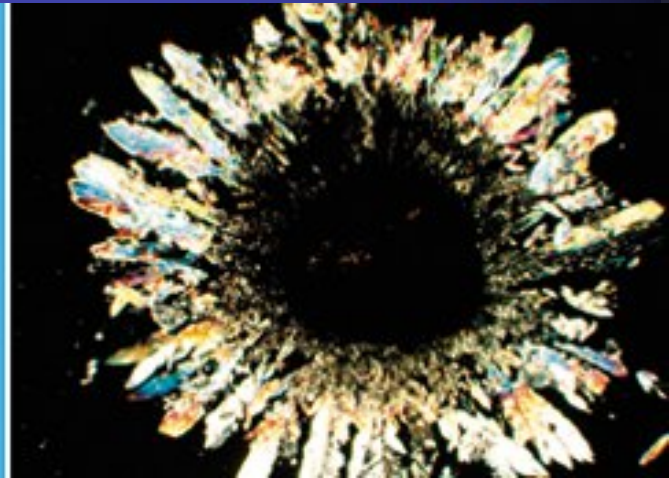


Urolithiasis



Urolithiasis: Epidemiology

Incidence is rising in Western countries.

In Germany, the current incidence is 1.47% and the prevalence is 4.7%.

This means that, at any given time, one in 21 people we encounter on the street suffers from some form of stone disease.

Urolithiasis: Epidemiology

Widespread condition of major significance

750,000 stone episodes at approx.

€2,500 each

€1.8 billion/yea



=

30% of urological patients

Urolithiasis: Epidemiology

men > women (3:1)

Urinary stones in children is rare, 1-5 % of stone patients

Peak age 40-50 years old

50-70 % recurrent within 10 years



Urolithiasis: causes

idiopathic

hereditary

overnutrition and dietary imbalances

dehydration

lack of physical activity

anatomical abnormalities of the urinary tract

metabolic disorders (hyperparathyroidism, cystinuria, renal tubular acidosis)

drug-induced (calcium, vitamin D, vitamin C (>4 g/day), sulfonamides, triamterene, indinavir)

inflammatory bowel disease (Crohn's disease), small bowel resection

Urolithiasis: Pathogenesis

Kidney stones consist of 95% crystalline substance and 5% organic matrix;

the pathogenesis of urinary stone disease is still not fully understood.

Urolithiasis: Pathogenesis

Crystallization theory:

As the concentration of dissolved substances increases, crystal and stone formation occurs in the urine.

However, individuals with healthy kidneys also excrete crystals when urine becomes supersaturated.

Consequently, crystalluria is not synonymous with a risk of stone formation.

Crystal excretion patterns:

Healthy people excrete small crystals ($<5\text{ }\mu\text{m}$).

Stone formers excrete large crystals and crystal conglomerates up to $300\text{ }\mu\text{m}$ in size.

Urolithiasis: Pathogenesis

Substances that inhibit crystal aggregation (inhibitors) play an important role in the formation of calcium-containing stones (>90% of urinary stones):

- Citrate
- Magnesium
- Bisphosphonate
- Polyanions
- Glycoproteins

Urolithiasis: Pathogenesis

substances
(Promoters)

- Oxalate
- Calcium
- Uric acid

Urolithiasis: Pathogenesis

- substances that promote stone formation (Promoters):
 - Oxalate
 - Calcium
 - Uric acid



Urolithiasis: Pathogenesis

substances that promote stone formation
(Promoters):

1 molecule **Oxalate** binding 50 molecule
Calcium

Urolithiasis: Pathogenesis

Forms of crystallization

- **Heterogeneous crystallization**

on a foreign surface such as:
cellular debris, urothelial lesions,
or implants/foreign bodies
under conditions of metastable supersaturation

- **Homogeneous crystallization**

increasing urinary supersaturation reaching the point of unstable
supersaturation, resulting in spontaneous crystal formation



Urolithiasis: Pathogenesis

Forms of crystallization

Unattached stone formation

Generally not possible in the urinary tract, as urine transit time under normal drainage conditions is too short for stones of significant size to form

Exceptions:

Cystinuria

Hyperuricosuria

Infections

Urinary tract obstruction

Urolithiasis: Pathogenesis

Forms of crystallization

- Fixed stone formation

Applies to stone formation in the collecting ducts or the interstitium

Caused by increased adhesion of crystals formed in the urine to structures such as tubular surfaces, followed by migration to the papillary surface (**papillary calcification**)

Urolithiasis: the most common types of stones

Calcium oxalate monohydrate 70%

Calcium oxalate dihydrate 20%

Uric acid 8–10%

Magnesium ammonium phosphate 5–7%

Calcium phosphate 4–7%

Cystine 0.5–3%

Urolithiasis: specific pathogenesis

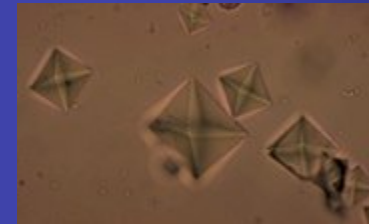
Calcium oxalate:



most commonly idiopathic
hypercalciuria

increased calcium intake

increased release (resorptive hypercalciuria
due to immobilization or hyperparathyroidism)



Urolithiasis: specific pathogenesis

Calcium oxalate:

Hyperoxaluria

- rare autosomal recessive hereditary form
- dietary (excessive intake of oxalate-rich foods)
- inflammatory bowel disease (Crohn's disease), small bowel resections
- malabsorption

Impaired **fat absorption** leads to increased intraluminal binding of calcium, which is then unavailable as ionized calcium to bind oxalate; unbound oxalate is consequently absorbed to a greater extent in the intestine and excreted renally.



