analysis of ionised (free) calcium.
2. Optional analysis.
3. Cystine test if cystinuria cannot be or has not been excluded by other means.
4. Urine culture in case of bacteriuria.

### Table 5: Analysis in patients with uncomplicated 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 analysed</td>
<td>Calcium</td>
<td>Fasting morning spot urine sample</td>
</tr>
<tr>
<td></td>
<td>Albumin$^1$</td>
<td>Dip-stick test:</td>
</tr>
<tr>
<td></td>
<td>Creatinine</td>
<td>pH</td>
</tr>
<tr>
<td></td>
<td>Urate$^2$</td>
<td>Leucocytes / Bacteria</td>
</tr>
<tr>
<td></td>
<td>Potassium</td>
<td>Brand's test</td>
</tr>
<tr>
<td></td>
<td></td>
<td>24 hour urine collection</td>
</tr>
<tr>
<td></td>
<td>Calcium</td>
<td>Magnesium$^{2,5}$</td>
</tr>
<tr>
<td></td>
<td>Oxalate</td>
<td>Phosphate$^{2,5,6}$</td>
</tr>
<tr>
<td></td>
<td>Citrate</td>
<td>Urea$^{2,6}$</td>
</tr>
<tr>
<td></td>
<td>Urate$^4$</td>
<td>Sodium$^{2,6}$</td>
</tr>
<tr>
<td></td>
<td>Creatinine</td>
<td>Choride$^{2,6}$</td>
</tr>
<tr>
<td></td>
<td>Volume</td>
<td>Potassium$^{2,6}$</td>
</tr>
</tbody>
</table>

1. Either analysis of calcium + albumin to correct for differences in calcium concentration attributable to the albumin concentration, or direct analysis of ionised (free) calcium.
2. Optional analysis
3. 24 h urine can be replaced by a collection during other periods of the day such as a 16h collection (7-10). A spot urine sample can be used with creatinine related variables (10).
4. Because uric acid precipitates in acid solutions, urate has to be analysed in a sample that has not been acidified or following alkalisation to dissolve uric acid. When a 16 h urine sample has been collected in a bottle with an acid preservative, the remaining 8 hours of the 24 h period can be used to collect urine with sodium azide for analysis of urate.
5. Analysis of magnesium and phosphate is necessary for calculating estimates of the supersaturation with calcium oxalate (CaOx) and calcium phosphate (CaP) such as AP(CaOx) index and AP(CaP) index (11-16).
6. Urea, phosphate, sodium and potassium are used to reflect the dietary habits of the patient.
### pH-profile (150)
- Repeated measurements of pH during the 24h period.
- Frequent samples should be collected for immediate pH measurement with PH paper or a glass electrode.
- Sampling every second hour or otherwise as convenient.

### Acid loading (150-155)
Together with blood sampling for conclusions on whether the patient has a complete or an incomplete acidification defect.

- **08.00** Breakfast + NH4Cl-tablets (0.1 g / kg body weight), drink 150 ml
- **09.00** Collect urine and measure pH, drink 150 ml
- **10.00** Collect urine and measure pH, drink 150 ml
- **11.00** Collect urine and measure pH, drink 150 ml
- **12.00** Collect urine and measure pH, drink 150 ml
- **13.00** Collect urine and measure pH, lunch

With a pH of 5.4 or lower: No RTA (Renal tubular acidosis)

### Findings in blood

<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>

### Calcium loading (150)
First day:
- Calcium-poor diet (i.e. without milk products)
- **18.00** Last meal
- **20.00** 300 ml calcium-poor water
- **23.00** 300 ml calcium-poor water

Second day:
- **07.00** Empty the bladder and drink 600 mL calcium-poor water
- **07.00-09.00** First urine collection (basic)
- **09.00** Breakfast (One sandwich, butter, jam, two cups of fruit tea) + 1000 mg calcium
- **09.00-13.00** Second urine collection (at 11 am: 300 ml of calcium-poor water)

### Interpretation
- Normal: Basic: < 0.34; After calcium load: < 0.56
- Absorptive hypercalciuria: Basic: < 0.34; After calcium load: > 0.56
- Renal/resorptive: Basic: > 0.34; After calcium load: > 0.56

NH4Cl = ammonium chloride

---

**Table 6: Analytical work up inpatients with calcium stone disease**
**Table 7: Principles for active stone removal (all sizes) in the proximal ureter.**

| Radio-opaque stones | 1. ESWL in situ  
| 2. ESWL following retrograde manipulation of the stone (‘push up’)  
| 3. Percutaneous URS in antegrade direction  
| 4. URS + contact disintegration:  
| - semirigid ureteroscopy  
| - flexible ureteroscopy |

| Infection stones  
Stones with infection | 1. Antibiotics + ESWL in situ  
| 2. Antibiotics + ESWL following retrograde manipulation of the stone (‘push up’)  
| 3. Antibiotics + PNL + URS in antegrade direction  
| 4. Antibiotics + URS + contact disintegration:  
| - semirigid ureteroscopy or flexible ureteroscopy |

| Uric acid/urate  
Stones | 1. Stent + oral chemolysis  
| 2. ESWL in situ (with i.v. or retrograde contrast) + oral chemolysis  
| 3. Percutaneous URS in antegrade direction  
| 4. URS + contact disintegration:  
| - semirigid ureteroscopy or flexible ureteroscopy |

| Cystine stones | 1. ESWL in situ  
| 2. ESWL following retrograde manipulation of the stone (‘push up’)  
| 3. PNL + URS in antegrade direction  
| 4. URS + contact disintegration:  
| - semirigid ureteroscopy or flexible ureteroscopy |

ESWL = extracorporeal shock wave lithotripsy, also including piezolithotripsy; URS = ureteroscopy; PNL = percutaneous nephrolithotomy with or without lithotripsy.
### Table 8: Principles for active stone removal (all sizes) in the mid ureter

<table>
<thead>
<tr>
<th>Radio-opaque stones</th>
<th>1. ESWL <em>in situ</em>, prone position</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1. URS + contact disintegration:</td>
</tr>
<tr>
<td></td>
<td>- semirigid ureteroscopy or flexible ureteroscopy</td>
</tr>
<tr>
<td></td>
<td>2. Ureteral catheter or intravenous contrast + ESWL</td>
</tr>
<tr>
<td></td>
<td>2. Ureteral catheter with retrograde manipulation (‘push up’) + ESWL</td>
</tr>
<tr>
<td></td>
<td>3. Percutaneous antegrade URS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infection stones</th>
<th>1. Antibiotics + ESWL <em>in situ</em>, prone position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stones with infection</td>
<td>1. Antibiotics + URS + contact disintegration:</td>
</tr>
<tr>
<td></td>
<td>- semirigid or flexible ureteroscopy</td>
</tr>
<tr>
<td></td>
<td>2. Antibiotics + ureteral catheter or intravenous contrast + ESWL</td>
</tr>
<tr>
<td></td>
<td>2. Antibiotics + ureteral catheter with retrograde manipulation (‘push up’) + ESWL</td>
</tr>
<tr>
<td></td>
<td>3. Percutaneous antegrade URS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Uric acid/ urate stones</th>
<th>1. ESWL <em>in situ</em>, prone position</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1. URS + contact disintegration:</td>
</tr>
<tr>
<td></td>
<td>- semirigid or flexible ureteroscopy</td>
</tr>
<tr>
<td></td>
<td>2. Ureteral catheter or intravenous contrast + ESWL</td>
</tr>
<tr>
<td></td>
<td>2. Ureteral catheter with retrograde manipulation (‘push up’) + ESWL</td>
</tr>
<tr>
<td></td>
<td>2. Stent + oral chemolysis</td>
</tr>
<tr>
<td></td>
<td>3. Percutaneous antegrade URS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cystine stones</th>
<th>1. ESWL <em>in situ</em>, prone position</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1. URS with lithotripsy:</td>
</tr>
<tr>
<td></td>
<td>- semirigid or flexible ureteroscopy</td>
</tr>
<tr>
<td></td>
<td>2. Ureteral catheter + ESWL</td>
</tr>
<tr>
<td></td>
<td>2. Ureteral catheter with retrograde manipulation (‘push up’) + ESWL</td>
</tr>
<tr>
<td></td>
<td>3. Percutaneous antegrade URS</td>
</tr>
</tbody>
</table>

ESWL = extracorporeal shock wave lithotripsy, also including piezolithotripsy; URS = ureteroscopy.
### Table 9: Principles for active stone removal (all sizes) in the distal ureter

