Urolithiasis

András Jávorházy MD, PhD

Epidemiology

- Prevalence: ~ 10%
  - EU: 5-9%
  - USA: 12-15%
  - „middle east”, North Africa: 10-15%
  - Asia: 1-5%

  Continous increase: since `90 +40%

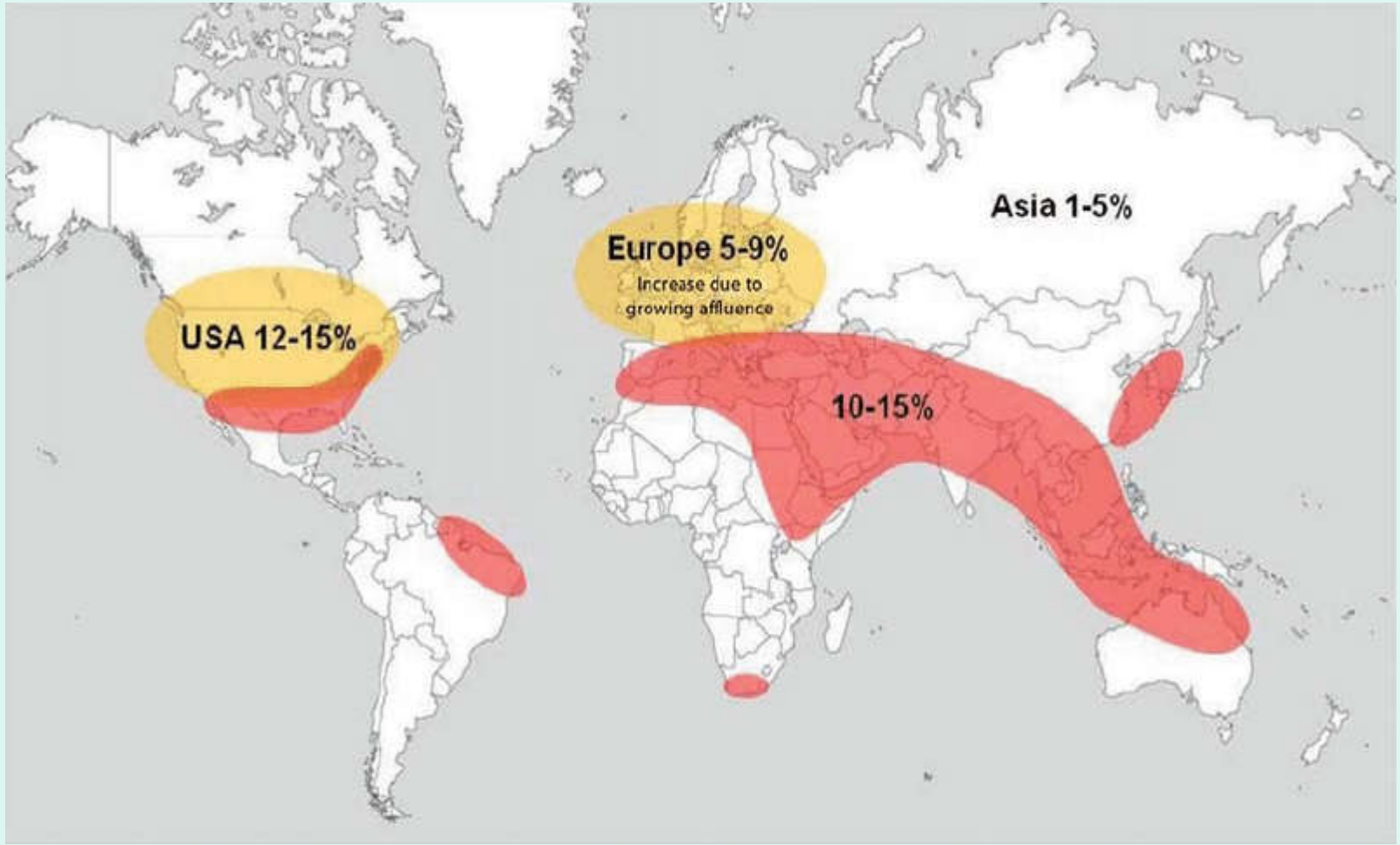
  2050: ~ 30%

- Incidence: ~ 1%
- Recidive risk:

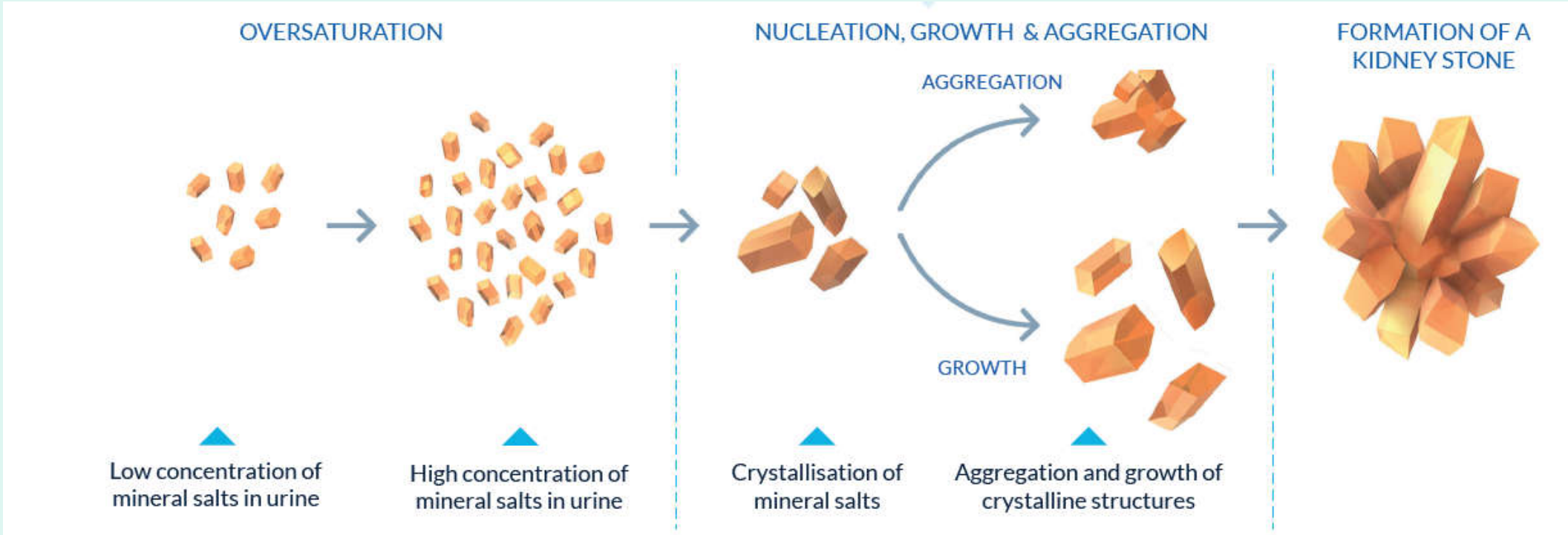
  w/o tx: 80% in 10y

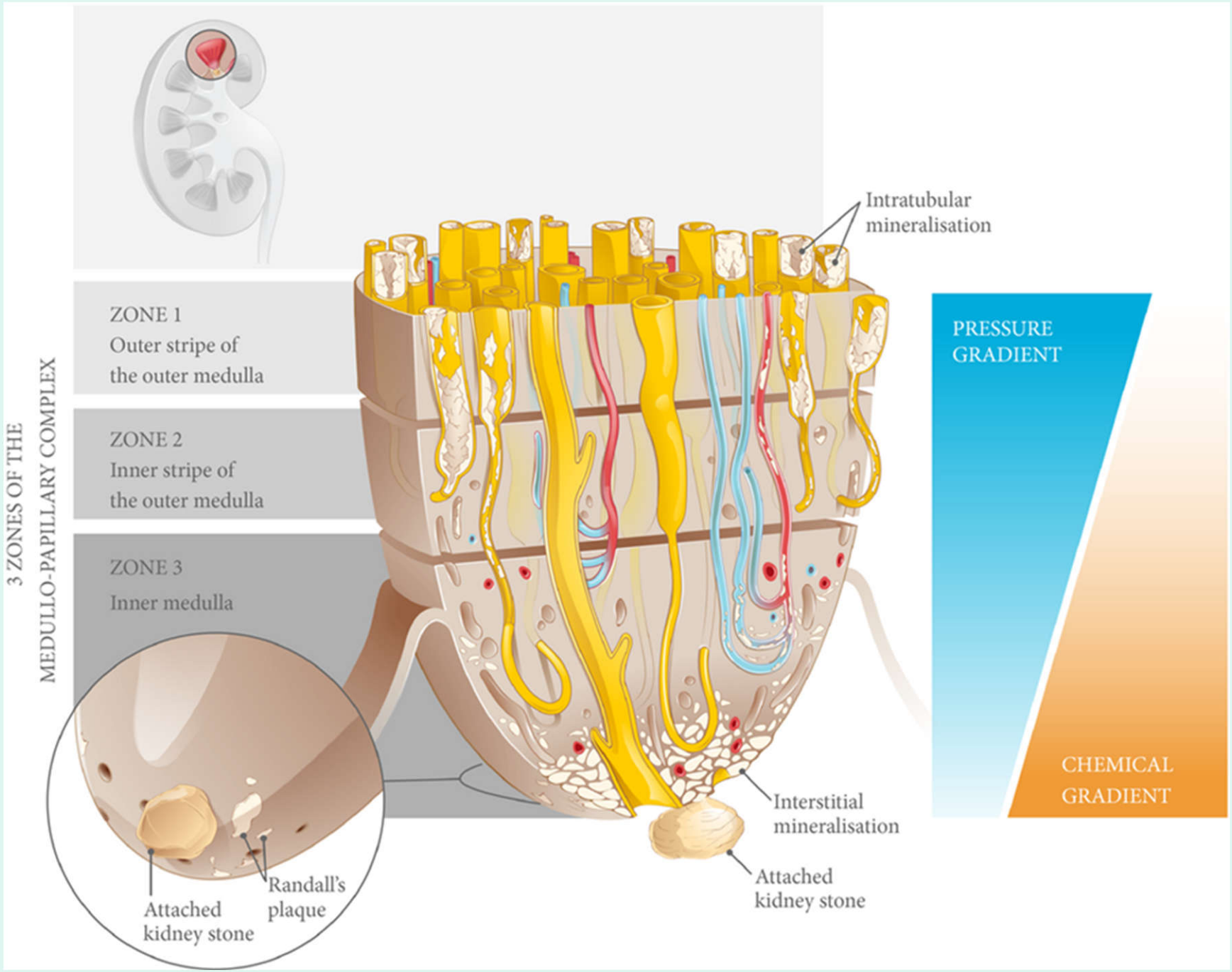
  w/ correcte sec. prevention: 10-15%

Urologic Disease of America, NIH, 2012.

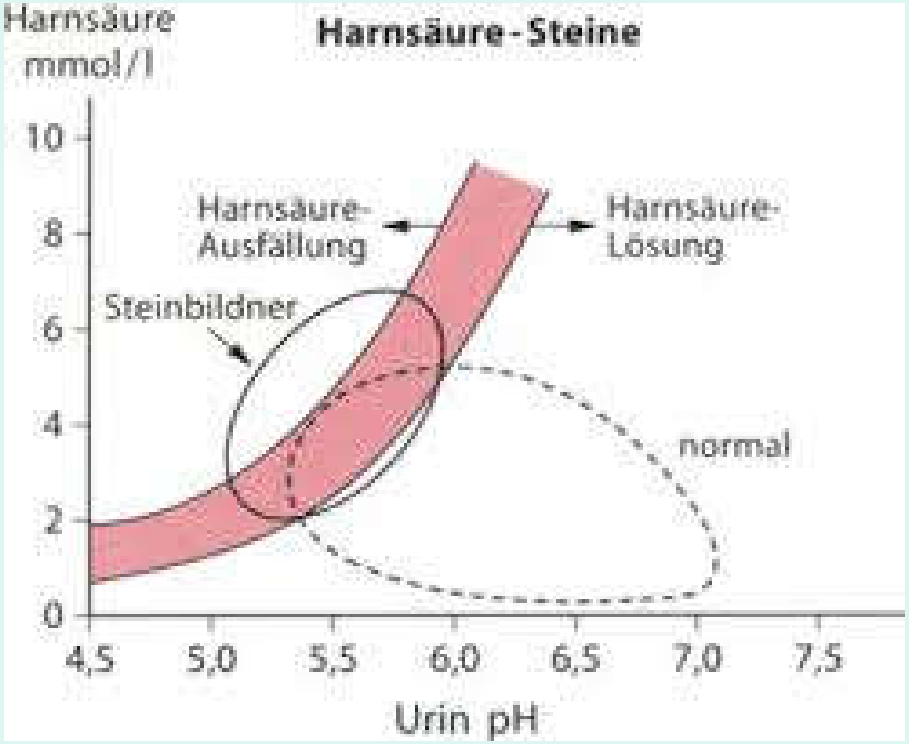

Asia 1-5%
Europe 5-9%
Increase due to growing affluence
USA 12-15%
10-15%

Formation of kidney stones

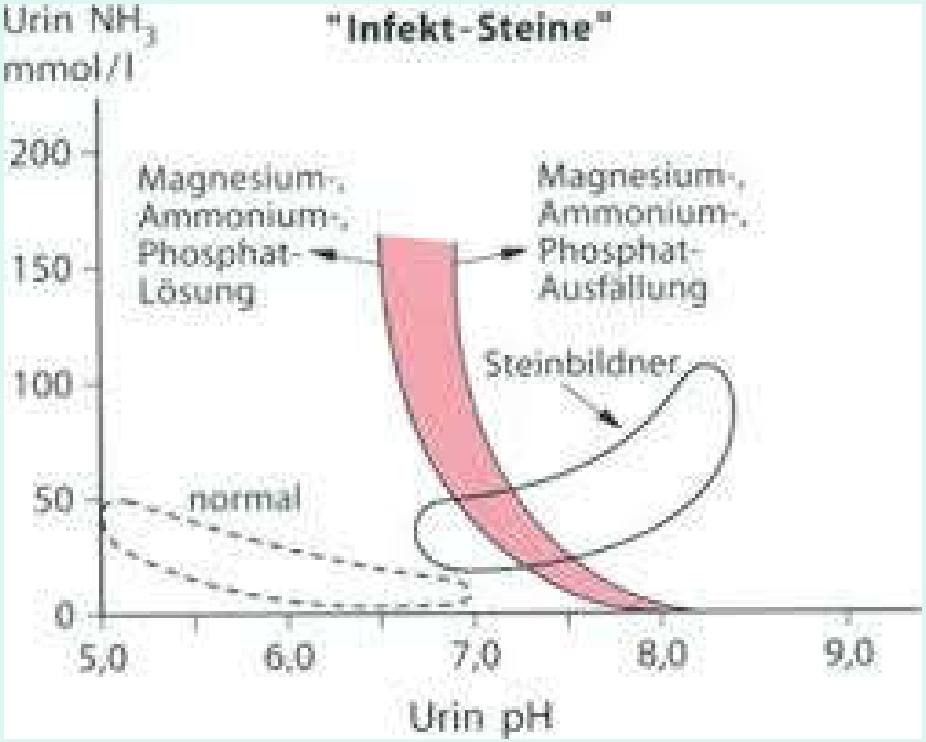



3 ZONES OF THE MEDULLO-PAPILLARY COMPLEX
ZONE 1
Outer stripe of the outer medulla
ZONE 2
Inner stripe of the outer medulla
ZONE 3
Inner medulla
Intratubular mineralisation
PRESSURE GRADIENT
CHEMICAL GRADIENT
Interstitial mineralisation
Attached kidney stone
Randall's plaque
Attached kidney stone

Urin-pH → solubility



URIC ACID



STRUVIT

Risk factors I.

