Urinalysis (Clinical Urine Tests) — Components and Results

See online here

Urinalysis is the test performed to analyze the physical, chemical and microscopic characteristics of urine. The information from this test might be used to diagnose or rule out diseases based on the findings. Urinalysis is most commonly used in identifying diseases of the urinary tract and diabetes. It includes macroscopic, microscopic/cytological and chemical analysis of the individual elements in urine.

Gold Standard test in the initial workup of renal disease:

- Urinalysis
- General Examination
Sample Collection

Mid-Stream Clean Catch

The ideal sample for urinalysis is the ‘mid-stream clean catch’ sample obtained from the patient. The sample of urine should be approximately 30–60 ml.

Procedure

Men: Discard the initial 200 ml of urine and obtain the midstream sample.

Women: It is advised to clean the external genitalia before urinating with disinfecting wipes to avoid contamination of the sample. Obtain the mid-stream sample after discarding the initial 200 ml. Alternatively, in some patients, the sample can be obtained by inserting a Foley’s catheter or even inserting a needle in the suprapubic area to obtain sterile samples. In case of a urinary tract infection, collect the sample before starting the patient on empiric antibiotics. Ideally, the sample should be tested about 30–60 minutes after collecting the sample. If a delay is expected, it is best to keep the sample refrigerated.

24-hour Sample Collection

The other kind of sample collection is the 24-hour sample collection, used to measure certain parameters like creatinine, protein, sodium, potassium, nitrogen, calcium, oxalate, urate and the total volume.

Procedure

On day 1, void urine normally in the toilet. Start collecting the urine voided after that in a
container provided. Continue collecting the sample throughout the 24-hour period, including the next day’s early morning sample. Store the sample in a refrigerator or a cool place during the period of collection.

Components of the Analysis of Urine

Analysis of urine includes:

- Macroscopic examination
- Chemical analysis
- Sulfosalicylic acid test
- Microscopic examination

Macroscopic Examination

Macroscopic examination involves observing the characteristics of the urine sample that can be observed by the naked eye. The macroscopic examination includes color and turbidity.

![Image](green Urine.png)

Image: “Green Urine” by openi.
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Color

The normal color of urine is said to be straw yellow in color (spectrum is light/pale to dark/deep amber). Variations in color can be observed with various conditions and medications.

<table>
<thead>
<tr>
<th>Physiological conditions</th>
<th>Urine Color</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food dyes (anthocyanins), beets, blackberries, rhubarb</td>
<td>Red</td>
</tr>
<tr>
<td>Carrot, vitamin C</td>
<td>Orange</td>
</tr>
<tr>
<td>Asparagus</td>
<td>Green</td>
</tr>
<tr>
<td>Fava beans</td>
<td>Brown</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Urine Color</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenolphthalein</td>
<td>Pink</td>
</tr>
<tr>
<td>Rifampicin, phenazopyridine, senna</td>
<td>Orange</td>
</tr>
<tr>
<td>Chlorpromazine, thioridazine, Ex-lax</td>
<td>Red</td>
</tr>
<tr>
<td>Propofol</td>
<td>Green</td>
</tr>
<tr>
<td>Methylene blue, Amitriptyline</td>
<td>Blue</td>
</tr>
<tr>
<td>Levodopa, Metronidazole, Nitrofurantoin, Primaquine, Chloroquine, Methocarbamol</td>
<td>Brown</td>
</tr>
</tbody>
</table>

Pathological Conditions | Urine Color
---|---
### Chemical Analysis (Dipstick test)

The dipstick is dipped into the urine sample and then let to settle after taking it out. The readings are noted after 2–5 minutes. The chemical agents on the strips change color based on the amount of the parameter in the urine. This includes:

- **pH**
- **Specific gravity**
- **Glucose**
- **Ketones**
- **Nitrites**
- **Leukocyte esterase**
- **Bilirubin**
- **Blood**
- **Protein**

#### pH

Normal urine is mildly acidic (normal range: 4.6–8). pH can be altered by normal compensatory physiological mechanisms of the body, or by disease. Urinary pH can be used to distinguish between the different types of RTA, in assessing the response to treatment of certain medication overdoses or assessing the treatment of rhabdomyolysis.

