Evaluation of urinary lithiasis

Background

- **Endocrine disorders:**
  - Hyperuricemia (uric stones).
  - Hyperparathyroidism and hyperthyroidism (oxalo-calcium stones).
  - Family history of cystinuria (cysteine stones).

- **Systemic diseases:**
  - Sarcoidosis.
  - Myeloma or lymphoproliferative diseases (calcium stones).

- **Intestinal diseases:**
  - Malabsorption.
  - Crohn’s disease and ulcerative colitis (oxalic and uric stones).
  - Intestinal diversions (oxalic and uric stones).

- **Lithogenic drugs:**
  - Diuretics: Acetazolamide, Triamterene.
  - Calcium antagonists, Vitamin D, High doses of Vitamin C.
  - Protease inhibitors: Indinavir.

- **Prolonged immobilization** (oxalo-calcium stones).

- **Changes in diet:**
  - Repeated intake of Alkalis or Calcium supplements.
  - Dietary imbalances (massive intake of proteins or oxalates) and obesity.

- **Urological abnormalities:**
  - UPJ stenosis.
  - Single or horseshoe kidney.
  - Vesicoureteral reflux or ureterocele.
  - Renal tubular ectasia (sponge kidney).
  - Calyceal diverticula.

- **Recurrent urinary infections** (magnesium ammonium phosphate stones).

Description of lithiasis

<table>
<thead>
<tr>
<th>Generic name</th>
<th>%</th>
<th>Crystallographic</th>
<th>Aspect</th>
<th>Hardness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium oxalate stones</td>
<td>60-80</td>
<td>Whewellite</td>
<td>Rough gray</td>
<td>Hard</td>
</tr>
<tr>
<td>Calcium oxalate monohydrate</td>
<td></td>
<td>Weddellite</td>
<td>White-yellow</td>
<td>Soft</td>
</tr>
<tr>
<td>Calcium oxalate dihydrate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium phosphate stones</td>
<td>6-20</td>
<td>Brushite</td>
<td>Yellowish</td>
<td>Hard</td>
</tr>
<tr>
<td>Calcium phosphate dihydrate</td>
<td></td>
<td>Whitlockite</td>
<td>White-yellow</td>
<td>Hard</td>
</tr>
<tr>
<td>Calcium phosphate</td>
<td></td>
<td>Apatite</td>
<td>Whitish</td>
<td>Hard</td>
</tr>
<tr>
<td>Carbonate apatite (phosphate)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infective lithiasis</td>
<td>10-15</td>
<td>Struvite</td>
<td>Rough,Yellowish</td>
<td>Fragile</td>
</tr>
<tr>
<td>Magnesium ammonium phosphate</td>
<td></td>
<td>Newberyte</td>
<td>Brownish</td>
<td>Soft</td>
</tr>
<tr>
<td>Magnesium phosphate</td>
<td></td>
<td>Calcite</td>
<td>White-Gray</td>
<td>Soft</td>
</tr>
<tr>
<td>Calcium carbonate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uric acid and ammonium urate</td>
<td>5-10</td>
<td>Whellite</td>
<td>Amber</td>
<td>Hard</td>
</tr>
<tr>
<td>Uric acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ammonium urate</td>
<td></td>
<td></td>
<td>Yellowish</td>
<td></td>
</tr>
<tr>
<td>Cystine stones</td>
<td>1</td>
<td></td>
<td>Honey-like</td>
<td>Very hard</td>
</tr>
<tr>
<td>In frequent stones</td>
<td>1</td>
<td></td>
<td>Grayish</td>
<td>Hard</td>
</tr>
<tr>
<td>Metabolic: Xanthine, Adenine</td>
<td></td>
<td></td>
<td>Yellow-brown</td>
<td>Soft</td>
</tr>
<tr>
<td>Drug stones: Indinavir, Triamterene</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Metabolic urinalysis

- **Candidates:** not necessary for first episodes in patients over 60 with no urological pathology or associated disease.

## Indications

<table>
<thead>
<tr>
<th>Indication</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent stones</td>
<td>Endocrine disease</td>
</tr>
<tr>
<td>Unilateral multiple stones</td>
<td>Metabolic disease</td>
</tr>
<tr>
<td>Bilateral stones</td>
<td>Gastrointestinal diseases</td>
</tr>
<tr>
<td>Single kidney</td>
<td>Sarcoidosis</td>
</tr>
<tr>
<td>Children</td>
<td>Obesity or bariatric surgery</td>
</tr>
</tbody>
</table>

## Requisites:

- Absence of gross **hematuria** or renal obstruction in the last 4 weeks.
- At least 15 days before or after a lithotripsy or endourological procedure.