Urolithiasis: specific pathogenesis

Calcium oxalate:

- Hypocitraturia/hypomagnesiuria:

Citrate forms soluble complexes with calcium, thereby inhibiting crystallization (in the formation of calcium oxalate and calcium phosphate stones)

- Hypocitraturia:

is the most common finding in patients with calcium oxalate stones (15–50%)

- Metabolic acidosis (type I renal tubular acidosis, chronic diarrhea) due to reduced tubular calcium reabsorption and hypercalciuria; increased citrate reabsorption

- High-protein diet

- Potassium deficiency (laxatives, diuretics)



Urolithiasis: specific pathogenesis

Uric acid stones:

- (radiolucent)
- Uric acid is extremely insoluble in the acidic pH range (<6)
- the most common cause is not hyperuricosuria, but rather acidic urine (fixed acidic pH: pH consistently <6 throughout the day)
increased urinary uric acid excretion in cases of:
 - Gout
 - Myeloproliferative syndrome
 - Hemolytic anemia
 - Use of uricosuric agents



Urolithiasis: specific pathogenesis

Magnesium ammonium phosphate (infection stone):

- Male-to-female ratio: 1:5
- Often large stones, potentially forming a staghorn calculus (filling the renal pelvis and calyces)



UTIs caused by urease-producing bacteria

- (Proteus, Klebsiella, Pseudomonas, Serratia)
- lead to high ammonium concentrations and an alkaline urinary pH, which promotes stone formation
- The bacteria consume citrate for energy production



Urolithiasis: specific pathogenesis

Calcium phosphate
usually mixed stones



apatite stones form at high urinary pH (> 6.8)
brushite can form at pH < 6.5 in the presence
of high calcium concentrations
otherwise similar to calcium oxalate stones



Urolithiasis: specific pathogenesis

Cystine stones:



often appear as early as childhood

Cystinuria: (autosomal recessive) impaired reabsorption of the amino acids cystine, ornithine, lysine, and arginine in the intestine and renal tubules

Cystine has very poor solubility in urine

Urolithiasis: Clinical Presentation

Renal colic caused by stone mobilization into the ureter presents a clinically striking picture with severe pain.



Rarely an incidental finding in asymptomatic patients (becoming more frequent due to improved ultrasound diagnostics).

Urolithiasis: Clinical Presentation

Key symptoms

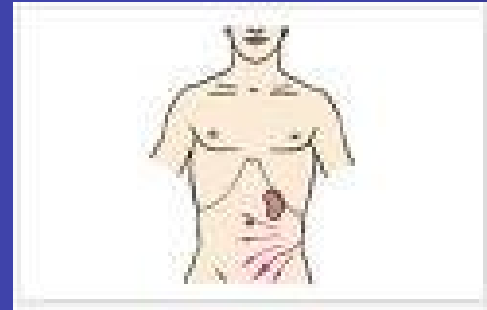
Dragging or colicky flank pain

Localisation of pain depending on stone location:

Kidney/proximal ureter: Flank

Mid-ureter: Groin region

Distal ureter: Testicles/labia



Urolithiasis: Clinical Presentation

Micro- or macrohematuria

In cases of colic: restless patient pacing about

Other symptoms:

- Fever
- Dysuria/pollakiuria
- Vomiting/nausea
- UTI/sepsis

Urolithiasis: Diagnosis

A basic evaluation should be performed for every patient with stones; an extended metabolic evaluation is indicated only for specific patient groups.

- Medical history
- Physical examination
- Basic diagnostics

Urolithiasis: Diagnosis

Basic diagnostics:

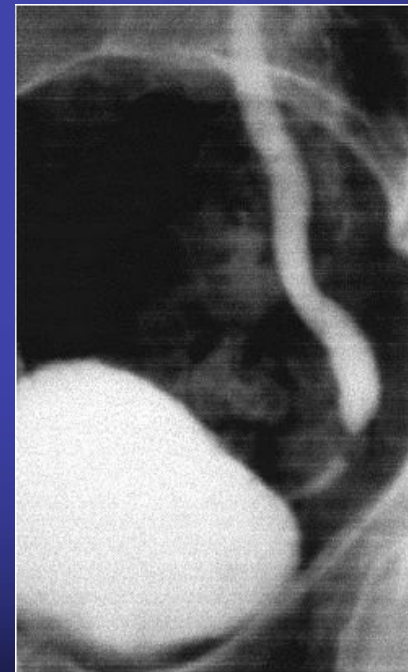
- Stone analysis: Infrared spectrometry/X-ray diffraction
- Blood sampling: Electrolytes, creatinine, uric acid, CRP, complete blood count (CBC)
- Urine: pH measurement, urinalysis, sediment (crystals?), culture
- Ultrasound: Stone localization, stone size, urinary tract obstruction, anatomical abnormalities



Urolithiasis: Diagnosis

Basic diagnostics:

Intravenous urography: stone localization, stone size, urinary tract obstruction, anatomical abnormalities



Urolithiasis: Diagnosis

Initial diagnostic workup:

In acute diagnostics, the trend is shifting away from IVU towards unenhanced helical CT (low-dose stone CT).