<table>
<thead>
<tr>
<th>Parameter (Physiological)</th>
<th>Change in pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cranberry, protein-rich food</td>
<td>Acidic</td>
</tr>
<tr>
<td>Citrus fruits, low carbohydrate diet</td>
<td>Alkaline</td>
</tr>
<tr>
<td>Respiratory alkalosis</td>
<td>Acidic</td>
</tr>
<tr>
<td>Respiratory acidosis</td>
<td>Alkaline</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter (Pathological)</th>
<th>Change in pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>RTA (renal tubular acidosis)</td>
<td>Acidic</td>
</tr>
<tr>
<td>Uric acid calculi, cystine calculi</td>
<td>Acidic</td>
</tr>
<tr>
<td>Calcium oxalate, calcium phosphate, struvite stones</td>
<td>Alkaline</td>
</tr>
<tr>
<td>UTI d/t urease splitting organisms</td>
<td>Alkaline</td>
</tr>
</tbody>
</table>

#### Specific Gravity

The normal specific gravity of urine is 1.005–1.025. It is a measure of the kidney’s concentrating ability. It can also give us an idea about the hydration status and the osmolality. For each rise in the specific gravity by 0.001 above 1, the urine osmolality
increases by about 30–35 mosmol/kg.

<table>
<thead>
<tr>
<th>Low Specific Gravity</th>
<th>High Specific Gravity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes insipidus</td>
<td>Dehydration</td>
</tr>
<tr>
<td>ATN</td>
<td>Heart failure</td>
</tr>
<tr>
<td>Sickle cell nephropathy</td>
<td>Excess Sugar or Protein in urine</td>
</tr>
<tr>
<td>Drinking too much fluid</td>
<td>SIADH</td>
</tr>
</tbody>
</table>

Glucose

The normal amount of glucose in urine should be $\leq 130 \text{ mg/dl}$. When blood glucose levels exceed 180 mg/dl, the proximal tubules lose their ability to absorb any more glucose. The excess glucose in the urine is called glucosuria and is detected in the dipstick test.

The most common conditions causing glucosuria are diabetes and pregnancy. The other conditions causing glucosuria are: SGLT-1 gene mutations, tubular dysfunction (Fanconi syndrome), Lowe’s syndrome (oculocerebrorenal dystrophy), tyrosinemia and Wilson’s disease.

A condition called benign glucosuria is generally discovered on routine urinalysis. It is of three types:

- **Type A**: Classic glucosuria, has decreased renal glucose threshold & maximal glucose reabsorption rate
- **Type B**: Has decreased glucose threshold and a normal reabsorptive rate
- **Type O**: Lack of glucose reabsorption

Ketones

Normal urine does not contain ketones at all. The presence of even a small amount of ketones in urine is abnormal. The most common ketones found in urine are acetone, acetoacetic acid and beta hydroxybutyrate. Ketones are seen in:

- Diabetic ketoacidosis
- Uncontrolled diabetes
- Severe vomiting and starvation
- Severe exercise and dehydration
- Pregnancy

Nitrites

They are not normally seen in urine. Presence of nitrates mostly occurs in the presence of bacteria with the inherent capability to convert urinary nitrates into nitrites such as *E. coli*, Klebsiella, Proteus, Pseudomonas, Enterobacter and Citrobacter; hence, the presence of nitrates in urine is highly suggestive of UTI.

However, it does not rule out a urine infection if nitrites are negative because the infection can also be caused by organisms that do not possess the ability to convert urine nitrates; hence, it is a test with high specificity but has low sensitivity.

Leukocyte Esterase
It is normally absent in urine. Leukocyte esterase is an enzyme produced by the lysis of WBCs. In normal sterile urine, the WBCs are very low in number to potentially produce a positive leucocyte esterase test. It is positive only with pyuria (increased number of WBCs). Pyuria is caused by infection and analgesic nephropathy (sterile pyuria).