Dietary failure

- Salt and protein rich diet (animal protein!)
- Obesitiy
  - BMI>25 kg/m²
- low daily fluid intake
  - < 2 Liter / 24h

Risk factors II.

Medicines

- Antibiotics

  →changes of the GI flora → oxalate resorbtion↑ → hyperoxaluria

- Ascorbic acid (Vitamin C)

  metabolised in the liver to oxalate → Hyperoxaluria

- Vitamin-D

  elevated calcium turnover → Hypercalciuria

- Urine alkalizers (Alkalicitrate, Bicarbonate)

  Urin pH↑ → Mg-ammoniumphosphat solubility↓ → stone formation

- Diuretics
  - Loop-diuretics: → Ca excretion↑ → → Nephrocalcinosis
  - Thiazid-diuretics: → Uric acid excretion ↑ → Ca excretion ↓

Risk factors III.

- Immobilisation

  Long immobilisation → Bone remodeling → Calcium + Phosphate excretion ↑

- Urinary tract infection

  urease positive strains → Urin pH↑ →
  Mg-ammoniumphosphate solubility↓ → Stone formation

- Urinary tract obstruction

  P-U Stenosis

  Ureteral stricture

  BPH

  Urethra stricture

  Neurogenic bladder disorders

  → Stasis → UTI → Stone formation

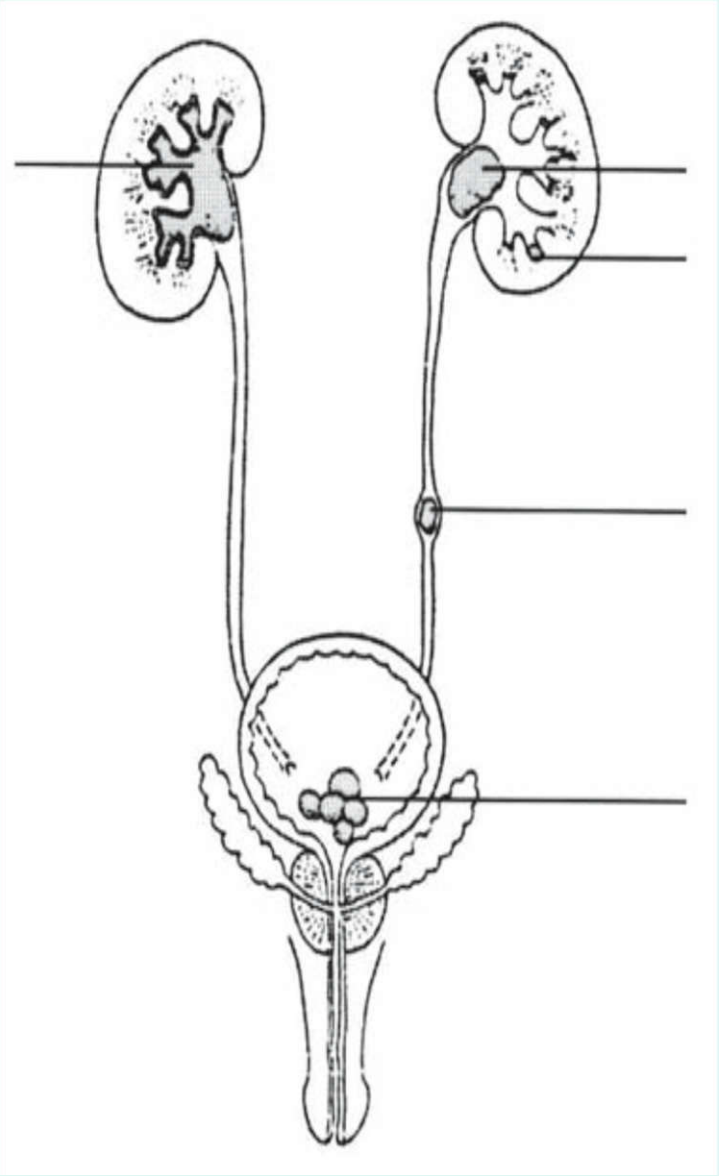
Deseases causing stone formation

- Hyperparathyreoidismus
- Renal tubular acidosis
- Metabolic Syndrome
- Primary Hyperoxaluria
- Hyperuricamia
- Cystinuria

Stone types

- **Classification of stones:**
  - Localisation
  - X-ray shadow
  - Etiology
  - Chemicals composition

Stone localisation



X-ray shadow

- **Provides shadow**
  - Calzium-oxalate (Whewellit/Weddellit)
  - Calzium-phosphate (Karbonatapatit, Brushit)
- **Provides pale shadow**
  - Magnesium-ammonium-phosphate (Struvit)
  - Cystin
- **Provides no shadow**
  - Uric acid
  - Ammonium-urate

Etiology

- **Infect stone**
  - Magnesiumammoniumphosphat (Struvit)
  - Karbonatapatit (Dahllite)
  - Ammoniumurat

- **Metabolic stone**
  - Kalziumoxalat
  - Harnsäure
  - Kalziumhydrogenphosphat Dihydrat (Brushit)

- **Genetic disorders**
  - Cystin, Xanthin, 2,8-Dihydroxyadenin

- **Drug stones**
  - Indinavir, Silicate, Sulfonamide

Chemical compostion

- **Oxalate**
  - Calcium-oxalate monohydrate (Whewellit)
  - Calcium-oxalate dihydrate (Weddellit)

- **Uric acide and Urate**
  - Uric acid (Uricit)
  - Monoammonium-urate

- **Phosphate**
  - Magnesium-ammonium-phosphate Hexahydrate (Struvit)
  - Carbonate-apatit (Dahllite)
  - Calcium-hydrogen-phosphate Dihydrat (Brushit)

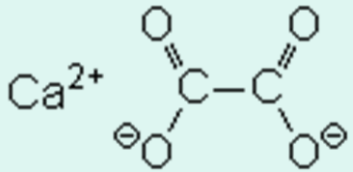
Calcium-oxalate

- Adults: 70% of all urinary stones
  - Idiopatic 60-70%
  - Hyperparathyreoidismus 5-7%
  - RTA 3-5%
  - primary Hyperoxalurie
  - enteral Hyperoxalurie
    - Malabsorption
    - St. P. intestinal resection
- Children: 48%
  - Idiopatic 14%
  - Serious metabolic defect: 34%

Idiopatic calcium-oxalate stone formation

- 24h collected urin

– Hypercalcuria	31%–61%
– Hyperoxaluria	26%–67%
– Hyperurikosuria	15%–46%
– Hypomagnesiuria	7%–23%
– Hypocitraturia	5%–29%



- **Calcium-oxalate Monohydrate** (Whewellit)
  - $Ca(C_2O_4)\cdot H_2O$
  - Very hard
  - Brownish-black stones

- **Calcium-oxalate Dihydrate** (Weddellit)
  - $Ca(C_2O_4)\cdot 2H_2O$
  - Loose textured, bright yellow crystals

Calcium-phosphate

~50% of all stones consist calcium-phosphate
- 4,8% monomineralic carbonate-apatit
- 1,5% monomineralic Brushit

- Carbonate-apatit (Dahllite)

  $Ca_5[(PO_4,CO_3)_3(OH)]$

  Urine pH >6,8 w/ high calcium and low citrate cc
  - UTI
  - RTA

- Brushit

  $CaHPO_4 \cdot 2H_2O$

  Urine pH between 6,5 and 6,8 w/ high calcium and phosphate cc.

  Urine pH > 6,8 Brushit→ carbonate-apatit

  quick growth

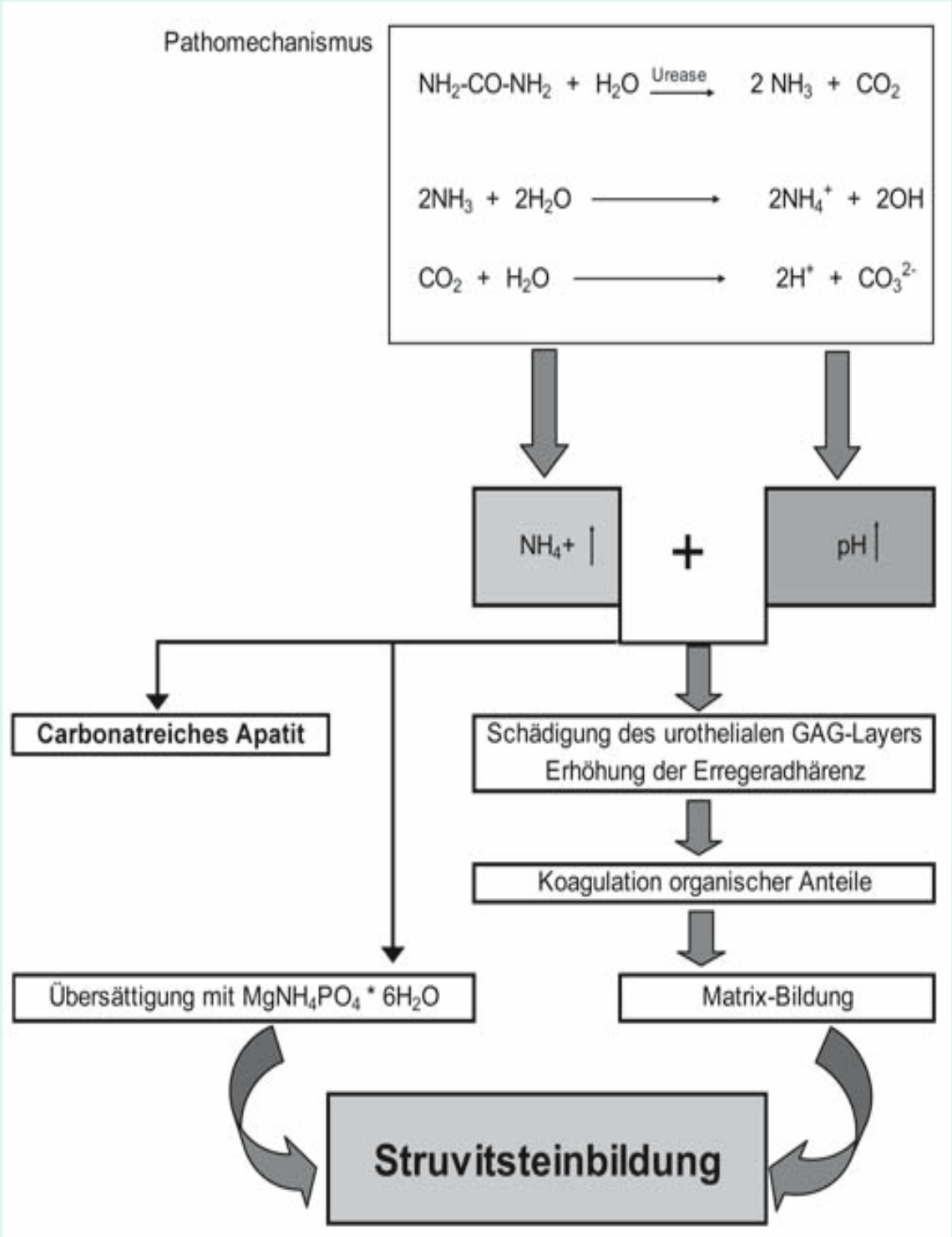
  very hard

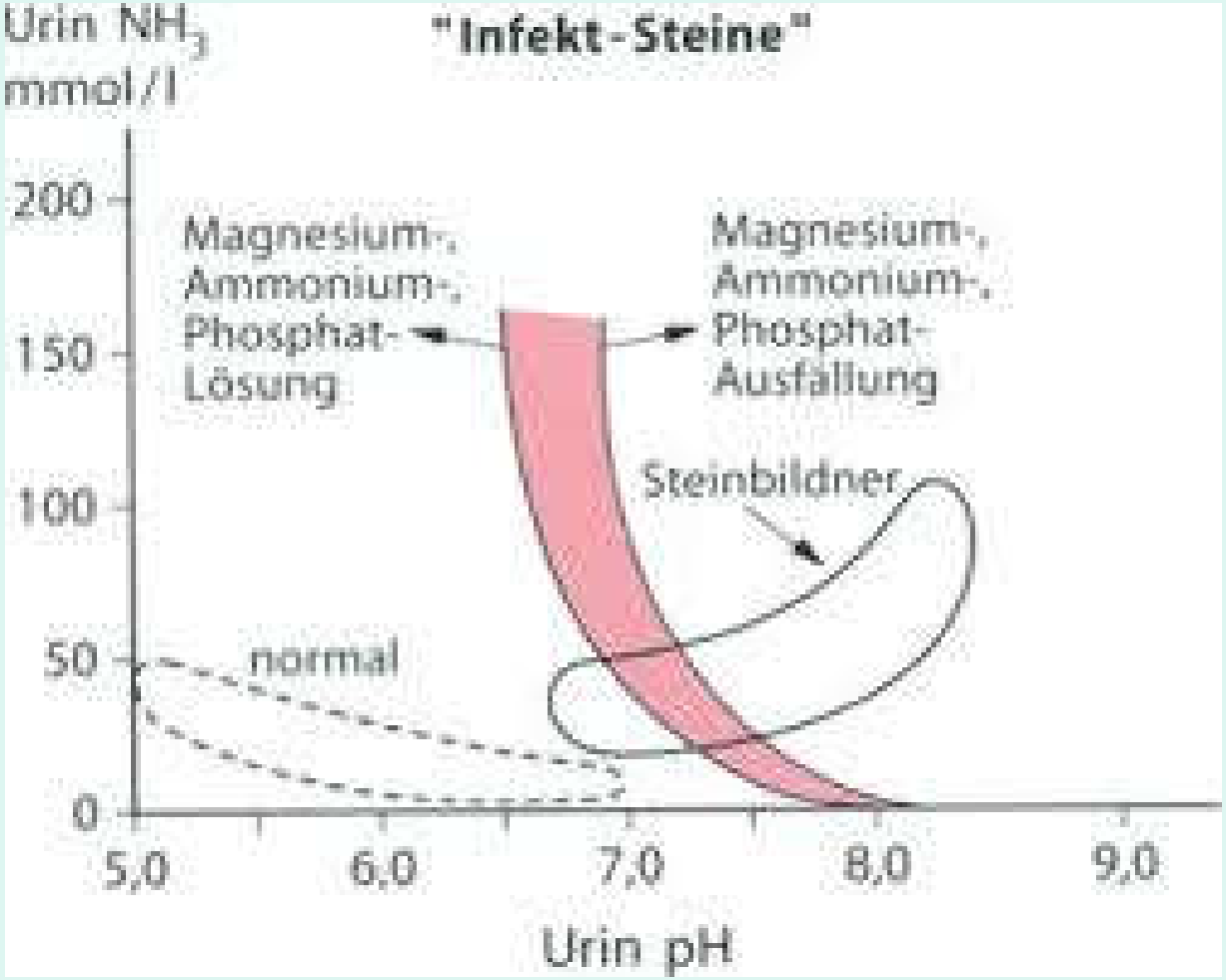
Struvit

Magnesium-ammonium-phoshate
$(NH_4)MgPO_4 \cdot 6H_2O$

UTI w/ **urease positive strains**

- Enterobacter aerogenes
- Haemophilus influenzae
- Klebsiella
- Proteus mirabilis und Proteus vulgaris
- Providencia
- Pseudomonas
- Serratia
- Staphylococcus aureus
- Ureoplasma urealyticum