CT:

- is independent of renal function
- but does not visualize the excretion status (important for treatment decisions)
- (detection limit for all imaging modalities: approx. 2–3 mm)

Urolithiasis: Diagnosis

Basic diagnostics:
Nativ-stone-CT



Urolithiasis: Diagnosis

Patient groups requiring extended metabolic evaluation:

all recurrent stone formers

or first-time stone formers with:

- non-calcium-containing stones
- Family history of kidney stones
- age <25 years
- chronic inflammatory bowel disease
- solitary kidney
- sarcoidosis (renal fibrosis?)
- hypercalcemia

Urolithiasis: Diagnosis

Renal tubular acidosis (RTA)

Nephrocalcinosis or multiple calculi

Osteoporosis

Lithogenic medication: calcium or vitamin D supplementation, ascorbic acid >4 g/day, sulfonamides, triamterene, indinavir

Specific occupational indications (pilots, professional drivers)



Urolithiasis: Diagnosis

Extended metabolic workup:

- Blood analysis (basic diagnostics + albumin, parathyroid hormone)
- Urine (same as basic examination)
- 24-hour urine collection (twice): Calcium, oxalate, uric acid, cystine, citrate, magnesium, phosphate, chloride, potassium, sodium, creatinine, volume
- Ammonium chloride loading test if indicated (in cases of high urine pH without UTI: suspected renal tubular acidosis [RTA])

Urolithiasis: Diagnosis

additional diagnostic imaging:

retrograde pyelography:

- in cases of contrast medium allergy
- renal insufficiency
- acute colic (risk of fornix rupture with IVU)
- non-visualizing kidney on IVU
- metformin medication
- for further intervention



Urolithiasis: Diagnosis

Additional diagnostic imaging:

Renal scintigraphy (MAG3)
to supplement the assessment of
renal function
and the determination of the
surgical procedure



Urolithiasis: Therapy

50% of asymptomatic stones become symptomatic over time. So, which patients with these stones should undergo treatment?

Initially, regular monitoring.

Treatment in the event of increasing stone size or the onset of symptoms.

Urolithiasis: Therapy

acute colic due to ureteral stones

(up to 80% of all stones ≤ 4 mm pass spontaneously)

- conservative management (analgesia, physical activity, oral fluid intake—"walk and drink"- and potentially alpha-blockers for prevesical stones)
- urinary drainage via ureteral stent or percutaneous nephrostomy (PCN) in cases of persistent pain or fever/sepsis due to obstruction
- the likelihood of spontaneous passage increases the lower the stone is located.

Urolithiasis: Therapiegrundsätze

Interventional therapy aimed at removing urinary stones is a form of symptomatic treatment.

In cases of recurrent stone formation, appropriate metaphylaxis should be employed to prevent the development of new stones.

For infection-induced stones, treatment initially involves empirical antibiotic therapy, which is subsequently adjusted to targeted antibiotic therapy once the results of susceptibility testing (resistogram) are available.

In the case of uric acid stones, treatment is supplemented by oral chemolitholysis.

Urolithiasis: Therapy

Ureteral stones:

- In situ ESWL, possibly following DJ stenting
- Primary ureterorenoscopy (URS), possibly following DJ stenting (laser fragmentation, basket extraction)
- Percutaneous antegrade URS