**Bilirubin**

Bilirubin is normally absent in urine. Bilirubin gets converted into urobilinogen in the intestine. Urobilinogen enters the portal circulation again and then is excreted in very small amounts (0.5-1 mg/dL) in the urine. Decreased bilirubin is seen in obstructive biliary disease and severe cholestasis. Excess bilirubin in urine is observed in the following conditions:
### Jaundice

**Physiological**
- Newborn jaundice

**Pathological**
- Biliary tract disease
- Hepatitis
- Cirrhosis
- Gallstones
- Tumors of liver or GB
- Excessive hemolysis
- Intestinal bacterial overgrowth

### Blood

The test checks for the peroxidase activity of RBCs. Normal amount of RBCs in urine is ≤ 3 RBCs. If the number of RBCs is > 3, blood is detected in the test. This test is qualitative in nature and does not give any information about the origin of the blood detected.

After centrifugation, if the sediment contains the blood (RBCs), it is indicative of hematuria. If the supernatant fluid contains blood, it is due to food dyes, porphyria, hydroxocobalamin and phenazopyridine. Myoglobinuria caused by rhabdomyolysis and hemoglobinuria caused by transfusion-related reactions.

Clostridium and Plasmodium infections do not contain RBCs on microscopic examination, which helps in differentiating them from hematuria, which shows RBC sediments on microscopic examination.

### Protein

The normal amount of protein in urine is ≤ 150 mg/dl. The Dipstick test measures only albumin and not the other proteins; hence, it is a highly specific test, but with low
sensitivity. The Dipstick test becomes positive with levels > 300 mg/ dl; therefore it cannot be used to detect microalbuminuria in diabetic patients.

It could give false positive results when tested immediately after giving contrast for testing and also with concentrated urine; hence, caution should be used to prevent such false positives. Approximate inference of dipstick values:

<table>
<thead>
<tr>
<th>Trace +</th>
<th>10-30 mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>1+</td>
<td>&gt; 30 mg/dl</td>
</tr>
<tr>
<td>2+</td>
<td>&gt; 100 mg/dl</td>
</tr>
<tr>
<td>3+</td>
<td>&gt; 300 mg/dl</td>
</tr>
<tr>
<td>4+</td>
<td>&gt; 1000 mg/dl</td>
</tr>
</tbody>
</table>

1+ to 2+ ⇒ equivalent to 24 hr excretion of < 0.5mg
2+ to 3+ ⇒ Glomerular disease more likely
3+ to 4+ ⇒ Nephrotic range, equivalent to 24 hr excretion of > 3g

<table>
<thead>
<tr>
<th>Types</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transient proteinuria</td>
<td>Vigorous exercise, fever, heart failure, UTIs</td>
</tr>
<tr>
<td>Orthostatic proteinuria</td>
<td>Upright posture (occurs only during the day)</td>
</tr>
<tr>
<td>Gross proteinuria</td>
<td>Nephrotic syndrome, nephritic syndrome</td>
</tr>
<tr>
<td>Microalbuminuria (not in urinalysis)</td>
<td>Diabetic nephropathy</td>
</tr>
<tr>
<td>Bence Jones proteinuria (not in urinalysis)</td>
<td>AL amyloidosis, B cell disorders, Multiple myeloma</td>
</tr>
<tr>
<td>Tubular proteinuria</td>
<td>Tubulointerstitial diseases (ATN, Fanconi syndrome, acute interstitial disease)</td>
</tr>
</tbody>
</table>
SSA- Sulfosalicylic Acid Test

This test detects all proteins like albumin, globulin and Bence Jones proteins in the urine at any amounts.

**Method**

Check turbidity of the solution made by 3 parts of 3% sulfosalicylic acid mixed with one part of urine supernatant.