## Baseline survey:

- **Urinalysis:** (crystalluria, presence of nitrites +, pH).
- **Urine culture:** the presence of ureolytic bacteria must be ruled out.
- **Blood biochemistry.**

## Two urine samples within 24 hours to determine:

<table>
<thead>
<tr>
<th>In blood</th>
<th>Normal value</th>
<th>In urine</th>
<th>Normal value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>9-10.5 mg/dL</td>
<td>Calcium</td>
<td>Hypercalciuria if &gt;300 mg (♂) 250 mg (♀)/24 h</td>
</tr>
<tr>
<td>Chloride</td>
<td>98-106 mEq/L</td>
<td>Oxalate</td>
<td>Hyperoxaluria if &gt;40 mg/24 h</td>
</tr>
<tr>
<td>Uric acid</td>
<td>&lt; 8(♂) mg/dL</td>
<td>Uric acid</td>
<td>Hyperuricosuria if &gt;750 mg(♀) y &gt;800 mg(♂)</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.5-5 mEq/L</td>
<td>Citrate</td>
<td>Hypocitraturia if &lt;300 mg/24 h</td>
</tr>
<tr>
<td>Urea</td>
<td>21-50 mg/dL</td>
<td>pH</td>
<td>Normal between 5-9 (mean 6.5)</td>
</tr>
<tr>
<td>Creatinine</td>
<td>&lt;1.5 mg/dL</td>
<td>Creatinine</td>
<td>1.0-1.6 g/24 h</td>
</tr>
<tr>
<td>Sodium</td>
<td>136-145 mEq/L</td>
<td>Sodium</td>
<td>100-260 mEq/24 h</td>
</tr>
</tbody>
</table>

## Extensive study:

- After the baseline study, **hypercalciuria** (most frequent anomaly) can be classified into three types (renal, absorptive, or resorptive). After a one-week dietary regimen restricting oxalates, calcium, and purines, a **calcium overload test** (Pak test) is performed:
  - First, the fasting urinary calcium/creatinine quotient is measured.
  - At 8:00 am: 1 g of calcium is administered orally.
  - Between 8:00 and 10:00 am: the urinary calcium/creatinine quotient is measured.
  - Between 10:00 and 1:00 pm: the urinary calcium/creatinine quotient is measured again.

### Types of Hypercalciuria according to Pak Test

<table>
<thead>
<tr>
<th>Determination</th>
<th>Renal leak</th>
<th>Absorptive I</th>
<th>Absorptive II</th>
<th>Absorptive III</th>
<th>Resorptive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca/creatinine pre-load</td>
<td>&gt;0.11</td>
<td>&lt;0.11</td>
<td>&lt;0.11</td>
<td>&lt;0.11</td>
<td>&gt;0.11</td>
</tr>
<tr>
<td>Ca/creatinine after calcium load</td>
<td>&gt;0.22</td>
<td>&gt;0.22</td>
<td>&gt;0.22</td>
<td>&gt;0.22</td>
<td>&gt;0.22</td>
</tr>
<tr>
<td>PTH</td>
<td>high</td>
<td>normal</td>
<td>normal</td>
<td>normal</td>
<td>high</td>
</tr>
<tr>
<td>Serum Calcium</td>
<td>normal</td>
<td>normal</td>
<td>normal</td>
<td>normal</td>
<td>high</td>
</tr>
<tr>
<td>Urine Calcium after Calcium restriction diet</td>
<td>high</td>
<td>normal</td>
<td>no changes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum Phosphate</td>
<td>normal</td>
<td>normal</td>
<td>low</td>
<td>low</td>
<td></td>
</tr>
</tbody>
</table>

## Acid load test to detect renal tubular acidosis.

- **Procedure:** Ammonium chloride (0.1 g/Kg) is administered at breakfast with a glass of water. Every hour for the next 4 hours the subject drinks another glass of water. The urine output is collected and urinary pH is measured.
- **Interpretation:** urinary pH <5.4 rules out renal tubular acidosis.

## Calculi analysis:

- by means of crystallographic studies and infrared spectroscopy. If no fragments of the stone can be recovered, its etiology can be determined by examining its radio-opacity, studying the sediment for crystalluria, evaluating urinary pH, determining the presence of urease-producing bacteria, or through specific tests, e.g. the Brand test for cystinuria.
Diagnostic imaging techniques

- **Ultrasound**: shows the morphology of the renal parenchyma, the presence of ectasia, and the presence and size of hyperechoic image that casts a shadow, which is characteristic of lithiasis. Suitable for pregnant women or women of childbearing age who do not want to be exposed to radiation. May not detect small or ureteral stones. Associated with an x-ray of the urogenital system, this technique has high sensitivity and specificity (90%).