<table>
<thead>
<tr>
<th>Stone Type</th>
<th>Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radio-opaque stones</strong></td>
<td>1. ESWL in situ&lt;br&gt;1. URS + contact disintegration:&lt;br&gt;- rigid ureteroscopy + US, laser or electrohydraulic disintegration&lt;br&gt;- semirigid ureteroscopy&lt;br&gt;2. Ureteral catheter + ESWL</td>
</tr>
<tr>
<td><strong>Infection stones</strong></td>
<td>1. Antibiotics + ESWL in situ&lt;br&gt;1. Antibiotics + URS + contact disintegration&lt;br&gt;2. Antibiotics + PN + ESWL in situ&lt;br&gt;2. Antibiotics + ureteral catheter + ESWL</td>
</tr>
<tr>
<td><strong>Stones with infection</strong></td>
<td>1. Antibiotics + ESWL in situ&lt;br&gt;1. Antibiotics + URS + contact disintegration&lt;br&gt;2. Antibiotics + PN + ESWL in situ&lt;br&gt;2. Antibiotics + ureteral catheter + ESWL</td>
</tr>
<tr>
<td><strong>Uric acid/urate stones</strong></td>
<td>1. ESWL in situ (i.v. contrast medium)&lt;br&gt;1. URS + contact disintegration&lt;br&gt;2. Ureteral catheter (+ contrast medium) + ESWL&lt;br&gt;3. PN + antegrade contrast + ESWL in situ</td>
</tr>
<tr>
<td><strong>Cystine stones</strong></td>
<td>1. ESWL in situ&lt;br&gt;1. URS + contact disintegration&lt;br&gt;- rigid ureteroscopy + US, laser or electrohydraulic disintegration&lt;br&gt;- semirigid ureteroscopy&lt;br&gt;2. Ureteral catheter + ESWL</td>
</tr>
</tbody>
</table>

ESWL = extracorporeal shock wave lithotripsy, also including piezolithotripsy; URS = ureteroscopy; PN = percutaneous nephrostomy
Table 10: Principles for active stone removal in stones sized \(\leq 20 \text{ mm}\) and \(> 20 \text{ mm}\) and in all positions in the kidney

<table>
<thead>
<tr>
<th>Stone size (\leq 20 \text{ mm})</th>
<th>1. ESWL</th>
<th>2. PNL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radio-opaque stones</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection stones</td>
<td>1. Antibiotics + Stent + ESWL</td>
<td>2. Antibiotics + PNL</td>
</tr>
<tr>
<td>Stones with infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uric acid/urate stones</td>
<td>1. Oral chemolysis</td>
<td>2. Stent + ESWL + oral chemolysis</td>
</tr>
<tr>
<td>Cystine stones</td>
<td>1. ESWL</td>
<td>2. PNL</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stone size (&gt; 20 \text{ mm})</th>
<th>1. PNL</th>
<th>2. ESWL with or without stenting</th>
<th>3. PNL + ESWL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radio-opaque stones</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection stones</td>
<td>1. Antibiotics + PNL</td>
<td>2. Antibiotics + ESWL (with or without stenting)</td>
<td>3. Antibiotics + PNL + ESWL</td>
</tr>
<tr>
<td>Stones with infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uric acid/urate stones</td>
<td>1. Oral chemolysis</td>
<td>2. Stent + ESWL + oral chemolysis</td>
<td></td>
</tr>
<tr>
<td>Cystine stones</td>
<td>1. PNL</td>
<td>2. PNL + ESWL</td>
<td>3. PNL + flexible nephroscopy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Open or videoendoscopic retroperitoneal surgery</td>
<td></td>
</tr>
</tbody>
</table>
Table 11: Active stone removal of complete and partial staghorn stones.

<table>
<thead>
<tr>
<th>Radio-opaque Stones</th>
<th>1. PNL</th>
<th>2. PNL + ESWL</th>
<th>3. ESWL + PNL</th>
<th>4. Open surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stones with Infection</td>
<td>1. PNL</td>
<td>2. PNL + ESWL</td>
<td>3. PNL/ESWL + oral chemolysis</td>
<td>3. ESWL + PNL</td>
</tr>
<tr>
<td>Uric acid/urate stones</td>
<td>1. PNL</td>
<td>2. PNL + ESWL</td>
<td>2. PNL/ESWL + oral chemolysis</td>
<td>3. ESWL + PNL</td>
</tr>
<tr>
<td>Cystine stones</td>
<td>1. PNL</td>
<td>2. PNL + ESWL</td>
<td>3. ESWL + PNL</td>
<td>4. Open surgery</td>
</tr>
</tbody>
</table>

Table 12: Recommendations for treatment of Steinstrabe.

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

PN = Percutaneous Nephrotomy
<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommended treatment</th>
<th>Sometimes useful</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypercalciuria</td>
<td>Thiazides</td>
<td>Orthophosphate</td>
<td>Potassium supplements should be given with thiazides&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Thiazides + Magnesium</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Alkaline citrate</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperoxaluria</td>
<td>Alkaline citrate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enteric hyperoxaluria</td>
<td>Alkaline citrate</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Calcium supplements</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary hyperoxaluria</td>
<td>Pyridoxine</td>
<td>Orthophosphate</td>
<td>These patients should be referred to someone with experience of this disease</td>
</tr>
<tr>
<td></td>
<td>Alkaline citrate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypocitraturia</td>
<td>Alkaline citrate&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RTA</td>
<td>Alkaline citrate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brushite stone</td>
<td>Thiazides + Magnesium</td>
<td></td>
<td>Potassium supplements should be given with thiazides&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Alkaline citrate&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperuricosuric and CaOx stone</td>
<td>Allopurinol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low inhibitory activity&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Alkaline citrate&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No abnormality</td>
<td>Alkaline citrate&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
<td>Repeated analysis of Urine composition!</td>
</tr>
</tbody>
</table>

<sup>1</sup> In case the inhibition of crystal growth or crystal aggregation has been assessed.

<sup>2</sup> Potassium citrate or potassium-magnesium citrate.

<sup>3</sup> Potassium citrate, sodium potassium citrate or potassium-magnesium citrate.

<sup>4</sup> Orthophosphate is not a first hand alternative, but it can be used in patients with hypercalciuria who do not tolerate thiazides.

<sup>5</sup> Potassium supplements are necessary to avoid hypokalemia and hypocitraturia caused by hypokalemic intracellular acidosis.
### Table 14: Pharmacological treatment of uric stone disease

<table>
<thead>
<tr>
<th>Prevention</th>
<th>A high fluid intake. 24h urine volume exceeding 2000 ml. Alkalinazation:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Potassium citrate 3 - 7 mmol x 2-3</td>
</tr>
<tr>
<td></td>
<td>• Sodium-potassium citrate 9 mmol x 2-3</td>
</tr>
<tr>
<td></td>
<td>In patients with a high S-urate or a high U-urate:</td>
</tr>
<tr>
<td></td>
<td>• Allopurinol 300 mg x 1</td>
</tr>
<tr>
<td>Medical dissolution of uric acid stones</td>
<td>A high fluid intake; 24 h urine flow exceeding 2000 ml</td>
</tr>
<tr>
<td></td>
<td>Alkalinazation:</td>
</tr>
<tr>
<td></td>
<td>• Potassium citrate 6-10 mmol x 3</td>
</tr>
<tr>
<td></td>
<td>• Sodium-potassium citrate 9-18 mmol x 3</td>
</tr>
<tr>
<td></td>
<td>In patients with a high S-urate or a high U-urate:</td>
</tr>
<tr>
<td></td>
<td>• Allopurinol 300 mg x 1</td>
</tr>
</tbody>
</table>

### Table 15: Pharmacological treatment of cystine stone disease.

- A high fluid intake should be recommended so that the 24 h urine volume exceeds 3000 ml. To achieve this goal the intake should be at least 150 ml/h.
- Alkaline citrate should be given to achieve a pH > 7.5:
  - potassium citrate 3-10 mmol x 2-3
- With a cystine excretion below 3 - 3.5 mmol/24h:
  - ascorbic acid 3 - 5 g / day
- With a cystine excretion above 3-3.5 mmol/24 h:
  - Thiola (Tiopronin) (250-2000 mg/day) or
  - Captopril (75-150 mg)

### Table 16: Pharmacological treatment of infection stone disease

<table>
<thead>
<tr>
<th>Definition</th>
<th>Stone composed of magnesium ammonium phosphate and carbonate apatite and caused by urease producing micro-organisms.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Surgical removal of the stone material as completely as possible</td>
</tr>
<tr>
<td></td>
<td>• Antibiotic treatment:</td>
</tr>
<tr>
<td></td>
<td>- short term antibiotic course</td>
</tr>
<tr>
<td></td>
<td>- long-term antibiotic course</td>
</tr>
<tr>
<td></td>
<td>• Acidification</td>
</tr>
<tr>
<td></td>
<td>Ammonium chloride 1 g x 2 - 3</td>
</tr>
<tr>
<td></td>
<td>Methionine 500 mg x 2 - 3</td>
</tr>
<tr>
<td></td>
<td>• In very selected cases with severe infections, treatment with acetohydroxamic acid (Lithostat) might be a therapeutic option.</td>
</tr>
</tbody>
</table>
REFERENCES

1. Tiselius HG.

2. Nawaz S, Cleveland T, Gaines PA, Chau P.


4. Hölzermann K, Hofbauer J, Szabo N.

5. Hess B, Hasler-Strub U, Ackermann D, Jaeger PH.

6. Bek-Jensen H, Tiselius HG.

7. Berg C, Larson L, Tiselius HG.

8. Tiselius HG.

9. Bek-Jensen H, Tiselius HG.

10. Strohmaier WL, Hoelz K-J, Bichler KH.

11. Tiselius HG.

12. Tiselius HG.

13. Tiselius HG.

14. Tiselius HG.

15. Tiselius HG.

16. Tiselius HG.

17. Halabé A, Sutton RAL.


19. Broadus AE.

20. Thomas WC.

21. Rose GA.

22. Alvarez-Arroyo MV, Traba ML, Rapade A, de la Piedra C.

23. Elliot JS, Sharp RF, Lewis L.
24. Chafe L, Gault MH.  

25. Brand E, Harris MM, Bildon S.  
Cystinuria: Excretion of a cystine complex which decomposes in the urine with the liberation of free cystine. J Biol Chem 1930; 86:315-.


