
This text has been prepared by the authors purely for educational purposes, in response to requests from many physicians who are confounded by complexities of medical approach to stone disease. There is no restriction on duplication or dissemination of the material. Enclosed recommendations represent a consensus view of the authors. They do not preclude other options or approaches.
Selection of simplified or extensive evaluation at initial visit. Apply a simplified evaluation in patients with single stone episode without risk. Consider an extensive evaluation in patients with recurrent episode or first episode at risk.
History constituting increased risk for stone development. If present in patients with first episode, an extensive evaluation is advised. If absent, a simplified evaluation may be applied.
SIMPLIFIED EVALUATION

Hx:
- Dietary aberrations
- Stone-provoking medications
- Fluid loss
- Urinary tract infection

Laboratory Tests:
- Stone analysis (e.g., StoneComp® Test)
- Serum Ca, P, electrolytes and uric acid
- 24-hour urine stone risk profile analysis (e.g., StoneRisk® Diagnostic Profile, UroRisk® Diagnostic Profile)
- Urinalysis & urinary sediment (crystals)
- Urine culture (if clinically indicated)
- KUB

DIETARY ABERRATIONS

- Low fluid intake
- High Ca intake
- High oxalate diet
- Sodium excess
- Animal protein excess
- Low citrus fruit intake

History and laboratory tests to be obtained during simplified evaluation.
During simplified evaluation, medications which might cause or exaggerate nephrolithiasis.

STONE-PROVOKING MEDICATIONS

- Acetazolamide
- Ca-channel blockers
- Vitamin C
- Triamterene
- Ca / Vitamin D
- Uricosuric agents
- P-binding antacids
- Furosemide
- Theophylline
### STONE ANALYSIS

Diagnostic importance of stone analysis.

<table>
<thead>
<tr>
<th>STONE TYPE</th>
<th>ETIOLOGY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radiopaque Stone</strong></td>
<td></td>
</tr>
<tr>
<td>Calcium oxalate</td>
<td>Hypercalciuria, hyperoxaluria, hyperuricosuria, hypocitraturia, hypomagnesuria, low urine volume</td>
</tr>
<tr>
<td>Calcium phosphate (hydroxyapatite)</td>
<td>Primary hyperparathyroidism, renal tubular acidosis, sodium alkali therapy</td>
</tr>
<tr>
<td>Struvite or carbonate apatite</td>
<td>Urinary tract infection with urea-splitting organisms</td>
</tr>
<tr>
<td>Cystine</td>
<td>Cystinuria</td>
</tr>
<tr>
<td><strong>Radiolucent Stones</strong></td>
<td></td>
</tr>
<tr>
<td>Uric acid</td>
<td>Gouty diathesis, hyperuricosuria, chronic diarrheal syndrome, dehydration, low urinary pH</td>
</tr>
<tr>
<td>2,8-Dihydroxyadenine</td>
<td>2,8-Dihydroxyadeninuria</td>
</tr>
<tr>
<td>Triamterene</td>
<td>Triamterene therapy</td>
</tr>
<tr>
<td>Xanthine</td>
<td>Xanthinuria</td>
</tr>
<tr>
<td>Silica</td>
<td>Magnesium trisilicate therapy</td>
</tr>
</tbody>
</table>
SERUM

↑ Ca, ↓ P : Primary hyperparathyroidism

↓ K, ↓ CO₂ : RTA

↑ Uric Acid : Gouty diathesis

↓ P : Hypophosphatemic AH

If present, extensive evaluation

During simplified evaluation, diagnostic utility of blood tests.

URINALYSIS

• Crystal identification

• pH (by electrode)
  < 5.50 = Gouty diathesis
  > 7.50 = Infection lithiasis

• Quantitative cystine (if suspect cystinuria)

• Culture
  If suspect presence of urea-splitting organisms: Infection stones
  If abnormal, extensive evaluation

During simplified evaluation, diagnostic value of urine analysis and culture.
Two forms of extensive evaluation to be applied in patients with recurrent episode or first episode at risk.

EXTENSIVE EVALUATION
Recurrent Episode
First Episode at Risk
• Full ambulatory protocol
• Simplified ambulatory evaluation

TREATMENT OF FIRST EPISODE
Conservative Measures
• Avoidance of stone-provoking drugs
• High fluid intake
• Dietary oxalate restriction
• Dietary sodium restriction
• Avoidance of animal protein excess
• Avoid extremes of calcium intake
  Do not restrict calcium if bone disease is present/suspected

Conservative measures to be applied in patients with single stone episode without risk.
FULL AMBULATORY PROTOCOL

Visit 1: Random diet
   History
   Serum Ca, P, electrolytes and uric acid
   24-hour urine for stone risk factors on customary diet and fluid intake

Visit 2: Restricted diet
   Serum Ca, P, electrolytes, uric acid and PTH
   24-hour urine for stone risk factors
   Fast and calcium load test (if warranted by persistent hypercalciuria)

Visit 1 and 2 - two weeks apart. If possible, bone density with hypercalcemia or marked hypercalciuria

