The particles of the urinary sediment and their clinical meaning

Cecilia Bellincioni and Giovanni B. Fogazzi

Clinical and Research Laboratory on Urinary Sediment
U.O. di Nefrologia
Fondazione IRCCS Ca’ Granda
Ospedale Maggiore Policlinico
Milano, Italy
THE PARTICLES OF THE URINARY SEDIMENT

- Cells
- Lipids
- Casts
- Crystals
- Microorganisms
- Contaminants
## Cells

<table>
<thead>
<tr>
<th>Type</th>
<th>Subtype</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Erythrocytes</strong></td>
<td>Isomorphic, Dysmorphic</td>
</tr>
<tr>
<td><strong>2. Leukocytes</strong></td>
<td>Neutrophil, Eosinophil, Lymphocyte</td>
</tr>
<tr>
<td><strong>3. Macrophages</strong></td>
<td>Granular, Vacuolar, Homogeneous, Phagocytic</td>
</tr>
<tr>
<td><strong>1. Renal Tubular Cells</strong></td>
<td>Proximal, Distal</td>
</tr>
<tr>
<td><strong>2. Transitional Cells</strong></td>
<td>Superficial, Deep</td>
</tr>
<tr>
<td><strong>3. Squamous Cells</strong></td>
<td>Superficial, Deep</td>
</tr>
</tbody>
</table>

### FROM BLOOD

- Erythrocytes
- Leukocytes
- Macrophages

### EPITHELIAL

- Renal Tubular Cells
- Transitional Cells
- Squamous Cells
a. CELLS FROM BLOOD

1. Erithrocytes
2. Leukocytes
3. Macrophages
Erythrocytes

Appearance
- Small cells, with a diameter ranging from 4 to 10 µm
- From perfectly round cells to very modified shapes

Clinical meaning
- Bleeding from the kidney
- Bleeding from the excretory urinary tract
- Genital contamination, especially in women
Isomorphic red blood cells
Dysmorphic red blood cells
Erythrocyte morphology
(isomorphic and dysmorphic)

See presentation by Dr A. Skoberne:
“Estimating erythrocyte shape-dysmorphism”
a. CELLS FROM BLOOD

1. Erithrocytes
2. Leukocytes
3. Macrophages
Leukocytes

3 types:

1. Polymorphonuclear
2. Lymphocytes
3. Eosinophils
### 1. Polymorphonuclear

<table>
<thead>
<tr>
<th>Source</th>
<th>Any segment of the urinary tract (without forgetting genital contamination)</th>
</tr>
</thead>
</table>
| Appearance | Round granular cells  
Diameter 7.0 - 15.0 μm  
Lobulated nucleus |
| Clinical meaning | Inflammation of whatever cause including immunological disorders (eg, glomerular diseases) |
POLYMORPHONUCLEAR LEUKOCYTES
2. Lymphocytes

Stains and cythological techniques needed

Appearance
small round cell, with big round nucleus and a thin cytoplasm

Clinical meaning
- they were considered an early marker of acute cellular rejection of renal allograft.
  Today, very rarely used in clinical practice
- typical finding in chyluria
3. Eosinophils

See presentation by Dr G.B. Fogazzi: “Urinary profiles”
a. CELLS FROM BLOOD

1. Erithrocytes
2. Leukocytes
3. Macrophages
Morphological features of macrophages

- Round cells
- Variable size (20 μm to >100 μm)
- One or more nuclei
- Five morphological types:
  - Granular
  - Vacuolar
  - Phagocytic
  - With a homogeneous appearance
  - Fatty
Granular macrophage