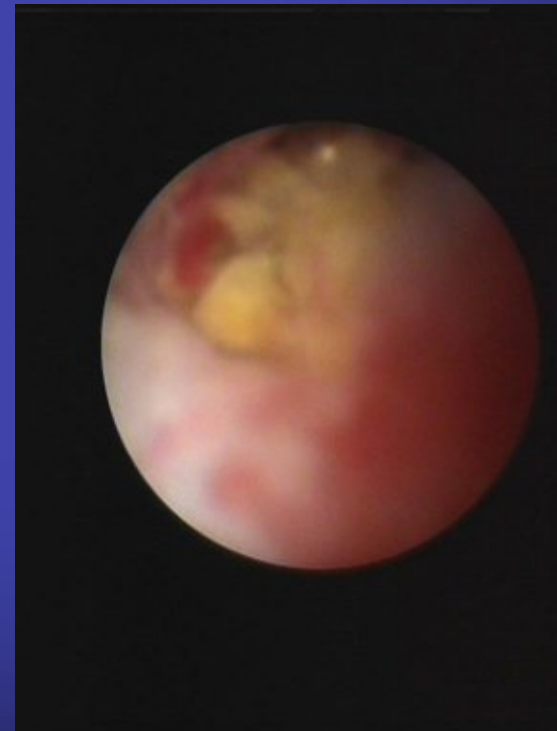
Urolithiasis: Therapy

Ureter stone: primary Ureterorenoscopy



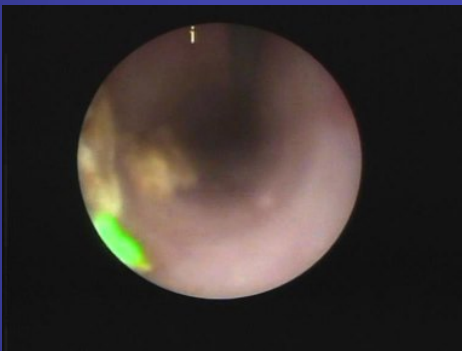
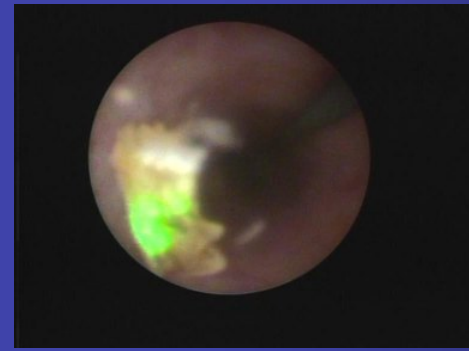
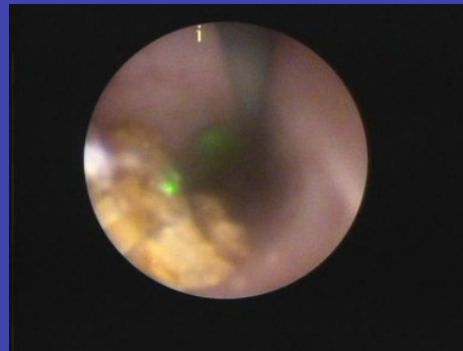
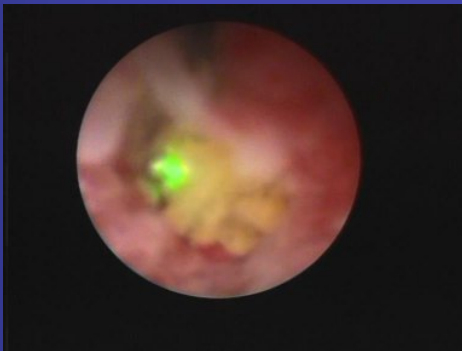
Urolithiasis: Therapy

Ureter stones: Laser lithotripsy URS



Urolithiasis: Therapy

Ureter stones: Laser- lithotripsy URS



Urolithiasis: Therapy

Kidney stones:

ESWL

URS (semirigid oder flexibel; desintegration per Laser, bascet)

PCNL (minimal invasive PCNL, 14 CH)

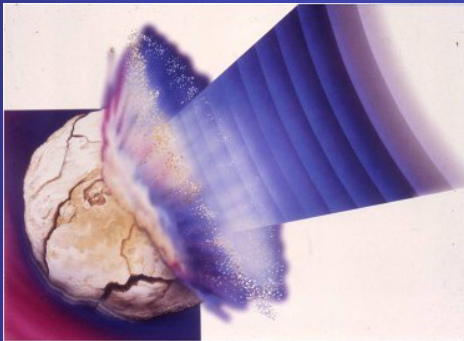
Kidney surgery (open, laparoscopic or roboter-assisted)