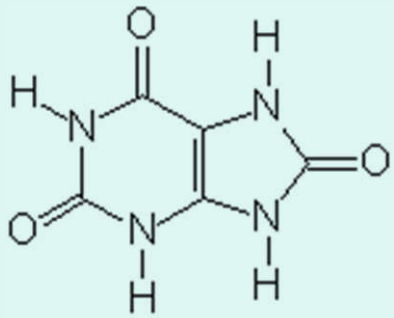

Pathomechanismus
NH_2-CO-NH_2 + H_2O Urease 2 NH_3 + CO_2
$2NH_3$ + $2H_2O$ $2NH_4^+$ + 2OH
CO_2 + H_2O $2H^+$ + CO_3^{2-}
NH_4+
+
pH
Carbonatreiches Apatit
Schädigung des urothelialen GAG-Layers
Erhöhung der Erregeradhärenz
Koagulation organischer Anteile
Übersättigung mit $MgNH_4PO_4$ * $6H_2O$
Matrix-Bildung
Struvitsteinbildung


Urin NH_3
mmol/l
"Infekt-Steine"
200
150
100
50
0
Magnesium-,
Ammonium-,
Phosphat-
Lösung
Magnesium-,
Ammonium-,
Phosphat-
Ausfällung
Steinbildner
normal
5,0
6,0
7,0
8,0
9,0
Urin pH

Ammonium-urate

- Urine pH > 7
- HWI + high uric acide excretion
- often mixed w/ Struvit

Uric acid



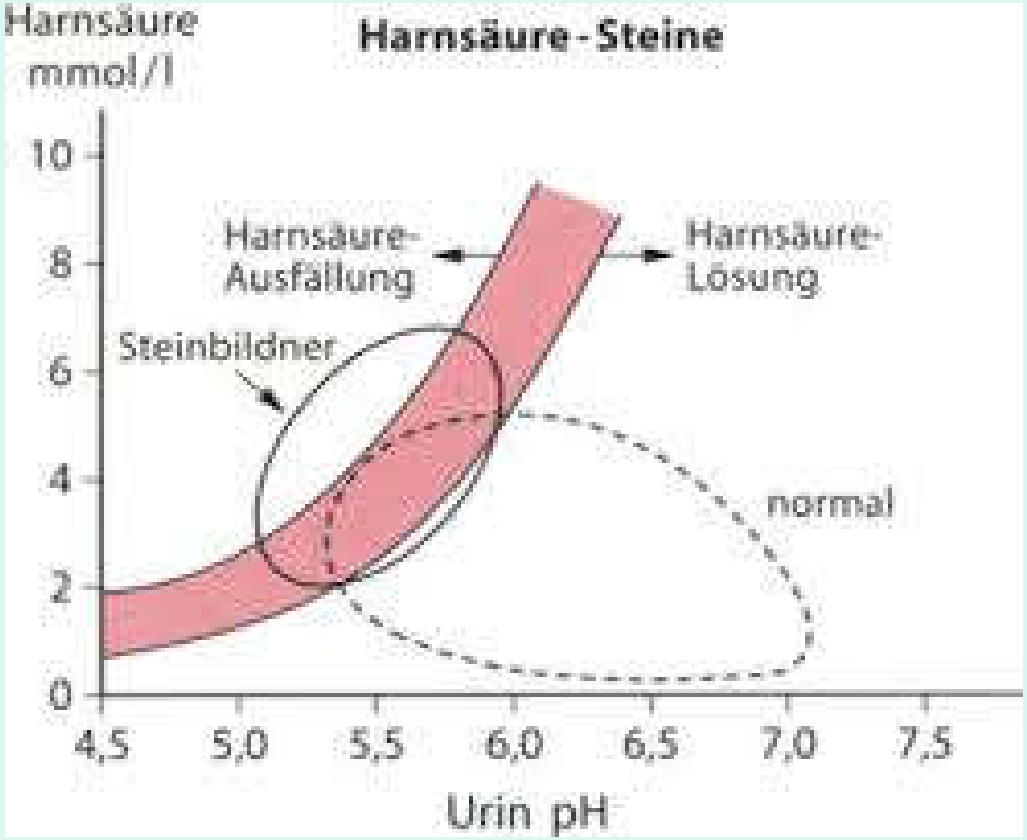
- 15% of all stones
- High uric acid cc in serum
  - endogene overproduction (cell disintegration)
  - high exogene intake

→ **Hyperuricosuria**

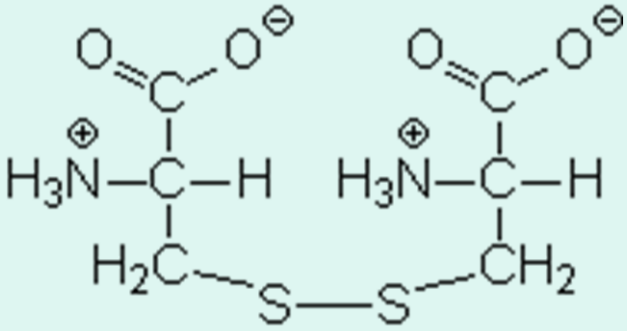
+ low Urin-pH

(Urin-pH permanently <6)

→ Stone formation


Harnsäure
mmol/l
Harnsäure-Steine
10
8
6
4
2
0
Harnsäure-
Ausfällung
Harnsäure-
Lösung
Steinbildner
normal
4,5
5,0
5,5
6,0
6,5
7,0
7,5
Urin pH

Cystin I.

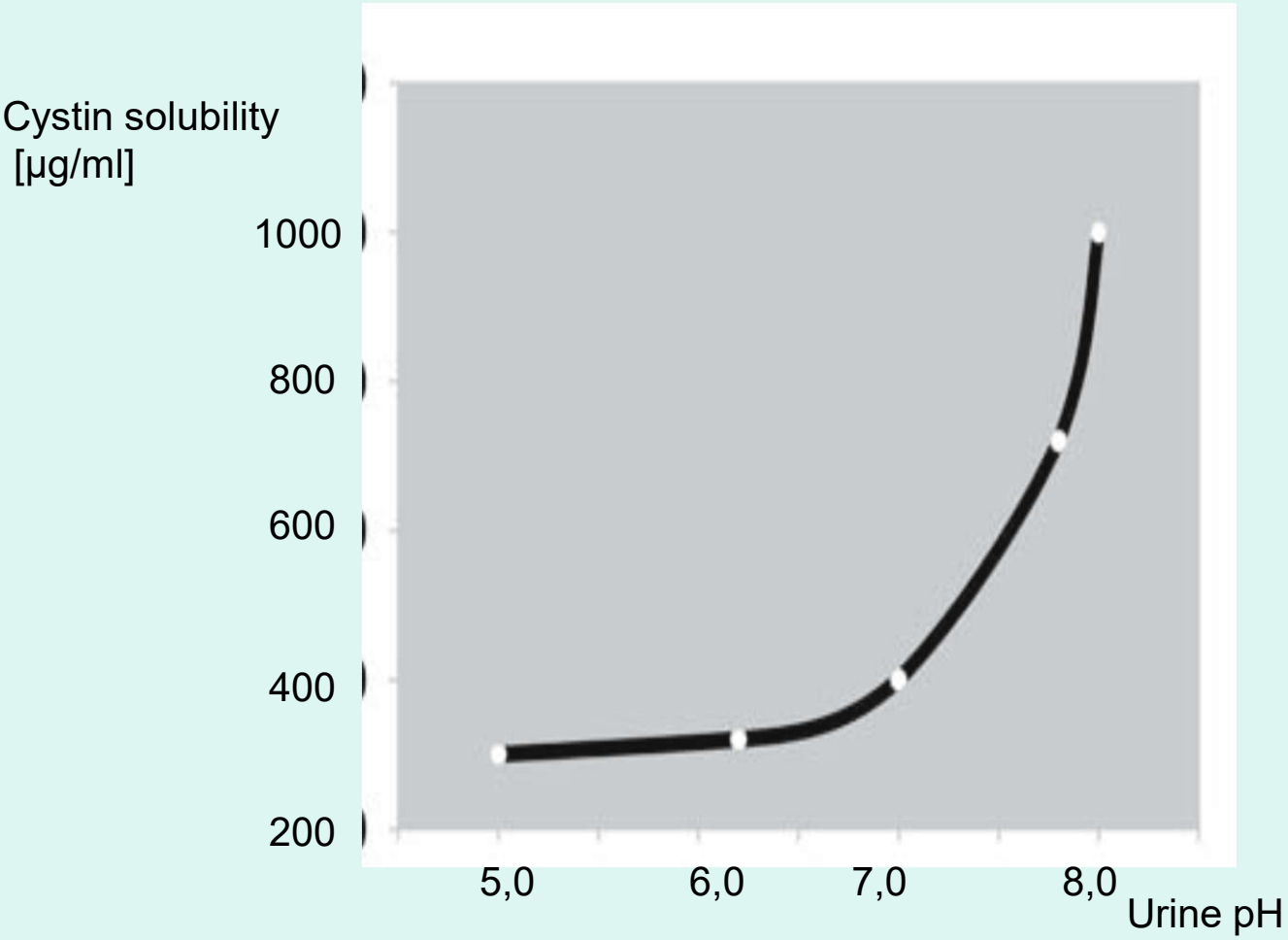


- 1–2%

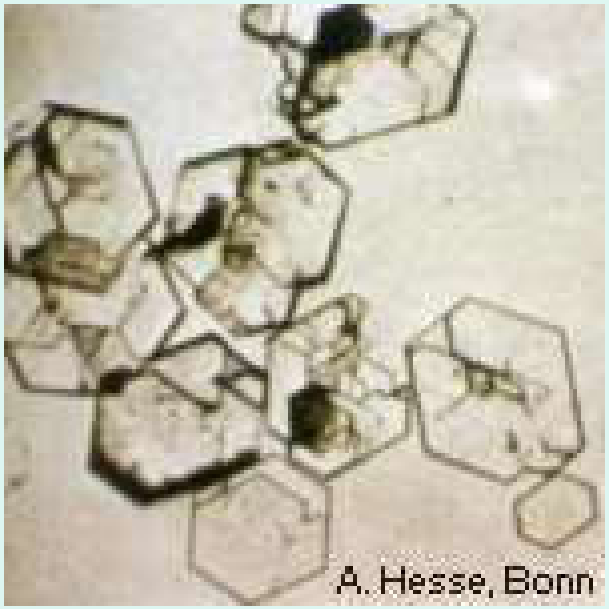
- autosomal-recessive hereditary metabolic disorder
- In the renal tubules the dibasic aminoacids (Cystin, Ornitin, Lysin, Arginin) are not reabsoprted
- The low solubility of cystin causes quick crystallisation an stone formation

Cystin II.

Mild acidotic urin pH + high protein intake



Cystin III.



- Bright yellow colour
- In urine sediment characteristic hexagonal crystals

Symptoms / Clinical aspects

- Asymptomatic
- Blunt renal pain
- Renal colic
- Obstructive pyelonephritis
- Urosepsis

Diagnostics

- Hystory
- PE
- Lab:
  - Creatinin, Natrium, Kalium, Chlorid, Kalzium, Uric acid, BB, CRP, INR
- Urine:
  - Urine sediment (RBC, WBC)
  - (Urin culture)
  - pH

Diagnostics

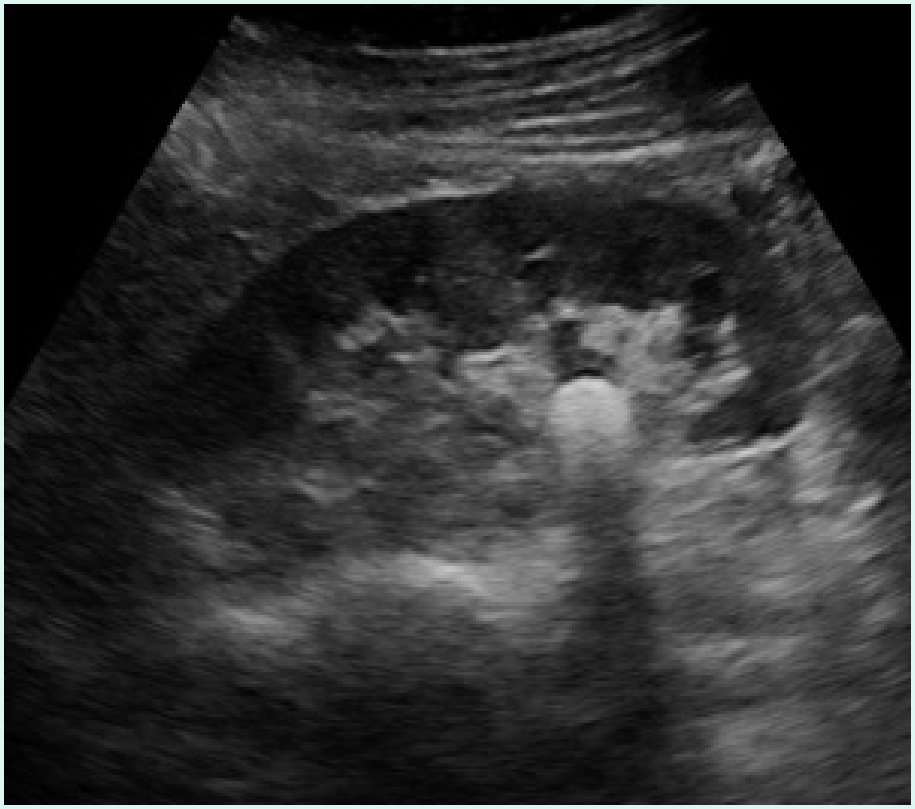
Imaging procedures

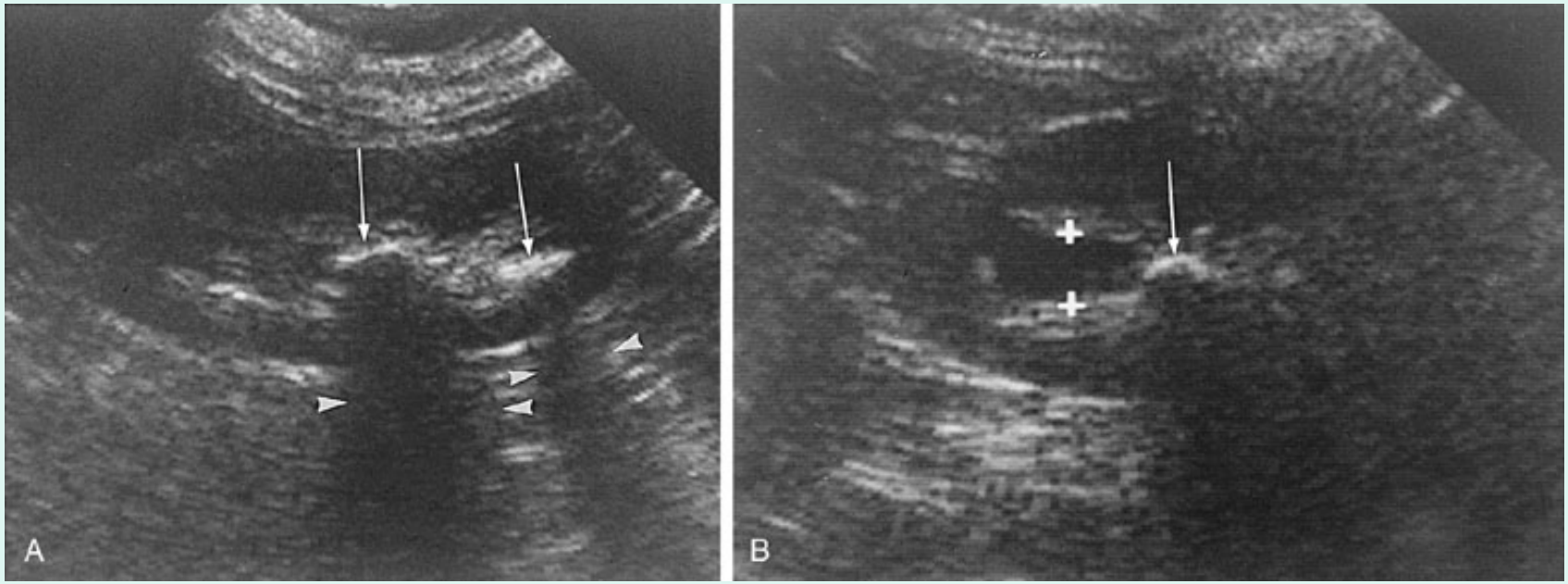
Stone?
Localisation?
Size?
How many stones?
Obstruction?
Anatomy of the collecting system?
Stone type?