Granular-vacuolar macrophage
Vacuolar macrophage

Homogeneous macrophage
Phagocytic macrophage
## Urinary macrophages

### Clinical meaning

<table>
<thead>
<tr>
<th>AUTHOR</th>
<th>METHOD</th>
<th>CLINICAL CONDITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITO 1992</td>
<td>Conventional microscopy with stain</td>
<td>Infection Inflammation</td>
</tr>
<tr>
<td>OTTA 2000</td>
<td>Flow cytometry</td>
<td>CD14⁺: proliferative GNs in active phase</td>
</tr>
<tr>
<td></td>
<td>Immunocytostaining</td>
<td>CD68⁺-ORO⁺: GNs associated with non selective proteinuria</td>
</tr>
<tr>
<td>MARUHASHI 2004</td>
<td>Immunofluorescence (CD68/MP-G1)</td>
<td>IgA nephropathy</td>
</tr>
<tr>
<td>KOPETSCHKE 2015</td>
<td>Flow cytometry Immunostaining</td>
<td>Active Lupus nephritis ANCA vasculitis, diabetes</td>
</tr>
</tbody>
</table>
Urinary macrophages
Clinical meaning

To date, however, macrophages seem to be just associated - but not diagnostic - particles.
Cells

**TYPE**

1. **ERYTHROCYTES**
2. **LEUKOCYTES**
3. **MACROPHAGES**

**SUBTYPE**

- Isomorphic
- Dysmorphic

1. **RENAL TUBULAR CELLS**
2. **TRANSITIONAL CELLS**
3. **SQUAMOUS CELLS**

**b. EPITHELIAL**

- a. **FROM BLOOD**
  - Neutrophil
  - Eosinophil
  - Lymphocyte
- Granular
- Vacuolar
- Homogeneous
- Phagocytic

- Proximal
- Distal
- Superficial
- Deep
b. EPITHELIAL CELLS

1. Renal tubular cells
2. Transitional cells
3. Squamous cells
Renal tubular cells

Source
Different tubular segments, more frequently from proximal tubule

Appearance
With conventional microscopy precise definition of the tubular segment of origin is difficult and can only be approximate.

- diameter 9-25 µm (mean 14 µm)
- Cells from proximal segments: round, oval, or rectangular, large central or eccentric nucleus, granular cytoplasm
- Cells from distal tubules: polygonal and smaller
- Cells from collecting ducts: columnar shape with a nucleus in basal position
Tubular fragments
Renal tubular cells

Clinical meaning

- Acute tubular necrosis
- Acute interstitial nephritis
- Glomerular diseases (especially proliferative types)
b. EPITHELIAL CELLS

1. Renal tubular cells
2. Transitional cells
3. Squamous cells
Transitional epithelial cells

Source: Uroepithelium
Superficial transitional cells

- Oval or round shape
- **Diameter** 17 to 43 μm
- Oval or round **nucleus** in central or slightly eccentric position
Deep transitional cells

- mostly ovoid or club-like shape
- longitudinal diameter 11 to 38 μm
- central or peripheral nucleus
- thin cytoplasm
Transitional epithelial cells

Clinical meaning

SUPERFICIAL CELLS
Mild uroepithelial damage (e.g., cystitis)

