Complete Summary

GUIDELINE TITLE

Guidelines on urolithiasis.

BIBLIOGRAPHIC SOURCE(S)

Tiselius HG, Alken P, Buck C, Gallucci M, Knoll T, Sarica K, Turk C. Guidelines on urolithiasis. Arnhem, The Netherlands: European Association of Urology (EAU); 2008 Mar. 128 p. [765 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Urolithiasis, particularly renal stones

Note: For recommendations for the management of patients with stones in the ureter, see the National Guideline Clearinghouse summary of the European Association of Urology and American Urological Association Education and Research 2007 guideline for the management of ureteral calculi.

GUIDELINE CATEGORY

Diagnosis
Management
Prevention

Risk Assessment
Treatment

CLINICAL SPECIALTY

Surgery
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide useful information for clinical practitioners on the classification, diagnosis, treatment, and management of patients with (or at risk for) urolithiasis

TARGET POPULATION

Adults and pediatric patients, including pregnant women, with urolithiasis or at risk for urolithiasis

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Management

1. Classification of type of stone former
2. Identification of risk factors for stone formation
3. Imaging (e.g., excretory urography [intravenous pyelography, IVP]), computed tomography (CT) with or without contrast, plain film of kidneys/ureter/bladder (KUB), ultrasonography (US), retrograde pyelography, antegrade pyelography, scintigraphy, contrast media (technetium-99, iodine), ureteroscopy (URS)
4. Analysis of stone size and composition
5. Biochemical investigation (e.g., blood levels of creatinine, electrolytes; urinalysis to include volume, minerals content; blood and urine pH, bacteria)

Treatment/Management

Renal Colic

1. Pain management (diclofenac sodium, indomethacin, ibuprofen, hydromorphine hydrochloride plus atropine, methamizol, pentazocine, tramadol)
2. Management of spontaneous stone passage
3. Medical expulsive treatment (MET)

Kidney Stone Removal

1. Extracorporeal shock-wave lithotripsy (ESWL), including frequency of treatments and power of shock waves
2. Percutaneous nephrolithotomy (PNL) with or without lithotripsy with US, electro-hydraulic, laser, or hydropneumatic probes
3. Retrograde removal of ureteral and renal stones (retrograde intrarenal surgery [RIRS])
4. Anesthesia (sedation, general anesthesia)
5. Open surgery
6. Laparoscopic surgery
7. Chemolytic percutaneous irrigation
8. Oral chemolysis
9. Treatment of staghorn stones
10. Management of complications of stone removal method

Management of Special Problems

1. Pregnancy
2. Children
3. Residual fragments
4. Steinstrasse
5. Internal stenting
6. Uric stone disease
7. Cystine stone disease
8. Infection stones
9. Special medical (e.g., patients with pacemakers or on anticoagulation) or physiological (e.g., horseshoe kidney) problems

Prevention

1. Recurrence prevention (diet, hydration)
2. Prevention therapy (thiazides, alkaline citrate, orthophosphate, magnesium, allopurinol, pyridoxine)
3. Management of patients with enteric hyperoxaluria

MAJOR OUTCOMES CONSIDERED

- Risk-benefit of diagnostic method or treatment
- Complication rates from treatment
- Incidence of adverse effects
- Morbidity and mortality
- Stone-free rates after treatment
- Recurrence rates of stone formation

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Up until 2007, the main strategy was to rely on the guidelines group members' knowledge and expertise on the current literature assuming that all, or almost all, relevant information would be captured. The method for literature selection was improved in the course of 2007. In updates produced from 2008 onwards, a structured literature search will be performed for all guidelines but this search will be limited to randomized controlled trials and meta-analyses, covering at least the past three years, or up until the date of the latest text update if this exceeds the three-year period.

Other excellent sources to include are other high-level evidence, Cochrane review and available high-quality guidelines produced by other expert groups or organizations. If there is no high-level data available, the only option is to include lower-level data. The choice of literature will be guided by the expertise and knowledge of the Guidelines Working Group.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

1a Evidence obtained from meta-analysis of randomized trials

1b Evidence obtained from at least one randomized trial

2a Evidence obtained from one well-designed controlled study without randomization

2b Evidence obtained from at least one other type of well-designed quasi-experimental study

3 Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies and case reports

4 Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

- The first step in the European Association of Urology (EAU) guidelines procedure is to define the main topic.
- The second step is to establish a working group. The working groups comprise about 4-8 members, from several countries. Most of the working group members are academic urologists with a special interest in the topic. In general, general practitioners or patient representatives are not part of the working groups. A chairman leads each group.
- The third step is to collect and evaluate the underlying evidence from the published literature.
- The fourth step is to structure and present the information. All main recommendations are summarized in boxes and the strength of the recommendation is clearly marked in three grades (A-C), depending on the evidence source upon which the recommendation is based. Every possible effort is made to make the linkage between the level of evidence and grade of recommendation as transparent as possible.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendation

A. Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomized trial
B. Based on well-conducted clinical studies, but without randomized clinical trials
C. Made despite the absence of directly applicable clinical studies of good quality

COST ANALYSIS

Published cost analyses were reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

There is no formal external review prior to publication.

The Appraisal of Guidelines for Research and Evaluation (AGREE) instrument was used to analyse and assess a range of specific attributes contributing to the validity of a specific clinical guideline.

The AGREE instrument, to be used by two to four appraisers, was developed by the AGREE collaboration (www.agreecollaboration.org) using referenced sources for the evaluation of specific guidelines. (See the "Availability of Companion Documents" field for further methodology information).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the levels of evidence (**LE = 1a-4**) and grades of recommendation (**GR = A-C**) are provided at the end of the "Major Recommendations" field.

Note from European Association of Urology: In several statements presented throughout the text the methods considered have been assigned Preference numbers, 1, 2, 3, etc. Preference numbers are used to indicate which treatment alternative was considered most appropriate or preferred, according to the literature or consensus reached. If two procedures were considered equally useful, they were given the same preference number. The first treatment alternative always has the preference number 1.

Classification

A system for subgrouping stone-forming patients into different categories according to type of stone and severity of the disease is shown in the following table.