**Interpretation**

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
<th>Proteinuria (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No turbidity</td>
<td>0</td>
</tr>
<tr>
<td>Trace</td>
<td>Slight turbidity</td>
<td>20</td>
</tr>
<tr>
<td>1+</td>
<td>Print visible through specimen</td>
<td>50</td>
</tr>
<tr>
<td>2+</td>
<td>Print invisible</td>
<td>200</td>
</tr>
<tr>
<td>3+</td>
<td>Flocculation</td>
<td>500</td>
</tr>
<tr>
<td>4+</td>
<td>Dense precipitate</td>
<td>≥1000</td>
</tr>
</tbody>
</table>

**Microscopic Examination**

Microscopic examination is done after **centrifuging the urine sample for about 3-5 minutes**. The supernatant fluid is discarded and the underlying sediment is observed under microscope. It is checked for parameters like cells, casts, crystals and living organisms.

**Normal/Few Hyaline Casts**

The presence of up to **0-5 hyaline casts/hpf** (“casts per high power field”) is considered to be normal. Hyaline casts can be seen in normal healthy people. It is composed mostly of **Tamm Horsfall protein**. They are formed only in the **distal convoluted tubule**, or the collecting duct. Low urine pH and high urinary salt concentration promote hyaline cast formation.

**RBCs/RBC Casts**

The normal amount of urine contains ≤ 2 RBCs/hpf. The presence of 3 or more RBCs/hpf in 2-3 samples is called hematuria. Red cell casts are diagnostic of glomerulonephritis or
vasculitis. Dysmorphic erythrocytes suggest the presence of nephritis.

Transient hematuria is seen in young patients and is considered benign. However, in the elderly, even if hematuria is transient, it needs to be worked up fully to exclude the possibility of cancer.

**WBCs/WBC Casts**

The normal amount of WBCs seen in urine is ≤ 2-5 WBCs/hpf. The presence of
leucocytes and bacteria in urine is indicative of a renal tract infection. White cell casts are strongly suggestive of pyelonephritis. WBCs and WBC casts are seen in:

- Interstitial nephritis
- Glomerulonephritis
- Pyelonephritis
- Allograft rejection
- Malignant infiltration of the kidney

**Renal Tubular Epithelial Cells/RTE Casts/Pigmented Casts**

The normal amount of squamous epithelial cells in urine is \( \leq 15-20 \) squamous epithelial cells/hpf. If it is > 15–20, it is considered to be an infection. Some of the conditions showing an increased count of cells are:

- Acute tubular necrosis
- Tubulointerstitial nephritis
- Acute cellular allograft rejection
- Myoglobinuria
- Hemoglobinuria

**Granular Casts**

They are seen in:

- Acute tubular necrosis
- Glomerulonephritis
- Vasculitis
- Tubulointerstitial nephritis

**Eosinophiluria**

They are observed in the following conditions:

- Allergic interstitial nephritis
- Atheroembolic disease
- Pyelonephritis
- Cystitis
- Glomerulonephritis

Crystalluria

Crystals are seen occasionally in normal urine. It should be noted that calcium oxalate and urate crystals can be found in normal urine that has been left to stand for some time.

Acute Uric Acid Nephropathy

[Image: “Uric acid crystals in a human urine sample with a pH of 5, as detected by an automated urinalysis system.” by Doruk Salanci. License: CC BY-SA 3.0]

Seen in tumor lysis syndrome, hyperuricosuria and gout

- Radiolucent
- Rhomboid or rosette shaped crystals

Calcium Oxalate Crystals

- Envelope or dumbbell-shaped crystals
- Seen in ethylene glycol intoxication
- Radio-opaque
- Conditions causing hypercalciuria

Cystine Crystals

- Hexagonal crystals
- Seen in cystinuria
- Radiopaque
- Nitroprusside test positive

Struvite Stones
Composed of magnesium ammonium phosphate, also called triple phosphate

- Shaped like a staghorn and radio-opaque
- Caused by urease positive organisms
- Coffin lid shaped crystals

**Bacteria**

**Normal urine is sterile and does not contain bacteria.** The presence of bacteria indicates an infection or contamination. The bacteria can be cultured in an appropriate medium to find out the exact species. Empiric antibiotics should be started while waiting for culture results.