Full ambulatory protocol representing an extensive evaluation useful in a research setting.
SIMPLIFIED AMBULATORY EVALUATION

1. 24-hour urine stone risk analysis (e.g., StoneRisk®, Diagnostic Profile, UroRisk® Diagnostic Profile)
2. Dietary modification pending results of 1
3. Abbreviated stone risk analysis (e.g. StoneTrack® Monitoring Test) plus serum Ca, P, electrolytes, uric acid and PTH following dietary modification
4. Bone density in hypercalcemia or marked hypercalciuria

StoneRisk®, UroRisk®, and StoneTrack® are registered trademarks of Mission Pharmacal Company.
**DIETARY MODIFICATION**  
(for diagnostic assessment)

<table>
<thead>
<tr>
<th>Finding</th>
<th>Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>TV &lt; 2 l/day</td>
<td>↑ Fluid intake</td>
</tr>
<tr>
<td>Na &gt; 200 meq/day</td>
<td>Na restriction</td>
</tr>
<tr>
<td>Ox &gt; 45 mg/day</td>
<td>Ox restriction</td>
</tr>
<tr>
<td>Ca &gt; 250 mg/day</td>
<td>Ca restriction (mod)</td>
</tr>
<tr>
<td>UA &gt; 600 mg/day</td>
<td>Restriction of</td>
</tr>
<tr>
<td>SO₄ &gt; 30 mmol/day</td>
<td>animal proteins</td>
</tr>
</tbody>
</table>

From 24-hour urine stone risk analysis, identify abnormal risk factors. Apply appropriate dietary measures as described here.
Description of various dietary measures. After 1-4 months of such a dietary modification, perform abbreviated stone risk profile. From results of full and abbreviated stone risk analysis, make diagnosis.

**DIETARY MODIFICATION**
(for diagnostic assessment)

- High fluid intake
  At least 10-10 oz glasses/day (enough to assure urine output of > 2 L/day)

- Sodium restriction
  Avoidance of salty foods and salt shaker

- Oxalate Restriction
  Avoidance of nuts, spinach, chocolate, tea, Vitamin C

- Calcium Restriction
  Avoidance of dairy products, spinach
  Diagnostic purpose only
DIETARY MODIFICATION
(for long-term treatment)

- High fluid intake
- Sodium restriction
- Oxalate restriction
- Avoidance of purine gluttony if possible
- Increased citrus fruit intake
- Calcium restriction (moderate) in hypercalciuria (only in the presence of normal bone density)

Whether or not metabolic abnormalities are present from preceding diagnostic evaluation, apply to all patients with recurrent episode or first episode at risk a dietary modification for long-term management. Provide additional specific measures for different metabolic abnormalities (to be described).
Treatment of hypercalciuria with low bone density and normocalcemia.

TREATMENT

Hypercalcemia:
Further work-up

Hypercalciuria with Low Bone Density and Normal Serum Ca:
Probable fasting hypercalciuria with normal PTH or Vitamin D-dependent AH

- Chlorthalidone 25 mg/day or
  - Indapamide 2.5 mg/day + K₃Cit
    (e.g., Urocit®-K) 20 meq bid, or
- Orthophosphate (e.g., Neutra-Phos-K®) 500 mg P tid/qid

Urocit®-K and Neutra-Phos-K® are registered trademarks of Mission Pharmacal Company and Alza Pharmaceuticals respectively.
ABSORPTIVE HYPERCALCIURIA TYPE I
FASTING HYPERCALCIURIA w Normal PTH
Urinary Ca > 250 mg/day on StoneRisk® Diagnostic Profile, UroRisk® Diagnostic Profile or StoneTrack® Monitoring Test
Normal serum Ca and PTH
Rx:
Chlorthalidone 25 mg/day or Indapamide 2.5 mg/day + K₃Cit (e.g., Urocit-K) 20 meq bid
Sodium restriction
SCP (e.g., Calcibind®) 5 g bid with oxalate restriction in TZ resistance/intolerance without bone disease
Avoidance of Ca restriction in the presence of low bone density

TREATMENT OF ABSORPTIVE HYPERCALCIURIA TYPE I OR FASTING HYPERCALCIURIA WITH NORMAL PARATHYROID FUNCTION.

ABSORPTIVE HYPERCALCIURIA TYPE II
Urinary Ca > 250 mg/day on StoneRisk® Diagnostic Profile or UroRisk® Diagnostic Profile
< 250 mg/day on StoneTrack® Monitoring Test (follow-up abbreviated test profile)
Normal Serum Ca and PTH
No evidence of bone disease
Rx:
Moderate dietary Ca restriction, or
Chlorthalidone 25 mg/day or Indapamide 2.5 mg/day + K₃Cit (e.g., Urocit-K) 10 meq bid

TREATMENT OF ABSORPTIVE HYPERCALCIURIA TYPE II.

StoneRisk®, UroRisk®, and StoneTrack®, Calcibind® and Urocit-K® are registered trademarks of Mission Pharmacal Company.
Treatment of renal hypercalciuria.