Table: Categories of Stone Formers

	Definition	Category
Non-calcium Stones	Infection stone: magnesium ammonium phosphate, carbonate apatite or ammonium urate*	INF
	Uric acid/ammonium urate*/sodium urate stone	UR
	Cystine stone	CY
Calcium Stones	First time stone former **without** residual stone or fragments	S_o
	First time stone former **with**	S_{res}

Table: Categories of Stone Formers		
	Definition	**Category**
	residual stone or fragments	
	Recurrent stone former with **mild** disease **without** residual stone(s) or fragments	R_{mo}
	Recurrent stone former with **mild** disease **with** residual stone(s) or fragments	$R_{m\text{-}res}$
	Recurrent stone former with **severe** disease with or without residual stone(s) or fragments *or* stone forming patient with **specific risk factor(s)** irrespective of otherwise defined category (see "Specific Risk Factors for Stone Formation" below)	R_s

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

Specific Risk Factors for Stone Formation

- Onset of disease early in life (i.e., below 25 years of age)
- Stones containing brushite (calcium hydrogen phosphate; $CaHPO_4 \cdot 2H_2O$)
- Strong family history of stone formation
- Only one functioning kidney (although only one kidney does not mean an increased risk of stone formation, these patients should be particularly considered for measures to prevent stone recurrence)

- Diseases associated with stone formation
  - Hyperparathyroidism
  - Renal tubular acidosis (partial/complete)
  - Cystinuria
  - Primary hyperoxaluria
  - Jejunoileal bypass
  - Crohn's disease
  - Intestinal resection
  - Malabsorptive conditions
  - Sarcoidosis
- Medication associated with stone formation
  - Calcium supplements
  - Vitamin D supplements
  - Acetazolamide
  - Ascorbic acid in megadoses (>4 g/day)
  - Sulfonamides
  - Triamterene
  - Indinavir
- Anatomical abnormalities associated with stone formation
  - Tubular ectasia (medullary sponge kidney)
  - Pelvi-ureteral junction obstruction
  - Caliceal diverticulum/caliceal cyst
  - Ureteral stricture
  - Vesico-ureteral reflux
  - Horseshoe kidney
  - Ureterocele

Diagnostic Procedures

Diagnostic Imaging

Imaging is imperative in patients with fever or a solitary kidney and when the diagnosis of stone is in doubt	**LE = 4** **GR = C**

Table: Imaging Modalities in the Diagnostic Work-Up of Patients with Acute Flank Pain

Preference Number	Examination	LE	GR	References
1	Non-contrast computed tomography (CT)	1	A	Smith et al., 1995; Smith et al., 1996; Kobayashi et al., 2003; Sudah et al., 2002; Homer, Davies-Payne, & Peddinti, 2001; Shokeir &

Table: Imaging Modalities in the Diagnostic Work-Up of Patients with Acute Flank Pain				
Preference Number	**Examination**	**LE**	**GR**	**References**
				Abdulmaaboud, 2001; Gray Sears et al, 2002; Miller et al., 1998; Dalrymple et al., 1998; Worster et al., 2002; Shine, 2008; Mindelzun & Jeffrey, 1997
1	Excretory urography	Standard procedure		
2	Plain film of kidney, ureters and bladder (KUB) + ultrasonography (US)	2a	B	Shokeir & Abdulmaaboud, 2001

Table: General Considerations Regarding the Use of Contrast Medium			
Contrast medium should not be given to, or avoided, in the following circumstances	**LE/GR**	**GR**	**Selected References**
• Patients with an allergy to contrast media	–	–	Morcos, Thomsen & Webb, 2001; Thomsen & Morcos, 2003
• When the serum or plasma creatinine level is >150 micromoles/L	4	C	Thomsen & Morcos, 2003
• To patients on medication with metformin	3	B	Thomsen & Morcos, 2003; Nawaz et al., 1998; McCartney et al., 1999; Thompson et al., 2000
• Untreated hyperthyroidism	3	B	–
• To patients with myelomatosis	3	B	Thomsen & Morcos, 2003

Analysis of Stone Composition

Stones that pass spontaneously, are removed surgically, or excreted as fragments following disintegration, should be subjected to stone analysis to determine their composition (Asper, 1990; Herring, 1962; Daudon & Jungers, 2004; Otnes, 1983; Leusmann, Blaschke, & Schmandt, 1990). The preferred analytical procedures are X-ray crystallography and infrared spectroscopy.

Biochemical Investigations

Analytical Work-up in the Acute Phase

Table: Biochemical Analyses Recommended for Patients with an Acute Stone Episode	
For all patients	Urinary sediment/dipstick test for demonstration of red cells White cells. Test for bacteriuria (nitrite) and urine culture in case of a positive reaction Serum creatinine should be analysed as a measure of the renal function
For patients with fever	C-reactive protein and blood cell count
For patients who vomit	Serum/plasma sodium Serum/plasma potassium
Optional useful information	Approximate pH level[a] Serum/plasma calcium[b] All other examinations that might be necessary in case of intervention

[a] Knowledge of pH might reflect the type of stone that the patient has formed.

[b] This might be the only occasion on which patients with hypercalcaemia are identified.

Analysis of Urine in Search for Risk Factors of Stone Formation

Two urine collections for each set of analyses are recommended. The urine collections are repeated when necessary (Hobarth, Hofbauer, & Szabo, 1994; Hess et al., 1997; Straub et al., 2005).

A Simplified Overview of the Principles of Analytical Work-Up in Patients

A correct categorization of the patients requires both information on the stone composition and an actual imaging procedure. The principles shown in the table below can be applied to all patients provided a reasonable assumption of the category can be made. If this is not possible an alternative analytical approach has to be chosen until more data have been collected.

Table: Recommendations Regarding Analysis of Stones, Blood and Urine in Different Categories of Stone Forming Patients			
Category of Stone Former*	**Stone**	**Blood**	**Urine**
INF	Yes	Creatinine	Culture Urease (in positive urine cultures) pH
UR	Yes	Urate Creatinine	Urate pH Volume
CY	Yes	Creatinine	Cystine pH Volume
Calcium stone S_o R_{mo}	Yes	Calcium Albumin Creatinine (Urate)	Bacteria Nitrate test pH
Calcium stone S_{res} $R_{m\text{-}res}$ Calcium stone R_s	Yes	Calcium Albumin Creatinine (Urate)	Bacteria Nitrate test pH ---------- - Calcium Oxalate Citrate Creatinine Volume (Magnesium) (Phosphate) (Urea) (Urate)

*See the table "Categories of Stone Formers" in the Classification section above for definitions of categories.

Treatment of Patients with Renal Colic

Pain Relief

The relief of pain is usually the most urgent therapeutic step in patients with an acute stone episode (see table below).

Table: Pain Relief for Patients with Acute Stone Colic				
Preference	**Pharmacological Agent**	**LE**	**GR**	**References**
1	Diclofenac sodium	1b	A	Holmlund & Sjodin, 1978; Lundstam, et al., 1982; Lundstam, Wahlander, & Kral, 1980; Walden, Lahtinen, & Elvander, 1993
1	Indomethacin Ibuprofen			
2	Hydromorphine hydrochloride + atropine Methamizol Pentazocine Tramadol	4	C	

The recommendation is to start with diclofenac whenever possible (see table below) and change to an alternative drug if the pain persists. Because of the increased risk of vomiting, avoid giving hydromorphone and other opiates without simultaneous administration of atropine.

Effects of Diclofenac on Renal Function

Although the renal function can be affected in patients with an already reduced function this is not the case for normally functioning kidneys (Lee et al. 2007) (**LE = 1b; GR = A**).