DEEP CELLS
Severe uroepithelial damage
### TABLE 2.3 Urinary sediment features and clinical conditions associated with the finding of $\geq 1$ deep transitional epithelial cell/high power field in authors’ experience.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age</th>
<th>Rbc</th>
<th>Wbc</th>
<th>Stc</th>
<th>Bacteria</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>71</td>
<td>+</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>Bladder carcinoma</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>65</td>
<td>+</td>
<td>+</td>
<td>--</td>
<td>--</td>
<td>Bladder carcinoma</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>57</td>
<td>+</td>
<td>+</td>
<td>--</td>
<td>+</td>
<td>Urolithiasis*</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>60</td>
<td>+</td>
<td>+</td>
<td>--</td>
<td>--</td>
<td>Urolithiasis*</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>69</td>
<td>+</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>Urolithiasis*</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>21</td>
<td>+</td>
<td>+</td>
<td>--</td>
<td>--</td>
<td>Urolithiasis*</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>63</td>
<td>+</td>
<td>--</td>
<td>+</td>
<td>+</td>
<td>Urolithiasis*</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>40</td>
<td>+</td>
<td>+</td>
<td>--</td>
<td>--</td>
<td>Hydronephrosis</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>78</td>
<td>+</td>
<td>+</td>
<td>--</td>
<td>--</td>
<td>Ureteric stenosis</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>37</td>
<td>+</td>
<td>+</td>
<td>--</td>
<td>--</td>
<td>Bladder carcinoma</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>73</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>UTI + bladder catheter (30 days)</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>51</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>--</td>
<td>Ureteric stent (60 days)**</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>45</td>
<td>+</td>
<td>+</td>
<td>--</td>
<td>--</td>
<td>Ureteric stent (68 days)**</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>40</td>
<td>+</td>
<td>--</td>
<td>+</td>
<td>--</td>
<td>Ureteric stent (30 days)**</td>
</tr>
<tr>
<td>15</td>
<td>F</td>
<td>59</td>
<td>+</td>
<td>--</td>
<td>+</td>
<td>--</td>
<td>Ureteric stent (34 days)**</td>
</tr>
<tr>
<td>16</td>
<td>F</td>
<td>31</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>Ureteric dilatation</td>
</tr>
<tr>
<td>17</td>
<td>M</td>
<td>61</td>
<td>+</td>
<td>+</td>
<td>--</td>
<td>--</td>
<td>Bladder catheter (26 days)</td>
</tr>
</tbody>
</table>

M: 10; F: 7 54.2±16.1  
16/17 (94.1%)  11/17 (64.7%)  6/17 (35.2%)  3/17 (17.60%)

RBC = Red blood cells (+ present; -- absent); WBC = white blood cells; STC = superficial transitional epithelial cells; * associated with ureteric stent; ** ureteric stent because of retroperitoneal fibrosis (patient 12) or prevention of ureteric stenosis in post kidney transplant period (patients 13-15).

From: Fogazzi GB. The Urinary Sediment an Integrated View 3rd Ed. Milano, Elsevier, 2010
b. EPITHELIAL CELLS

1. Renal tubular cells
2. Transitional cells
3. Squamous cells
Squamous cells

Source
Exfoliation of the epithelium of urethra and vagina

Appearance
The largest cells of the urine sediment, with a large cytoplasm containing few organelles

Clinical meaning
Small amounts → a normal finding
Large amounts → contamination of the urine from genital secretions
Squamous epithelial cells
FOUR TYPES OF FATTY PARTICLES

1. Free lipid droplets (isolated or in aggregates)
2. Oval fat bodies
3. Fatty casts
4. Cholesterol crystals
1. LIPID DROPLETS

Phase contrast

Polarized light
2. “OVAL FAT BODIES”

Phase contrast

Polarized light
3. FATTY CAST

Phase contrast

Polarized light
4. CHOLESTEROL CRYSTAL
Clinical meaning of fatty particles

Clinical conditions associated with fatty particles

- MARKED PROTEINURIA (glomerular diseases)
- LIPID STORAGE DISEASE (Fabry disease)
Fatty particles in Fabry disease

Phase contrast: irregular shapes, protrusions, spiral internal pattern
Polarized light: irregular or truncated Maltese crosses
Transmission electron microscopy: zebra-like and myelin-like bodies
CASTS
CASTS

**Formation** → Distal tubules and collecting ducts of the kidneys

**Matrix** → Tamm-Horsfall glycoprotein

**Different types** → Different clinical meanings
IMPORTANT TAKE HOME MESSAGE ABOUT CASTS

Since casts form

WITHIN THE KIDNEYS

whatever particle is contained

in a cast

COMES

FROM THE KIDNEYS!!!
Factors favouring cast formation

From: Fogazzi GB. The Urinary Sediment an Integrated View 3rd Ed. Milano, Elsevier, 2010
## Classification of casts

