

Calcium oxalate stones

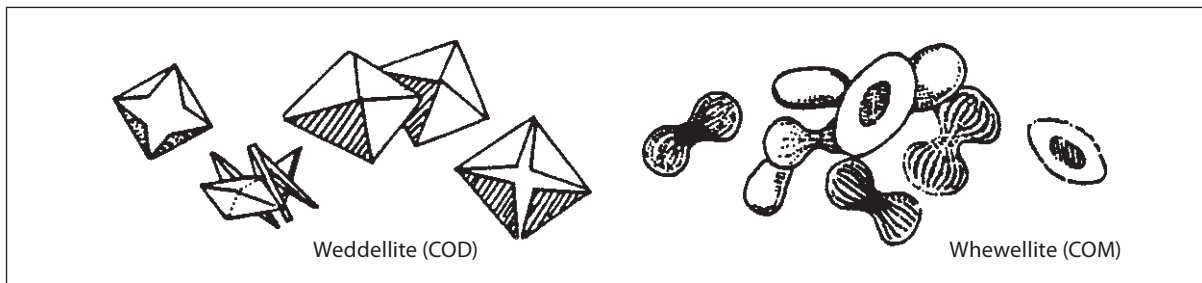
Introduction

Calcium oxalate stones are the most frequent urinary stones of all. 70–75% of all stones contain calcium oxalate. Men are afflicted two times more frequently than women; people aged 30–50 years run the highest risk.

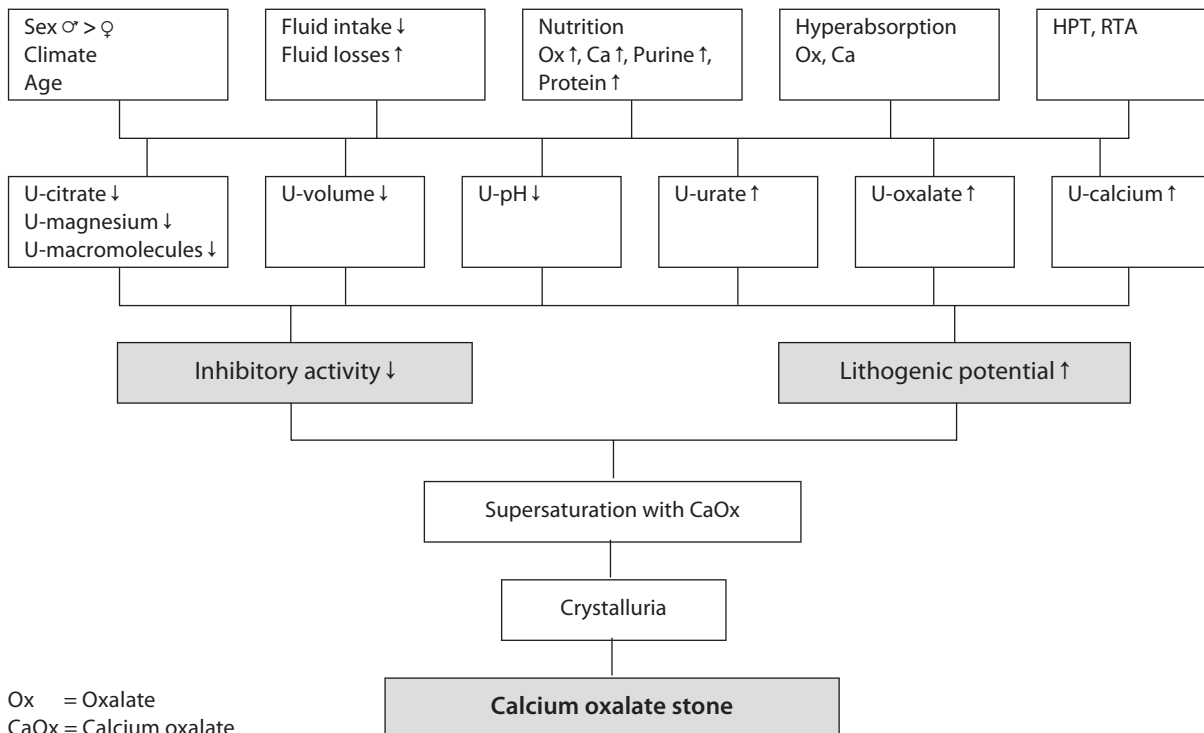
Calcium oxalate stones develop as a multifactorial process in which an imbalance between crystallization-driving and -inhibiting forces plays a fundamental role. Dietary factors might be of great importance in stone development. Inborn errors of metabolism as well as acquired metabolic disorders are important contributing factors. So are most certainly also subepithelial calcifications (Randall's plaques), and it is of note that a large fraction of calcium oxalate-containing stones also contain calcium phosphate.

