2ND EDITION - ABC's

ABC's of Medical Management of Stones

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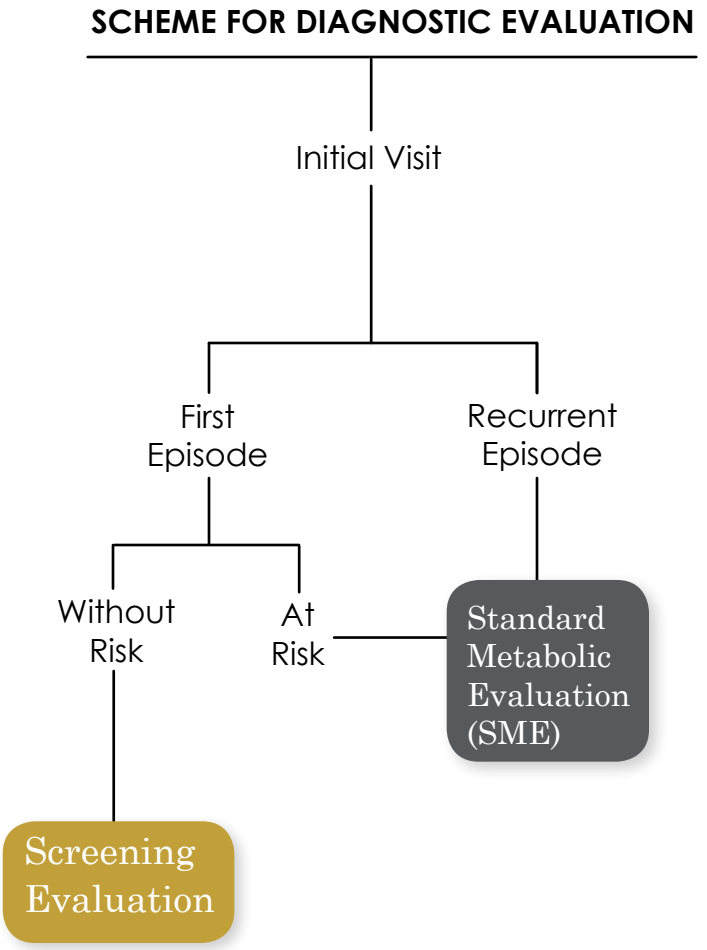
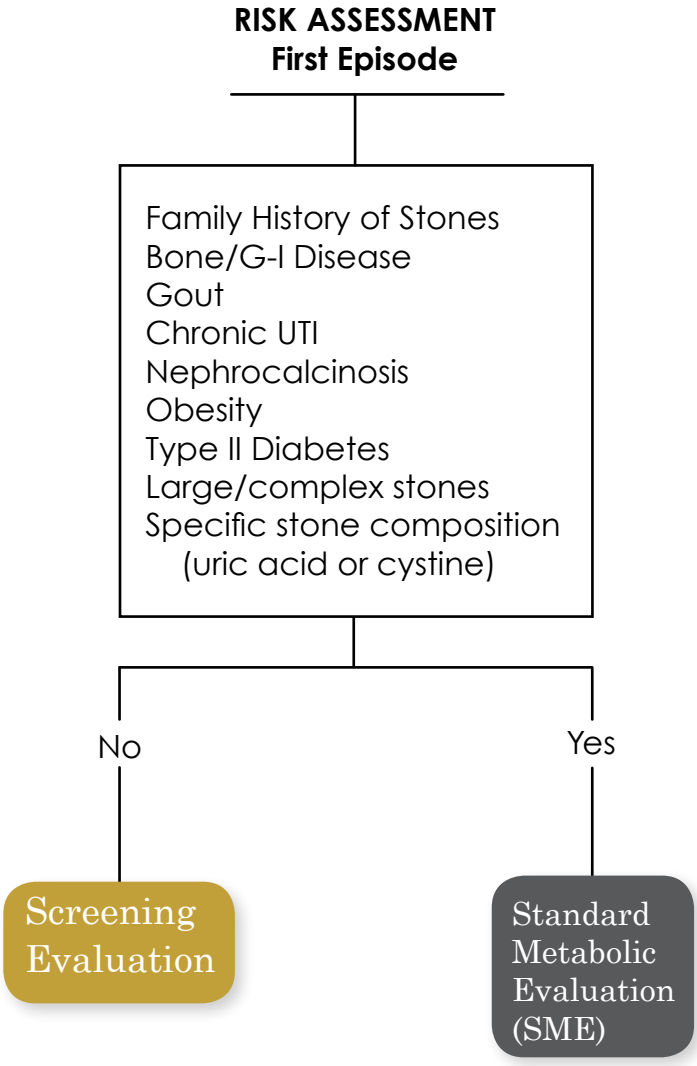
A simple, step-by-step approach to the diagnosis and prevention of nephrolithiasis.