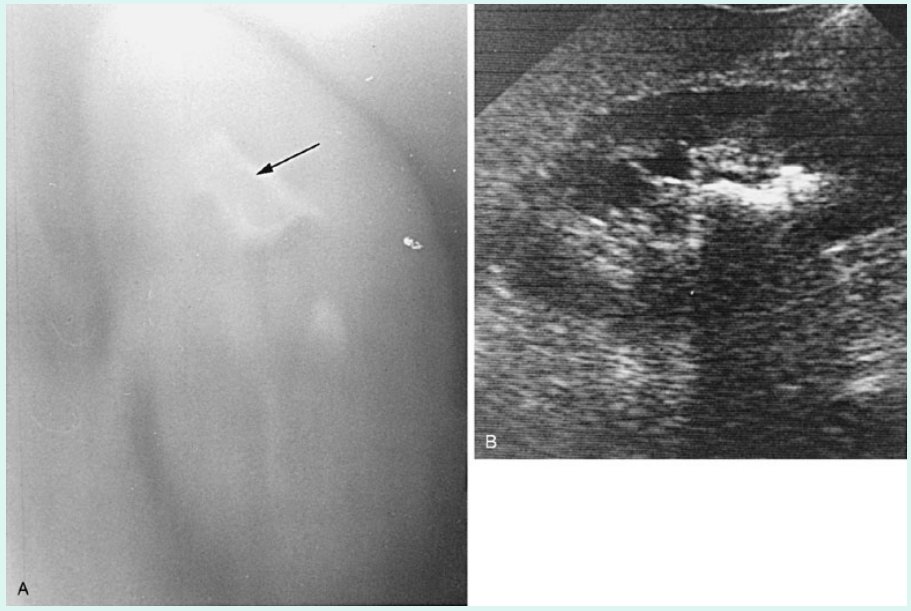
Diagnostics

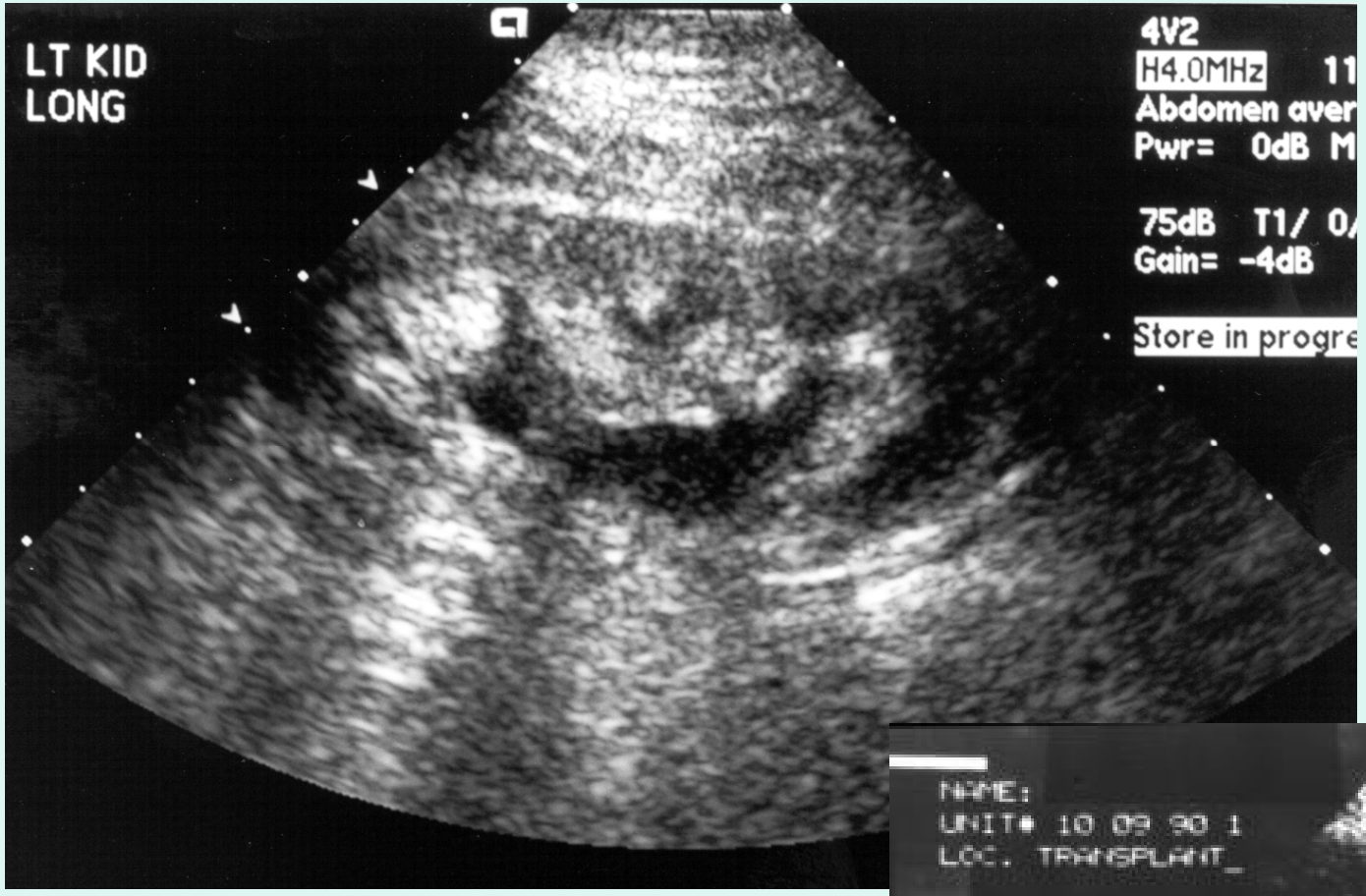
Imaging

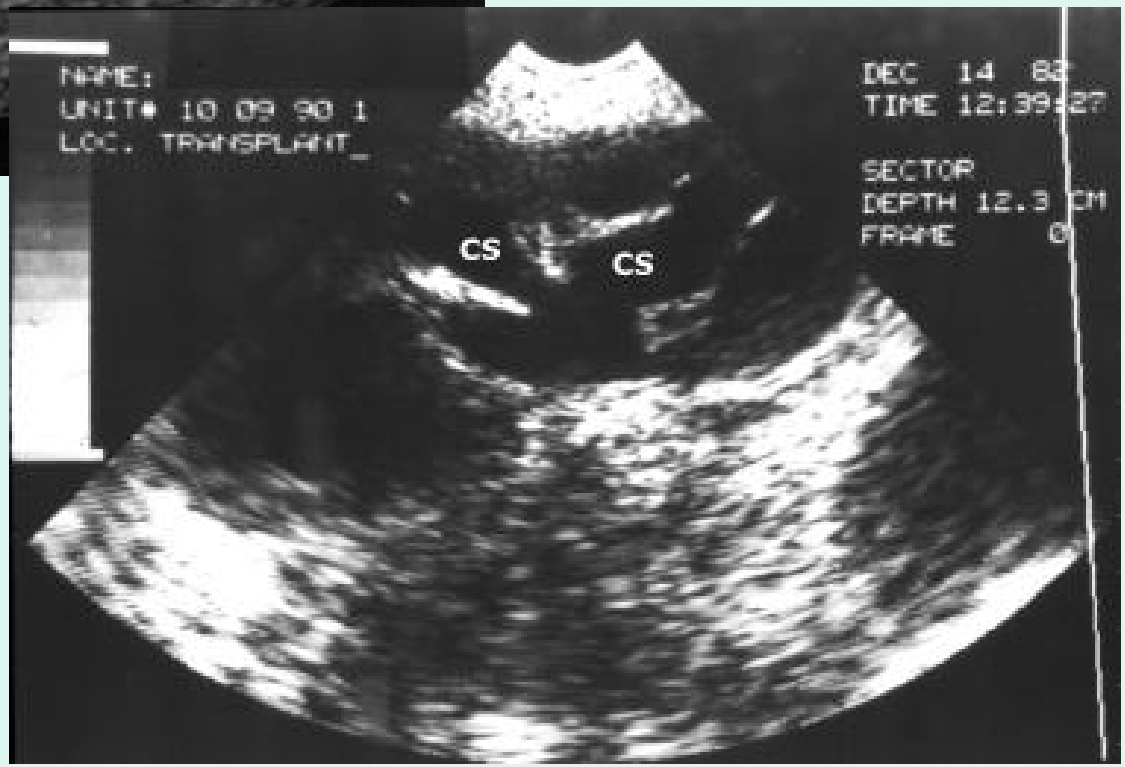
- US
- Native Spiral-CT
- KUB
- Excretory urographies
  - IVU
  - CT-Urography
- MR-Urography
- Retrograde Pyelography
- Antegrade Pyelography



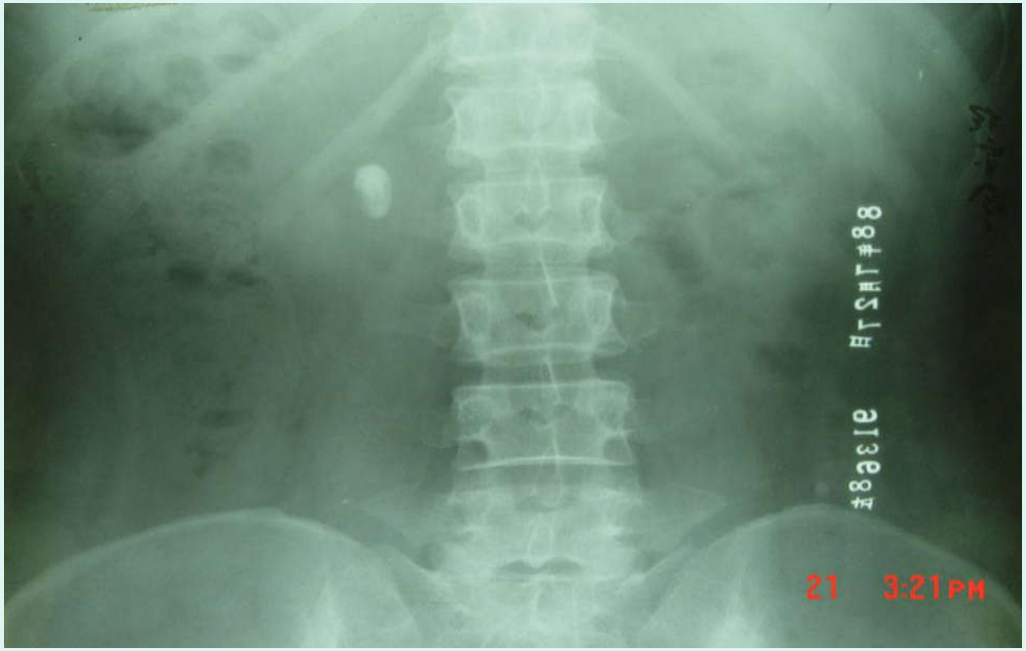

A
B


A
B

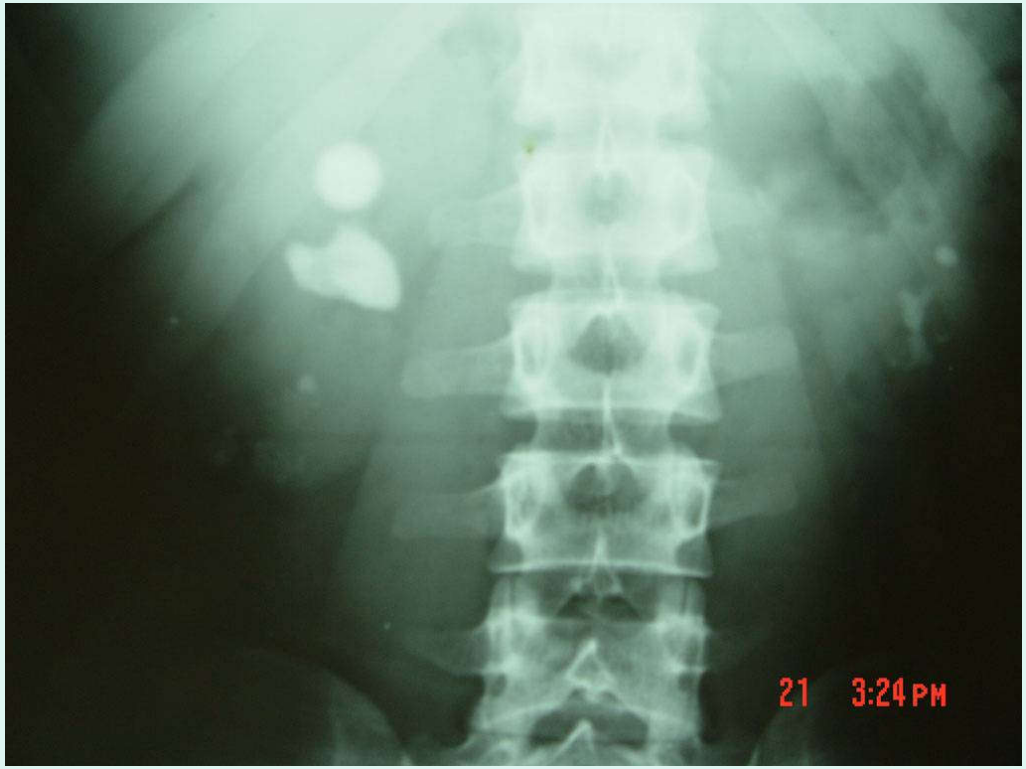

LT KID
LONG
4V2
H4.0MHz
Abdomen aver
Pwr= 0dB M
75dB T1/ 0
Gain= -4dB
Store in progre