Calcium oxalate occurs in two different forms. Whewellite (CaOx monohydrate; COM) is compact and of brown or black color. Its formation is favored by high urinary oxalate concentrations. However, high concentrations of calcium and magnesium result in weddellite (CaOx dihydrate; COD) stone formation. Weddellite crystals are of light yellow color and during lithotripsy they disintegrate much more easily than whewellite stones. The recurrence risk is considered higher for COD than for COM stones.

Calcium oxalate stones



- Frequency: 70–75%
- Develop as a result of a multifactorial process



Specific notes for CaOx stone disease

Medical history

Lifestyle:

Overweight, lack of physical activity, stress

Pathophysiologic factors:

Disturbances in the metabolism of calcium, oxalate and uric acid

see *General aspects*, page

22 f.

Imaging

Radiograms with calcifications

Ultrasonography:

Echogenic structures

24 f.

Minimal program

Urine analysis:

pH low

Envelope and dumb-bell shaped crystals in the sediment

26 f.

213 f.

Serum analysis:

Calcium >2.5 mmol/l (5.0 meq/l)
or normal

Uric acid >380 μ .mol/l (6.4 mg/100 ml)
or normal

Establishment of the diagnosis by

stone analysis: CaOx stone (whewellite, weddellite)

192 f.

Quick reference with known serum and urine composition

(in case of unclear findings, first episode of stone, etc.: consider the following pages on diagnostic work-up)



Serum analysis

Calcium	>2.5 mmol/l	▶		Exclude HPT	▶	42 f.
Urate	>380 μmol/l	▶		Diet	▶	56 f.
		▶		Medication	▶	62 f.



24h urine analysis

Volume	<2 l/24h	▶		Urine dilution	▶	52 f.
Density	>1.010 g/cm ³	▶		Urine dilution	▶	52 f.
Calcium	>5.0 mmol/24h	▶		Diet	▶	54 f.
				Medication	▶	58 f.
Oxalate	>0.5 mmol/24h	▶		Diet	▶	56 f.
				Medication	▶	64 f.
Urate	>4.0 mmol/24h	▶		Diet	▶	56 f.
				Medication	▶	62 f.
Citrate	<2.5 mmol/24h	▶		Diet	▶	56 f.
				Medication	▶	62 f.
Magnesium	<3.0 mmol/24h	▶		Medication	▶	58 f.
pH	>6.8	▶		Exclude RTA	▶	46 f.
				Treat RTA	▶	48 f.

Reference values for children see ▶ [206](#) f.

Biochemical investigations

Serum analysis

Calcium

Disturbances in calcium metabolism result in hypercalciuria or hypercalcemia or both. The combination of high serum and urine values is observed in only 3–5% of patients, and the levels are usually parallel.

The serum concentration of calcium is usually strictly controlled within the narrow limits of 2.0 and 2.5 mmol/l (4.0–5.0 meq/l). Ionized serum/plasma calcium is usually between 1.15–1.30 mmol/l.

Suspicion of hyperparathyroidism (HPT)

Additional diagnostic procedures in patients with hypercalcemia

Increased serum concentrations of calcium raise the *suspicion of primary HPT* (but can also be seen with osteolytic malignant processes and in renal failure). It is therefore necessary to measure the *serum concentration of parathyroid hormone*.