Table: Recommendations and Considerations Regarding Treatment of the Patient with Renal Colic			
Recommendations	**LE**	**GR**	**Selected References**
Treatment should be started with an non-steroidal anti-inflammatory drug (NSAID)	1b	A	Holmlund & Sjodin, 1978; Lundstam et al, 1982; Lundstam, Wahlander, & Kral, 1980; Walden, Lahtinen, & Elvander, 1993
Diclofenac sodium affects glomerular filtration rate (GFR) in patients with reduced renal function, but not in patients with normal renal function	2a	2a	Lee et al., 2007
Diclofenac sodium is recommended as a method to counteract recurrent pain after an episode of ureteral colic	1b	A	Laerum et al., 1995

Indications for Active Stone Removal

The size, site, and shape of the stone at the initial presentation are factors that influence the decision to remove the stone (see table below):

Table: Indications for Active Stone Removal			
Indications for Considering Active Stone Removal	**LE**	**GR**	**Selected References**
• When stone diameter is ≥7 mm because of a low rate of spontaneous passage	2a	B	Sandegard, 1956; Morse & Resnick, 1991; Ibrahim et al., 1991; Miller & Kane, 1999; Andersson & Sylven 1983
• When adequate pain relief cannot be achieved	4	B	
• When stone obstruction is associated with infection*	4	B	
• When there is a risk of pyonephrosis or urosepsis*	4	B	
• In single kidneys with obstruction*	4	B	
• Bilateral obstruction*	4	B	

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

Active Removal of Stones in the Kidney

Extracorporeal Shock-Wave Lithotripsy (ESWL) for Removal of Stones in the Kidney

In the case of infected stones or bacteriuria, antibiotic therapy should be given before ESWL treatment and continued for at least 4 days after the treatment	**LE = 4** **GR = C**

Shorter intervals between treatment sessions are usually acceptable for stones in the ureter. Clinical experience supports this view	**LE = 4** **GR = C**

It has been concluded, however, that a frequency of 1 to 1.5 Hz is acceptable and optimal (Yilmaz et al., 2005)	**LE = 3** **GR = C**

Insertion of an internal stent before ESWL is recommended for stones with a diameter $\geq$20 mm (~300 mm^2) (Sulaiman, Buchholz & Clark, 1999)	**LE = 3** **GR = B**

A study concluded that the routine use of internal stents does not improve the outcome (Musa, 2008) (**LE = 1b, GR = A**).

A multicentre randomized comparison between ESWL and ureteroscopic removal of stones from the lower calix system failed to show a significantly better result with ureteroscopy (Pearle et al., 2005) (**LE = 1b; GR = A**).

Percutaneous Removal of Renal Stones

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 those cases likely to have a less favourable outcome after ESWL.

Pre-procedural plain film of kidney, ureters and bladder (KUB) and intravenous urography or computed tomography (CT) scan should be used to plan access.

The percutaneous puncture may be facilitated by the preliminary placement of a balloon ureteral catheter to dilate and opacify the collecting system.

In lower pole stones, ESWL, PNL and flexible uretero-nephroscopy are competing procedures with different success and complication rates and patient acceptance (Pearle et al., 2005; Albala et al., 2001) (**LE = 1b; GR = A**).

Stones can be extracted straightaway, or following disintegration by US-, electro-hydraulic-, laser- or hydro-pneumatic 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 tamponading the tract and maintaining access to the collecting system is preferred in complicated procedures or when a second intervention is necessary. Tubeless percutaneous nephrolithotomy, with or without tract fulguration, application of a sealant or double-J stenting, is a safe alternative in uncomplicated cases (Feng et al., 2001; Desai et al., 2004) (**LE = 1b; GR = A**).

Retrograde Removal of Ureteral and Renal Stones (Retrograde Intrarenal Surgery [RIRS])

Antibiotic prophylaxis should be administered before the procedure to ensure sterile urine (Knopf, Graff, & Schulze, 2003; Grabe, 2001)	**LE = 4** **GR = C**

Stone extraction with a basket without endoscopic visualization of the stone (blind basketing) should not be performed (see Chapter 9 of the original guideline document)	**LE = 4** **GR = C**

Holmium:yttrium aluminium garnet (Ho:YAG) laser lithotripsy is a reliable method for the treatment of urinary calculi, regardless of the hardness of the stone (Grasso, 1996; Grasso & Chalik, 1998; Jeon, Hyun, & Lee, 2005; Gupta, 2007). It is the preferred method when performing flexible ureteroscopy (URS) (Smith & Patel, 2007; Gupta, 2007; Gould, 1998; Tawfiek & Bagley, 1999) (**LE = 3; GR = B/C**).

Nitinol baskets preserve tip deflection of flexible ureterorenoscopes and the tipless design reduces the risk of mucosa injury (Michel et al., 2002). They are therefore most suitable for use in flexible URS	**LE = 2b/3** **GR = B**

Stenting following uncomplicated URS is optional (see also Chapter 9 in the original guideline document)	**LE = 1a** **GR = A**

Flexible URS has been demonstrated to be an effective treatment for ESWL-refractory calculi (Johnson, Portela, & Grasso, 2006; Mariani, 2007).

Ureteroscopy can also be applied when ESWL might be contraindicated or ill-advised	**LE = 4** **GR = C**

Open Surgery for Removal of Renal Stones

Indications for open and laparoscopic surgery

Indications for open surgery for stone removal include:

- Complex stone burden
- Treatment failure with ESWL and/or PNL or failed ureteroscopic procedure
- Intrarenal anatomical abnormalities: infundibular stenosis, stone in the caliceal diverticulum (particularly in an anterior calyx), obstruction of the ureteropelvic junction, stricture
- Morbid obesity
- Skeletal deformity, contractures and fixed deformities of hips and legs
- Co-morbid medical disease
- Concomitant open surgery
- Non-functioning lower pole (partial nephrectomy), non-functioning kidney (nephrectomy)
- Patient choice following failed minimally invasive procedures (i.e., single procedure in preference to possibly more than one PNL procedure)
- Stone in an ectopic kidney where percutaneous access and ESWL may be difficult or impossible.
- Cystolithotomy for giant bladder calculus
- A large stone burden in children because of easy surgical access and the need for only one anaesthetic procedure

Operative Procedures

Operative procedures that can be carried out include:

- Simple and extended pyelolithotomy
- Pyelo-nephrolithotomy
- Anatrophic nephrolithotomy
- Ureterolithotomy
- Radial nephrolithotomy
- Pyeloplasty
- Partial nephrectomy and nephrectomy
- Removal of calculus with re-implantation of the ureter (i.e., ureteroneocystotomy)

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

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

Where the expertise is available the laparoscopic approach should be an alternative before proceeding to open surgery (Marberger, 1999)	**LE = 4** **GR = C**

Recommendations for Removal of Renal Stones

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

More than 20 years of experience with low invasive methods have clearly shown that open surgery is necessary only in exceptional cases and mainly for those patients in whom anatomical reconstruction is necessary. Video-endoscopic retroperitoneal or laparoscopic surgery has no place as a standard procedure for removal of stones from the kidney. However, this technique should be considered as an alternative before proceeding to open surgery, and it is advantageous in some types of reconstructive surgery.