27. Wandzilak TR, D’Andre SD, Davis PA, Williams HE.  

28. Asper R.  

29. Herring LC.  

30. Reveillaud RJ, Daudon M, Protat MF, Ayrole G.  

31. Otnes B.  

32. Leusmann DB, Blaschke R, Schwan dt W.  


34. O’Regan S, Laberge I, Homsy Y.  

35. Kroovand RL.  

36. Marberger M, Hofbauer J.  

37. Carringer M, Swartz R, Johansson JE.  

38. Scarpa RM, De Lisa A, Usai E.  


40. Sandegård E.  

41. Morse RM, Renick MI.  

42. Ibrahim AIA, Shetty SE, Awad RM, Patel KP.  

43. Miller OF, Kane CJ.  

44. Wilson CM.  
Clinical and laboratory approaches for evaluation of nephrolithiasis. J Urol 1987; 141: 770-.


47. Valancien G, Deformestraux N, Leo JP et al.  


72. Gaur DD.
73. Gaur DD.
74. Gaur DD, Agarwal DK, Purohit KC, Darshane AS.
76. Locke DR, Newman RC, Steinbock GS, Finlayson B.
77. Chen KK, Chang LS, Chen MTC, Lee YH.
78. Weinerth JL, Webster GD.
79. Khatri VP, Walden T, Pollack MS.
80. Chin JL, Denstedt JD.
82. Cohen TD, Streem SB, Lammet G.
83. Terai A, Ueda T, Kakehi Y et al.
84. Assimos DG.
85. Ramsay JWA, Miller RA, Kellett MJ, Blackford WN, Wickham JEA, Whitfield HN.
86. Brannen GE, Bush WH, Lewis GP.
87. Payne SR, Coptcoat MJ, Kellett MJ, Wickham JEA.
89. Kuenkel M, Korth K.
90. Gelet A, Martin X, Dessouki T.
91. Cassis AN, Brannen GE, Bush WH, Correa RJ, Chambers M.
92. Motola JA, Badlani GH, Smith AD.
93. Klahr S, Chandhoke P, Clayman RV.
94. Motola JA, Fried R, Badlani GH, Smith AD.
95. Gerber GS, Lyon ES.
96. Nakamura K, Baba S, Tazaki H.
97. Bagley DH, Liu JB, Goldberg BB, Grasso M.
98. Danuser H, Ackermann DK, Böhlen D, Studer UE.

99. Van Cangh PJ.
Editorial: Endopyelotomy - a panacea for ureteropelvic junction obstruction? J Urol 1998; 159: 66-.

100. Gallucci M, Alpi G, Ricciuti GP, Cassanelli A, Persechino F, Di Silverio F.

101. Chowdhury SD, Kenogbon J.

102. Chandhoke PS, Bogaert GA, Mevorach RA, Kogan AB, Stoller ML.

103. Bolton DM, Combe M, Ramackers JM et al.

104. Conlin MJ, Bagley DH.

105. Krings F, Tuerk C, Steinkogler I, Marberger M.


107. Eisenberger F, Bub P, Schmidt A.

108. Streem SB, Yost A, Mascha E.

109. Liedl B, Schuster C, Lunz C.

110. Cicerello E, Merlo F, Gambararo G et al.

111. Fine JK, Pak YC, Preminger GM.


123. Sabnis RB, Naik K, Patel SH, Desai MR, Bapat SD.

124. Tolley DA.

125. Griffith DP.


128. Ebusino S, Morimoto S, Yasukawa S, Ohkawa T.

129. Hess A, Tiselius HG, Jahnem A.
Urine stones - Diagnosis, Treatment and Prevention of Recurrence. Karger 1996; pp. 62-.

130. Wandelzak TR, D’André SD, Davis PA, Williams HE.

131. Sutton RAL, Walker VR.

132. Auer BL, Auer D, Rodger AL.

133. Robertson WG.

134. Yendt ER.

135. Iguchi M, Umekawa T, Ishikawa Y et al.

136. Kok DJ, Iestra JA, Doorenbos CM, Papapoulos SE.

137. Goldfarb S.

138. Hughes J, Norman RW.

139. Holmes RP, Goodman HO, Hart LJ, Assimos DG.

140. Buck AC.

141. Curhan GC, Willett WC, Rimm EB, Stampfer MJ.

142. Coe FL.

143. Pak CYC, Holt K, Britton F, Peterson R, Crowther C, Ward D.
144. Hofbauer J, Zechner O.

145. Sarig S.

146. Zechner O.

147. Ettinger B.

Urinary stones - diagnosis, treatment and prevention of recurrence. Karger, 1996; 88-.

149. Ahlstrand C, Sandvall K, Tiselius HG.

Urinary stones - diagnosis, treatment and prevention of recurrence. Karger 1996: 52-.


152. Knispel HH, Fitzner R, Kaiser M, Butz M.

153. Nutahara K, Higashihara E, Ishii Y, Niijima T.

154. Osther PJ, Hansen AB, Røhl HF.

155. Buckalew VM Jr.
APPENDIX

1. THE INFUNDIBULO-PELVIC ANGLE

2. ESWL FOR REMOVAL OF RENAL STONES

Fifteen years after the world-wide spread of the extracorporeal shock wave lithotripsy (ESWL) technology with consequent deep changes in lithotripters, indications, the types of complication and complication rate have changed. In fact, lithotripter machines are smaller and in the vast majority of cases, part of a uroradiological table which allows the performance of all diagnostic and ancilliary procedures related to an ESWL treatment. All these measures give an efficacy that is the same or superior to that of the first lithotripters, with lower cost and greater affordability. Even the indication criteria have been modified by the advent of this new technology. Currently, the absolute contraindications to the ESWL treatment are restricted to severe skeletal malformations, severe obesity, pregnancy and aortic and/or renal artery aneurysms (1, 2). Based on the classification proposed by Di Silverio and Gallucci (3) and the evaluation of the stone surface area proposed by Lam et al (4), ESWL is most efficacious for stones smaller than 20 mm in diameter. If the calculus is localised in the lower calix, percutaneous surgery should be the best treatment alternative for stones with a diameter greater than 1.5 cm. Otherwise the percutaneous approach should be considered as the best treatment. Stones with a diameter smaller than 10 mm have an 84% (64-92%) stone free rate. This percentage decreases to 77% (59-81%) for stones with a diameter between 10 mm and 20 mm and is 63% (39-70%) for stones with a diameter greater than 20 mm (5-7).

Stone composition can play an important role in the processes of fragmentation and subsequent elimination of these fragments. Uric acid stones and calcium oxalate dihydrate stones have a better coefficient of fragmentation than calcium oxalate monohydrate, and cystine stones are harder and more resistant to ESWL. Success rates from these two groups of stones were shown to be 38-81% and 60-63%, respectively (8). Considering cystine stones with a diameter less than 15 mm, the stone free rate is about 71%, a figure that drops to 40% for stones with a diameter exceeding 20 mm (9). Thus, for cystine stones with a diameter greater than 15 mm, ESWL as monotherapy is not to be recommended.

The retreatment rate for calcium oxalate monohydrate stones was 10.3%, for struvite stones 6.4 % and for stones composed of calcium oxalate dihydrate 2.8% (10). In the presence of a hydrenephrotic and/or an infected kidney, a nephrostomy should be positioned before the ESWL procedure and antibiotic therapy administered 5 days before the planned treatment. Hydrenephrosis can seriously affect the result of ESWL; in fact the percentage of success can change from 83% without hydrenephrosis to 50% with medium grade hydrenephrosis and to a complete failure with severe hydrenephrosis (11).

The number of ESWL sessions should not exceed the three to five (dependent on the lithotripter), otherwise a percutaneous lithotripsy should be considered as a valid option. In case of infected stones, antibiotic therapy should be administered 3 days before the ESWL treatment and continued for at least 4 days after the treatment. From the literature, it is not clear what the interval between two ESWL sessions should be. Generally, this interval should be greater if an electrohydraulic lithotripter is employed (4-5 days) and shorter if a piezoelectric one is used (2 days).
The maximum number of shock waves that should be delivered at each session has not been defined. This number depends exclusively on the type of lithotripter. With the electrohydraulic lithotripter (which is most powerful), not more than 3500 shock waves per session should be given. While with the piezoelectric lithotripter, this limit could be 5000 shock waves per session.

A problem that could affect the results of ESWL is a malformed kidney. These malformations can be the reason for the stone formation due to altered mechanisms of urine elimination and thus to an impaired stone fragment passage. The rate of auxiliary procedures in these patients is high and only 50% of the patients are stone free at 3-month follow-up (12). In the horseshoe kidney, the incidence of stones is around 20%. Success rate depends mainly on the lithotripter used and varies between 53% to 60%; the incidence of auxiliary procedures is 24% and the retreatment rate 27% (13). Some authors claim that percutaneous surgery is the treatment of choice for these patients (14, 15), but the greater morbidity and complication rate of this technique has prompted us to affirm that percutaneous lithotripsy could be used when the previous ESWL treatment has failed. Concerning medullary sponge kidneys and nephrocalcinosis, some recent papers claimed the validity of ESWL for patients with these pathologic conditions (16, 17). In ectopic kidneys, the efficacy of ESWL is strictly related to the position of the kidney. Regardless, ESWL could be considered as the first option in the management of stones in these cases. In transplanted kidneys, the efficacy of ESWL is similar to that of normal kidneys. ESWL treatment is well tolerated in the transplanted kidney without any particular side effects (18).