Serum phosphate (low in primary HPT) and *alkaline phosphatase* (sometimes high in primary HPT) are also indicators of a disturbed metabolism of calcium. The analysis of *ionized serum calcium* is very helpful in diagnosis of HPT.

Urate

Disturbances in urate metabolism are sometimes considered to be of pathognomonic importance for the formation of calcium oxalate stones. It might therefore be worthwhile to be attentive to an *increased serum level of urate*: $>380 \mu\text{mol/l}$ (6.4 mg/100 ml). It is of note that an increased serum or plasma urate concentration parallels increased levels of creatinine.

**Calcium >2.5 mmol/l****Suspicion of pHPT****Further diagnostic procedures**

Variable	Normal range	Findings
Calcium	2.0–2.5 mmol/l	always increased
Phosphate	0.84–1.45 mmol/l	decreased or normal
PTH	depends on method	increased
Ionized calcium	1.15–1.3 mmol/l	increased

**Ultrasonography**

(scintigraphy; CT; MR)

**The diagnosis of pHPT is established****Urate >380 μmol/l (>6.4 mg/100 ml)****The diagnosis of hyperuricemia is established**

Analysis of urine

24h urine

Numerous factors influence the formation of calcium oxalate stones. Therefore, it is important that the relevant components of the 24h urine are carefully analyzed according to the principles for the quality standard (see p. 28 f.).

The patient has to collect a complete *24h urine sample*.

► Detailed instructions how to collect the sample are essential:

- the first portion of urine in the morning is discarded and the time noted
- collect all urine during the following 24h in the bottle
- the last voiding should be made at the same time as the collection was started on the previous day
- if possible, store the urine in a cool place and bring it to analysis as soon as possible after the collection has been completed

(for detailed instructions how to collect urine, see p. 190 f.)

Note: Analysis of urate and pH cannot be carried out in acidified urine samples. Another preservative should be used such as 10 ml of 5% thymol in isopropanol or 30 ml of 0.3 mol/l sodium azide (for 24h urine collections).

Calcium

The *excretion of calcium* is particularly interesting inasmuch as increased values are observed in up to 56% of patients with calcium oxalate stone disease, and particularly in recurrent stone formers. *Hypercalciuria* is defined as an *excretion of ≥ 8 mmol of Ca per 24h*, but it is justified to start calcium reduction *therapy even at a 24h excretion of 5 mmol* (children: >0.1 mmol/kg body weight/24h).

Oxalate

Increased *excretion of oxalate* can be demonstrated in 20–50% of patients with calcium oxalate stone disease. A high oxalate excretion is associated with a high risk of recurrent stone formation. It is therefore essential that oxalate is analyzed in this group of patients. The intestinal oxalate absorption rate can be determined through the [$^{13}\text{C}_2$]oxalate absorption test (see p. 178 f.).

Urate

Urate might contribute to the formation of stones because high concentrations of urate lead to decreased solubility of calcium oxalate. The occurrence of increased urate excretion varies between different populations but figures between 20 and 60% have been reported.

Citrate and magnesium

Citrate and magnesium are the two most important inhibitors of crystallization that can be influenced by therapy. A low excretion of citrate which is associated with a high risk of stone formation has been demonstrated in up to 50% of all patients with calcium oxalate stone disease. The analysis of citrate is an important part of the quality standard.



24h urine collection



Part of the quality standard

particularly relevant:

calcium, oxalate, urate, citrate, magnesium, pH

▶ 28 f.

Calcium

≥8mmol/24h

▶ Hypercalciuria

Therapy is justified at a level of 5 mmol/24h

Oxalate

≥0.5 mmol/24h

▶ Hyperoxaluria

Urate

≥4 mmol/24h

▶ Hyperuricosuria

Citrate

≤2.5 mmol/24h

▶ Hypocitraturia

Magnesium

≤3 mmol/24h

▶ Hypomagnesuria

pH

The pH day profile does not show any values below 5.8

▶ Exclude RTA

▶ 46 f.

Reference values for children see ▶ 206 f.