<table>
<thead>
<tr>
<th>Type</th>
<th>Subtype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyaline</td>
<td>--</td>
</tr>
<tr>
<td>Granular</td>
<td>Finely granular</td>
</tr>
<tr>
<td></td>
<td>Coarsely granular</td>
</tr>
<tr>
<td>Waxy</td>
<td>--</td>
</tr>
<tr>
<td>Cellular</td>
<td>Erythrocytic</td>
</tr>
<tr>
<td></td>
<td>Leukocytic</td>
</tr>
<tr>
<td></td>
<td>Containing renal tubular epithelial cells (epithelial casts)</td>
</tr>
<tr>
<td>Fatty</td>
<td>--</td>
</tr>
<tr>
<td>Containing crystals</td>
<td>--</td>
</tr>
<tr>
<td>Containing microorganisms</td>
<td>Bacterial</td>
</tr>
<tr>
<td></td>
<td>Candidal</td>
</tr>
<tr>
<td>Pigmented</td>
<td>Haemoglobinic</td>
</tr>
<tr>
<td></td>
<td>Myoglobinic</td>
</tr>
<tr>
<td></td>
<td>Bilirubinic</td>
</tr>
<tr>
<td>Mixed</td>
<td>Hyaline-granular</td>
</tr>
<tr>
<td></td>
<td>Granular-waxy</td>
</tr>
<tr>
<td></td>
<td>Granular-cellular</td>
</tr>
<tr>
<td></td>
<td>Granular-fatty</td>
</tr>
<tr>
<td></td>
<td>Etc.</td>
</tr>
</tbody>
</table>

From: Fogazzi GB. The Urinary Sediment an Integrated View 3rd Ed. Milano, Elsevier, 2010
Granular cast
Waxy cast
Erythrocytic cast
Leukocytic cast
Renal tubular epithelial cell cast ("epithelial cast")
Fatty cast

Phase contrast

Polarized light
Cast containing crystals
Pigmented casts

Haemoglobin cast

Myoglobin cast

Bilirubin cast
Mixed casts

Hyaline-granular

Haemoglobin-granular

Waxy-erythrocytic
Clinical meaning of the different types of casts

<table>
<thead>
<tr>
<th>Cast</th>
<th>Clinical meaning</th>
<th>Clinical conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyaline</td>
<td>Variable</td>
<td>Normal subjects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After physical exercise</td>
</tr>
<tr>
<td></td>
<td></td>
<td>During episodes of fever or dehydration</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acute congestive heart failure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>All renal diseases</td>
</tr>
<tr>
<td>Granular</td>
<td>Renal disease</td>
<td>Acute tubular necrosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glomerulonephritis</td>
</tr>
<tr>
<td>Waxy</td>
<td>Renal disease</td>
<td>Renal failure (acute or chronic)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glomerular diseases (especially amyloidosis and acute post-infectious GN)</td>
</tr>
<tr>
<td>Erythrocytic</td>
<td>Glomerular bleeding (mostly)</td>
<td>Glomerulonephritis, especially proliferative types</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acute interstitial nephritis (rare)</td>
</tr>
</tbody>
</table>
Clinical meaning of the different types of casts

<table>
<thead>
<tr>
<th>Cast</th>
<th>Clinical meaning</th>
<th>Clinical conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocytic</td>
<td>Renal inflammation</td>
<td>Pyelonephritis, Acute interstitial nephritis, Active proliferative GN</td>
</tr>
<tr>
<td>Epithelial</td>
<td>Severe tubular damage</td>
<td>Acute tubular necrosis, Acute interstitial nephritis, Glomerular disease</td>
</tr>
<tr>
<td>Fatty</td>
<td>Proteinuria</td>
<td>GN with variable proteinuria, especially in nephrotic range</td>
</tr>
<tr>
<td>Containing crystals</td>
<td>Precipitation of crystals within the tubular lumen</td>
<td>Crystalline nephropathies</td>
</tr>
</tbody>
</table>
## Clinical meaning of the different types of casts