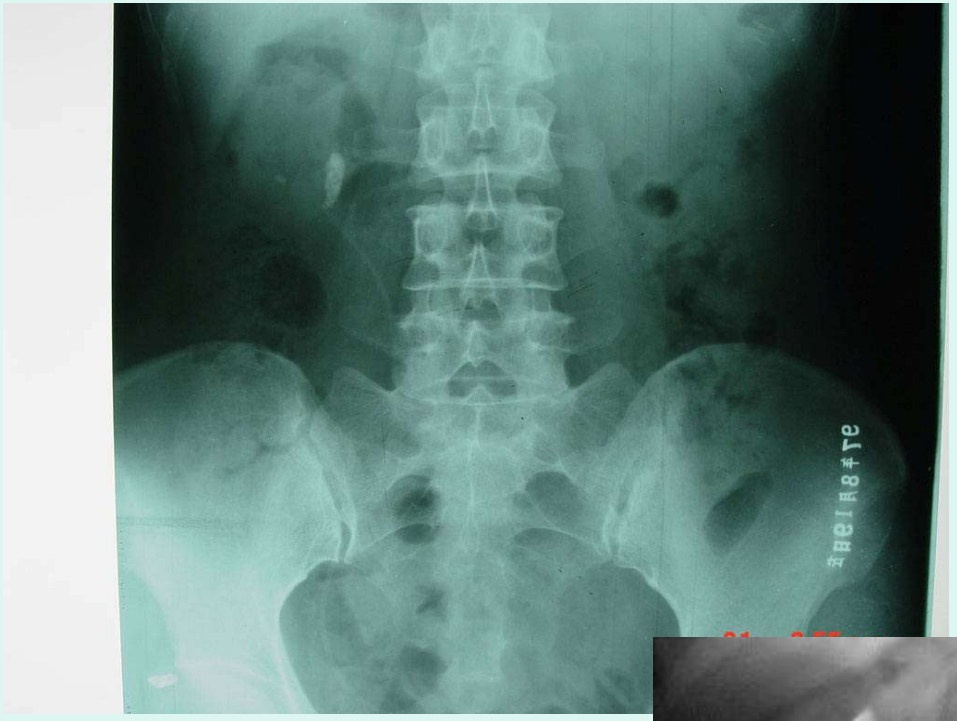

NAME:
UNIT# 10 09 90 1
LOC. TRANSPLANT
DEC 14
TIME 12:39:27
SECTOR
DEPTH 12.3 CM
FRAME
CS
CS

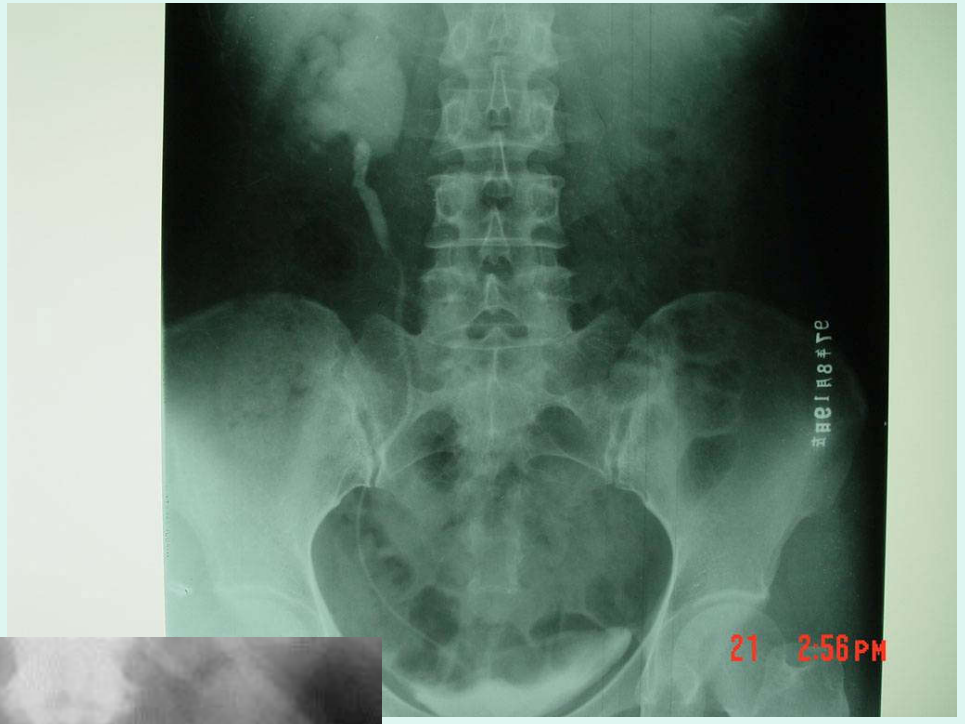

21 3:27

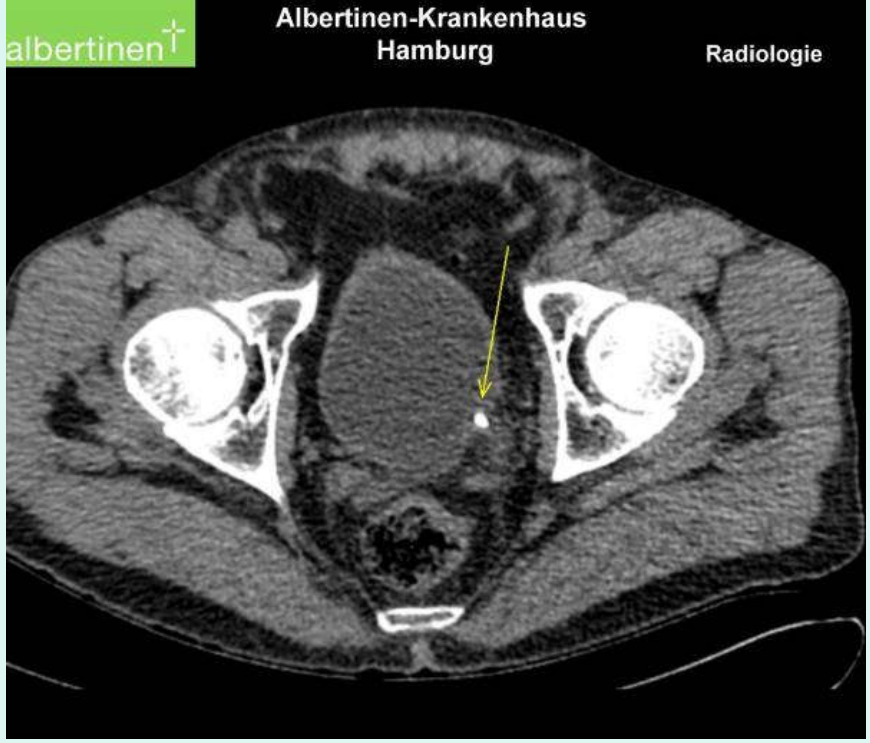

21 3:21PM


21 3:22PM

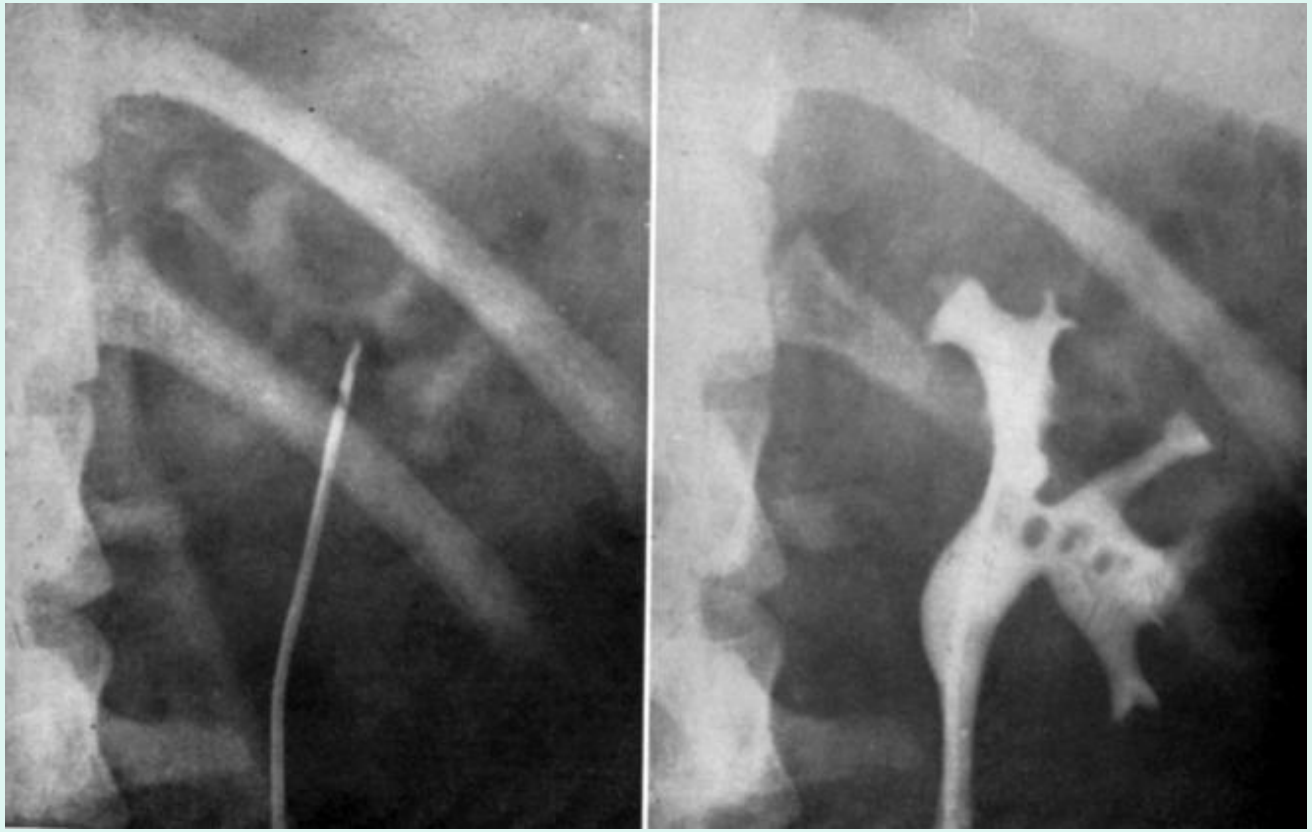

21 3:24PM




21 2:56 PM


albertinen
Albertinen-Krankenhaus
Hamburg
Radiologie


P39




Radiology Archives

Therapy of urolithiasis

Acute therapy

Spasmolysis

Urinary diversion

Conservative treatment

- Observation
- Medical expulsive treatment (MET)
- Medical litholysis

ESWL

Surgical therapy

- URS
- PCNL
- RIRS
- ECIRS
- Laparoscopy (open surgery)

Profilaxis, Metafilaxis

Acute therapy of renal colic

- Acute analgesy
  - metamizol (Algopyrin®) 1-2g iv.
  - drotaverine (No-Spa®) 40-80mg iv.
  - diclophenac (Voltaren®) 75 mg iv.
  - pethidine (Dolargan®) 100mg im.
- Continuos analgesy
  - metamizol (Algopyrin®) 3x500mg po.
  - drotaverine (No-Spa®) 3x 40-80mg po.
  - diclophenac (Voltaren®) 3x50mg po.
  - tamsulosin (Omnic®) 1x0,4mg po.

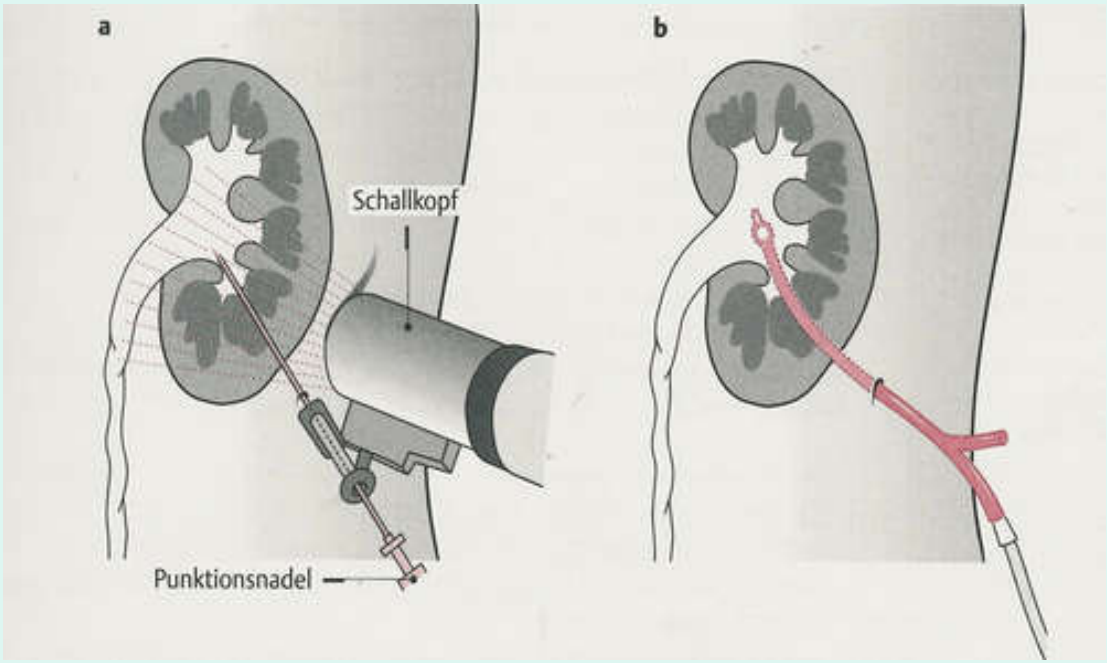
Acute therapy of renal colic

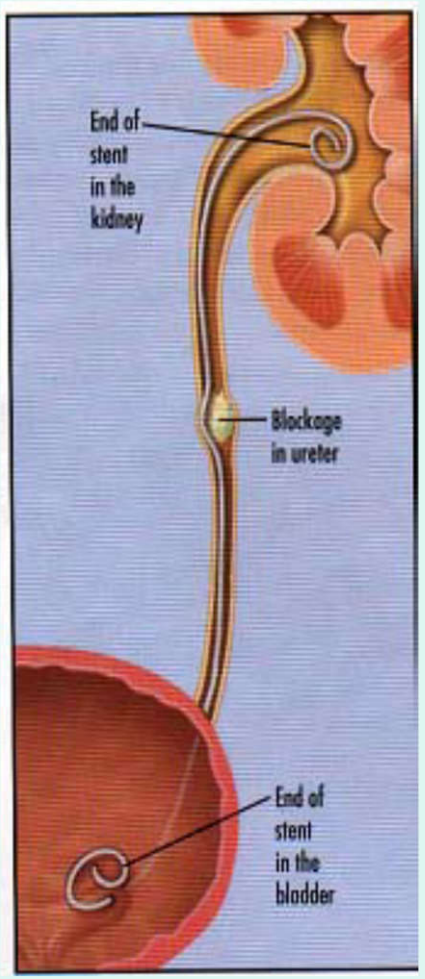
- Colics non responding to pain killers:

  → urine diversion

  » D-J ureteral stent

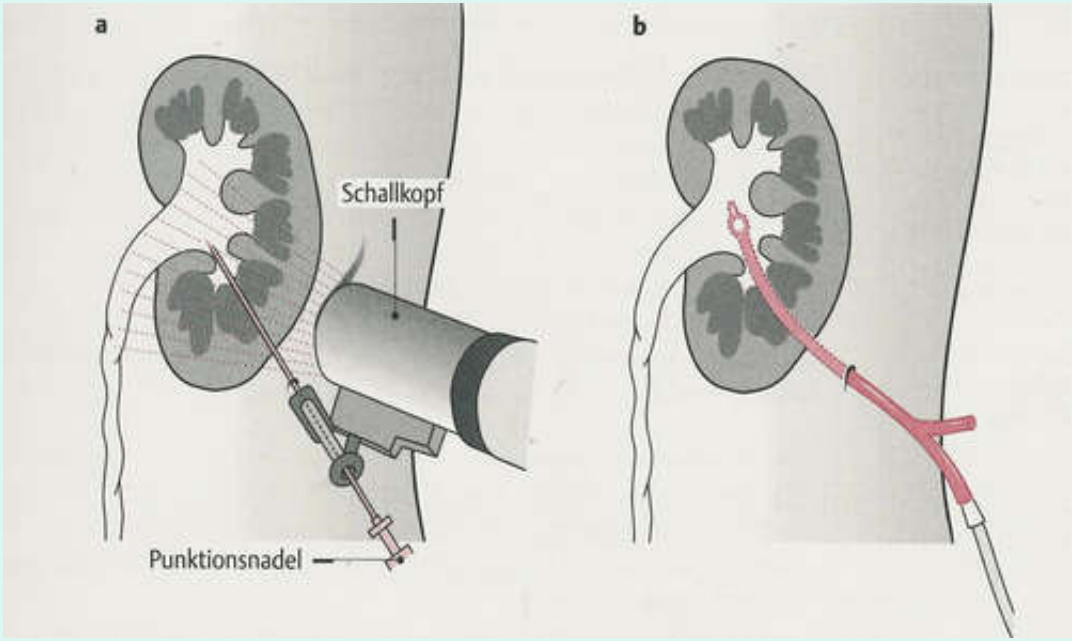
  » Percutane Nephrostomy

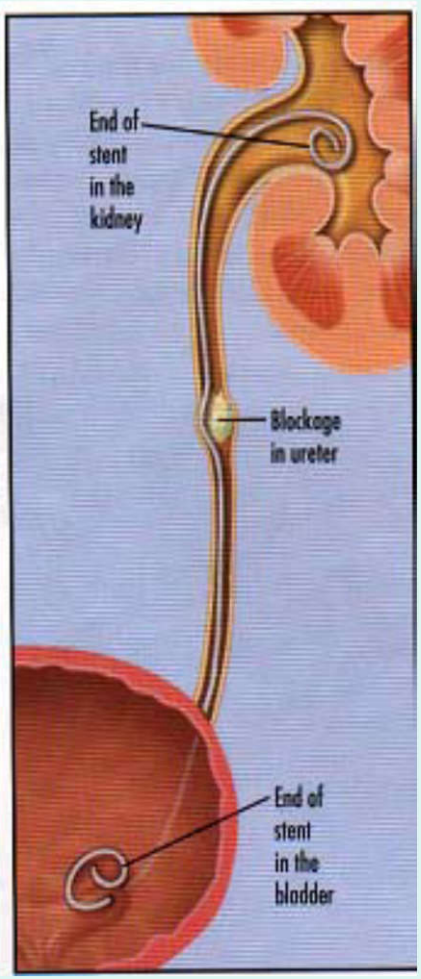




Acute therapy of obstructive pyelonephritis

- iv. antibiotic Tx
- Urine diversion
  - D-J Ureteral stent
  - Percutane Nephrostomy





Conservative treatment

- Observation
- Medical expulsive treatment (MET)
- Litholysis

Observation

Ureteral stones

- Spontaneous stone passage is likely
  - < 4 mm → 95% passage in 40 days
  - Upper limit? **< 10 mm**
- No symtoms
- No signs of complications

Observation

Renal stones

- No symptoms
- Stone size: <15 mm
- No progression
- No obstruction
- Low risk for stone formation

Medical expulsive tretment (MET)

- Medicine → Stone passage to facilitate

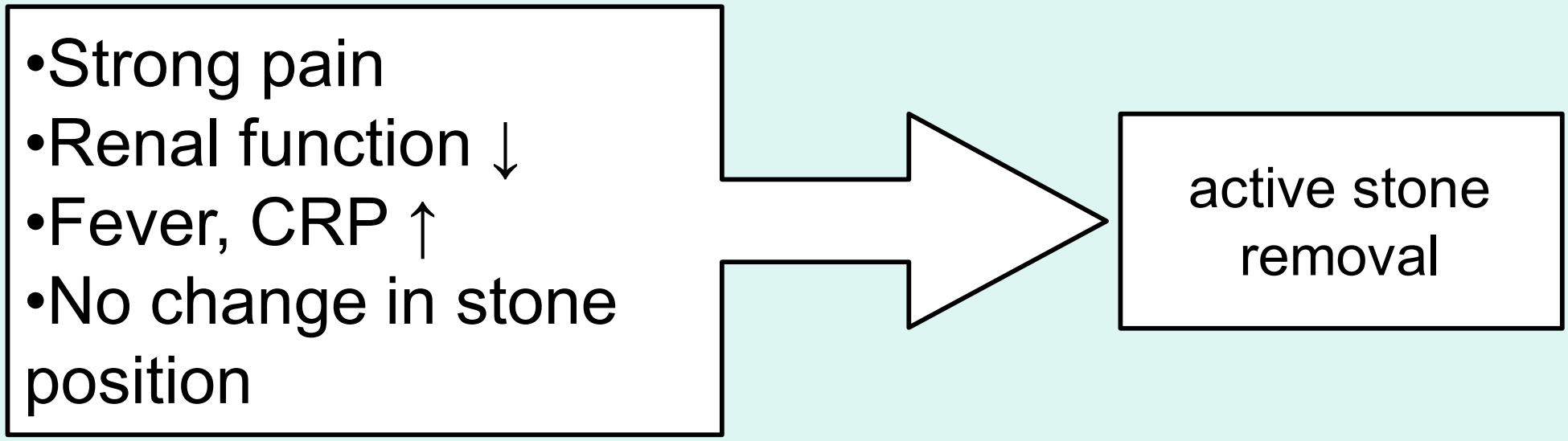
!!! No indication of active stone removal!!!

  - Stone passage is possible
    - < 4 mm → 95% in 40 days
    - Upper size limit? **< 10 mm**
  - Pain is under controll
  - No obstruction
  - No renal failure
  - No UTI

Preminger, G.M., et al. Eur Urol, 2007. 52: 1610.

MET

- Sever F/U
  - Lab (renel function, CRP)
  - Imaging (US, X-ray, CT)



How long???

MET

- Alpha-Blockers

  (tamsulosin, alfuzosin, silodosin)

→ Smoot muscle relaxation

→ Ureteral tonus↓

→Flow↑

→ Stone passage

Medical Litholysis

- Percutane Litholysis
- Oral Litholysis

Medical Litholysis

Percutane Litholysis

- Struvit stones
  - Suby G-Solution (10% hemiacidrin; pH 3.5-4)
  - RENACIDIN®
    (Citric acid, glukono-delta-lacton, $MgCO_3$)
- Stone free rate (SFR): 55-60%

Kachrilas, S., et al. The current role of percutaneous chemolysis in the management of urolithiasis: review and results. Urolithiasis, 2013. 41: 323

Tiselius, H.G., et al. Minimally invasive treatment of infection staghorn stones with shock wave lithotripsy and chemolysis. Scand J Urol Nephrol, 1999. 33: 286.

Medical Litholysis

Oral Litholysis

- **Uric acid stones**
- Urine alkalisation
  - Alkalcitrate, Na-Bikarbonate → pH: 7,0-7,2
  - High urine pH → Ca-Phosphate stone fromation !!!
  - Continuous pH control → Dose modification
- Imaging (US, CT)
- Obstruction → Urine diversion + Litholysis
- Ureteral stone: Urine alkalisation + tamsulosin

Rodman, J.S., et al. Dissolution of uric acid calculi. J Urol, 1984. 131: 1039.

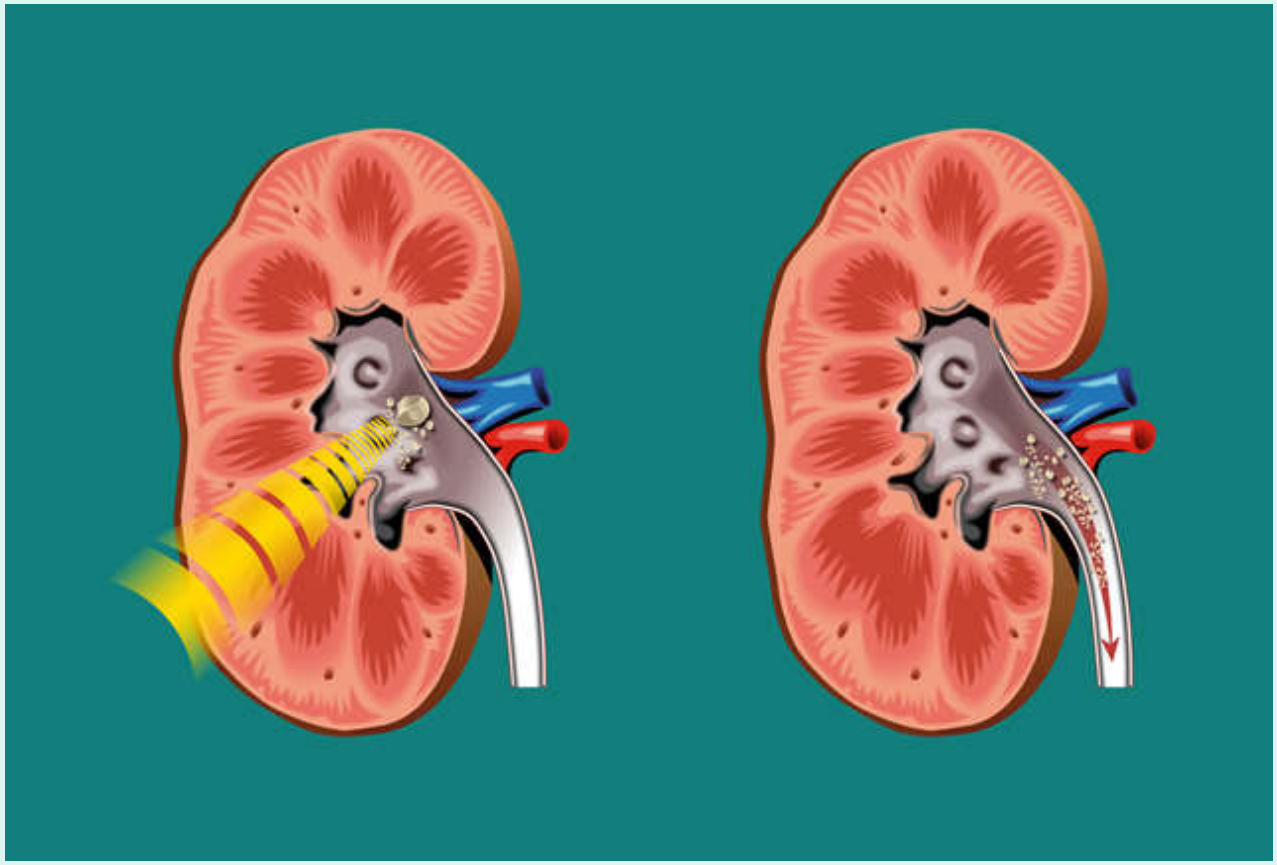
Becker, G. Uric acid stones. Nephrology, 2007. 12: S21.

El-Gamal, O., et al. Role of combined use of potassium citrate and tamsulosin in the management of uric acid distal ureteral calculi. Urol Res, 2012. 40: 219.

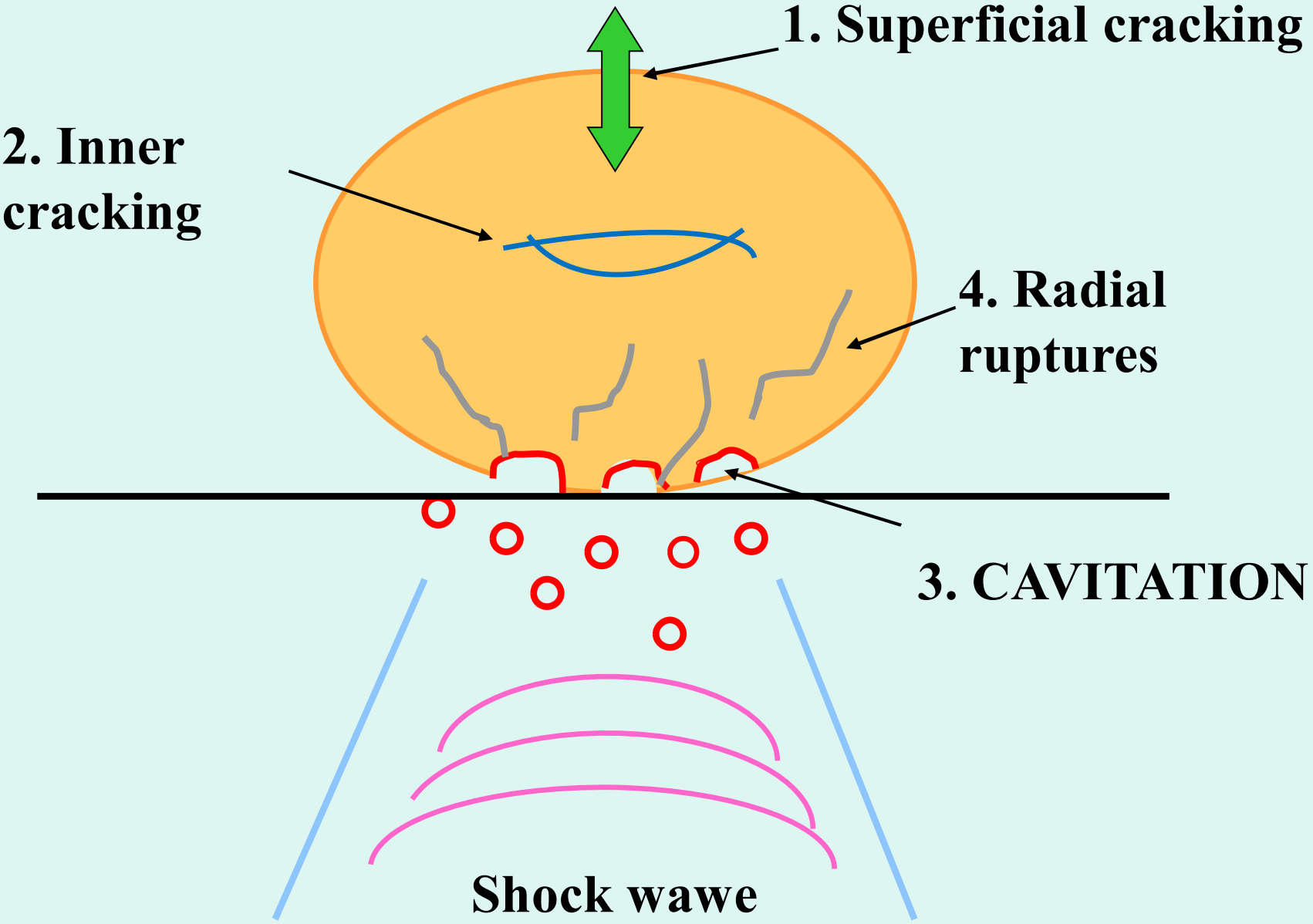
ESWL

- **E**xtracorporeal **S**hock **W**awe **L**ithotripsy

- in situ stone desintegration w/ focused shock wawes
- Spontaneos passage of the fragments