This text has been prepared by the authors purely for educational purposes, in response to requests from many physicians who are confounded by the complexities of medical approaches to stone disease. There is no restriction on duplication or dissemination of the material. The enclosed recommendations represent a consensus view of the authors. They do not preclude other options or approaches.

Selection of screening or standard metabolic evaluation at the initial visit. Apply a screening evaluation in patients with a single stone episode without risk. Consider a standard metabolic evaluation in patients with recurrent stone episodes or after a first episode in patients who are at risk.



History conferring an increased risk for stone development. If present in patients experiencing their first stone episode, a standard metabolic evaluation is advised. If absent, a screening evaluation is sufficient.



SCREENING EVALUATION

History and laboratory tests to be obtained during screening evaluation.

Hx:

Dietary aberrations

Stone-provoking medications

Fluid loss

Urinary tract infection (UTI)

Laboratory Tests:

Stone analysis

Serum Ca, P, electrolytes (creatinine, potassium, bicarbonate) and uric acid

Urinalysis & urinary sediment (stone crystals)

Urine culture (if clinically indicated)

Imaging studies to quantify stone burden and identify nephrocalcinosis (KUB, non-contrast CT or ultrasound)

Hx: Dietary aberrations

- Low fluid intake
- High or low Ca intake
- High oxalate diet
- High salt intake
- High animal protein diet
- Low citrus fruit intake

Hx: Stone-provoking medications

Medications associated with stones or causing abnormal risk factors

MEDICATION	MECHANISM
Acetazolamide	Metabolic acidosis
Topiramate	Metabolic acidosis
Vitamin C	Hyperoxaluria
Triamterene	Triamterene stones
Ca / Vitamin D	Hypercalciuria
Uricosuric agents	Hyperuricosuria
Phos-binding antacids	Hypercalciuria
Guaifenesin	Guaifenesin stones
Ephedrine	Ephedrine stones
Some retrovirals	Indinavir stones, others

Laboratory Tests: Stone Analysis

STONE TYPE	ETIOLOGY
Radiopaque Stones	
Calcium oxalate	Hypercalciuria Hyperoxaluria Hyperuricosuria Hypocitraturia Low urine volume Low urinary pH
Calcium phosphate (hydroxyapatite)	Primary hyperparathyroidism Renal tubular acidosis (RTA) Over alkalinization
Struvite or carbonate apatite	Urinary tract infection (UTI) with urea-splitting organisms
Cystine	Cystinuria
Radiolucent Stones	
Uric acid	Idiopathic uric acid nephrolithiasis Hyperuricosuria Chronic diarrheal syndrome (CDS) Dehydration Low urinary pH Diabetes Metabolic syndrome
2,8-Dihydroxyadenine	2,8-Dihydroxyadeninuria
Triamterene	Triamterene therapy
Xanthine	Xanthinuria

Laboratory Tests: Serum

↑Ca, ↓P	:	Primary hyperparathyroidism
↓ K, ↓CO_2	:	Renal tubular acidosis (RTA)
↑ Uric Acid	:	Idiopathic uric acid nephrolithiasis and/or hyperuricosuric calcium nephrolithiasis

If present, extensive evaluation

Laboratory Tests: Urinalysis

- Crystal identification
- pH (by electrode)

  < 5.50 = Idiopathic uric acid nephrolithiasis

  > 7.50 = Infection lithiasis
- Quantitative cystine (if cystinuria suspected or cystine crystals detected)
- Culture

Urea-splitting organisms: suspect infection stones

If abnormal, proceed to standard metabolic evaluation

TREATMENT OF FIRST EPISODE

Conservative measures to be applied in patients after a single stone episode without risk.