<table>
<thead>
<tr>
<th>Cast</th>
<th>Clinical meaning</th>
<th>Clinical conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Containing microorganisms</td>
<td>Infection of the kidney</td>
<td>Acute pyelonephritis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Visceral candidiasis</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>Renal bleeding</td>
<td>Glomerulonephritis</td>
</tr>
<tr>
<td></td>
<td>Intravascular haemolysis</td>
<td>Intravascular haemolysis</td>
</tr>
<tr>
<td>Myoglobin</td>
<td>Tubular damage caused by myoglobin</td>
<td>AKI associated with rhabdomyolysis</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>Tubular damage caused by bilirubin</td>
<td>Jaundice</td>
</tr>
<tr>
<td>Mixed</td>
<td>Variable according to the components they contain</td>
<td>Variable according to the components they contain</td>
</tr>
</tbody>
</table>
CRYSTALS
OUR CLASSIFICATION OF CRYSTALS

a. "COMMON" CRYSTALS

b. PATHOLOGICAL CRYSTALS

c. OTHER (RARE) CRYSTALS

d. CRYSTALS DUE TO DRUGS
HOW TO IDENTIFY CRYSTALS

The knowledge of the following **THREE** features is mandatory:

1) The commonest appearances of each type of crystal
2) The birefringence features
3) The urinary pH
### a. Main Types of “Common” Crystals and Their Prevalence in a Two-Year Period in Our Unit

<table>
<thead>
<tr>
<th>Crystal</th>
<th>Number</th>
<th>pH Range</th>
<th>pH &lt;5.8 (%)</th>
<th>pH &gt;7.0 (%)</th>
<th>Polar %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca-oxalate dihydrate</td>
<td>67</td>
<td>&lt;5.4-6.7</td>
<td>82</td>
<td>__</td>
<td>25</td>
</tr>
<tr>
<td>Uric acid</td>
<td>36</td>
<td>&lt;5.4-5.6</td>
<td>100</td>
<td>__</td>
<td>100</td>
</tr>
<tr>
<td>Amorphous phosphates</td>
<td>27</td>
<td>6.2-&gt;7.0</td>
<td>__</td>
<td>78</td>
<td>__</td>
</tr>
<tr>
<td>Triple phosphate</td>
<td>25</td>
<td>6.2-&gt;7.0</td>
<td>__</td>
<td>73</td>
<td>100</td>
</tr>
<tr>
<td>Ca-oxalate monohydrate</td>
<td>18</td>
<td>&lt;5.4-6.4</td>
<td>89</td>
<td>__</td>
<td>100</td>
</tr>
<tr>
<td>Amorphous urates</td>
<td>7</td>
<td>&lt;5.4-5.8</td>
<td>100</td>
<td>__</td>
<td>100</td>
</tr>
<tr>
<td>Ca-phosphate plates</td>
<td>3</td>
<td>6.7-&gt;7.0</td>
<td>__</td>
<td>67</td>
<td>__</td>
</tr>
<tr>
<td>Ca-phosphate crystals</td>
<td>2</td>
<td>&gt;7.0</td>
<td>__</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>
URIC ACID (U-pH < 5.8)

Phase contrast

Polarized light
AMORPHOUS URATES (U-pH <5.8)
AMORPHOUS PHOSPHATES (U-pH 6.2-7.0)

By phase contrast, amorphous urates and phosphates are identical (A), however the former polarize light (B) while phosphates do not.
MONOHYDRATED CALCIUM OXALATE

U-pH 5.4 - 6.7

BIHYDRATED CALCIUM OXALATE
CALCIUM PHOSPHATE (U-pH 6.7-7.0)
TRIPLE PHOSPHATE (pH 6.2 - 7.0)

Phase contrast

Polarized light
CLINICAL IMPORTANCE OF “COMMON” CRYSTALS (I)

• In most instances, UA, Ca-Ox, and Ca-P crystals are due to a transient supersaturation of the urine caused by foods, dehydration, or changes of urine pH and/or temperature upon standing.

• However, especially when they are persistent, large and in aggregates they may be associated with metabolic disorders such as hyper-calciuria, -oxaluria, or -uricosuria.