For small stones (up to a maximum diameter of 20 mm or a surface area of approximately 300 mm^2), ESWL has been established as the standard procedure because it is non-invasive, has a low rate of complications and there is (at least for adults) no need for regional or general anaesthesia.

There continues to be a debate about whether large renal stones are best treated with ESWL or with PNL. Although larger stones can also be treated successfully with ESWL, the drawbacks of ESWL are a frequent need for repeated treatments and the relatively common occurrence of residual fragments. Although PNL might be preferable to ESWL for faster debulking of the stone, it must be emphasized that considerable expertise and experience is required for complete clearance of stones from the caliceal system. Unless percutaneous surgery is carried out with a meticulous technique, residual fragments of the stone may also be left behind following PNL.

Residual fragments of infection stones, associated with the most pronounced risk of recurrent stone formation, can be eliminated with PNL, with or without

percutaneous chemolysis. Such a step might also be used as an auxiliary procedure in the treatment of cystine stones.

For uric acid stones, oral chemolysis is the first choice of treatment for stone elimination. However, an increased rate of dissolution can be obtained by combining stone disintegration and chemolysis, and treatment in this way may be considered for removal of large uric acid stones. The approximate estimates of surface area corresponding to oval stone projections with certain diameters are given in Appendix 2 of the original guideline document.

An overview of treatment recommendations according to size and stone type as discussed above is shown in the following tables.

Table: Active Removal of Radiopaque (Calcium) Renal Stones with a Largest Diameter ≤ 20 mm (Surface Area ~ ≤ 300 mm^2)			
Preference	**Procedure**	**LE**	**GR**
1	Extracorporeal shock-wave lithotripsy (ESWL), also including piezolithotripsy	1b	A
2	Percutaneous nephrolithotomy	1b	A
3	Retrograde intrarenal surgery	2a	C
4	Laparoscopic surgery	2a	C
5	Open surgery	4	C

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

For all patients with infection stones or recent history of urinary tract infection, bacteriuria antibiotics should be administered before the stone removing procedure for at and continued least 4 days afterwards	**LE = 4** **GR = C**

Table: Active Removal of Uric Acid Renal Stones with a Largest Diameter ≤ 20 mm (Surface Area ~ ≤ 300 mm^2)			
Preference	**Procedure**	**LE**	**GR**

Table: Active Removal of Uric Acid Renal Stones with a Largest Diameter ≤ 20 mm (Surface Area ~ ≤ 300 mm^2)			
Preference	**Procedure**	**LE**	**GR**
1	Oral chemolysis	2a	B
2	ESWL + oral chemolysis	2a	B

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

Table: Active Removal of Cystine Stones with a Largest Diameter ≤ 20 mm (Surface Area ~ ≤ 300 mm^2)			
Preference	**Procedure**	**LE**	**GR**
1	ESWL	2a	B
1	Percutaneous nephrolithotomy	2a	B
2	Retrograde intrarenal surgery	4	C
3	Laparoscopic surgery	4	C
4	Open surgery	4	C

Table: Active Removal of Radiopaque (Calcium) Renal Stones with a Largest Diameter >20 mm (Surface Area >300 mm^2)			
Preference	**Procedure**	**LE**	**GR**
1	Percutaneous nephrolithotomy	1b	A
2	ESWL	1b	A
3	Percutaneous nephrolithotomy + ESWL	2b	B
4	Laparoscopic surgery	4	C
4	Open surgery	4	C

Table Active Removal of Uric Acid Renal Stones with a Largest Diameter >20 mm (Surface Area ~ >300 mm^2)			
Preference	**Procedure**	**LE**	**GR**
1	Oral chemolysis	2a	B
2	ESWL + oral chemolysis	2a	B
3	Percutaneous nephrolithotomy	3	C
3	Percutaneous + chemolysis	3	C

For patients with uric acid stones and a percutaneous nephrostomy catheter in place, stone disintegration with ESWL combined with percutaneous chemolysis is a good alternative to quickly dissolve the stone material (see Section 7.5 of the original guideline document).

Table: Active Removal of Cystine Stones with a Largest Diameter >20 mm (Surface Area >300 mm^2)			
Preference	**Procedure**	**LE**	**GR**
1	Percutaneous nephrolithotomy	2a	B
1	Percutaneous nephrolithotomy + ESWL	2a	B
1	Percutaneous nephrolithotomy + chemolysis	3	C
2	ESWL + chemolysis	3	C
3	Laparoscopic surgery	4	C
3	Open surgery	4	C

Patients, who are planned for ESWL-treatment of stones with a diameter exceeding (20 mm ~300 mm^2), should have an internal stent to avoid problems related to Steinstrasse	**LE = 3** **GR = B**

<u>Staghorn Stones</u>

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

Patients with staghorn stones can usually be treated according to the principles given for large stones (diameter >20 mm/300 mm^2) (see Chapter 7 of the original guideline document)	**LE = 1b** **GR = A/B**

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

Management of Patients with Stones in the Ureter

For recommendations for the management of patients with stones in the ureter, see the National Guideline Clearinghouse (NGC) summary of the European Association of Urology (EAU) and American Urological Association (AUA) Education and Research, Inc. 2007 guideline for the management of ureteral calculi.

General Recommendations and Precautions for Stone Removal

Infections

A test for bacteriuria should be carried out in all patients in whom stone removal is planned. Screening with dipsticks might be sufficient in uncomplicated cases. In others, urine culture is necessary. In cases with clinically significant infection and obstruction, several days of drainage procedures by a stent or a percutaneous nephrostomy should precede the active intervention for stone removal.

Aspects of Anticoagulation and Stone Treatment

Patients with bleeding diathesis or medical anticoagulation should be referred to an internist for appropriate therapeutic measures prior to, and during, the stone-removing procedure.

Avoiding electro-hydraulic lithotripsy seems to be crucial to decrease bleeding complications (Watterson et al., 2002; Kuo et al., 1998)	**LE = 4** **GR = C**

Pacemaker

It is recommended that the patient's cardiologist is consulted before undertaking ESWL treatment. Patients with implanted cardioverter defibrillators need to be

treated with special care because some of these devices need deactivation during ESWL.

