MICROSCOPIC EXAMINATION OF THE URINE: CRYSTALS

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<thead>
<tr>
<th>Normal Acid Crystals</th>
<th>Abnormal Crystals of Metabolic Origin</th>
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<tbody>
<tr>
<td>Amorphous urates</td>
<td>Cystine</td>
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<tr>
<td>Uric acid</td>
<td>Tyrosine</td>
</tr>
<tr>
<td>Acid urates</td>
<td>Leucine</td>
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<tr>
<td>Monosodium urate or sodium urates</td>
<td>Cholesterol</td>
</tr>
<tr>
<td>Calcium oxalate (also neutral and alkaline urine)</td>
<td>Bilirubin</td>
</tr>
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<table>
<thead>
<tr>
<th>Normal Alkaline Crystals</th>
<th>Abnormal Crystals of Iatrogenic Origin (Drugs)</th>
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<td>Amorphous phosphates</td>
<td>Sulfonamides</td>
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<td>Ampicillin</td>
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<td>Ammonium biurate</td>
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<tr>
<td>Calcium phosphate</td>
<td>Acyclovir</td>
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<tr>
<td>Calcium carbonate</td>
<td></td>
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</tbody>
</table>
## Microscopic Examination of the Urine: Crystals

<table>
<thead>
<tr>
<th>Crystal</th>
<th>pH</th>
<th>Color</th>
<th>Shape</th>
<th>Heat</th>
<th>Alkali (10% NaOH)</th>
<th>Acetic Acid (Glacial)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normal Acid Crystals</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amorphous urates (Na, K, Mg, Ca) (common)</td>
<td>Acid</td>
<td>Yellow-red or red-brown</td>
<td>Amorphous (are very small crystals)</td>
<td>Soluble at 60°C</td>
<td>Soluble</td>
<td>Changed to uric acid</td>
</tr>
<tr>
<td>Uric acid (common)</td>
<td>Acid (low)</td>
<td>Yellow or red-brown (rarely, color-less hexagons)</td>
<td>Large variety - rhombic, rosettes, 4-sided plates, “whetstones” lemon-shaped</td>
<td>Soluble at 60°C</td>
<td>Soluble</td>
<td>Insoluble</td>
</tr>
<tr>
<td>Acid urates (Na, K, NH₄)</td>
<td>Acid (or neutral)</td>
<td>Brown</td>
<td>Small spheres, clusters, resemble biurates</td>
<td>Soluble at 60°C</td>
<td></td>
<td>Changed to uric acid</td>
</tr>
<tr>
<td>Monosodium urate (uncommon)</td>
<td>Acid</td>
<td>Colorless</td>
<td>Slender needles or amorphous ppt.</td>
<td>Insoluble (soluble dilute HCl)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium oxalate (dihydrate)</td>
<td>Acid, neutral or alkaline</td>
<td>Colorless</td>
<td>Octahedral, “envelopes”</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium oxalate (monohydrate) (uncommon)</td>
<td>Acid, neutral or alkaline</td>
<td>Colorless</td>
<td>Oval, ovoid rectangle, dumbbell</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Amorphous Urates

- Yellow-brown color
- Found in acidic urine with pH > 5.7
- Forms pink precipitate upon refrigeration (uroerythrin accumulates on surface of crystal) – “brick-dust”
- Precipitate redissolves when warmed or alkali added

Amorphous urates X400
Uric Acid Crystals

- Rhombic, 4-sided shapes, rosettes,...
- Found in acidic urine with pH < ~5.7
- Usually yellow-brown
- Birefringent
- Associated with increased purine metabolism

Uric acid, whetstone shape X160

Uric Acid Crystals

Uric acid crystals, urine sediment X100
**Acid Urates**
- Granules with spicules
- Brown

**Sodium Urates**
- Needle-shaped, blunt ends
- Light yellow, colorless
Calcium Oxalate Crystals

- Seen in urine of any pH
- Dihydrate → octahedral (2 pyramids joined at base)  
  most common form
- Found in 67% of renal calculi in US
- Associated with a diet rich in oxalic acid