- Avoidance of stone-provoking drugs
- High fluid intake (at least 3.0 L/day)
- Dietary oxalate restriction
- Dietary sodium restriction
- Limited intake of animal protein
- Avoidance of extremes of calcium intake

Do not restrict calcium if osteoporosis or family history is present/suspected

STANDARD METABOLIC EVALUATION (SME)

Recurrent Episode or First Episode at Risk

1. Perform screening evaluation

2. Perform 24-hour urine stone risk analysis on a random diet

3. Measure PTH when serum calcium is > 10 mg/dl or urinary calcium excretion is > 500 mg/day.

    - Alternative approach: 24-hour urine collection for stone risk analysis on a restricted diet (after dietary modification).

4. Bone density in hypercalcemia or marked hypercalciuria

IDENTIFICATION OF URINARY ABNORMALITIES DUE TO DIETARY OR ENVIRONMENTAL DISTURBANCES

From the initial 24-hour urine stone risk analysis obtained on a random diet, identify abnormalities. Some of these abnormalities may be the result of underlying dietary or environmental disturbances.

Finding	Implicated Dietary-Environmental Disturbances
TV < 2 L/day	Low fluid intake, excessive sweating
Na > 200 mEq/day	Salt abuse
Ox > 45 mg/day	↑ intake of oxalate-rich foods, very low calcium intake
Ca > 250 mg/day	High intake of calcium in some cases
UA > 600 mg/day	High animal protein intake
SO_4 > 30 mmol/day	Excessive animal protein intake
Citrate < 500 mg/day	High intake of animal protein and salt

Rx: DIETARY MODIFICATION

(For long-term treatment)

Whether or not metabolic abnormalities are present from the preceding diagnostic evaluation, apply the following dietary modifications for long-term management of those with recurrent stone episodes or those with a single stone episode and risk factors. Apply calcium restriction only in select patients.

- High fluid intake (> 3000 ml/day)
  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 (2000-3000 mg sodium daily)
- Oxalate restriction
  Avoidance of nuts, spinach, chocolate, tea, potatoes, vitamin C supplements
- Avoidance of excessive intake of animal protein
- Increased intake of potassium-rich citrus products

Applied to Those with Hypercalciuria

- 24-hour urine for stone risk analysis after dietary modification (if no restricted urine was collected at initial SME)
- Modest calcium intake in patients with hypercalciuria if pharmacological treatment is contemplated

Dx: HYPERCALCIURIA

Urinary Ca > 250 mg/day

Normal serum Ca

Rx: Indapamide 1.25-2.5 mg/day
(or Chlorthalidone 25 mg/day)

+ K_3Cit (e.g., Urocit®-K) 15 mEq with breakfast and 30 mEq with dinner (45 mEq qd)

Sodium restriction

Ensure a minimum amount of calcium intake (800 mg/day, i.e. 2-3 dairy servings/day) in patients with hypercalciuria

Hypercalciuria Special Circumstances:

a) **Dx: HYPERCALCIURIA WITH LOW BONE DENSITY AND NORMAL SERUM *Ca*:**

Rx: Further work-up for osteoporosis

b) **Dx: HIGH URINE pH** (≥ 6.5) and normal urine citrate

Rx: Indapamide 1.25-2.5 mg/day
(or Chlorthalidone 25 mg/day)

+ K_3Cit (e.g., Urocit®-K) 15 mEq with breakfast, 30 mEq with dinner (potassium chloride 20 mEq/day, if there is concern for over-alkalinization)