Recommendations for Special Considerations

Table: Recommendations for Special Considerations		
Special Considerations	**LE**	**GR**
Treatment with antibiotics should precede stone-removing procedures in case of a positive urine culture, positive dip-stick test or suspicion of an infective component	3	B
Treatment with salicylates should be stopped 10 days before the planned stone removal	3	B
Extracorporeal shock-wave lithotripsy (ESWL) and percutaneous nephrolithotomy (PNL) are contraindicated in pregnant women	4	C
ESWL is possible in patients with a pacemaker	4	C

Management of Stone Problems During Pregnancy

Diagnostic Evaluation

Ultrasonography (using the change in resistive index and transvaginal ultrasound [US] when necessary) has become the primary radiological diagnostic tool	**LE = 1a** **GR = A**

Management of the Stone Problem

In 70 to 80% of patients, the stones will pass spontaneously	**LE = 1a** **GR = A**

Preference 1	Conservative management with bed rest, appropriate hydration and analgesia should be the first line treatment for all pregnant women with non-complicated urolithiasis	**LE = 4** **GR = C**

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

Preference 2	The placement of an internal stent or a percutaneous nephrostomy catheter are suggested first line treatment alternatives	**LE = 4** **GR = C**

Preference 3	Ureteroscopy, although more invasive, has been accepted as a minimally invasive treatment alternative (Stothers & Lee 1992; Parulkar et al., 1998; Lewis et al., 2003; Cormier et al., 2006; Denstedt & Razvi, 1992)	**LE = 1b** **GR = A**

When conservative management fails and urinary diversion is desired, both nephrostomy tube placement and internal ureteral insertion are appropriate alternatives	**LE = 3** **GR = B**

Caution must be exercised when performing URS during pregnancy with a solitary kidney. Ureteroscopy in experienced hands can be an effective treatment alternative to removal of ureteral stones during pregnancy (**LE = 1b; GR = B**).

Due to the established risks of radiation exposure on the growing fetus, ESWL and PNL are contraindicated in pregnancy	**LE = 4b** **GR = C**

<u>Management of Stone Problems in Children</u>

Investigations

Paediatric patients with urinary stones are considered to be a high-risk group for developing recurrent stones.

Therefore, investigations for stone diagnosis as well as metabolic abnormalities are crucial (Straub et al., 2005).	**LE = 2a** **GR = B**

A urine culture is mandatory (Straub et al., 2005)	**LE = 2** **GR = A**

Imaging

When selecting diagnostic procedures to identify urolithiasis in paediatric patients, the investigator must consider the fact that the patients may be uncooperative, require anaesthesia for some modalities, or be sensitive to ionizing rays.

Ultrasound

Ultrasound evaluation should include the kidney the filled bladder and adjoining portions of the ureter (Palmer, 2006)	**LE = 4** **GR = B**

In addition, colour-Doppler US showing differences in the ureteric jet (Darge & Heidemeier, 2005) (**LE = 4; GR = C**) and differences in the resistive index of the arciform arteries of both kidneys are indicative of the grade of obstruction (Pepe et al., 2005) (**LE = 4; GR = C**).

Thus, US is able to provide information about the presence, size and location of a stone, the grade of dilatation and obstruction. It is also able to indicate signs of abnormalities that facilitate the formation of stones. Ultrasound also is a part of the metaphylactic work-up.

Nevertheless **US fails to identify stones in more than 40% of paediatric patients** (Oner et al., 2004; Palmer et al., 2005) (**LE = 4**) and provides no information about renal function.

Recently developed CT protocols may further reduce the radiation exposure (Cody et al., 2004) (**LE = 4; GR = C**). However, the radiation dose and the extent of information about renal function must be considered when using non-enhanced helical CT.

Intravenous Urography (IVU)

Conventional imaging models are indispensable in some cases (Riccabona, Lindbichler, & Sinzig, 2002; Chateil et al., 2004)	**LE = 4** **GR = C**

Helical Computed Tomogram (CT)

In paediatric patients, only 5% of stones escape detection by non-enhanced helical CT (Djelloul et al., 2006; Palmer et al., 2005; Thomson et al., 2001)	**LE = 4**

Sedation or anaesthesia is rarely needed when a modern high speed CT apparatus is used (Palmer, 2006)	**LE = 4**

Magnetic Resonance Urography (MRU)

Magnetic resonance urography is unable to demonstrate a urinary stone. However, it may provide detailed information about the anatomy of the urinary collecting system, the location of an obstruction or stenosis in the ureter, and the morphology of renal parenchyma (Leppert et al., 2002) (**LE = 4**).

Nuclear Imaging

A diuretic renogram with injection of a radiotracer (mercaptoacetyltriglycine [MAG_3] or diethylene triamine penta-acetic acid [DPTA]) and furosemide are able to demonstrate renal function, identify obstruction in the kidney after injection of furosemide, as well as indicate the anatomical level of the obstruction (Palmer, 2006) (**LE = 4; GR = C or B**).

Metaphylactic Investigations

The most common non metabolic disorders are vesico ureteral reflux, ureteropelvic junction obstruction, a neurogenic bladder, or other voiding difficulties (Sternberg et al., 2005)	**LE = 4**

If suspected, suitable investigations must be performed (see appropriate chapter of the original guideline document).

Metabolic investigations are based on a proper stone analysis. According to the current standard, infrared spectroscopy or X-ray diffraction are mandatory for adult patients. A wet chemistry analysis is insufficient (Hesse et al., 2005)	**LE = 2b** **GR = B**

Based on the composition of stones (see also the appropriate Chapter 16 in the original guideline document).

Additional serum chemistry and 24 hour urine collections may be required (Straub et al., 2005)	**LE = 2**

	GR = A

Stone Removal

In principle, the same treatment modalities are used for adults and children. However, the specific circumstances of paediatric therapy must be taken into account when treating children.

Spontaneous passage of a stone is more likely to occur in children than in adults (Sternberg et al., 2005)	**LE = 4** **GR = C**

For invasive stone removal in paediatric patients, both ESWL and endourologic procedures are effective alternatives. Several factors must be considered when selecting the therapeutic procedure:

- Compared to adults, children pass fragments more rapidly after ESWL.
- For endourological procedures, the smaller organ size must be considered when selecting instruments for PNL or URS.
- Use of US for localization during ESWL in order to eliminate radiation exposure.
- Anticipated stone composition (cystine stones are more resistant to ESWL).
- Co-morbidity involving the use of concomitant treatment.
- The need for general anaesthesia for ESWL (depending on the patient's age and the lithotripter used).

Endourological Procedures

The improvement of intracorporeal lithotripsy devices and the development of smaller instruments facilitate both PNL and URS in children. For PNL, nephroscopes that are sized 15F or less are available (Jackman et al., 1998; Lahme, 2006) (**LE = 4; GR = C**). Smaller 'needle ureteroscopes' and flexible scopes are also available.

During URS, dilatation of the ureteral orifice is rarely needed (Gedik et al., 2007)	**LE = 4** **GR = C**

As in adults (see Chapters 7 and 9 of the original guideline document).