REFERENCES

3. **ESWL FOR REMOVAL OF URETERAL STONES**

ESWL has been used extensively for treatment of patients with stones in the proximal, middle and distal parts of the ureter. It was recognized early, however, that ureteral stones were less easily disintegrated than renal stones and frequently required a higher shock wave energy as well as a greater number of shock waves. With increased experience and technical achievements, with or without low invasive auxiliary procedures, it is possible in most cases to remove the stone(s) without general or regional anaesthesia and with a low rate of complications and side-effects. There is, however, a variable success rate reported in the literature, obviously related to the type of equipment, size and composition of the stone, degree of impaction and to what extent repeated shock wave sessions are accepted. The experience of the operator is also a factor of great importance.

Ureteral stones can be treated *in situ* with or without a ureteral catheter or stent bypassing the stone, with a catheter up to the stone or following retrograde manipulation of the stone up to the kidney (push back procedure). A detailed comparison of different results is indeed very difficult because of the diversity with which the data are presented in the reports.

It is obvious from the reported results that with adequate equipment the vast majority of ureteral stones at all levels of the ureter can be successfully disintegrated and eliminated following ESWL with sedo-analgesia only, and occasionally with the assistance of limited intrarureteral manipulation.

### 3.1 PROXIMAL URETERAL STONES

ESWL treatment of proximal ureteral stones with or without low-invasive auxiliary procedures gives a stone free rate of 62-100%. Retreatment is carried out in up to 38% of patients, with an average number of sessions of 1.0-1.8 (1-14).

### 3.2 MID URETERAL STONES

A stone-free rate of 46-100%, a retreatment rate up to 38% and 1.0-1.9 sessions per patient were recorded for ESWL treatment of mid ureteral stones (1-4,11,12,15-17).

### 3.3 DISTAL URETERAL STONES

For distal ureteral stones, the stone free rate varied between 72 and 100%. Retreatment rate and the number of sessions were comparable with those for proximal ureteral stones (1-4,6,10-12,18,19).

### 3.4 IN SITU DISINTEGRATION

When only those patients were considered in whom it was clearly stated that the treatment had been carried out *in situ* without manipulation, the success rate varied between 62 and 100%. (1,2,4,5,8,10,13,15,20,22)

### 3.5 RETROGRADE MANIPULATION OF THE STONE

The ‘push-back’ technique has been applied in order to avoid problems with insufficient disintegration of ureteral stones. In comparative studies, retrograde manipulation resulted in stone-free rates of 73-100%, (8,13, 20, 21) which should be compared with stone-free rates of 62-97% following *in situ* treatment. (1,2,4,5,8,10,13,15,20,22) It needs to be emphasized, however, that the success rate in pushing the stone up to the kidney varied considerably and it can be extremely difficult to manipulate large or impacted stones.

### 3.6 STENTING

The value of an expanding chamber around the stone is the rational for using a ureteral catheter that either bypasses the stone or is placed just below the stone. Although slightly better results have been reported, the retreatment rate was usually not significantly altered by this procedure (4,11,15,20-24). It might, however, be of some help to use a ureteral catheter when large and impacted ureteral stones are treated, but it is difficult to find definite evidence for this assumption in the literature. Another reason for stenting might be to aid in the
localization of small and less radio-opaque stones, as well as to fill the collecting system with contrast medium for detecting radiolucent stones.

REFERENCES


4. URETEROSCOPY FOR REMOVAL OF URETERAL STONES.

During the past two decades ureteroscopy has dramatically changed the management of ureteral calculi. Ureteroscopy is extensively used in many urologic departments all over the world. However, it is more invasive than ESWL, and the treatment of choice for stones 1 cm or larger is still controversial.

New ureteroscopes and lithotripsy devices have recently become available. Literature during the last 3 years was reviewed to assess whether improvements in the field of ureteroscopy has lead to new therapeutic modalities and therefore new recommendations.

4.1 STANDARD 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 preoperative plain film of the urinary tract will confirm the location of the stone. The operating room must have a fluoroscopic equipment.

Under general, spinal anaesthesia or intravenous sedation the patient will be placed in the lithotomy position. The procedure starts with rigid or flexible cystoscopy. Then 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 the 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) or a semi-rigid ureteroscope (6.0-8.5 F), alongside a second 0.035-inch safety guide wire with floppy tip.

Endoscopic lithotripsy requires the use of different devices in order to brake the stone into dust or fragments with a diameter of 2 mm or less. The stone may be fragmented either by ultrasonic lithotripsy, electrohydraulic lithotripsy, laser lithotripsy or ballistic (or pneumatic) lithotripsy. Small stones and fragments under 5 mm in diameter are better retrieved with a basket or a grasper (3,4).

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

Stent placement at the end of the procedure is optional (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 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 between 10 to 60 minutes. If the stone is impacted, the best approach is to insert a ureteral stent for a couple of days, prior to the ureteroscopy (2). Patients should be followed by plain abdominal film, ultrasonography or IVP after 2 to 12 weeks (2, 5).

4.2 ANAESTHESIA
Improvement of ureteroscopes and stone retrieval instruments allow ureteroscopic procedures under sedation analgesia with a similar success rate (88-97%) to general anaesthesia. This is particularly true for distal ureteral stones in women (2,6,7).

4.3 ASSESSMENT OF DIFFERENT DEVICES
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 dilatation of the intramural ureter in more than 75% of cases. In the lower ureter, a flexible ureteroscope is not suitable because of its tendency to fall back into the bladder (1,3).

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 ureteroscopy (12,17,18). A 365 mm Holmium:YAG laser fibre is the best choice for ureteral stones, as minimal deflection is required to access the stone. The 200 mm fibre is more expensive and should be reserved for fragmentation of intrarenal calculi (12,19). The ideal energy and frequency settings are less than 1.0 J and 5-10 Hz. If manipulated with care, laser does not damage the ureteral mucosa (16,18,20). The operating time for laser lithotripsy between 7 to 45 min is acceptable (18).

Laser lithotripsy using Candela has similar results to the Holmium:YAG laser (21). Holmium:YAG lithotripsy seems to give better stone-free results at 3 months than electrohydraulic lithotripsy (97% vs. 87%) for distal ureteral stones (5). But for ureteral calculi less than 15 mm in diameter, laser lithotripsy will require longer time than the electrohydraulic technique (5).

Ballistic lithotriptors (pneumatic or electropneumatic) using a 2.4 probe in a semi-rigid ureteroscope provide excellent fragmentation rates (90-96%). Low capital cost and simple and safe handling are major advantages of this type of device. Its cost-effectiveness is three fold that of laser lithotripsy (9,14,22-24). Nevertheless, migration toward the renal pelvis from mid or proximal ureter might be a limiting factor of ballistic lithotripsy (25).

Basket stents
Ureteroscopic removal of small ureteral stones with a basket is a relatively quick procedure with a lower morbidity rate than with 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 tip-less basket is more effective than flat wire basket (4,13,23). Laser or electrohydraulic lithotripsy might break the wires of the basket (16).

4.4 DILATATION AND STENTING
Attempts to modify the standard technique of dilatation and stenting have been conducted during recent years. Reduced dilatation (0-40%), operating time and post-operative ureteral stenting have resulted from the use of thin ureteroscopes. Patients are easily treated on an out-patient basis. Routine stent placement following uncomplicated ureteroscopy may be unnecessary. Patient discomfort is modest and satisfactorily controlled by oral analgesics (21,26).

4.5 CLINICAL RESULTS
The Ureteral Clinical Guidelines Panel of the American Urological Association has conducted a meta-analysis of relevant studies between 1966 and 1996. Members produced a report for guidelines in August 1997, which was published in *J Urol* (27). When the material was stratified into proximal and distal ureteral stones, the overall stone-free rates were 72% and 90%, respectively. For ureteral stones with a diameter of 10 mm or less 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 the 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 higher than the results reviewed before 1997 (25,28,29). Similar results were observed in children and in obese patients (11,30).

With only one endoscopic procedure, 95% of patients could be successfully treated. The best results were reported with the Holmium:YAG laser lithotripsy, especially in the proximal ureter (5). This last technique might be a good alternative to ESWL, for example, in obese patients or in those with less visible stones (9,11).

4.6 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 reported complication; estimated rate was 1%.

There is a pronounced relationship between the complication rate and the equipment used and/or the expertise of the urologist (31,32). The overall complication rates reported in the 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). Autologus transplantation or uretero-ileoplasty are the methods of choice in case 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).
4.7 CONCLUSION

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

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 of the operating time and complication rate. Randomized and prospective studies are needed in order to compare all forms of stone removal from the ureter.