Dx: HYPERCALCEMIA

Further work-up for primary hyperparathyroidism

Consider sarcoidosis

Dx: HYPERURICOSURIC Ca NEPHROLITHIASIS

Urinary uric acid > 700 mg/day

pH > 5.50

CaOx stones (recurrent)

History of excessive dietary intake of animal protein

Normocalcemia

Normocalciuria

Rx: Allopurinol (e.g., Zyloprim®) 300 mg/day, if urinary uric acid > 800 mg/day and fails to correct with dietary measures (reduced intake of animal protein)

K_3Cit (e.g., Urocit®-K) 15 mEq bid, may be useful

Limit animal protein to 6-8 oz daily

Zyloprim® and Urocit®-K are registered trademarks of Prometheus Laboratories and Mission Pharmacal Company respectively.

Dx: HYPOCITRATURIC Ca NEPHROLITHIASIS

Relative hypocitraturia:
urinary citrate 320-500 mg/day

Hypocitraturia:
urinary citrate < 320 mg/day

Due to distal renal tubular acidosis (RTA), chronic diarrheal syndrome (CDS), K-losing diuretic Rx, or unknown cause

Rx: Apply dietary modification if hypocitraturia is due to high intake of animal protein, deficient intake of citrus fruits or sodium abuse

Relative hypocitraturia:
K_3Cit (e.g., Urocit®-K) 15 mEq bid with breakfast and dinner

Hypocitraturia:
K_3Cit (e.g., Urocit®-K) 15-30 mEq bid with breakfast and dinner

to achieve urinary citrate > 500 mg

Dx: IDIOPATHIC URIC ACID NEPHROLITHIASIS

(Sometimes called gouty diathesis)

Urinary pH < 5.50 on both random and restricted diets

Uric acid and/or Ca stones

In most patients: high BMI

In some patients: personal/family history of gout

In some patients: high serum uric acid and triglycerides

No history of chronic diarrheal syndrome (CDS)

Rx: K_3Cit (e.g., Urocit®-K) to achieve urine pH between 6.0-6.5 (usual dose 15-30 mEq bid with breakfast and dinner)

Allopurinol (e.g., Zyloprim®) 300 mg/day, for failure to alkalinize urine with K_3Cit or recurrent stones despite alkalinization; or if serum uric acid > 8 mg/dl and gout

Dx: INFECTION STONES

Urinary pH > 7.50

High urinary ammonium

Positive urine culture with urea-splitting organism

Struvite or carbonate apatite stones

Rx: Antibiotics

Stone removal

Treatment of associated metabolic abnormalities

Acetohydroxamic Acid (e.g., Lithostat®) a urease inhibitor, 250 mg bid (especially if the entire struvite stone cannot be removed, or with persistent infection)

Dx: CYSTINE STONES

Positive quantitative test for cystine

Cystine on stone analysis

Rx: High fluid intake: maintain TV > 4.0 L/day

K_3Cit (e.g., Urocit®-K) to maintain urinary pH between 6.5 - 7.0 (usual dose 15 mEq bid with breakfast and dinner)

If urinary cystine concentration is > 500 mg/l, Tiopronin (e.g., Thiola®) (starting dose 200 mg bid) adjust dose to keep cystine < 200 mg/l

ABBREVIATIONS

1. SME .....standard metabolic evaluation
2. CDS .....chronic diarrheal syndrome
3. GI.....gastrointestinal
4. UTI.....urinary tract infection
5. Ox.....oxalate
6. RTA .....renal tubular acidosis
7. TV .....total volume

Physician's Disclosure: Urocit®-K, one of the drugs discussed in this educational publication, is manufactured by Mission Pharmacal Company, and was developed by Mission and Dr. Charles Pak at the University of Texas Southwestern Medical Center. Dr. Pak and the University receive a royalty from Mission Pharmacal Company from the sale of Urocit®-K. None of the authors have equity interest in Mission Pharmacal Company.

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