The Ho:YAG laser is the preferred device for intracorporeal lithotripsy (Gupta, 2007)	**LE = 4**

	GR = C

For PNL or URS with larger instruments US or pneumatic lithotripsy are appropriate alternatives (Desai, 2005)	**LE = 3** **GR = C**

The indications for ESWL are similar to those in adults. Children with renal pelvic stones or caliceal stones with a diameter up to 20 mm (~300mm^2) are ideal cases for this form of stone removal. The success rates tend to decrease as the stone burden increases.	**LE = 1a** **GR = A**

Open or Laparoscopic Surgery

The rate of open procedures in stone patients has dropped significantly in all age groups. Open surgery, if required, may be replaced by laparoscopic procedures. Indications for surgery include failure of primary therapy for stone removal (Casale et al., 2004), abnormal position of the kidney (Holman & Toth, 1998), or an additional target of therapy apart from stone removal, such as the treatment of stones in a primary obstructive megaureter (Hemal et al., 2003) (**LE = 4; GR = C**).

Residual Fragments

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

Identification of biochemical risk factors and appropriate stone prevention is particularly indicated in patients with residual fragments or stones (Kang et al., 2007)	**LE = 1b** **GR = A**

In symptomatic patients, it is important to rule out obstruction and to treat this problem if present. In other cases, necessary therapeutic steps need to be taken to eliminate symptoms. In asymptomatic patients where the stone is unlikely to pass, treatment should be applied according to the relevant stone situation.

For well-disintegrated stone material residing in the lower calix, it might be worthwhile considering inversion therapy during high diuresis and mechanical percussion (Chiong et al., 2005)	**LE = 1a** **GR = A**

Table: Recommendations for the Treatment of Residual Fragments		
Residual Fragments, Stones (Largest Diameter)	**Symptomatic Residuals**	**Asymptomatic Residuals**
<4-5 mm	Stone removal	Reasonable follow-up
>6-7 mm	Stone removal	Consider appropriate method for stone removal

<u>Steinstrasse</u>

Table: Recommendations for Treatment of Steinstrasse				
Position of Stone	**Unobstructed**	**Obstructed and/or Symptomatic**	**LE**	**GR**
Proximal ureter	1. Extracorporeal shock-wave lithotripsy (ESWL)	1. Percutaneous nephrostomy catheter (PN)		
	2. Ureteroscopy (URS)	1. Stent	4	C
		1. URS		
		1. ESWL		
Mid-ureter	1. ESWL	1. PN		
	2. URS	1. Stent	4	C
		1. URS		
		1. ESWL		

Table: Recommendations for Treatment of Steinstrasse				
Position of Stone	**Unobstructed**	**Obstructed and/or Symptomatic**	**LE**	**GR**
Distal ureter	1. ESWL	1. PN		
	1. URS	1. Stent	4	C
		1. URS		
		1. ESWL		

<u>Internal Stenting – When and Why</u>

The Use of Stents in the Ureter

The indications for stenting for urgent relief of obstruction are:

- Presence of infection with urinary tract obstruction
- Urosepsis
- Intractable pain or vomiting or both
- Obstruction in a solitary or transplanted kidney
- Bilateral obstructing stones
- Relief of ureteral calculus obstruction in pregnancy, pending definitive therapy in the post-partum period

For decompression of the renal collecting system ureteral catheters, stents and percutaneous nephrostomy catheters are apparently equally effective	**LE = 1b** **GR = A**

The recommendation is that stent insertion prior to shock wave lithotripsy (SWL) for obstructing ureteral stones 2 cm or less provides no advantage and is unnecessary.

The recommendation is that ureteric stents are not necessary following uncomplicated URS for stones.

<u>Recurrence Preventive Treatment</u>

Recurrence Preventive Treatment of Patients with Calcium Stone Disease

Table: Dietary and Pharmacological Treatment Regimens for Prevention of Recurrent Calcium Stone Formation

Treatment	Biochemical Effects	References	LE	GR
Increased fluid intake	Dilution of urine	Borghi et al., 1996; Curhan et al., 1997	1b	A
Reduced intake of oxalate	Reduced excretion of oxalate			
Reduced intake of animal protein	Reduced excretion of: • Calcium • Oxalate • Urate Increased excretion of: • Citrate Increased pH	Borghi et al., 2002	1b	A
Reduced intake of sodium	Reduced excretion of calcium Increased excretion of citrate	Borghi et al., 2002	1b	A
Increased intake of fibres		Hess et al., 1999; Ebisuno et al., 1991	2b	B
Increased intake of vegetables, provided there is a simultaneous adequate intake of calcium		Siener & Hesse, 2002	3	B
Avoid excessive intake of vitamin C	Reduced urinary oxalate	Taylor, Stampfer, & Curhan, 2004	2b	B
Thiazide	Reduced excretion of calcium	Wilson, Strauss & Manuel, 1984; Robertson et al., 1985; Ettinger et al., 1988; Ohkawa et al., 1992; Borghi et al., 1993; Ahlstrand, Sandwall, & Tiselius, 1996; Ala-Opas et al., 1987; Coe & Kavalach, 1974; "Do thiazides," 1981; Ljunghall et al., 1981; Ahlstrand et	1a	A

Table: Dietary and Pharmacological Treatment Regimens for Prevention of Recurrent Calcium Stone Formation				
Treatment	**Biochemical Effects**	**References**	**LE**	**GR**
		al., 1984; Marangella et al., 1999; Tiselius et al., 1993		
Potassium citrate	Increased excretion of citrate Increased urine pH Increased inhibition of crystal growth and crystal agglomeration	Hofbauer et al., 1994; Ettinger et al., 1997	1b	A
Potassium magnesium citrate	Increased urine pH Increased excretion of citrate Increased inhibition of crystal growth and crystal agglomeration Reduced supersaturation with calcium oxalate (CaOx) as a result of increased urinary magnesium Increased inhibition of calcium phosphate (CaP) crystal growth and aggregation	Pak & Fuller, 1986	1b	A
Allopurinol (in patients with hyperuricuric calcium oxalate stone formation)	Reduces urinary urate Decreased risk of calcium oxalate crystal formation	Fellstrom et al., 1985	1b	A
Pyridoxine	In patients with primary hyperoxaluria: reduced excretion of oxalate	Takei et al., 1998	3	C

Drinking Recommendations

The general recommendation for calcium stone formers is to maintain a high urine flow by a generous intake of fluids. The aim should be to obtain a 24-hour urine volume of at least 2 L (**LE 1b; GR A**).

Although most beverages can be drunk to increase fluid intake and help prevent stone formation, grapefruit juice has been shown to be associated with an increased risk of stone formation (Curhan et al., 1998) (**LE 3; GR C**).