REFERENCES

1. Grasso M, Conlin M, Bagley D.
2. Elashry OM, Elbahnasy AM, Rao GS, Nakada SY, Clayman RV.
3. Harmon WJ, Sershon PD, Blute ML, Patterson DE, Segura JW.
4. Netto Junior NR, de Almeida Claro J, Esteves SC, Andrade EFM.
5. Teichman JM, Rao RD, Rogenes VJ, Harris JM.
6. Hosking DH, Bard RJ.
7. Yalçinkaya F, Topaloglu H, Ozmen E, Unal S.
8. Ferraro RF, Abraham VE, Cohen TD, Preminger GM.
10. Yip KH, Lee CW, Tam PC.
11. Nguyen TA, Belis JA.
12. Tawfiek ER, Bagley DH.
13. Honey RJ.
14. Gould DL.
16. Yiu MK, Liu PL, Yiu TF, Chan AYT.
17. Razvi HA, Denstedt JD, Chun SS, Sales JL.


5. 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 percutaneous nephrolithotomy (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 anatomical relations in order to avoid complications.

Preprocedural KUB (Radiograph of kidney, ureter and bladder) and IVU (intravenous urography) allow the identification of those stones with limited success after ESWL. These images are also used to plan the access. Preprocedural sonography of the kidney and the surrounding structures is recommended to determine the optimal access site, the position of the stone in the kidney - ventral or dorsal - and to rule out that neighbouring organs, such as spleen, liver, large bowel or pleura and lungs are within the planned percutaneous path.
The percutaneous puncture may be facilitated by the preliminary placement of a balloon ureteral catheter to dilate and opacify the collecting system. The puncture can be performed under combined ultrasound and x-ray control or under biplane fluoroscopy. The most frequently used access 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 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. This also applies to the stone 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.

Major complications are lesions to adjacent organs, which can be avoided by puncture under ultrasound guidance. Bleeding is generally avoided by an anatomy oriented access as described above. Sepsis and ‘TUR-syndrome’ indicate a false technique with high pressure within the collecting system during manipulation. They can be avoided by using continuous flow instruments or an Amplatz sheath. Major bleeding during the procedure requires termination, placement of a nephrostomy and a secondary intervention at a later date.

As with open surgery, percutaneous procedures have different degrees of difficulty. Anatomical conditions that offer only limited space for the initial puncture and dilation and instrumentation, such as stones in diverticles or stones completely filling the target calix, indicate a difficult procedure. These cases should be limited to experienced surgeons.

6. PERCUTANEOUS SURGERY VS. ESWL FOR REMOVAL OF RENAL STONES

PNL and ESWL are not competing but complementing procedures. Principally, the indication for PNL can also be extended to include so-called easy cases when ESWL is not available. Stones below 2 cm in diameter in the renal pelvis, the upper and middle caliceal group without obstruction and dilatation of the collecting system are generally accepted as ideal indications for ESWL. Lower pole stones have a clearance rate of less than 50% and the percutaneous procedure is preferential if the calix is obstructed, the stone is larger than 2 cm in diameter, or if the infundibulum is long and the infundibulo-pelvic angle is steep. (2, 4, 5)

6.1 MALFORMATIONS

In horseshoe kidneys, spontaneous passage of fragments after ESWL can only be expected if there is no obstruction and no high insertion of the ureter. Otherwise, PNL is preferred. Stones an caliceal diverticle are frequently very dense and respond poorly to EWSL. Stone clearance is achieved in less than 20% of cases. Percutaneous procedures are difficult, but in the hand of the experienced surgeon generally successful. (3)

6.2 STONE COMPOSITION

Dense, round calculi with a smooth surface are frequently composed of either brushite or calcium oxalate Monohydrate. In these cases, ESWL leads to large fragments which do not pass easily(1). PNL should be preferred in these cases just as in patients with cystine stones which respond poorly to ESWL. Uric acid stones are best treated with oral chemolysis. ESWL plus stenting is possible, but it is difficult to determine fragment size and the need for further sessions, and larger fragments that pass into the ureter may require frequent retrograde manipulations.

REFERENCES

4. Bon D et al.

5. Netto NR et al.

7. DEVICES FOR ENDOSCOPIC DISINTEGRATION OF STONES

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

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

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

7.4 LASER LITHOTRIPSY
The pulsed dye laser delivers short (one microsecond) pulsation at 5-10 Hz produced from a coumarin green dye. A plasma is formed at the stone surface, resulting in a highly localized shock wave. The 504 nm wave length produced by the dye laser is selectively absorbed by the stone but not by the surrounding ureteral wall. As the field continues to advance, new lasers (Alexandrite, q-switched YAG and Holmium) are now being used as sources for laser lithotripsy units. The reported results indicate that the Holmium:YAG laser effectively fragments all types of urinary stones, wherever they are located and whatever their composition, including cystine stones. The Holmium:YAG system produces light of 2100 nm, with a tissue penetration of less than 0.5 mm. It is also a pulsed laser and laser fibres are available at 200 and 365 µm in diameter. In combination with the actively deflectable, flexible ureteroscope, the Holmium:YAG laser has proven ideally suited for fragmenting stones in the upper ureter. Potential complications of the Holmium:YAG laser when used for removal of ureteral stones include stricture and possible perforation of the ureteral wall.

8. SHOCK WAVE LITHOTRIPSY FOR REMOVAL OF LARGE (>20 MM) STONES IN THE KIDNEY
ESWL for the treatment of large renal stones often causes problems. Frequent complications are pain, hydronephrosis, fever, occasional urosepsis due to difficulties in passage of the stone disintegrates or insufficient disintegration (3).

By using a double-J stent, the obstructive and infective complications after ESWL due to large renal stones are reduced. The insertion before ESWL is advocated for stones with a diameter larger than 2 cm (3). Stone particles might pass easily along stents, urine flows in and around stents, which prevents obstruction with loss of ureteral contraction in most cases. Sometimes, the 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 percutaneous nephrostomy tube is necessary, even when the 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.

8.1 LOCATION OF THE STONE MASS
Lower caliceal stones are considered to have a lower success rate than stones located elsewhere in the kidney. A faster clearance of upper pole stones was observed. It is an experience of many authors that stone debris are collected in the lower calices. The best results are reported for stones located primarily in the renal pelvis.

8.2 TOTAL STONE BURDEN
There is no clear cut-off for critical stone size. It appears that an area of 40 x 30 mm could represent a limiting value. With ESWL monotherapy (only stent) a success rate of 86% (stone-free or residual material likely to undergo spontaneous discharge) after 3 months is described for stones with an area smaller than 40 x 30 mm. The success rate for larger stones was only 43% at 3 months after 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 a success rate of 71-96% and acceptable morbidity and complications. ESWL after PNL seems to be better than PNL after ESWL. The indication for open stone-surgery has become extremely rare because of the invasiveness of this approach.

8.3 STATE OF CONTRALATERAL KIDNEY
ESWL monotherapy is a minimally invasive treatment. PNL or sandwich approach may provide the best outcome for removal of very large stones or staghorn calculi. However, the risk of complications of the combined therapy or the PNL alone is higher than for ESWL monotherapy. In case of a solitary kidney, it could be feasible to try ESWL monotherapy first, even if the stone has an area larger than 40 x 30 mm.

8.4 COMPOSITION AND HARDNESS OF THE STONE
ESWL monotherapy of large calcium or struvite containing stones provides reasonable results with respect to stone removal and complications. About 1% of all patients treated for urinary tract stones by ESWL have cystine stones. A total of 76% of the cystine stones have a maximal 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 patients with other stone patients. 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 cystine stone patients.

The first line treatment of uric acid stones is oral chemolysis. In large uric acid stones, dissolution might be accelerated by increasing the stone surface by ESWL. It is possible to treat large uric acid stones with ESWL and oral chemolysis at success rates up to 85%.

REFERENCES

9. ASPECTS ON STAGHORN-STONE TREATMENT AND IMPORTANCE OF STONE BURDEN

Staghorn-stones may vary tremendously in size, composition, 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 the determination of success and complication rates of a single or combined procedures. Thus all techniques - ESWL, PNL, surgery and partial or complete nephrectomy - are included in the treatment strategy (11). If the global kidney function is reduced or in the case of bilateral stone disease, every effort has to be made to preserve functioning nephrons.

9.1 ESWL
Staged ESWL in combination with a double-J stent may be used in those cases where the stone image mimics a normal contrast filled collecting system, that is there is no dilatation of the collecting system and the stone is of a small volume (10).

9.2 PNL
PNL may be used in larger stone volume cases, which expand and obstruct the collecting system when the majority of the stone volume lies within the target calix and the renal pelvis. These are the cases with a large centrally located stone volume. The use of two or more percutaneous accesses should follow the same rules (12).

9.3 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 a good indication for a combined procedure. Large volume extensions into the calices with obstruction of the collecting system are not suited to this approach.

9.4 OPEN SURGERY
Whenever the major stone volume is located peripherally in the calices and especially if these calices are obstructed so that either several percutaneous accesses and several probably unsuccessful shock-wave-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 the patients to a centre where the techniques of extended pyeolycalicotomy (2), anatrophic nephrolithotomy (1, 4, 5, 7) and multiple radial nephrotomies (3, 8) and renal surgery under hypothermia are still mastered. The latest progress in this area was the introduction of intra-operative b-mode scanning and Doppler-sonography (6, 9) to identify avascular areas in the real parenchyma close to the stones or the dilated calices to enable removal of large staghorn stones by multiple small radial nephrotomies without loss of kidney function.

REFERENCES

1. Boyce WH, Smith MJV.
2. Gil-Vernet J.
3. Wickham JEA, Coe N, Ward JP.
4. Harrison LH.
5. Boyce WH.
6. Thüroff JW, Frohneberg D, Riedmiller R et al.  