DESINTEGRATION



ESWL

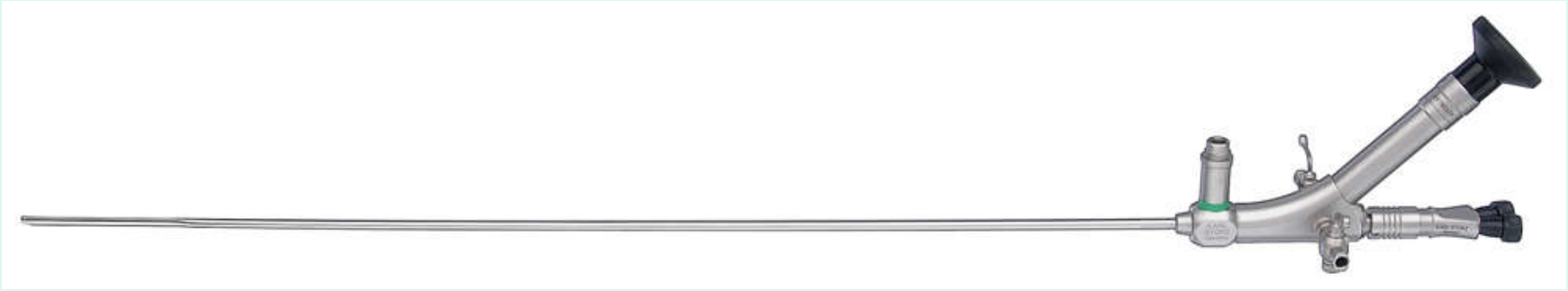
Surgical treatment

- URS
- PCNL
- RIRS
- ECIRS

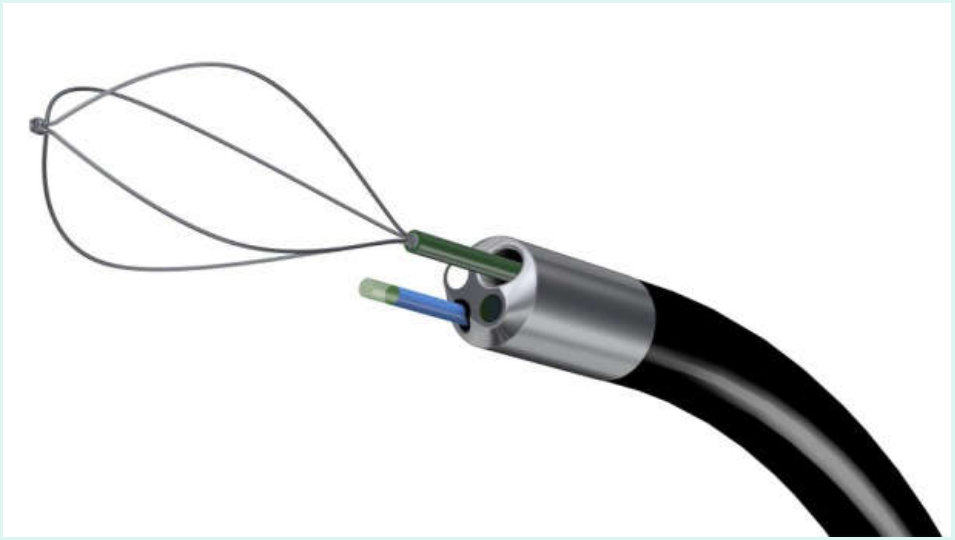
- Laparoscopy
- Open surgery

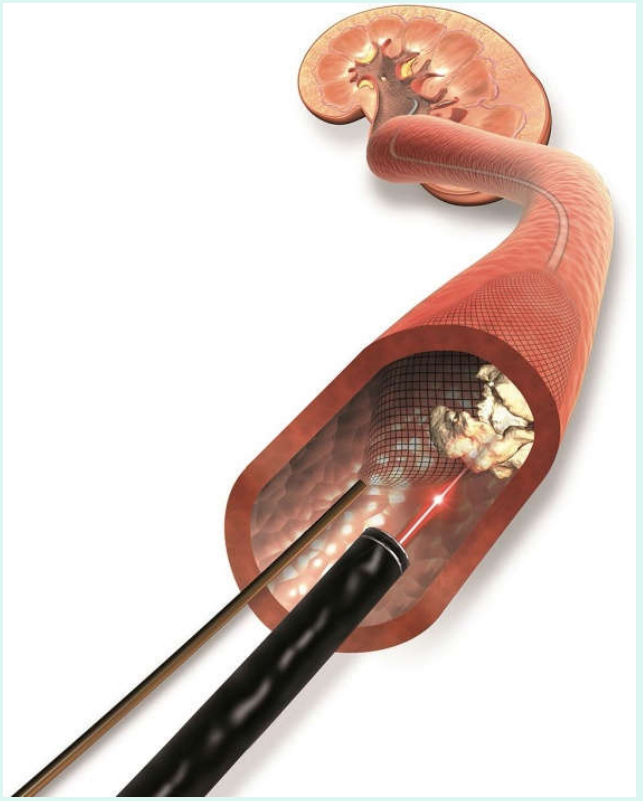
Ureterorenoscopy (URS)

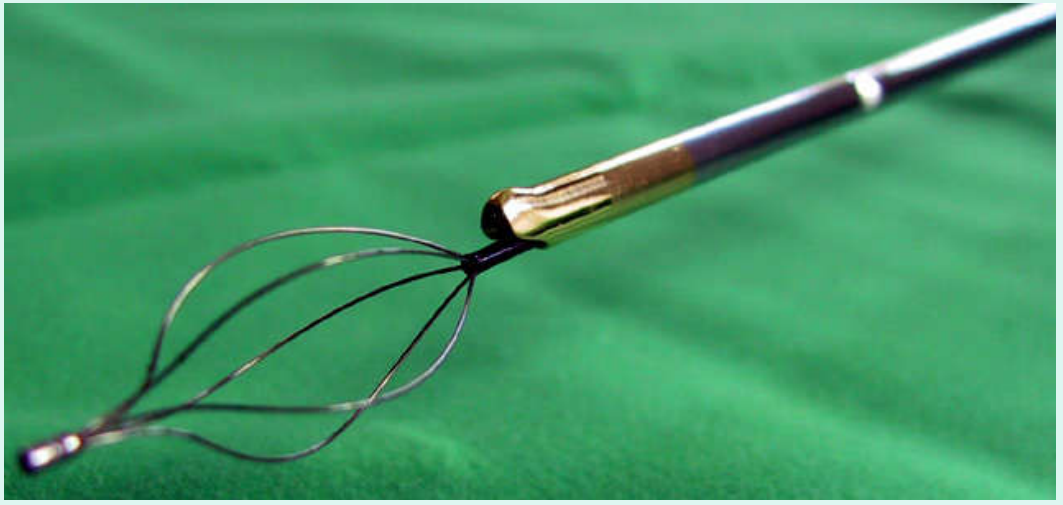
- Semirigid
- Flexible



Ureterorenoscopy (URS)

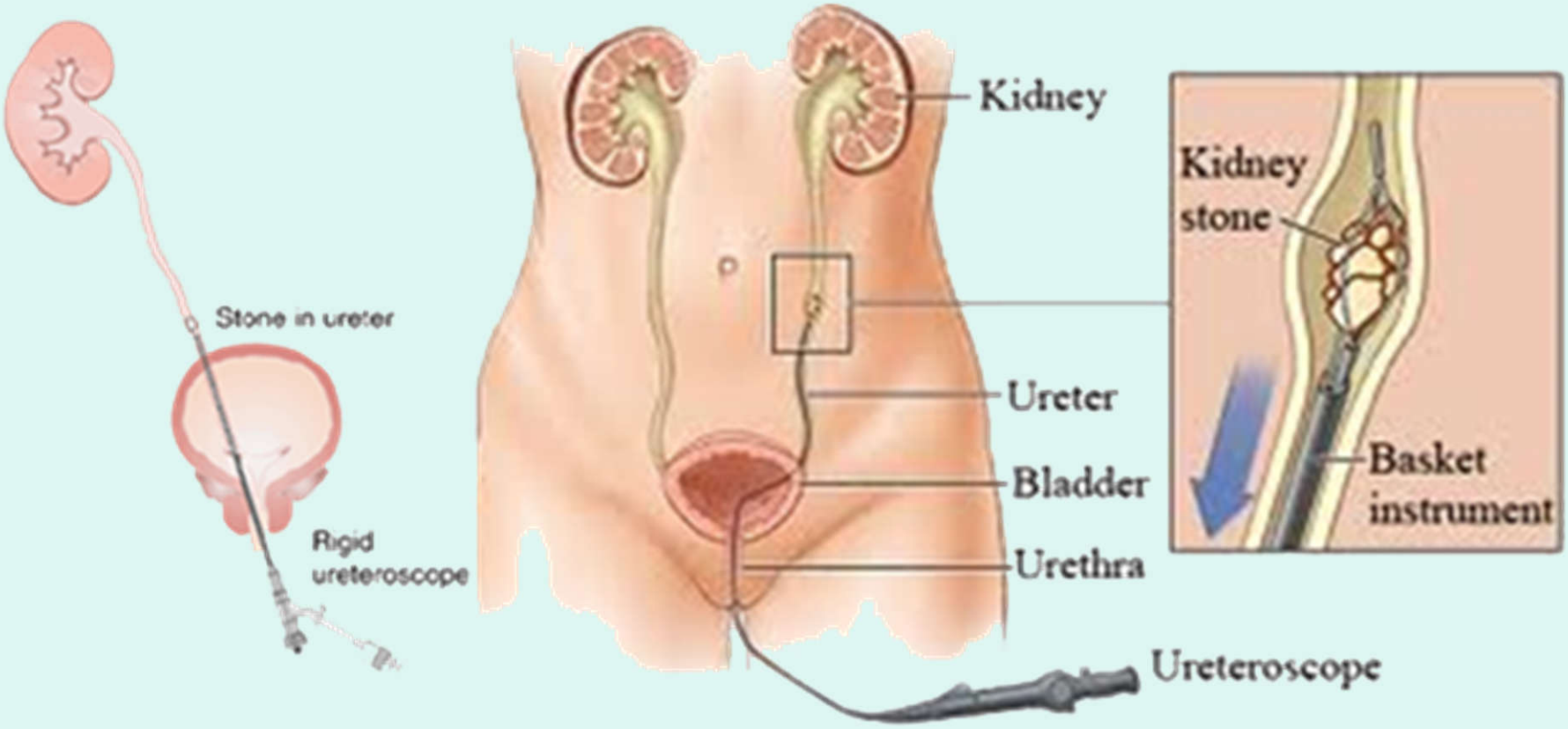






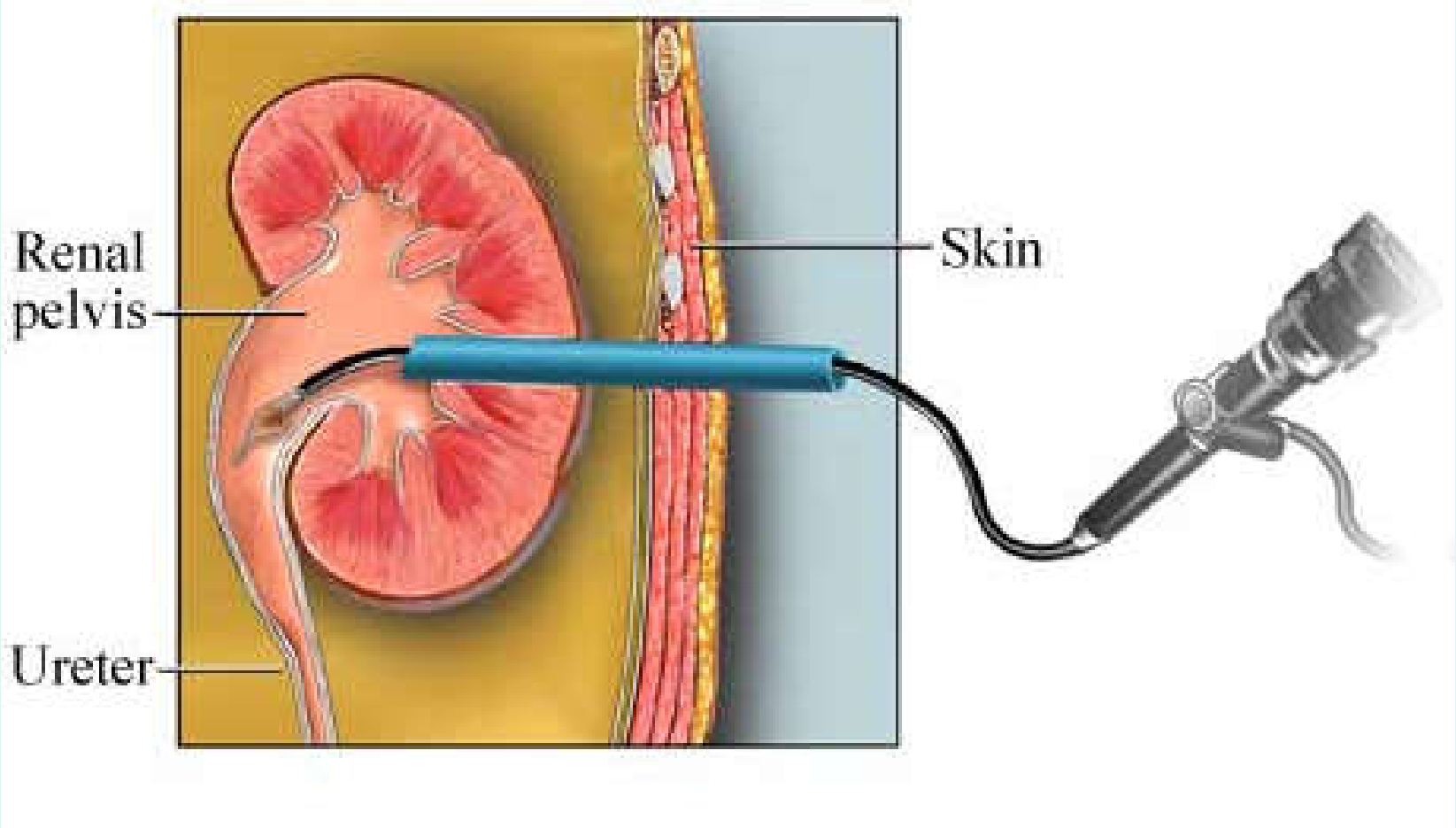
Ureterorenoscopy (URS)

- Retrograde



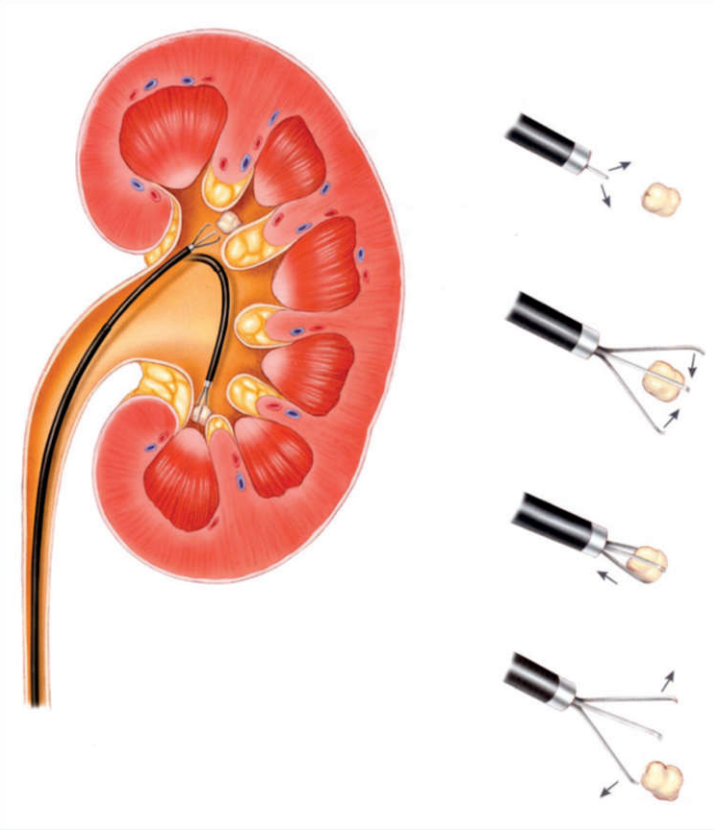
Ureterorenoscopy (URS)