Table: Suggested Treatment for Patients with Specific Abnormalities in Urine Composition

Urinary Risk Factor	Suggested Treatment	LE	GR
Hypercalciuria	Thiazide + potassium citrate	1a	A
Hyperoxaluria	Oxalate restriction	2b	A
Hypocitraturia	Potassium citrate	1b	A
Enteric hyperoxaluria	Potassium citrate	3-4	C
	Calcium supplement	2	B
	Oxalate complex formation	3	B
High excretion of sodium	Restricted intake of salt	1b	A
Small urine volume	Increased fluid intake	1b	A
Urea level indicating a high intake of animal protein	Avoid excessive intake of animal protein	1b	A
Distal renal tubular acidosis	Potassium citrate	2b	B
Primary hyperoxaluria	Pyridoxine	3	B
No abnormality identified	High fluid intake	2b	B

Table: When Should Calcium Stone Formers Be Offered Recurrence Preventive Treatment and How?

Category**	Analysis of Urinary Risk Factors	Recurrence Prevention
First time stone former **without** residual stone or fragments (S_o)	No	General advice
First time stone former **with** residual stone or	Yes*	Specific advice, with or without a pharmacological

fragments (S_{res})		agent
Recurrent stone former with **mild** disease and **without** residual stone(s) or fragments (R_{mo})	No	General advice
Recurrent stone former with **mild** disease **with** residual stone(s) or fragments ($R_{m\text{-}res}$)	Yes*	Specific advice, with or without a pharmacological agent
Recurrent stone former with **severe** disease with or without residual stone(s) or fragments *or* stone forming patient with **specific risk factor(s)** irrespective of otherwise defined category (see "Specific Risk Factors for Stone Formation" below) (R_s)	Yes	Specific advice, with or without a pharmacological agent

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

Table: Pharmacological Treatment of Uric Acid Stone Disease

Objective	Therapeutic Measures	References	LE	GR
Prevention	**Urine Dilution** A high fluid intake; 24-hour urine volume exceeding 2-2.5 L	Rodman, Sosa & Lopez, 1996; Low & Stoller, 1997; Shekarriz & Stoller, 2002; Hesse, Tiselius, & Jahnen, 2002	3	B
	Alkalinization Potassium citrate 3-7 mmol x 2-3	Coe, Evan, & Worcester, 2005; Welch et al., 2006; Pak et al., 1977; Wilcox et al., 1972	2b	B
	In patients with a high serum or urine level of urate Allopurinol 300 mg x 1	Pak, Sakhaee, & Fuller, 1986	3	B
Medical dissolution of uric acid	**Urine dilution** A high fluid intake;		4	C

Table: Pharmacological Treatment of Uric Acid Stone Disease				
Objective	**Therapeutic Measures**	**References**	**LE**	**GR**
stones	24-hour urine volume exceeding 2-2.5L			
	Alkalinization Potassium citrate 6-10 mmol x 2-3	Mattle & Hess, 2005; Shekarriz & Stoller, 2002	1b	A
	Always reduce urate excretion Allopurinol 300 mg x 1		4	C

Medical Treatment of Cystine Stone Disease

Table: Pharmacological Treatment of Patients with Cystine Stone Disease			
Therapeutic Measures	**References**	**LE**	**GR**
Urine Dilution A high fluid intake should be recommended so that the 24-hour urine volume exceeds 3000 mL. To achieve this goal, the intake should be at least 150 mL/h	Ng & Streem, 1999; Biyani & Cartledge, 2006; Dent & Senior, 1955	3	B
Alkalinization *For patients with a cystine excretion below 3 mmol/24 h:* Potassium citrate 3-10 mmol x 2-3 should be given to achieve a pH >7.5	Ng & Streem, 1999; Biyani & Cartledge, 2006; Dent & Senior, 1955	3	B
Complex Formation with Cystine *For patients with a cystine excretion above 3 mmol/24 h or when other measures are insufficient* Tiopronin (α-mercaptopropionyl glycine), 250-2000 mg/day **or**	Ng & Streem, 1999; Biyani & Cartledge, 2006; Dent & Senior, 1955; Tiselius, 1996; Freed, 1975; Rogers et al., 2007; Chow & Streem, 1998	3	B

Table: Pharmacological Treatment of Patients with Cystine Stone Disease			
Therapeutic Measures	**References**	**LE**	**GR**
Captopril, 75-150 mg			

Management of Patients with Infection Stones

It is fundamental that the renal collecting system is cleared from stone material	**LE = 3** **GR = C**

Table: Pharmacological Treatment of Infection Stone Disease			
Therapeutic Measures	**References**	**LE**	**GR**
Stone Removal Surgical removal of the stone material as completely as possible	Wilson, 1989	4	C
Antibiotic Treatment			
Short-term antibiotic course	Wong, Riedl, & Griffith, 1996	3	B
Long-term antibiotic course		3	B
Acidification			
Ammonium chloride 1 g x 2-3	Wall & Tiselius, 1990	3	B
Methionine 500 mg 1-2 x 3	Jarrar, Boedeker, & Weidner, 1996	3	B
Urease Inhibition	Griffith et al., 1991; Williams, Rodman, & Peterson, 1984	1b	A*
In very selected cases with severe infections, treatment with acetohydroxamic acid (Lithostat) might be a therapeutic option			

* Although treatment with acetohydroxamic acid (Lithostat) has proven effective in controlled studies, due to the potentially severe side effects, this form of treatment is used only in selected cases with severe infections.

Definitions:

Levels of Evidence

1a Evidence obtained from meta-analysis of randomized trials

1b Evidence obtained from at least one randomized trial

2a Evidence obtained from one well-designed controlled study without randomization

2b Evidence obtained from at least one other type of well-designed quasi-experimental study

3 Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies and case reports

4 Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities

Grades of Recommendation

A. Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomized trial
B. Based on well-conducted clinical studies, but without randomized clinical trials
C. Made despite the absence of directly applicable clinical studies of good quality

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate diagnosis and management of urolithiasis

POTENTIAL HARMS

Diagnosis

- Precautions should be taken when contrast medium needs to be administered to patients who have either reported allergic reactions or who may be at such a risk.
- The administration of metformin (a drug used to treat diabetes type II) may give rise to lactic acidosis in case of contrast-induced anuria.
- Intravenous administration of contrast medium may result in a reduced renal perfusion and toxic effect on tubular cells.