Urolithiasis: Therapie

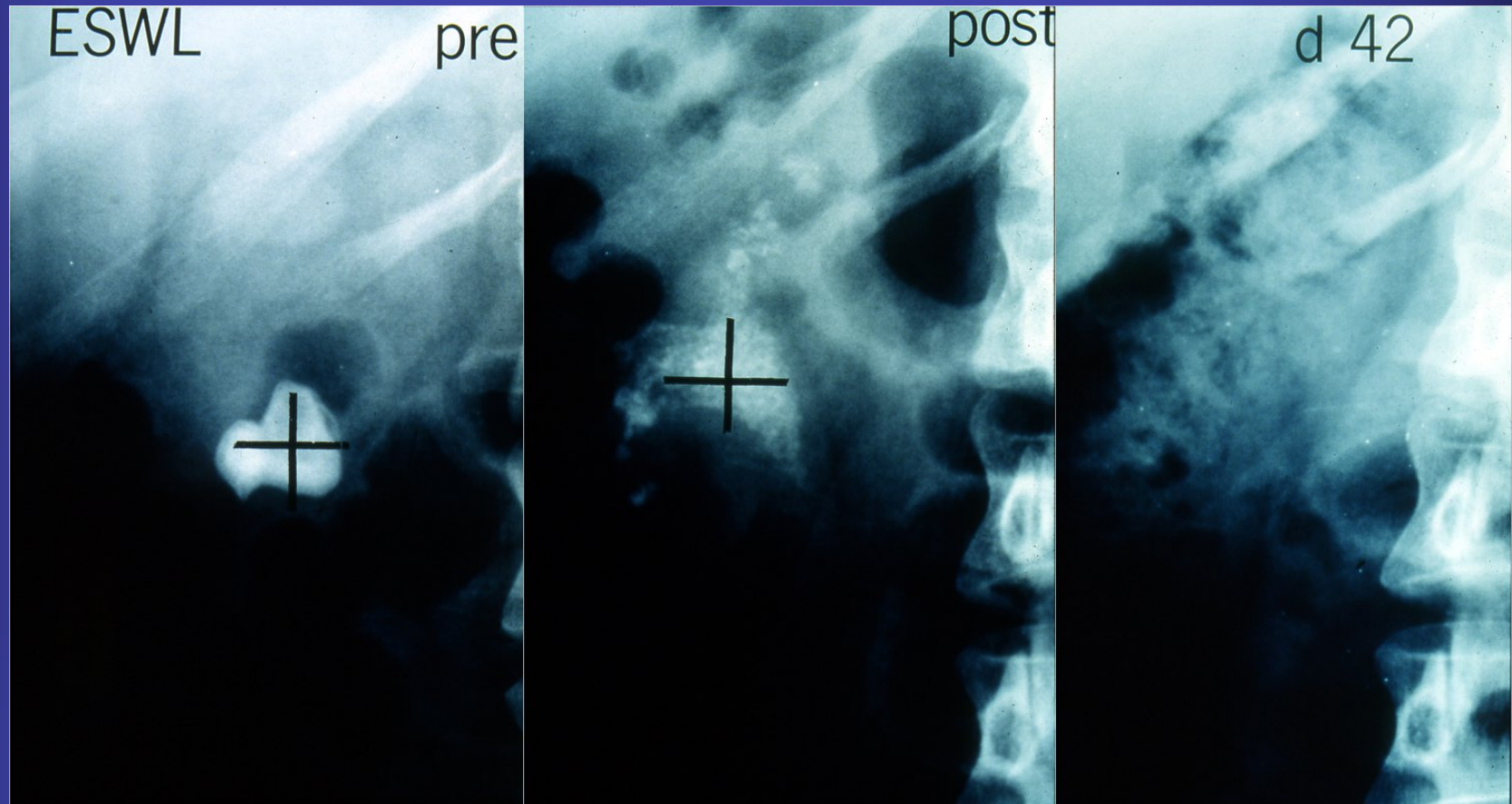
ESWL (analgo-sedation sufficient):

- Stones <15 mm
- Focused shock waves (behaving like an acoustic wave)
- Strong tensile and compressive stresses occur at interfaces of differing acoustic impedance (tissue/stone)
- Disintegration of the stone
- Fragments are excreted
- Multiple interventions usually required

Urolithiasis: Therapy ESWL



Urolithiasis: Therapy ESWL



Urolithiasis: Therapy

Ureterorenoscopy (URS):

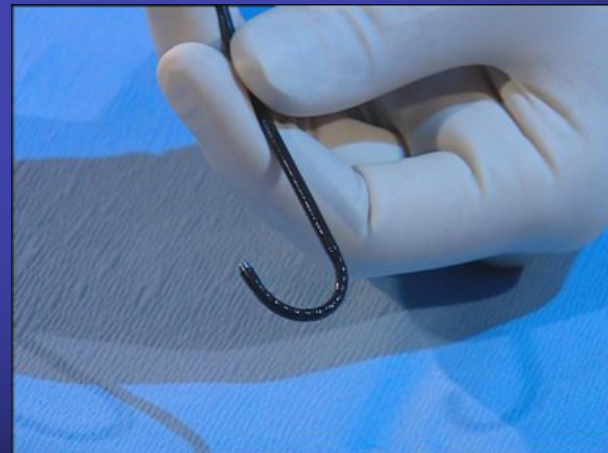
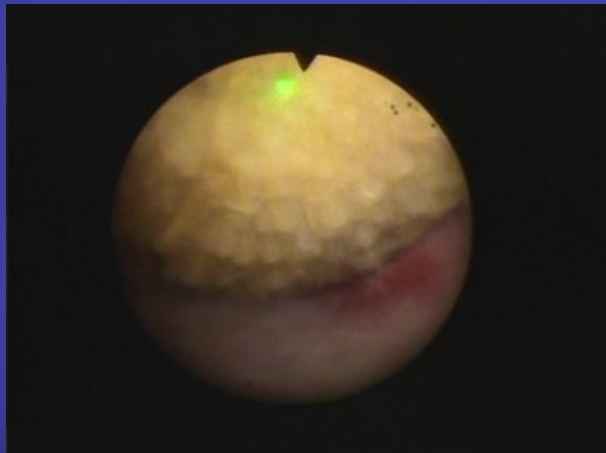
- Stones 10–20 mm
- Most stones are amenable to URS
- Repeat procedures rarely required

Rigid, semi-rigid, or flexible instruments (6–11 Fr.)