Calcium oxalate, three typical octahedrals, X160

Calcium Oxalate Crystals

- Monohydrate form → oval or dumbbell
- Found in ethylene glycol poisoning

Calcium oxalate, rare large ovoid form, X400
Hippuric Acid Crystals

- Elongated needles, prisms
- Yellow-brown or colorless
- Found in high vegetable diets

<table>
<thead>
<tr>
<th>Crystal</th>
<th>pH</th>
<th>Color</th>
<th>Shape</th>
<th>Heat</th>
<th>Acetic Acid (Glacial)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amorphous phosphates (Mg, Ca)</td>
<td>Alkaline</td>
<td>Colorless</td>
<td>Amorphous granules</td>
<td>Insoluble</td>
<td>Soluble</td>
</tr>
<tr>
<td>(common)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triple Phosphate (NH₄, Mg)</td>
<td>Alkaline or neutral</td>
<td>Colorless</td>
<td>3-6 sided prisms – “coffin lids” (common) flat, fern leaf, sheets, flakes (less common)</td>
<td>Soluble</td>
<td></td>
</tr>
<tr>
<td>(common)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium phosphate</td>
<td>Alkaline</td>
<td>Colorless</td>
<td>Slender prisms with 1 wedgelike end, often in rosettes, flat plate (rare)</td>
<td>Insoluble</td>
<td>Soluble</td>
</tr>
<tr>
<td>(uncommon)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ammonium biurate</td>
<td>Alkaline</td>
<td>Dark yellow or brown – like uric acid/urates</td>
<td>Spheres or “thorn apples”</td>
<td>Soluble at 60°C with acid</td>
<td>Slowly change to uric acid</td>
</tr>
<tr>
<td>(common in old urine)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium carbonate</td>
<td>Alkaline</td>
<td>Colorless</td>
<td>Tiny spheres in pairs or fours (crosses)</td>
<td>Soluble</td>
<td>Effervescence</td>
</tr>
<tr>
<td>(uncommon)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Amorphous Phosphates

- Granular, colorless
- Found in alkaline urine
- Forms white precipitate upon refrigeration
- Does NOT redissolve upon warming but dissolves in acetic acid

Triple Phosphate Crystals

- Ammonium, Magnesium, Phosphate precipitates
- "Coffin-lid" prism shape most common
- Can also see flat sheets or fern-leaf shapes
- Colorless
- Birefringent
- Often seen in highly alkaline urine associated with UTI
MICROSCOPIC EXAMINATION OF THE URINE: CRYSTALS

**Triple Phosphate Crystals**

Triple phosphate, unusual fern-leaf form of crystals going into solution, X400.

**Calcium Phosphate Crystals**

- Slender prisms with one tapered end and one blunt end
- Often arranged in rosettes
- Flat rectangular plates also seen
- Colorless
- Common constituent of renal calculi

Calcium phosphate, X400
**Calcium Phosphate Crystals**

- Small round or dumbbell shape
- Often in clumps
- Colorless
- Forms CO₂ when mixed with acetic acid
- Birefringent

![Calcium Phosphate crystals, X400](image)

**Calcium Carbonate Crystals**

- Small round or dumbbell shape
- Often in clumps
- Colorless
- Forms CO₂ when mixed with acetic acid
- Birefringent

![Calcium Carbonate crystals (X 400)](image)
**Ammonium Biurate Crystals**

- Spicule covered spheres; “thorny apples”
- Yellow-brown
- Dissolves at 60°C
- Converted to uric acid crystals when acetic acid added

![Ammonium Biurate Crystals (X 400)](image)