7. Resnick Ml; Pounds DM, Boyce WH.  

8. Sleight MW, Gower RL, Wickham JEA.  


10. Lam HS et al.  
Stone surface area determination techniques: a unifying concept of staghorn stone burden assessment.  

11. Segura JW et al.  
Nephrolithiasis Clinical Guidelines Panel summary report on the management of staghorn calculi. The  

12. Lam HS et al.  
Evolution of the technique of combination therapy for staghorn calculi: a decreasing role for  

10. STONE REMOVAL WITH OPEN SURGERY

With the advances in extracorporeal shock wave lithotripsy (ESWL) and endourological surgery (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. Because most of these cases will usually involve difficult stone situations, it is  
important that urologists maintain proficiency, skills and expertise of 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  
the experience of consensual opinion and the technical limitations of the less invasive alternative approaches.

10.1 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 caliceal diverticulum particularly in  
an anterior calix, uretero-pelvic junction obstruction, 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 procedures in preference to  
possibly more than one PNL procedure.
- Stone in a transplanted kidney where there may be a risk of damage to overlying bowel.
- Stone in an ectopic kidney where percutaneous access and ESWL may be difficult or impossible.
- Cystolithotomy for giant bladder calculus.

10.2 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
There is proven superiority of open surgery over less invasive therapy for stone free rates.

REFERENCES


11. 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 residuals. 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 treatment alternative for removal of uric acid stones. There follows a brief 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 in order to prevent chemolytic fluid from draining into the bladder and to reduce the risk of an increased renal pressure. In case of a large stone burden, the ureter should be protected by a double-J stent during the procedure (1,2).

11.1 INFECTION STONES
Stones composed of magnesium ammonium phosphate and carbonate apatite can be dissolved with a 10% solution of Renacidin®, 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 shock wave lithotripsy. The time required for dissolution depends on the stone burden, but for a complete staghorn stone several weeks will be necessary. The major advantage of this therapeutic approach is that it can be carried out without anaesthesia and might thus be an option in high-risk patients or in any other patients in whom anaesthesia or other surgical procedures must be avoided (3-13).

11.2 BRUSHITE STONES
Brushite is also soluble in the acid solutions mentioned above. This option should be considered in patients with residual brushite fragments after other stone removing procedures, particularly in view of the very high recurrence rate of brushite stones.

11.3 CYSTINE STONES
Cystine is soluble in an alkaline environment. For this purpose 0.3 or 0.6 mol/L THAM solution can be used. The pH of these solutions is in the range 8.5 - 9.0. Another option is acetylcystine. 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).

11.4 URIC ACID STONES
A high concentration of urate and a low pH are the determinants of uric acid stone formation. Percutaneous dissolution can be made with THAM solutions. Oral chemolysis is, however, the most attractive alternative whereby the urate concentration is lowered by allopurinol and a high fluid intake and the pH increased by alkali (19-21).

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

1. Tiselius HG, Hellgren E, Andersson A, Borrud-Ohlsson A, Eriksson L.
   Minimally invasive treatment of infection staghorn stones with shock wave lithotripsy and chemolysis.
   Scand J Urol Nephrol 1999; 33, 286-290


3. Sheldon CA, Smith AD.

4. Griffith DP.

5. Lingeman JE.

6. Wall I, Tiselius HG, Larsson L.

7. Rodman JSA, Reckler JM, Israel AR.

8. Weirich W, Haas H, Alken P.

9. Klein RS, Cattolica EV, Rankin KN.

10. Dretler SP, Pfister RC.

11. Fam B, Rossier AB, Yalla S, Berg S.

12. Burns JR, Joseph DB.

13. Levy DA, Resnick MI.

14. Kachel TA, Vijan SR, Dretler SP.

15. Tseng CH, Talwalkar YB, Tank ES, Hatch T, Alexander SR.


17. Smith AD, Lange PH, Miller RP, Reinke DB.
    Dissolution of cystine calculi by irrigation with acetylcystein through percutaneous nephrostomy. Urology 1979; 8: 422-423.

18. Schmeller NT, Kersting H, Schüller J, Chaussy C, Schmiedt E.

19. Sharma SK, Indudhara R.

20. Rodman JS, Williams JJ, Peterson CM.

    Local chemolysis of obstructive uric acid stones with 0,1 MTHAM and 0,02% chlorhexidine. Urol Int 1993; 51: 147-151.

22. Oosterlinck W, Verbeeck R, Cuvelier C, Vergauwe D.
12. **EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY IN CHILDREN**

*In situ* ESWL gives remarkably good results in children due to the friability of newly formed stones, as well as the compliance of the urinary tract (1-3). The great majority of upper urinary tract calculi that are not spontaneously eliminated have to be fragmented by ESWL. The first generation of lithotriptors required special equipment for positioning young children and for protecting their lungs from the shock waves. Recent machines enable ESWL with less difficulty in positioning children. Treatment frequently requires general anaesthesia, but intravenous sedation may be sufficient in selected cases. ESWL, especially piezoelectric, is possible without any anaesthesia, but it is necessary to reduce the number and the strength of the shock waves and often to increase the number of sessions. Stone location under fluoroscopy exposes children to x-rays, but the association with echography reduces the radiation dose (3-6). The stone-free rate is 63-100% with one to three sessions, according to the size and location of the stones (7).

Parietal and visceral trauma may be induced by ESWL; its delayed consequences have not yet been evaluated. However, no clinically significant disturbances have been detected and animal experiments have not revealed any anomaly in overall growth or renal development. Potentially, lithogenic abnormalities of the urinary tract can interfere with the treatment of calculi. The detection of an evident obstructive anomaly favours a single procedure for correcting the anatomical abnormality and removing the stone. Relative contraindications for ESWL treatment are especially represented by multiple or voluminous stones, such as staghorn calculi, which often require repeated sessions with unknown long-term consequences (8).

ESWL remains the treatment of choice for upper urinary tract stones in children. ESWL requires a regular follow-up because long-term effects are unknown. Repeated sessions should be strictly controlled. It is therefore important to rule out any underlying pathology and to prevent stone recurrence.

**REFERENCES**


13. **PREVENTIVE TREATMENT FOR RECURRENCE OF CALCIUM STONES**

*Summary of a Consensus Conference in Mannheim 23 November 1999*

13.1 **INCREASED FLUID INTAKE**

13.1.1 Mechanism of action

An increased intake of fluid gives an increased urine flow and thereby a reduction in the supersaturation level of all salts of importance for stone formation.

13.1.2 Indication

General advice to patients with all types of stone.
13.1.3 Evidence in the literature
There is no doubt that an increased urine flow is of great value in patients with stone disease irrespective of the stone composition. There are, however, few studies carried out to support this assumption. The ‘stone clinic effect’ described by Hoskin (1) is one example of the usefulness of a high fluid intake. Recently Borghi and co-workers (2) reported in a randomized study a clear inverse association between urine volume and recurrent stone formation.

13.1.4 Side-effects
None.

13.1.5 Compliance
There is very little information regarding the compliance to drinking advice.

13.1.6 Conclusion
Drinking advice is an important basic form of treatment in patients with stone disease.

13.2 ADVICE REGARDING CALCIUM INTAKE
13.2.1 Mechanism of action
A high calcium excretion is the most frequently encountered abnormality in urine composition. A reduced intake of calcium has been commonly recommended with the aim of decreasing urinary calcium excretion, particularly in patients with absorptive hypercalciuria. In this way, supersaturation with calcium oxalate and calcium phosphate would be avoided.

A low intake of calcium has a deleterious effect on the bone density. In as much as calcium is also of importance for complex formation with oxalate in the intestine, it is of value in reducing oxalate absorption. For this reason administration of calcium has been recommended as well.

13.2.2 Indication
Recurrent calcium oxalate stone disease.

13.2.3 Evidence in the literature
Curhan in large population studies in men (3) and women (4) found an inverse relationship between dietary calcium and the age-related risk of stone formation. Manipulation of the dietary calcium level showed that the highest intake of calcium resulted in the lowest excretion of oxalate. When patients were given an oxalate load of 2 g per day, a dose of 1 g of calcium per day resulted in calcium oxalate aggregates not seen when the calcium dose was increased to 4 g per day (5).

For calcium supplements, the effect is different to that seen with a diet high in calcium. In men as well as in women, supplements of calcium brought about an approximately 20% increase in the relative risk of stone formation (3,4).

13.2.4 Side-effects
A calcium intake below 800 mg per day will cause a negative calcium balance and a loss of bone. An uncontrolled increase in calcium will increase urine supersaturation with calcium salts.

13.2.5 Compliance
The compliance of this kind of advice can be considered reasonably good.

13.2.6 Conclusion
A low calcium intake is harmful, whereas a normal to moderately high calcium content of the diet appears to be of clinical value. Elemental supply of calcium not taken together with food is probably harmful. Although dietary calcium has definite benefits in terms of urine composition and the risk of stone formation, an excessive intake of calcium cannot be recommended and should be avoided.

13.3 FIBRES
13.3.1 Mechanism of action
An inverse relationship has been shown between dietary fibre and the incidence of stone disease. Several mechanisms have been proposed: (a) calcium binding in the gut; (b) reduced transit time; (c) altered intestinal environment; (d) changed hormone response; (e) less calories with more fibres. The net effect would be a reduced excretion of oxalate, calcium and urate and increased crystallization inhibitory properties of urine.
13.3.2 Indication
Recurrent calcium oxalate stone disease.