**RENA L HY PERCALCIURIA**

Urinary Ca > 250 mg/day

High serum PTH

Rx:

Chlorthalidone 25 mg/day or
Indapamide 2.5 mg/day + K₃Cit
(e.g., Urocit-K) 20 meq bid

Urocit-K is a registered trademark of Mission Pharmacal Company.
HYPERURICOSURIC CALCONEPHROLITHIASIS

Urinary uric acid > 700 mg/day
pH > 5.50
CaOx stones (recurrent)
History of animal protein excess (purine gluttony)
Normocalcemia

Rx:
Allopurinol (e.g., Zyloprim®) 300 mg/day, if
serum uric acid > 8 mg/dl
urinary uric acid > 800 mg/day
Potassium Citrate (e.g., Urocit®-K)
15 meq bid, if hypocitraturic
urinary uric acid 600-800 mg/day

Zyloprim® and Urocit®-K are registered trademarks of Prometheus Laboratories and Mission Pharmacal Company respectively.
Treatment of hypocitraturic Ca nephrolithiasis. Apply dietary modification if hypocitraturia is due to animal protein excess, deficient intake of citrus fruits or sodium abuse.

**HYPOCITRATURIC CA NEPHROLITHIASIS**

Urinary citrate < 450 mg/day  
Evidence of RTA, CDS or TZ Rx

Rx:

K$_3$Cit (e.g., Urocit*-K) 20-40 meq bid

---

Treatment of gouty diathesis.

**GOUTY DIATHESIS**

Urinary pH < 5.50  
Uric acid/Ca stones  
Personal/family history of gout  
High serum uric acid and triglycerides  
No animal protein excess or CDS

Rx:

K$_3$Cit (e.g., Urocit*-K) 20-40 meq bid  
Allopurinol (e.g., Zyloprim*) 300 mg/day for  
  Serum uric acid > 8 mg/dl  
  Urinary uric acid > 800 mg/day

---

Zyloprim* and Urocit*-K are registered trademarks of Prometheus Laboratories and Mission Pharmacal Company respectively.
Comparative effects of potassium citrate and sodium citrate.

<table>
<thead>
<tr>
<th></th>
<th>Potassium Citrate</th>
<th>Sodium Citrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary calcium</td>
<td>↓</td>
<td>=, ↑</td>
</tr>
<tr>
<td>Urinary citrate</td>
<td>↑ ↑ ↑</td>
<td>↑ ↑</td>
</tr>
<tr>
<td>Inhibitor activity, calcium oxalate</td>
<td>↑</td>
<td>=, ↓</td>
</tr>
<tr>
<td>Prevention of calcium stones</td>
<td>+ + +</td>
<td>+ +</td>
</tr>
<tr>
<td>Urinary pH</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Prevention of uric acid stones</td>
<td>+ +</td>
<td>+ +</td>
</tr>
</tbody>
</table>
Treatment of cystine stones.

**CYSTINE STONES**

- Positive quantitative test for cystine
- Cystine on stone analysis

**Rx:**

- $K_3$Cit (e.g., Urocit-K) 10-20 meq bid to maintain urinary pH between 6.50 - 7.00
- If urinary cystine concentration is > 300 mg/l, Tiopronin (e.g., Thiola) or d-Penicillamine (e.g., Cuprimine) 300 mg tid
- Adjust dose to keep cystine < 200 mg/l

---

Treatment of infection stones.

**INFECTION STONES**

- Urinary pH > 7.50
- High urinary ammonium
- Positive culture with urea-splitting organism
- Struvite or carbonate apatite stones

**Rx:**

- Acetohydroxamic Acid (e.g., Lithostat) a urease inhibitor, 250 mg tid/qid
- Antibiotics
- Stone removal
- Treatment of associated metabolic abnormalities

---

*Lithostat* and *Thiola* are registered trademarks of Mission Pharmacal Company. *Cuprimine* is a registered trademark of Merck and Company.
ABBREVIATIONS

1. AH ............................................. absorptive hypercalciuria
2. CDS ............................................. chronic diarrheal syndrome
3. G-I ............................................. gastrointestinal
4. UTI ............................................. urinary tract infection
5. Ox ............................................. oxalate
6. RTA ............................................. renal tubular acidosis
7. SCP ............................................. sodium cellulose phosphate
8. StoneComp® Test .................. identifies chemical components of stones
9. StoneRisk® Diagnostic Profile . assessment of urinary metabolic, environmental and physicochemical factors
   UroRisk® Diagnostic Profile
10. StoneTrack® Monitoring Test . simplified profile with Ca, oxalate, uric acid, citrate, sodium, total volume and pH
11. TV ............................................. total volume
12. TZ ............................................. thiazide
A B C s of Medical Management of Stones

Charles Y. C. Pak, M.D.
with
Donald P. Griffith, M.D.
Mani Menon, M.D.
Glenn M. Preminger, M.D.
Martin I. Resnick, M.D.