- Antegrade



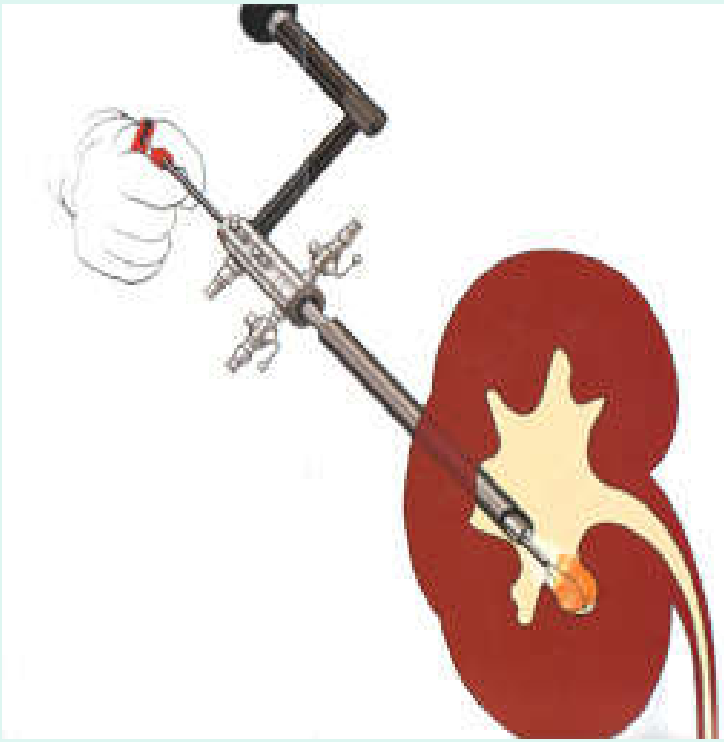
RIRS

- Retrograde Intrarenal Surgery
  - Flexible URS + LASER



PCNL

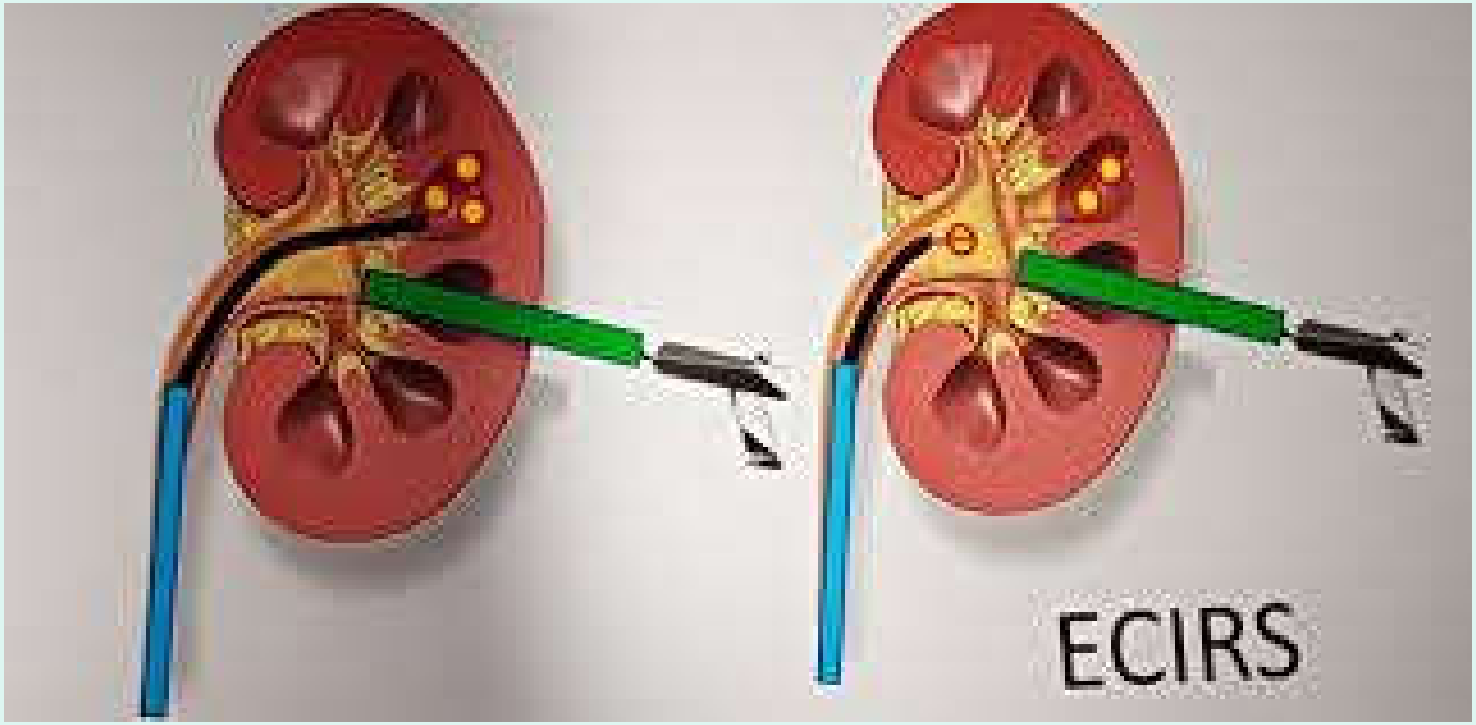
= **P**er**k**utane **n**ephro**l**itolapaxy



ECIRS

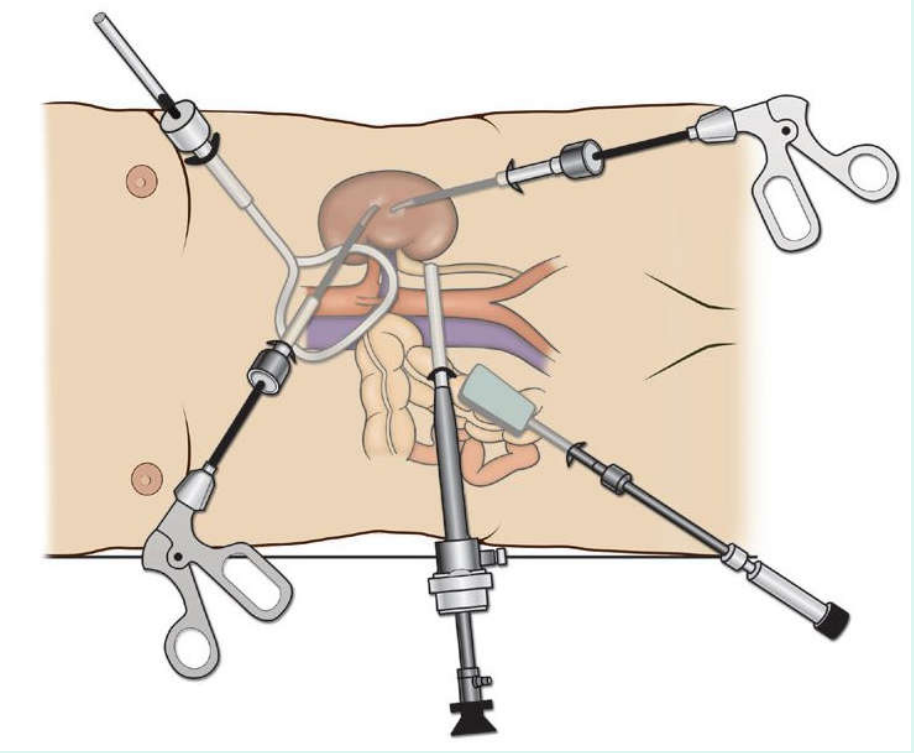
- **E**ndoscopic **C**ombined **I**ntra**r**enal **S**urgery

  = RIRS + PCNL



Laparoscopy

- Lap. Ureterotomy
- Lap. Pyelotomy
- Lap. partial Nephrectomy
- Lap. nephrectomy



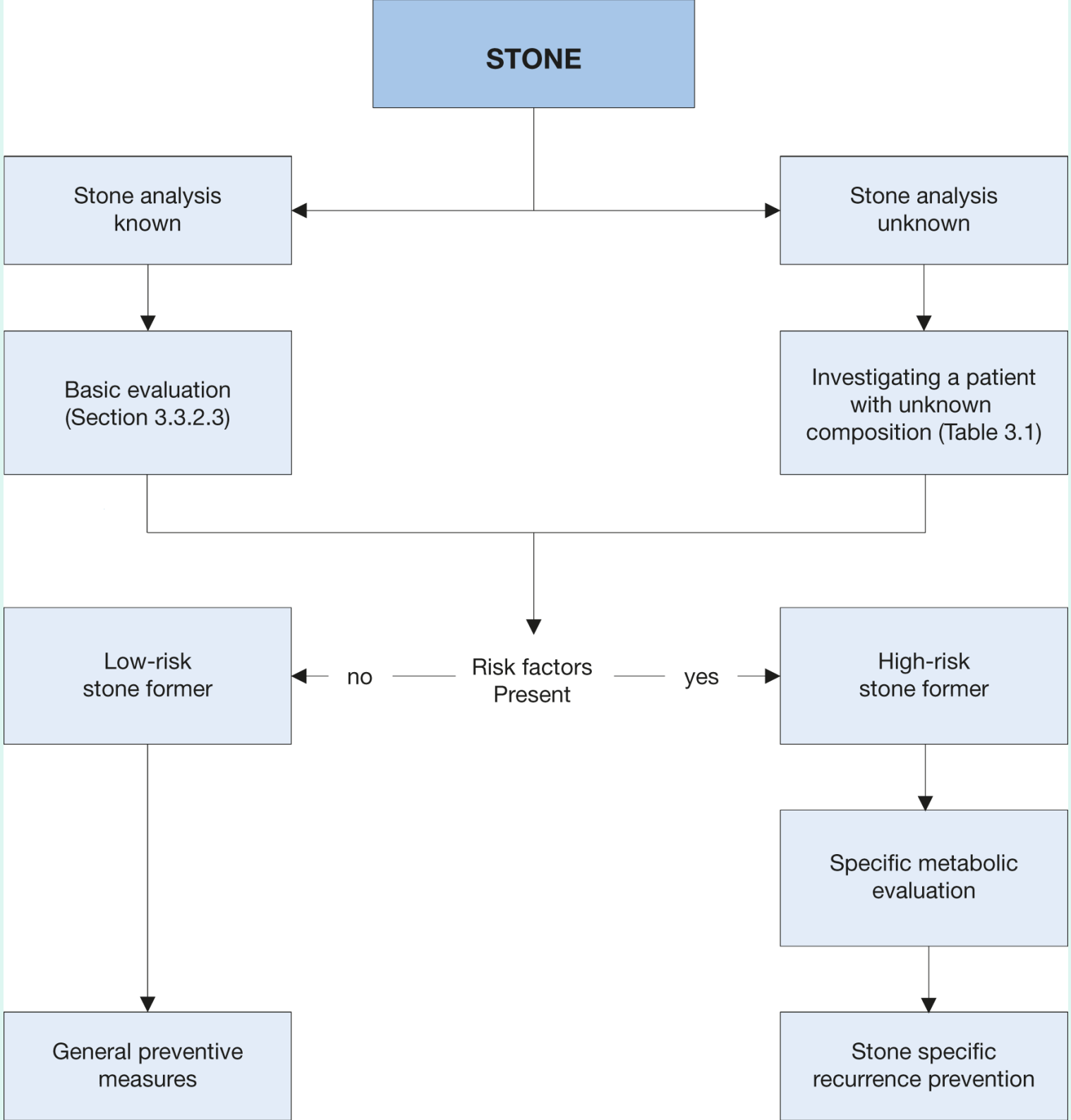
Open surgery: rarely

Metabolic therapy and metaphylaxis

- Recidive risk:

  w/o tx: 50-100%
  w/ correct secundary prevention: 10-15%

- General stone profilaxis
  - Fluid prophylaxis
    - Fluid intake: 2,5-3,0 L/day
  - Dietary prophylaxis
    - Balanced
    - Vega
    - Rich in fibres
    - Low salt and protein intake
  - Normalising general risk factors
    - BMI: 18-25


STONE
Stone analysis known
Stone analysis unknown
Basic evaluation (Section 3.3.2.3)
Investigating a patient with unknown composition (Table 3.1)
Low-risk stone former
no
Risk factors Present
yes
High-risk stone former
Specific metabolic evaluation
General preventive measures
Stone specific recurrence prevention

High risk stone formers:

- High desease activity (≥3 stones in 3 years)

- Infect stones (Struvit, carbonate-apatit, amonium-urate)
- Uric acid stones
- Brushit stones
- genetic determined stone formation (Cystinuria)

- Hyperparathyreoidismus
- Nephrocalzinosis
- Gastrointestinal deseases (Colitis, Morbus Crohn, Malabsorption)

- Solo kidney situation
- bilateral large stones
- Children and juveniles
- positive family hystory

Basic evaluation

- Blood
  - Kreatinin
  - Calcium
  - Uric acid

- Urine
  - Urine sediment, pH
  - Urine culture

Specific metabolic evaluation

Basic evalutation +

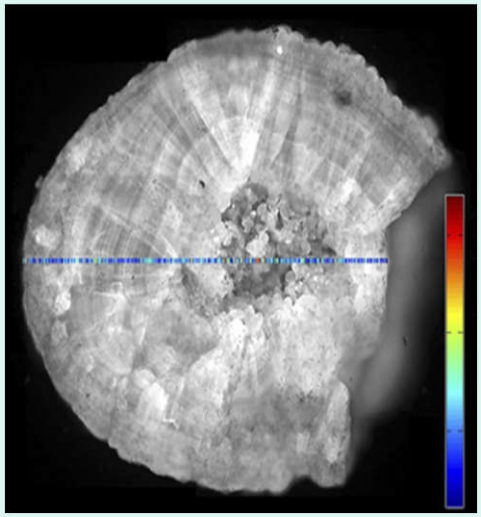
- Blood
  - Parathormon
  - Natrium
  - Kalium
  - Chlorid

- Urine
  - Urine pH profile (4x / day)

  - 2x24h collected urine
    - Volume
    - Kalzium
    - Oxalat
    - Zystin
    - Harnsäure
    - Phosphat
    - Zitrat
    - Magnesium

Stone analysis

- (Chemical)
- X-ray Diffraktometry
- Infrared/Raman Spektroscopy
- Polarisation microscopy



Indications:

- First stone episode
- Recidive stone formation:
  - Recidive in spite of metafilaxis
  - Quick recurrence after complete stone removal
  - New stone formation after long stone free periode

Stone specific metaphylaxis

- **Calcium-oxalate stones**
  - Hypercalcuria → Alkalicitrate, HCT
  - Hypocitraturia → Alkalicitrate
  - Hyperoxaluria → Mg, Alkalicitrate
  - Hyperuricosuria → Alkalicitrate, Allopurinol
  - Hypomagnesiuria → Mg

Stone specific metaphylaxis

- **Calcium-phosphat stones**
  (Karbonatapatit, Brushit)

  – Alkaline Urine pH → L-Methionin
  – Hypercalcuria → HCT

Stone specific metafilaxis

- **Struvit stones**

  - UTI → Antibiotics
  - Alkaline Urine pH → L-Methionin
  - Complete stone removal

Stone specific metaphylaxis

- **Uric acid stones**
  - Urine pH < 6,0 → Urine alkalinization
    - Alkalicitrate
    - Na-bicarbonate

    Metaphylaxis: Urine pH 6,2-6,8
    Lytholysis: Urine pH 7,0-7,2
  - Hyperuricosuria → Allopurinol
- **Ammoniumuratstein**
  - UTI → Antibiotics
  - Urin-pH > 6,5 → L-Methionin (pH 5,8-6,2)
  - Hyperuricosuria → Allopurinol

Stone specific metaphylaxis

- **Cystin stones**
  - Urine dilution: fluid intake 3,5-4 l/day
  - Urine alkalinization to enhance the solubility of cystin
    - Alkalicitrate
    - Na-bicarbonate
  - Ascorbic acid, Tiopronin

    → Cystin excretion↓

Thank you for your attention