13.3.3 Evidence in the literature
In four papers, the fibre intake was compared between stone formers and controls (6-8). No difference was recorded. Administration of 24 g of fibres per day brought about a reduced excretion of calcium (9-11). The fibre effect on urinary oxalate has been contradictory. There are no controlled clinical studies with fibre, but a reduced recurrence rate was noted in a short-term follow-up study (12-13), as well as in a 5-year follow-up of stone formers. No control group was used.

13.3.4 Side-effects
None

13.3.5 Compliance
Probably reasonably good.

13.3.6 Conclusion
The intake of products with a high fibre content (fruits and vegetables) might be of value, but it is important to avoid products that also are rich in oxalate (such as wheat bran).

13.4 OXALATE RESTRICTION
13.4.1 Mechanism of action
Although usually less than 10-15% of urinary oxalate is derived from dietary oxalate, a reduced intake of food-stuffs rich in oxalate has been considered useful in view of the powerful influence of oxalate on the ion-activity product of calcium oxalate. The relationship between dietary and urinary oxalate is weak with a normal oxalate intake (less than 2 mmol/day), but increases significantly following an oxalate load. A low intake of calcium increases oxalate absorption and excretion. An increase in a low calcium intake 15-20 mmol/day resulted in a reduction of urinary oxalate. Administration might thus be beneficial in decreasing oxalate absorption, but this approach might not be effective in all patients. Ascorbate and vitamin D might contribute to an increased oxalate excretion.

13.4.2 Indication
Hyperoxaluria (more than 0.45 mmol/24h, more than 0.30 mmol/16h).

13.4.3 Evidence in the literature
There are no prospective randomized studies on the efficacy of a reduced intake of oxalate. Only one report deals with the clinical effect of a low oxalate diet (14). In this study, a subgroup of patients with a diet low in calcium (500 ± 200 mg) and low in oxalate was followed for 5 years. The annual frequency of stone formation was reduced from 3.1 to 1.1 and the fraction of patients free of recurrent stone formation was 55%. These data should be compared with those in a group of patients only given drinking advice, in whom the frequency of stone formation was reduced from 2.65 to 0.9 with 52% remaining stone-free.

13.4.4 Side-effects
None.

13.4.5 Compliance
No information available.

13.4.6 Conclusion
Advice should be given on avoiding an excessive intake of food-stuffs rich in oxalate (rhubarb, sorrel, beet-roots, spinach, chocolate, wheat bran, nuts and black tea). The inverse relationship between dietary calcium and urinary oxalate is of note. It needs to be emphasized, however, that many other nutrient factors influence oxalate absorption and excretion.

A reduced intake of oxalate might be most useful in patients with enteric hyperoxaluria, but in these patients, oxalate restriction should be combined with other therapeutic measures.

13.5 REDUCED INTAKE OF VITAMIN C
13.5.1 Mechanism of action
The natural conversion of ascorbate to oxalate is the rational for recommending patients with calcium oxalate stone disease to avoid excessive intake of vitamin C.
13.5.2 **Indication**
Recurrent calcium oxalate stone disease.

13.5.3 **Evidence in the literature**
The results in the literature are contradictory. Whereas some authors have recorded an increased excretion of oxalate following administration of gram-doses of ascorbic acid, others have not (15-17). In some of these studies, the conversion to oxalate might have occurred *in vitro*. The general impression from recent studies is that an intake of up to 4 g of vitamin C can be made without harm (17).

There are no studies associating a high intake of vitamin C to an increased recurrence rate or that a reduced intake of vitamin C is of clinical value.

13.5.4 **Side-effects**
Provided the minimum requirement of vitamin C is achieved, there are probably no negative effects of a reduced intake.

13.5.5 **Compliance**
No information is available, but the compliance in avoiding large doses of vitamin C is probably good.

13.5.6 **Conclusion**
There is presently no convincing evidence that an intake of large doses of vitamin C (up to 4 g) has a negative influence on calcium stone recurrence.

13.6 **REDUCED INTAKE OF PROTEIN**

13.6.1 **Mechanism of action**
Animal protein has been incriminated as one important risk factor in stone formation (18). An excessive intake might affect urine composition by increasing the excretion of calcium and oxalate and by decreasing the excretion of citrate and the urinary pH.

13.6.2 **Indication**
Recurrent calcium oxalate stone disease.

13.6.3 **Evidence in the literature**
In a comparative study of 121 patients treated with a high or a low protein intake during a 3-year period, no difference in stone recurrence between the two groups was recorded.

13.6.4 **Side-effects**
No side-effects should be anticipated if the protein intake is decreased within reasonable limits.

13.6.5 **Compliance**
The compliance of this form of treatment can be considered low.

13.6.6 **Conclusion**
As part of a common sense diet, excessive intake of animal protein should be avoided.

13.7 **THIAZIDES**
Hydrochlorothiazide, bendroflumethiazide, trichlorothiazide and indapamide.

13.7.1 **Mechanisms of action**
The major effect of thiazide treatment is a reduction of hypercalciuria. According to the original work by Yendt (19), thiazides also reduced urinary calcium in normocalciuric patients. In addition, it was reported that thiazides reduced urinary oxalate as well as the intestinal absorption of calcium. A reduction of urinary calcium by 20-30% can be expected.

Thiazides also provide bone protection. A reduced bone turnover has been observed and thereby the reduced bone density seen in hypercalciuric stone formers can be counteracted.

13.7.2 **Indication**
Hypercalciuric calcium stone disease.
13.7.3 Evidence in the literature
There are 10 randomized or controlled studies reported in the literature (20-29). A beneficial effect was recorded in eight (22-29), whereas in two studies, the stone-free rate was similar in the treatment and control groups (20,21). In the latter studies, however, the treatment period was only 1.0-1.6 years. In general, the number of patients included was small, the statistical power low and the drop-out of patients high. The recurrence rate was also reduced in placebo treated and control patients. This can probably be explained by the ‘stone clinic effect’.

13.7.4 Side-effects
Several side-effects have been reported, such as unmasking of normocalcemic hyperparathyreoidism and development of diabetes and gout. Erectile dysfunction is a common complaint. It is essential to follow thiazide treated patients with analysis of serum levels of calcium, potassium, urate and glucose.

13.7.5 Compliance
Side-effects cause a fairly high drop-out rate in the range of 30-50%.

13.7.6 Conclusion
Although the statistical power of the reviewed studies is weak and the severity of side-effects high, thiazides seem beneficial in reducing stone formation in hypercalciuric calcium stone forming patients and its use appears justified in patients with recurrent hypercalciuric calcium stone disease. Further studies are, however, highly desirable to further verify the stone preventive effects of this form of treatment and to increase our understanding of its mechanism of action.

13.8 ORTHOPHOSPHATE

13.8.1 Mechanism of action
Two types of orthophosphate - acidic and neutral - have been used clinically to treat patients with calcium urolithiasis. Orthophosphate is assumed to work by reducing the formation of 1.25 (OH)2-D vitamin. The decreased absorption of calcium brings about a reduced calcium excretion as well as reduced bone reabsorption. The effect is most pronounced for neutral orthophosphate, which in addition to reduced calcium and an increased phosphate excretion, increases urinary citrate. The combined effect of an increased pyrophosphate and citrate excretion increases the crystallization inhibitory properties of urine.

13.8.2 Indication
Hypercalciuria.

13.8.3 Evidence in the literature
There are only two double-blind studies in this area (30-31). In the first one, there was no difference between treated and untreated patients. The latter study showed a reduced rate of stone formation. Other less well controlled studies have usually demonstrated a beneficial effect of orthophosphate therapy, but a comparison between different studies is difficult because of various doses, dosage regimens and periods of treatment. The number of patients is usually small.

13.8.4 Side-effects
Diarrhoea, abdominal cramps, nausea and vomiting are common complaints. The possible effect on PTH needs attention.

13.8.5 Compliance
Usually good and in most patients successfully managed by a dose reduction.

13.8.6 Conclusion
Orthophosphate is a low-rated alternative in case of hypercalciuria. There are insufficient data to prove its absolute efficacy. It may have a place in treatment of selected cases, but cannot be recommended as a first-line option.

13.9 CELLULOSE PHOSPHATE
Cellulose phosphate (CP) and sodium cellulose phosphate (SCP).
13.9.1 Mechanism of action
Reduced absorption of calcium by complex formation between CP / SCP and calcium.

13.9.2 Indication
Treatment of patients with absorptive hypercalciuria.

13.9.3 Evidence in the literature
There are three studies on CP and six on SCP, none of which included a control or placebo group (32-39). In the CP and SCP studies, 89 and 67%, respectively, were without recurrences; failure rates were 57 and 22%. Accordingly, 40% of patients formed new stones (32).

13.9.4 Side-effects
Diarrhoea is a common side-effect. As a result of intestinal complexation, these patients develop hyperoxaluria and hypomagnesiuria. Also, other ions might be affected.

13.9.5 Compliance
Limited information is available, but treatment with CP and SCP is described as acceptable.

13.9.6 Conclusion
CP and SCP cannot be recommended for therapeutic use in patients with stone disease. They may be used for diagnostic purposes.

13.10 ALKALINE CITRATE
13.10.1 Mechanism of action
Alkaline citrate increases the excretion of citrate mainly by increasing the pH of tubular cells. A small fraction of the citrate absorbed is excreted in urine, but the major part of administered citrate is metabolised.