• Triple phosphate crystals are associated with UTI caused by urea-splitting bacteria (e.g., Ureaplasma or Corynebacterium urealyticum).
Acute kidney injury associated with crystalluria:

- Acute urate nephropathy (uric acid)
- Ethylene glycol poisoning (calcium oxalate)
Massive uric acid crystalluria in a patient with AKI and acute leukemia
Massive oxalic crystalluria after ethylene glycol ingestion
b. Pathological crystals

- CHOLESTEROL
- CYSTINE
- 2,8-DI-HYDROXYADENINE
- LEUCINE
- TYROSINE

Very rare (liver disease and inherited disorders)
Cholesterol
Cystine crystals

CYSTINURIA

- Autosomic recessive disease
- Clinical phenotype: Renal stone disease with possible CKD
- CYSTINE CRYSTALS:
  - pathognomonic of the disease
  - found in acidic urine and are insoluble up to a pH of 7.4
Occasionally, uric acid and cystine crystals are identical, both coming as hexagons. Polarized light enables differentiation.
2,8-DIHYDROXYADENINE (2,8-DHA)
ADENIN PHOSPHORIBOSYLTANSFERASE (APRT) DEFICIENCY

• Autosomal recessive disease
• 2,8-DHA → highly insoluble at any pH
• Clinical manifestations (Edvarsson V, Am J Kidney Dis 2001):
  • Recurrent radiolucent stone disease (65%)
  • AKI due to intratubular 2,8-DHA precipitation (26%)
  • CKD probably due to chronic interstitial nephritis (17%)
  • 2,8-DHA crystalluria (96%)
Role of urinary sediment examination

“Skilful urine microscopy is the single most important diagnostic procedure because urinary 2,8-DHA crystals are usually abundant in untreated patients”

c. OTHER (RARE) CRYSTALS

- IPPURIC ACID
- CALCIUM CARBONATE
- AMMONIUM BIURATE

MOST PROBABLY WITHOUT CLINICAL RELEVANCE
OTHER CRYSTALS: Hippuric acid
OTHER CRYSTALS: Calcium carbonate

Phase contrast

Polarized light
OTHER CRYSTALS: Ammonium biurate

Phase contrast

Polarized light
d. CRYSTALS DUE TO DRUGS

Two main categories:

1. Drugs which cause atypical crystals which are made up of the drugs themselves

2. Drugs which cause calcium oxalate crystals
## Drugs Causing Atypical Crystalluria (1)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Type of Crystals</th>
<th>Clinical Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfadiazine</td>
<td>Birefringent shocks of wheat or shells with striations</td>
<td>Isolated crystalluria, hematuria, AKI, stones</td>
</tr>
<tr>
<td>Amoxycillin</td>
<td>Birefringent needles, shocks of wheat</td>
<td>Isolated crystalluria, hematuria, AKI</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Birefringent needles, sheaves, stars, fans, butterflies, etc</td>
<td>Isolated crystalluria, AKI</td>
</tr>
<tr>
<td>Acyclovir</td>
<td>Birefringent thin needles</td>
<td>? Isolated crystalluria, AKI</td>
</tr>
</tbody>
</table>
## Drugs Causing Atypical Crystalluria (2)

<table>
<thead>
<tr>
<th>DRUG</th>
<th>Type of Crystals</th>
<th>Clinical Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indinavir</td>
<td>Strongly birefringent plate-like rectangles, star-like structures, irregular plates</td>
<td>Isolated crystalluria, stones, AKI</td>
</tr>
<tr>
<td>Felbamate</td>
<td>Thin needles</td>
<td>AKI</td>
</tr>
<tr>
<td>Primidone</td>
<td>Birefringent hexagons</td>
<td>Isolated crystalluria, transient proteinuria and hematuria</td>
</tr>
<tr>
<td>Piridoxylate</td>
<td>Asymmetrical hexagons or rectangles with rounded extremities</td>
<td>Stones</td>
</tr>
<tr>
<td>Sulfamethoxazole</td>
<td>Birefringent “coffin lid, notched edges suggestive of UA crystals, rosettes”</td>
<td>AKI</td>
</tr>
</tbody>
</table>
# Drugs Which Cause CA-OX Crystaluria