### Abnormal Crystals in the Urine Sediment: Description and Confirmatory Tests

<table>
<thead>
<tr>
<th>Crystal</th>
<th>pH</th>
<th>Color</th>
<th>Shape</th>
<th>Confirmatory Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystine (most common physiologic/abnormal crystals)</td>
<td>Acid</td>
<td>Colorless</td>
<td>Transparent, usually refractile six-sided plates; May polarize (depending on thickness)</td>
<td>Cyanide nitroprusside reaction—red purple color</td>
</tr>
<tr>
<td>Tyrosine (rare)</td>
<td>Acid</td>
<td>Colorless (usually appear black w/focusing)</td>
<td>Fine silky needles arranged in sheaves or rosettes usually occur with leucine</td>
<td>Nitrosomaphthol test—orange color</td>
</tr>
<tr>
<td>Leucine (extremely rare)</td>
<td>Acid</td>
<td>Yellow</td>
<td>Oily-appearing spheres with radial and concentric striations usually occur with tyrosine</td>
<td>Amino acid separation</td>
</tr>
<tr>
<td>Cholesterol (rare)</td>
<td>Acid or neutral</td>
<td>Colorless</td>
<td>Flat plate with corner notch (seen with large proteinuria and after refrigeration)</td>
<td></td>
</tr>
<tr>
<td>Bilirubin (uncommon)</td>
<td>Acid</td>
<td>Reddish brown</td>
<td>Amorphous needles, rhombic plates or cubes; may color uric acid crystals</td>
<td></td>
</tr>
<tr>
<td>Hemosiderin</td>
<td>Acid or neutral</td>
<td>Golden brown</td>
<td>Granules, in clumps, in cells, casts</td>
<td>Blue with Prussian blue reaction (Rous Test)</td>
</tr>
</tbody>
</table>
### Cystine Crystals

- Indicative of cystinuria or cystinosis
- Hexagonal plates but sides uneven
- Can be thick or thin; often in layers

### Crystals of Iatrogenic Origin (Drugs)

<table>
<thead>
<tr>
<th>Crystal</th>
<th>pH</th>
<th>Color</th>
<th>Shape</th>
<th>Confirmatory Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonamides (most common drugs seen)</td>
<td>Acid</td>
<td>Yellow to brown</td>
<td>Various—depends on the drug. Mimics various forms of uric acid/urates/biurates.</td>
<td>For all forms: Hydrolyze with heat and acid. Apply diazo reaction—magenta color.</td>
</tr>
<tr>
<td>Acetylsulfa-diazine</td>
<td>Acid</td>
<td>Yellow-brown</td>
<td>Sheaves of wheat with eccentric bindings</td>
<td></td>
</tr>
<tr>
<td>Sulfadiazine</td>
<td>Acid</td>
<td>Brown</td>
<td>Dense globules</td>
<td></td>
</tr>
<tr>
<td>Acetylsulfa-methoxazole</td>
<td>Acid</td>
<td>Brown</td>
<td>Dense spheres or irregularly divided spheres</td>
<td></td>
</tr>
<tr>
<td>Ampicillin (Penicillins)</td>
<td>Acid</td>
<td>Colorless</td>
<td>Long slender needles, form clusters. Sheaves after refrigeration.</td>
<td></td>
</tr>
<tr>
<td>Radiographic media (meglumine diatrizoate)</td>
<td>Acid</td>
<td>Colorless</td>
<td>Flat plates, some with corner notch like cholesterol; elongated crystals</td>
<td>Specific gravity &gt;1.035 False-positive SSA protein test</td>
</tr>
<tr>
<td>Acyclovir (rare) (7.5)</td>
<td>Alkaline</td>
<td>Colorless</td>
<td>Fine slender needles</td>
<td>Infrared analysis and/or clinical history</td>
</tr>
</tbody>
</table>

**Cystine Crystals (X400)**
**Cholesterol Crystals**

- Found in lipid disorders, nephrotic syndrome
- Rectangular plates with notched corners
- Birefringent
- Seen in conjunction with fatty casts, oval fat bodies and protein

![Cholesterol crystals. Notice the notched corners (X 400)](image1)

**Radiographic Dye Crystals**

- Similar to cholesterol in appearance
- Associated with markedly elevated SG

![Radiographic contrast media, meglumine diatrizoate (Renografin), appearing somewhat like cholesterol, X400](image2)

![Radiographic contrast media (meglumine diatrizoate) X400](image3)
**Tyrosine Crystals**

- Fine needles
- Arranged in clumps or rosettes
- Colorless to yellow
- Usually occur with leucine crystals and a positive bilirubin