- Fragmentation—primarily via laser—is highly effective today
- Extraction of fragments using forceps or tipless baskets

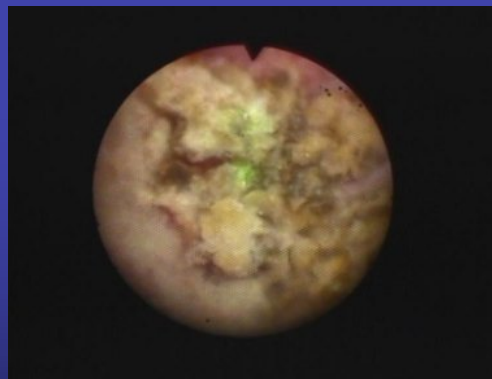
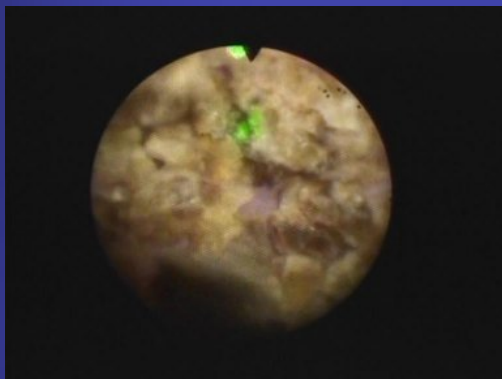
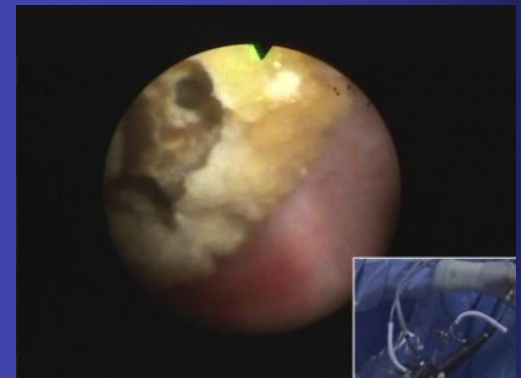
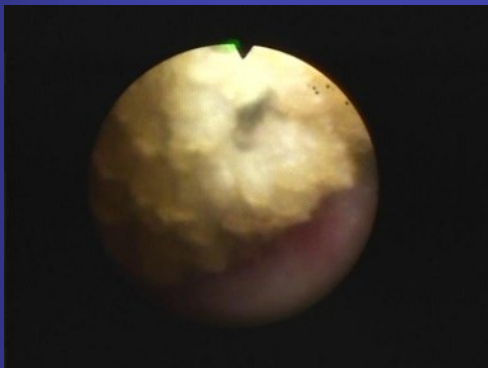
Urolithiasis: Therapy

Kidney pelvis stone: Laser-URS



Urolithiasis: Therapie

Kidney pelvis stone: Laser-URS



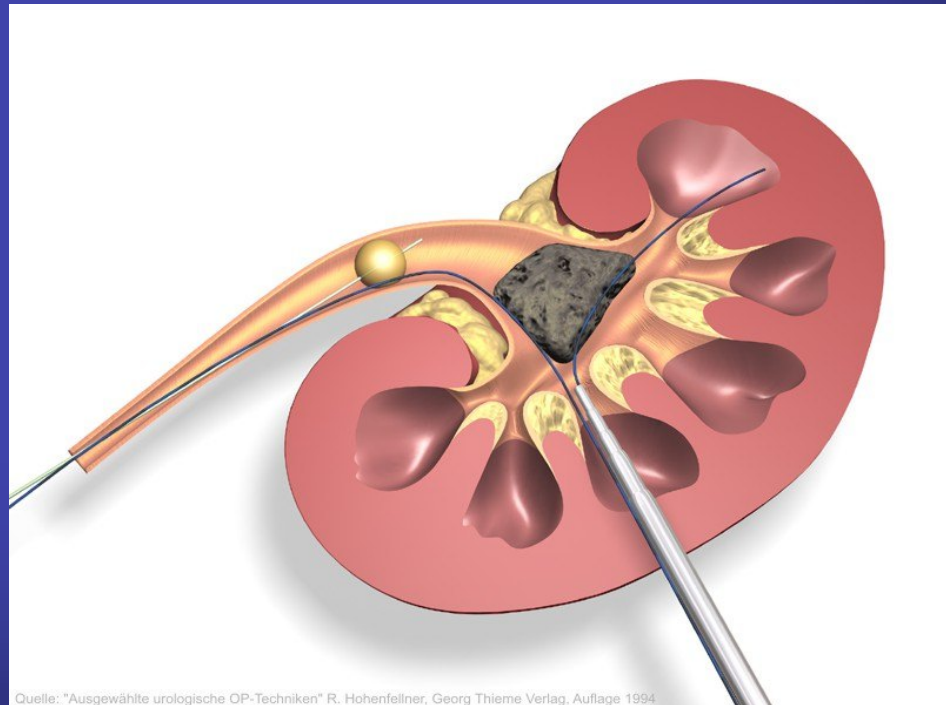
Urolithiasis: Therapy

percutaneous nephrolithotomy (PCNL):

- important standard minimally invasive procedure
- kidney stones >15 mm to staghorn calculi
- good visualization of the collecting system
- rigid and flexible nephroscopes
- fragmentation via ballistic, ultrasonic probe, mechanical, or laser methods
- working sheath diameter is decreasing due to device advancements (currently 10–20 Fr.)
- second-look procedure possible