- **KUB x-ray**: mandatory in single kidney patients, when associated with fever >38°C, or in case of diagnostic doubt. Indicates the location, size, volume \((length \times width \times 0.8)\), and radiological density of the stone. Disadvantages: does not detect radio-transparent stones, small stones, or stones that overlap bony structures.

  Depending on their radiopacity, stones can be classified into three main groups:

<table>
<thead>
<tr>
<th>Radiopaque</th>
<th>Poor Radiopacy</th>
<th>Radiolucent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium oxalate monohydrate</td>
<td>Magnesium ammonium phosphate</td>
<td>Uric acid</td>
</tr>
<tr>
<td>Calcium oxalate dihydrate</td>
<td>Cystine</td>
<td>Ammonium urate</td>
</tr>
<tr>
<td>Calcium phosphate</td>
<td>Apatite</td>
<td>Xanthine</td>
</tr>
<tr>
<td>Calcium carbonate</td>
<td></td>
<td>Hydroxyadenine</td>
</tr>
<tr>
<td>Brushite</td>
<td></td>
<td>Indinavir</td>
</tr>
</tbody>
</table>

- **IVU**: considered to be the standard procedure and technical reference. Allows assessment of renal function and morphology as well as the location, size, radiopacity, and repercussions of lithiasis. Less accurate than unenhanced helical CT. Not recommended if there is a history of:
  - Allergy to the contrast medium.
  - Creatinine >1.7 mg/dL.
  - Untreated hyperthyroidism.
  - Myelomatosis.
  - Concomitant treatment with Metformin.

- **Unenhanced CT**.
  - **High diagnostic yield** with high level of evidence and recommendation for its use.
  - **The duration of the test** is, on average, 30 minutes faster than IVU.
  - **Its use is limited** due to the need for sophisticated radiological equipment.
  - **Measuring the Hounsfield units (HU)** can predict the hardness of the stone and thus its capacity for fragmentation (>1000 HU=more difficult to fragment).
  - **Low-energy CT** is an ideal method with good prospects for the future.

- **Other tests**: possible, but not common:
  - **Retrograde pyelography**.
  - **MRI**. Used infrequently as it only detects the filling defect produced by the stone.
  - **Isotope renogram**.

- **Determining the mass of stones**: The size of the stone is expressed in different ways:
  - **Length**: the greatest diameter in mm.
  - **Area** (in \(mm^2\)) with the formula:
    \[
    Area: L (length) \times W (width) \times 0.25 \times 3.1416.
    \]
  - **Volume** (in \(mm^3\)) with the formula:
    \[
    Volume: L (length) \times W (width) \times D (depth) \times 0.167 \times 3.1416.
    \]
Serum Calcium

>10.2 mg/dL
- ↑ PTH
  - Hyperparathyroidism
  - Surgery
- normal PTH
  - Hyperthyroidism
  - Renal insufficiency
  - Sarcoidosis
  - Tumors
  - Metastases
  - Leukemia
  - Lymphoma
  - Hypervitaminosis D
- Etiologic treatment

<10.2 mg/dL
- Evaluation of two 24-hour urine samples
  - Hyperoxaluria >40 mg/24 h
  - Hyperuricosuria >750 mg/24 h
  - Hypocitraturia <300 mg/24 h
  - Hypomagnesiuria <30 mg/24 h
  - Hypercalciuria >250-300 mg/24 h
Hypercalciuria
>250-300 mg/24 h (4 mg/kg/24 h)

Renal leak Hypercalciuria
- Ca++/creatinine pre-load >0.11
- Ca++/creatinine after load >0.22
- Normal Serum Calcium
- Slightly increased PTH

Resorptive Hypercalciuria
- Ca++/creatinine pre-load >0.11
- Ca++/creatinine after load >0.22
- Increased Serum Calcium
- Increased PTH

Absorptive Hypercalciuria
- Ca++/creatinine pre-load <0.11
- Ca++/creatinine after load >0.22
- Normal Serum Calcium
- Normal PTH

Type I
- No Hypercalciuria reduction despite Ca++ restrictive diet

Type II
- Normocalciuria after Ca++ restrictive diet

Type III
- Associated with Hyperphosphaturia
- Hypophosphatemia

Thiazides

Pak Test or Calcium (Ca++) loading test
- Urinary evaluation of Ca++/creatinine before loading
- Urinary evaluation of Ca++/creatinine after 1 g of Ca++

Thiazides + Potassium citrate

Ca++ restriction

phosphates

Surgery