![Tyrosine crystals; urine sediment; X 400](image)

**Leucine Crystals**

- Yellow-brown spheres with concentric circles and radial striations
- Usually occur with tyrosine crystals

![Leucine crystals; urine sediment; X 400](image)
**Bilirubin Crystals**

- Clumps of needles, granules or plates
- Highly colored yellow to reddish brown
- Present in liver disorders producing large amounts of bilirubin in urine

![Bilirubin Crystals; urine sediment; X 400](image)

**Hemosiderin**

- Appears in urine 2-3 days following a severe hemolytic episode
- Coarse, yellow-brown granules
- Found free-floating or within cells
- Stains with Prussian blue

![Free-floating hemosiderin granules Brightfield X400](image)  ![Hemosiderin granules stained with Prussian Blue](image)
Sulfonamide Crystals

- Sulfa drugs used in treatment of UTI
- Variety of drugs, therefore a variety of shaped crystals
- Needles, rhombus forms, sheaves of wheat, rosettes
- Colorless to yellow-brown

Acetylsulfadiazine, as sheaves of wheat with eccentric binding and red blood cells, X 400

Sulfamethoxazole (Septra) rosette, and red blood cells, X 400
Sulfonamide Crystals

- Rarely seen; found after massive doses of ampicillin and inadequate patient hydration
- Slender needles in clusters; colorless
- Form sheaves following refrigeration

Ampicillin Crystals

- Rarely seen; found after massive doses of ampicillin and inadequate patient hydration
- Slender needles in clusters; colorless
- Form sheaves following refrigeration
Acyclovir Crystals

- Rarely seen
- Acyclovir: antiviral drug for treatment for herpes simplex infections
- Found in alkaline urine
- Fine needles; colorless

Urinary Sediment Artifacts:

Starch Granules

- Highly refractive
- Spherical with dimpled center
- Maltese cross formation when polarized
Starch Granules

Starch granules, showing typical dimpled appearance with brightfield illumination, unlike cholesterol esters of fat, and Maltese cross formation with polarized and compensated polarized light, ×400. A, Brightfield. B, Polarized light showing Maltese cross formation and similarity to fat as cholesterol. C, Compensated polarized light showing so-called beach-ball appearance.

Urinary Sediment Artifacts:

Oil Droplets / Air Bubbles

- Highly refractive
Urinary Sediment Artifacts:

Glass Fragments

Glass fragments from coverslip, appearing like crystals, \( \times 100 \).

Urinary Sediment Artifacts:

Pollen
- Seasonal contaminant
- Large spheres
- Has cell wall and occasionally concentric circles

Pollen grain. Notice the concentric circles, \( X \ 400 \).
Urinary Sediment Artifacts:

Hair and Fibers

• Similar in appearance to casts BUT longer and more refractile

Fiber, probably hair (left), waxy casts (right), Sedi-stain, X400

Fibers

Fiber (left), granular cast (right), and many yeast, ×400.
Urinary Sediment Artifacts:

Fecal Contaminants

- Plant and meat fibers
- Brown amorphous material

Identification Errors that Occur in the Microscopic Examination of Urine Sediment

<table>
<thead>
<tr>
<th>Element</th>
<th>Identification Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red blood cells</td>
<td>Yeast, oil droplets, air bubbles</td>
</tr>
<tr>
<td>White blood cells</td>
<td>Renal tubular epithelial cells</td>
</tr>
<tr>
<td>Oval fat bodies</td>
<td>Air bubbles</td>
</tr>
<tr>
<td>Squamous cells (folded)</td>
<td>Casts</td>
</tr>
<tr>
<td>Transitional and RTE cells</td>
<td>Resemble each other</td>
</tr>
<tr>
<td>Mucus threads</td>
<td>Hyaline casts</td>
</tr>
<tr>
<td>Bacteria</td>
<td>Amorphous urates, phosphates</td>
</tr>
<tr>
<td>Trichomonas</td>
<td>WBCs, renal tubular epithelial cells</td>
</tr>
</tbody>
</table>