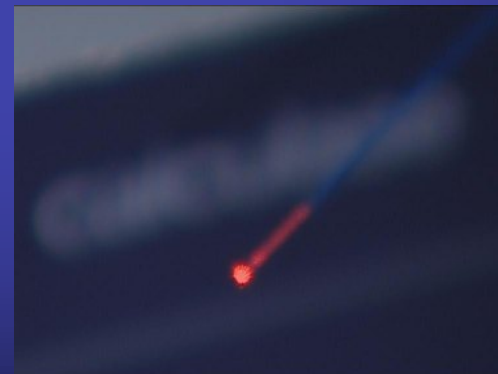
Urolithiasis: Therapy

percutane Nephrolithotomy (PCNL)



Urolithiasis: Therapy

percutane Nephrolithotomy (PCNL)



Urolithiasis: Therapy

Percutane Nephrolithotomy (PCNL)



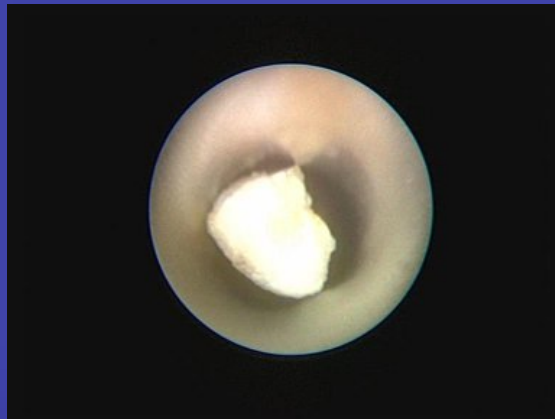
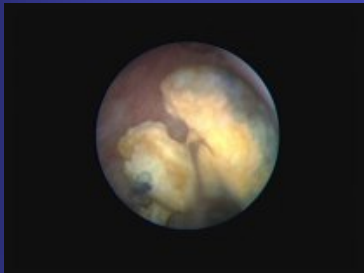
Urolithiasis: Therapy

Percutane Nephrolithotomy (PCNL)



Urolithiasis: Therapy

Percutane Nephrolithotomy (PCNL)



Urolithiasis: Therapy

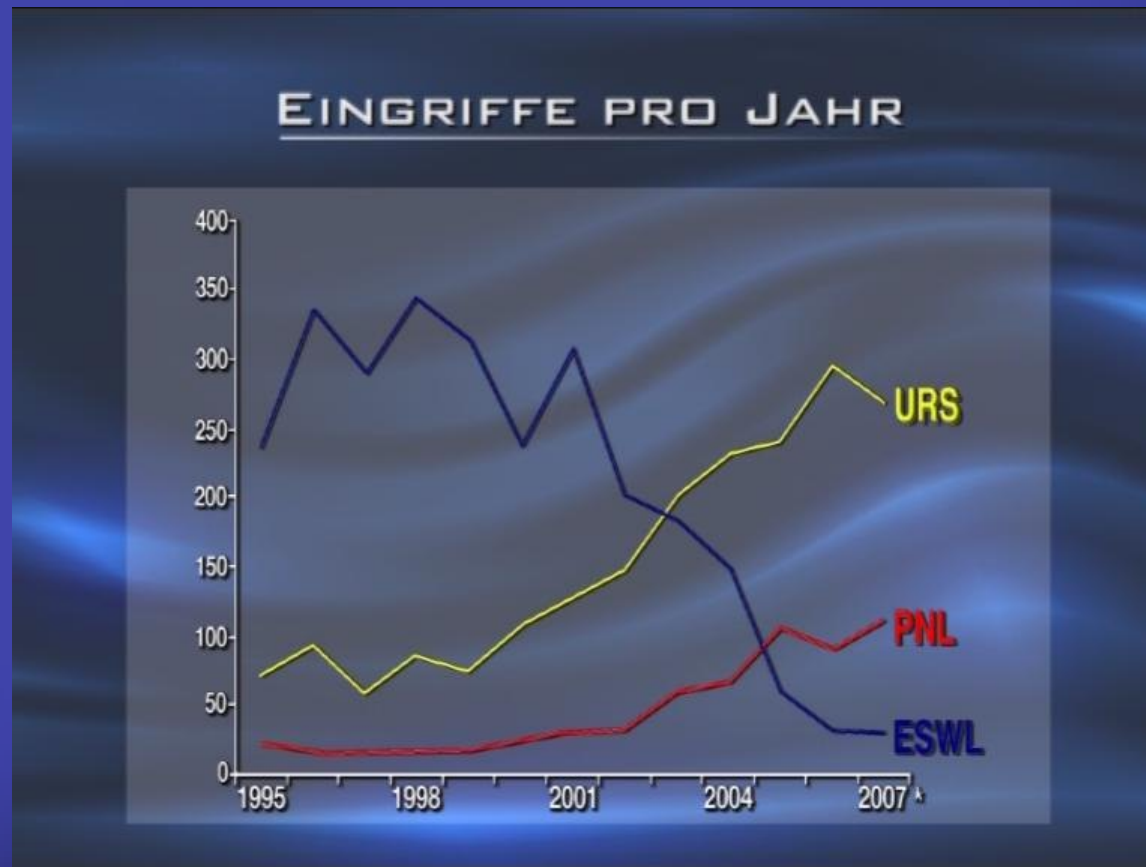
All the above-mentioned procedures can be readily combined.