<table>
<thead>
<tr>
<th>Drug</th>
<th>Crystal</th>
<th>Clinical Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naftidrofuryl oxalate</td>
<td>Birefringent monohydrate calcium oxalate</td>
<td>AKI</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Birefringent monohydrate calcium oxalate</td>
<td>AKI</td>
</tr>
<tr>
<td>Orlistat</td>
<td>(? Mono- ?Bi- hydrate) calcium oxalate</td>
<td>AKI</td>
</tr>
</tbody>
</table>
Sulfadiazine

Phase contrast

Polarized light
Acyclovir

Phase contrast  Polarized light

(From: Mason WJ & Nickols HH. NEJM 2008: 358: e14)
Indinavir

Phase contrast

Polarized light
Ciprofloxacin
FACTORS FAVOURING DRUG CRYSTALLURIA

- Drug overdose
- Dehydration
- Hypoalbuminaemia
- Urine pH
FORMATION OF CRYSTALS DUE TO DRUGS ACCORDING TO U-pH

- **Sulfadiazine**: pH ≤ 5.5
- **Amoxycillin**: U-shaped (peaks at pH ~ 4.0 and > 7.0)
- **Ciprofloxacin**: pH > 7.3
- **Indinavir**: pH > 6.0
CLINICAL MANIFESTATIONS OF DRUG CRYSTALLURIA

- Isolated and asymptomatic crystalluria
- Haematuria (micro or gross) ± leukocyturia
- Obstructive uropathy due to drug stones
- AKI due to intratubular precipitation of crystals
GENERAL RULES TO REMEMBER ABOUT CRYSTALLURIA DUE TO DRUGS

1) Think of a drug whenever you come across crystals with unusual and pleomorphic appearance (*)

2) Ask the patient *if and which* drug(s) she/he is taking

3) Check the renal function

4) Hydrate the patient and reduce or discontinue the drug to prevent AKI

(*) Naftidrofyl oxalate, Vitamin C and orlistat → calcium oxalate crystals
MICROORGANISMS

Bacteria: Rods, Cocci

Yeast: Candida

Protozoa: Trichomonas vaginalis, Balantidium coli

Parasites: Schistosoma haematobium
Bacteria

Rods

Cocci
Yeasts: Candida
Trichomonas vaginalis
Balantidium coli
Schistosoma haematobium

See presentation by Dr. G.B. Fogazzi: “Urinary profiles”
## Principal sources of contamination of the urine

<table>
<thead>
<tr>
<th>Patient</th>
<th>Laboratory</th>
<th>Enviroment</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC/WBC*</td>
<td>Starch</td>
<td>Pollen granules</td>
</tr>
<tr>
<td>Squamous cells</td>
<td>Glass fragments</td>
<td>Plant cells</td>
</tr>
<tr>
<td>Bacteria*</td>
<td>Air bubbles</td>
<td>Fungal spores</td>
</tr>
<tr>
<td>Spermatozoa</td>
<td></td>
<td>Alternaria</td>
</tr>
<tr>
<td><em>Trichomonas V.</em></td>
<td></td>
<td>Helminthosporium</td>
</tr>
<tr>
<td>Public hair</td>
<td></td>
<td>Epicoccum</td>
</tr>
<tr>
<td>Pediculosis pubis</td>
<td></td>
<td>Cladosporium</td>
</tr>
<tr>
<td>Faeces</td>
<td></td>
<td>Fibres</td>
</tr>
<tr>
<td>Intestinal cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Enterobius vermicularis</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cloth fibres/Talcum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oil /Creams</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Contaminants when deriving from urethra or genital secretions*
Spermatozoa
Talcum powder

Phase contrast

Polarized light
Cloth fibre
Synthetic fibre

Phase contrast

Polarized light
Starch

Phase contrast

Polarized light
Alternaria
Thank you for your kind attention