13.10.2 Indication
To reduce supersaturation with calcium oxalate and calcium phosphate, to inhibit the crystallisation process in terms of growth and aggregation (agglomeration) of the corresponding crystal phases and to decrease supersaturation with uric acid.

13.10.3 Evidence in the literature
There are only three randomized studies on the recurrence rate in calcium stone formers (40-42) and one on the clearance of fragments from the kidney (43). There are no randomized trials in patients with uric acid stone disease.

During a 3-year follow-up period, the fraction of patients who remained stone-free on K-citrate, NaK-citrate and KMg-citrate were 72, 31 and 87%, respectively. The corresponding figures for untreated controls were 20, 27 and 36%. In the three groups treated with alkaline citrate, the frequency of stone formation was reduced from 1.2 to 0.1, from 2.1 to 0.9 and from 0.57 to 0.08, respectively (40-42).

13.10.4 Side-effects
Mild side-effects were recorded in 42% of patients, moderate in 26% and severe (diarrhoea) in 12%.

13.10.5 Compliance
The compliance was only slightly above 50%. As many as 48% of patients had stopped their participation in the studies.

13.10.6 Conclusion
Alkaline citrate is obviously efficient in reducing the recurrence rate in patients with calcium stone disease. The side-effects are pronounced and the patient compliance surprisingly low. Studies with better tolerable preparations over longer periods of time are desirable. Although alkaline citrate might be most useful in patients with hypocitraturia, there is reason to believe that its indication can be extended to all calcium stone formers irrespective of urinary findings. However, additional evidence is mandatory.
13.11 MAGNESIUM

13.11.1 Mechanism of action
Complex formation between magnesium and oxalate and thus a reduced supersaturation with calcium oxalate and to some extent the growth of calcium oxalate crystal. In addition, magnesium urinary citrate and pH are increased. Magnesium also has a direct inhibitory influence on calcium phosphate crystal growth.

13.11.2 Indication
Calcium oxalate stone formation with or without hypomagnesuria.

13.11.3 Evidence in the literature
There are two prospective, double-blind, placebo controlled randomized studies. In 30 patients treated with 650 mg of magnesium hydroxide and 21 with 1300 mg daily, 65 and 59%, respectively, remained without recurrent stone formation during the treatment. The corresponding figure in the placebo group was 56% (44). The frequencies of stone formation in the patients given 650 mg magnesium hydroxide was 0.71 before and 0.15 during treatment. In those treated on 1300 mg, the corresponding frequencies were 0.73 and 0.17. Magnesium hydroxide did not significantly reduce the recurrence rate compared with placebo.

In 31 patients treated with KMG-citrate, 87% were stone free compared with 36% in the placebo group. The pretreatment stone frequency was 0.57 and that during treatment 0.07 (45). KMG-citrate substantially reduced the 3-year recurrence rate of calcium oxalate stone formation.

13.11.4 Side-effects
Diarrhoea, central nervous disorders, tiredness, sleepiness and paresis. Increased excretion of calcium.

13.11.5 Compliance
Good: reported as 70-80% in above studies.

13.11.6 Conclusion
Magnesium salts not containing citrate cannot be recommended as monotherapy in prevention of recurrent calcium stone disease.

13.12 ALLOPURINOL

13.12.1 Mechanism of action
Reduces the production of urate and the serum urate concentration, as well as the excretion of urate. A high urinary urate excretion might induce crystallization of uric acid and/or sodium urate. These crystal phases might theoretically cause heterogeneous nucleation of calcium oxalate or induce its nucleation by a salting out mechanism. Uric acid or colloidal urate can bind inhibitory glycosaminoglycans. There are also reports of reduced oxalate excretion following administration of allopurinol. Administration of allopurinol may thus be of value in patients with hyperuricosuric calcium stone disease.

13.12.2 Indication
Uric acid stone formation. Calcium oxalate stone formation in association with a high excretion of urate.

13.12.3 Evidence in the literature
Ettinger, in a randomized placebo-controlled study, found that 75% of patients treated with allopurinol were free of recurrent stone formation after 3 years compared with only 45% in the placebo group (46). In two open studies, Coe and associates showed a significant reduction of the risk of stone formation in allopurinol treated hyperuricosuric patients (47-48). These results have not been confirmed in other studies (49-51).

13.12.4 Side-effects
Severe side-effects have been reported with high doses of allopurinol, but this form of medication is usually well tolerated.

13.12.5 Compliance
No information available.

13.12.6 Conclusion
Allopurinol is recommended for hyperuricosuric patients with calcium oxalate stone disease or uric acid stone formation. Moreover, it may be useful to lower the urate concentration in urine during dissolution of uric acid stones irrespective of the urate excretion.
13.13 GLYCOSAMINOGLYCANS (GAGS)

13.13.1 Mechanism of action
Inhibition of calcium oxalate crystal growth.

13.13.2 Indication
Recurrent calcium oxalate stone disease.

13.13.3 Evidence in the literature
There are presently no efficient ways of significantly increasing urinary GAG-concentration. Although sodium pentosan polysulphate (SPP) in some studies has been reported to have positive effects on the crystallization properties of urine, there are no controlled studies supporting its clinical value.

13.13.4 Side-effects
Administration of large doses of GAGs may have a toxic effect.

13.13.5 Compliance
No information available.

13.13.6 Conclusion
There is so far no evidence that administration of synthetic or semisynthetic GAGs have a place in the preventive treatment for recurrence of calcium stones.

REFERENCES
14. Elomaa I, Ala-Opas M, Porkka L.


16. Urivetzky M, Kessaris D, Smith AD.

17. Auer BL, Auer D, Rodgers AL.

18. Hiatt RA, Ettinger B, Caan B, Quesenberg CP Jr, Duncan D, Citron JT.

19. Yendt ER, Cohanim M.


21. Scholz D, Schwille PO, Sigel A.


23. Laerum E, Larsen S.

24. Robertson WG, Peacock M, Selby PL et al.

25. Mortensen JT, Schultz A, Ostergaard AH.

26. Ala-Opas M, Elomaa I, Porkka L, Alfthan O.

27. Ettinger B, Citron JT, Livermore B, Dolman LI.


29. Borghi L, Meschi T, Guerra A, Novanni A.

30. Ettinger B.

31. Bresalu NA, Heller HJ, Reza-Albarran AA, Pak CYC.

32. Hallson PC, Rose GA.

33. Hautmann R, Herem FJ, Lutzeyer W.

34. Pak CYC.

36. Pak CYC.

37. Knebel L, Tscöpe W, Ritz E.
   A one day cellulose phosphate test discriminates non-absorptive from absorptive hypercalciuria.

38. Marickar YMF, Rose GA.

39. Burke JR, Cowley DM, Mottram BM, Buckner P.

40. Barcelo B, Wuhl O, Servitge E, Rousaud A, Pak CYC.

41. Hofbauer J, Höbarth K, Szabo N, Marberger M.


43. Cicerello E, Merlo F, Gambaro G et al.

44. Ettinger B, Citron JT, Livermore B, Dolman LL.


47. Coe FL, Raisen L.

48. Coe FL.

49. Fellsström B, Backman U, Danielson BG et al.

50. Miano L, Petta S, Gallucci M.

51. Tiselius HG, Larsson L, Hellgren E.

14. OTHER CONTRIBUTORS

For the metabolic evaluation and preventive treatment members of the Advisory Board of European Urolithiasis Research have contributed:

W. Achilles; D. Ackermann; P. Alken; JM Baumann; B. Dussol; KH Bichler; R. Caudarella; M. Daudon; B. Hess; A. Hesse; Ph. Jaeger; DJ Kok; BD Leussmann; PN Rao (Vice-President); K. Sarica; PO Schwille; WL Strohmaier; HG Tiselius (President).
15. **ABBREVIATIONS USED IN THE TEXT**

This list is not comprehensive for the most common abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CaOx</td>
<td>calcium oxalate</td>
</tr>
<tr>
<td>CaP</td>
<td>calcium phosphate</td>
</tr>
<tr>
<td>CarbAp</td>
<td>carbonate apatite</td>
</tr>
<tr>
<td>COD</td>
<td>calcium oxalate dihydrate</td>
</tr>
<tr>
<td>COM</td>
<td>calcium oxalate monohydrate</td>
</tr>
<tr>
<td>ESWL</td>
<td>extracorporeal shock wave lithotripsy, also including piezolithotripsy</td>
</tr>
<tr>
<td>HAP</td>
<td>hydroxyapatite</td>
</tr>
<tr>
<td>MAP</td>
<td>magnesium ammonium phosphate</td>
</tr>
<tr>
<td>PN</td>
<td>percutaneous nephrostomy catheter</td>
</tr>
<tr>
<td>PNL</td>
<td>percutaneous nephrolithotomy with or without lithotripsy</td>
</tr>
<tr>
<td>Ud</td>
<td>distal part of the ureter between the bladder and the lower part of the sacroiliac joint.</td>
</tr>
<tr>
<td>Um</td>
<td>middle part of the ureter from pelvic brim to lower sacroiliac joint.</td>
</tr>
<tr>
<td>Up</td>
<td>proximal part of the ureter from UPJ to the level of the pelvic brim.</td>
</tr>
<tr>
<td>URS</td>
<td>ureteroscopy</td>
</tr>
</tbody>
</table>