Endourological treatments are increasing and show high stone-free rates.

ESWL treatments are declining (multiple sessions often required).

There is hardly any remaining indication for open stone surgery (<1% of all stone treatments).

Urolithiasis: development of therapy



Urolithiasis: Therapy

Metaphylaxis:

- Causal therapy
- Measures to prevent disease recurrence
- Reduction of recurrences prevents painful stone episodes
- Reduction of healthcare system costs

Urolithiasis: Therapy

general metaphylaxis:

General metaphylaxis should be implemented for all patients with urinary stones (stone-specific metaphylaxis for patients at high risk of recurrence).

- normalization of body weight
- physical activity
- adequate fluid intake (>2 L/day)
- low-fat and low-meat diet (max. 150 g animal protein/day)
- reduction of salt intake
- reduction of alcohol, coffee, tea, and sweetened drinks

Urolithiasis: Therapie

allgemeine Metaphylaxe:

Diureseerhöhung (Trinkprophylaxe)

- Flüssigkeitszufuhr 2,5-3 l/Tag
- zirkadianes Trinken
- harnneutrales Trinken
- Diurese 2-2,5 l/Tag



Urolithiasis: Therapy

General Metaphylaxis: Nutrition

- Balanced diet
- high in fiber
- rich in vitamins (no excessive intake of vitamin supplements)
- vegetable-based
- calcium 1,000-1,200 mg/day
- salt 4-5 g/day
- protein intake 0.8-1.0 g/kg body weight/day

General metaphylaxis:

- Normalization of general risk factors
- BMI 18-25 kg/m² (guideline)
- Stress reduction
- Adequate physical activity



Urolithiasis: Therapy

Specific metaphylaxis:

- **Calcium-containing stones** (in high-risk patients and those with recurrent stone formation)
- Reduction of oxalate, especially in enteric hyperoxaluria
- High-fiber diet (fruits, vegetables) to shorten the enteral transit time of food: enteral binding of calcium
- Increasing citrate intake using alkali citrate (caution: contraindicated in renal insufficiency due to the potassium content)
- Normalization of calcium intake (0.8 g/day); no calcium reduction
- Urinary alkalinization; target pH 6.8 using citrus juices or alkali citrate (2-3 daily doses)
- Administration of sodium bicarbonate
- Possibly magnesium supplementation in hypomagnesiuria
- In hyperoxaluria: cholestyramine for intestinal binding of oxalate

Urolithiasis: Therapy

Specific metaphylaxis:

Foods high in oxalate, calcium, and uric acid

Oxalate:

Rhubarb, spinach, cocoa, black tea, nuts

Calcium:

Yogurt, milk, cheese, rhubarb, chocolate

Uric acid:

Calf thymus, liver, kidney, poultry skin, herring, sardines, anchovies

Urolithiasis: Therapy

Specific metaphylaxis:

Uric acid stones

can often be dissolved pharmacologically by urinary alkalization with alkali citrates (oral chemolitholysis)

for metaphylaxis: pH 6.8–7

for therapy: pH 7–7.2

in cases of proven hyperuricemia/

hyperuricosuria: chemolitholysis + allopurinol
300 mg/day

Urolithiasis: Therapy

Specific metaphylaxis:

Infection stones (complete stone removal required)

- Avoidance of alkalizing foods (citrus juices, purely vegetarian diets, bicarbonate-rich mineral waters)
- Antibiotic treatment, even low-dose, until stone removal
- Temporary urinary acidification: L-methionine, until pH <6.2

Urolithiasis: Therapy

Specific Metaphylaxis:

Cystine Stones

- To reduce the frequency of stone formation, intensive and regular medical monitoring is necessary.
- Quarterly: 24-hour cystine excretion, ultrasound (cystine excretion should be <300 mg/day)
- Reduction of animal protein (contains L-methionine, the precursor of cystine)
- Reduction of acidifying foods (animal protein, alcohol, soft drinks)
- Reduction of table salt

Urolithiasis: Therapy

Specific metaphylaxis: Cystine stones

Urine dilution:

Continuous urine dilution

Day and night,

Daily urine output >3 liters (fluid intake 4-7 liters)

Urine alkalinization:

Cystine solubility increases significantly in alkaline conditions; alkalization with medication to at least pH 7.5

Urolithiasis: Therapy

Specific metaphylaxis:

Cystine stones

Recommendation of the German Society of Urology (DGU):

For cystine excretion up to 840 mg/day, administer 3-5 g of **ascorbic acid**/day as an effervescent tablet
alkalinizing effect due to the **bicarbonate** content
reducing effect of the ascorbic acid

If necessary, administer **tiopronin**: reduces cystine to the more soluble cysteine

Urolithiasis