Treatment

- Extracorporeal shock-wave lithotripsy (ESWL) for the treatment of large renal stones often causes problems. Frequent complications are pain, hydronephrosis, fever and occasional urosepsis, due to difficulties in the passage of stone particles, especially in cases of insufficient disintegration.
- Major but rare complications from percutaneous nephrolithotomy (PNL) are lesions to adjacent organs.
- As with open surgery, percutaneous procedures have different degrees of difficulty. A difficult procedure is to be expected when anatomical conditions offer only limited space for the initial puncture, dilatation and instrumentation, such as stones in diverticulae or stones completely filling the target calix, as well as a large stone burden caused by complete or partial staghorn stones. The procedure should only be carried out by experienced surgeons in these cases.
- There are complications associated with ureteral stenting, including stent migration, urinary tract infection, breakage, encrustation and obstruction.
- Sometimes, stents are not efficient in draining purulent or mucoid material, leading to a risk of obstructive pyelonephritis.
- Potential complications of the Holmium:yttrium aluminium garnet (Ho:YAG) laser when used to fragment ureteral stones include possible perforation of the ureteral wall and consecutive formation of strictures.
- As in all situations when pharmacological treatment is considered, a judgment must be made between the benefits and risks of the medication.
- It should be noted that hemiacidrin and Suby G solutions carry a potential risk of mortality (cardiac arrest) from hypermagnesemia if there is leakage and magnesium absorption occurs. This form of treatment must only be used when there is good evidence that the renal tract has healed following surgery and should never be infused in the immediate post-operative stage.

<u>Special Populations</u>

Pregnancy

- The most important factor complicating the radiological evaluation of stone disease in pregnancy is the risk of radiation exposure to the fetus, which includes possible teratogenesis, carcinogenesis, and mutagenesis. The risk is critically dependent on the gestational age and the amount of radiation delivered.
- Although no drug is absolutely free of risk during pregnancy, acetaminophen and narcotic analgesic drugs appear to have a minimal risk when used judiciously in usual doses under medical supervision.

- Epidural blocks have been commonly used to reduce maternal pain and their safety for mother and fetus are well accepted, provided maternal hypotension is avoided.
- The disadvantages of external tubes are the inconvenience of dealing with a collection device, the risk for accidental dislodgement and bacterial colonization. Moreover, the insertion of a percutaneous nephrostomy catheter may be complicated by significant bleeding because of tract creation and dilatation.
- Infection and migration are other complications of internal stents and because of these difficulties, reservation of ureteral stent placement for the later stages (>22 weeks) of pregnancy has been advocated.
- Ureteroscopy may require general anaesthesia and one must always be aware of the potential risk of ureteral perforation and sepsis.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Contrast medium should not be given to in the following circumstances: patient has allergy to contrast media, patient has serum or plasma creatinine level >150 micromoles/L, patient is on metformin, patient has untreated hyperthyroidism, patient has myelomatosis.
- The most obvious contraindications to extracorporeal shock-wave lithotripsy (ESWL) treatment are pregnancy, severe skeletal malformations, severe obesity and aortic and/or renal artery aneurysms, uncontrolled blood coagulation or uncontrolled urinary tract infections.
- Due to the established risks of radiation exposure on the growing fetus, percutaneous nephrolithotripsy (PNL) is contraindicated in pregnancy.
- The most important contraindications to ureteroscopy (URS) during pregnancy are inexperience and inadequate endoscopic instruments, stones with a diameter exceeding 1 cm, multiple calculi, transplanted kidney and sepsis (because of the higher risk of complications).

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- For all clinical problems, the various recommendations in this guideline are supported by comments based on the most important relevant publications or by panel opinion when data from the literature are contradictory or lacking. It must be emphasized, however, that no attempt was made to perform a structural analysis of the available literature since such an effort was beyond the possibilities and scope of the work.
- When recommendations were made, the main focus was on medical aspects. A discussion of the associated economic issues is beyond the scope of a European guideline document because of the wide geographical diversity of, and variation between, different financial systems in the European healthcare sector.
- The guideline developers are very well aware of the different treatment and technical facilities available geographically. Their intention has been to highlight the alternatives that appear most convenient for the patient in terms

of low invasiveness and risk of complications. This does not mean that other methods are not applicable. However, when a certain form of therapy is not recommended, this has been specifically stated.
- The purpose of this text is not to be proscriptive in the way a clinician should treat a patient but rather to provide access to the best contemporaneous consensus view on the most appropriate management currently available. European Association of Urology (EAU) guidelines are not meant to be legal documents but are produced with the ultimate aim to help urologists with their day-to-day practice.
- The EAU believe that producing validated best practice in the field of urology is a very powerful and efficient tool in improving patient care. It is, however, the expertise of the clinician which should determine the needs of their patients. Individual patients may require individualized approaches which take into account all circumstances and treatment decisions often have to be made on a case-by-case basis.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The European Association of Urology (EAU) Guidelines long version (containing all 19 guidelines) is reprinted annually in one book. Each text is dated. This means that if the latest edition of the book is read, one will know that this is the most updated version available. The same text is also made available on a CD (with hyperlinks to PubMed for most references) and posted on the EAU websites Uroweb and Urosource (www.uroweb.org/professional-resources/guidelines/ & http://www.urosource.com/diseases/).

Condensed pocket versions, containing mainly flow-charts and summaries, are also printed annually. All these publications are distributed free of charge to all (more than 10,000) members of the Association. Abridged versions of the guidelines are published in European Urology as original papers. Furthermore, many important websites list links to the relevant EAU guidelines sections on the association websites and all, or individual, guidelines have been translated to some 15 languages.

IMPLEMENTATION TOOLS

Pocket Guide/Reference Cards

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Tiselius HG, Alken P, Buck C, Gallucci M, Knoll T, Sarica K, Turk C. Guidelines on urolithiasis. Arnhem, The Netherlands: European Association of Urology (EAU); 2008 Mar. 128 p. [765 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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Working Group Members: H.G. Tiselius (*Chairman*); P. Alken; C. Buck; M. Gallucci; T. Knoll; K. Sarica; C. Türk

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All members of the working group submit a conflict of interest form.

All members of the Urolithiasis Guidelines Writing Panel have provided disclosure statements of all relationships that they have and that may be perceived as a potential source of conflict of interest. The information is kept on file in the European Association of Urology (EAU) database. This guideline document was developed with the financial support of the EAU. No external sources of funding and support have been involved. The EAU is a non-profit organization and funding is limited to administrative assistance, travel, and meeting expenses. No honoraria or other reimbursements have been provided.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the European Association of Urology Web site.

Print copies: Available from the European Association of Urology, PO Box 30016, NL-6803 AA ARNHEM, The Netherlands

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- EAU guidelines office template. Arnhem, The Netherlands: European Association of Urology (EAU); 2007. 4 p.
- The European Association of Urology (EAU) guidelines methodology: a critical evaluation. Arnhem, The Netherlands: European Association of Urology (EAU); 18 p.

The following are also available:

- Guidelines on urolithiasis. Pocket guide. Arnhem, The Netherlands: European Association of Urology (EAU); 2008 Feb. 34 p.
- Introduction. European Association Urology Guidelines. Arnhem, The Netherlands: European Association of Urology (EAU); 2008 Mar. 4 p.

Print copies: Available from the European Association of Urology, PO Box 30016, NL-6803 AA ARNHEM, The Netherlands

PATIENT RESOURCES

None available

NGC STATUS

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