**Overview**

<table>
<thead>
<tr>
<th>General Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Color</strong></td>
</tr>
<tr>
<td>Dark yellow: Concentrated urine, bilirubinuria, ↑ UBG, vitamins</td>
</tr>
<tr>
<td>Red or pink: Hematuria, hemoglobinuria, myoglobinuria, drugs (e.g., phenazopyridine, a urinary aesthetic), porphyria</td>
</tr>
<tr>
<td>Smoky-colored urine: Acid pH urine converts Hb to hematin; common finding in the nephritic type of glomerulonephritis</td>
</tr>
<tr>
<td>Black urine after exposure to light: Alkaptonuria (AR disease with deficiency of homogentisate oxidase) with an increase in homogentisic acid in the urine; turns black when exposed to light</td>
</tr>
<tr>
<td><strong>Clarity</strong></td>
</tr>
<tr>
<td>Cloudy urine with alkaline pH: Normal finding most often due to phosphates</td>
</tr>
<tr>
<td>Cloudy urine with acid pH: Normal finding most often due to uric acid</td>
</tr>
<tr>
<td>Other: Bacteria, WBCs, Hb, myoglobin also decrease clarity</td>
</tr>
<tr>
<td><strong>Specific gravity</strong></td>
</tr>
<tr>
<td>Evaluates urine concentration and dilution</td>
</tr>
<tr>
<td>Specific gravity &gt; 1.023 (UOsm 900 mOsm/kg) indicates urine concentration and excludes intrinsic renal disease</td>
</tr>
<tr>
<td>Hypotonic urine has a specific gravity &lt; 1.015 (~ UOsm 220 mOsm/kg)</td>
</tr>
<tr>
<td>UOsm is the best indicator of urine concentration/dilution</td>
</tr>
<tr>
<td>Fixed specific gravity (1.008—1.010): correlates with UOsm; lack of concentration and dilution (e.g., chronic renal failure)</td>
</tr>
<tr>
<td><strong>Chemical Dipstick</strong></td>
</tr>
<tr>
<td><strong>pH</strong></td>
</tr>
<tr>
<td>Determined by diet and acid-base status of the patient; pure vegan usually has alkaline pH (citrate converted into bicarbonate); meat eater usually has acid pH (organic acids in meat)</td>
</tr>
<tr>
<td>Alkaline pH + smell of ammonia: Urease-producing pathogen (e.g., Proteus)</td>
</tr>
</tbody>
</table>
| Protein | Detects albumin (not globulins)  
SSA: Detects albumin and globulins (e.g. BJ protein)  
Albuminuria: Reagent strip and SSA have the same results  
BJ protein: SSA greater than reagent strip result; always confirm BJ protein with urine immunoelectrophoresis |
|---|---|
| Glucose | Specific for glucose; will not detect fructose or other sugars  
Detect glucose in urine as los as 30 mg/dL  
↑ Serum glucose + glucosuria: Diabetes mellitus  
Normal serum glucose + glucosuria: Normal pregnancy (normally have a low renal threshold for glucose), benign glucosaria (low renal threshold for glucose)  
Microalbuminuria dipsticks: More sensitive than standard dipstick; sensitive to 1.5—8 mg/dL; microalbuminuria is the first sign of diabetic nephropathy |
| Ketones | Detects acetone, acetoacetic acid (not β-OHB); nitroprusside in the test system only reacts with AcAc and acetone, not β-OHB |
| Bilirubin | Detects conjugated (water-soluble) bilirubin  
Bilirubinuria: Viral hepatitis, obstructive jaundice |
| Urobilinogen | Normal to have trace amounts (normal urine color is due to urobilin)  
Absent urine UBG, ↑ urine bilirubin: Obstructive jaundice  
↑ Urine UBG, absent urine bilirubin: Extravascular hemolytic anemia (e.g., hereditary spherocytosis)  
↑ Urine UBG, ↑ urine bilirubin: Hepatitis |

**Review Questions**

The solutions are located below the sources.

1. **Prolonged treatment with propofol can produce which of the following color in urine?**
   - A. Green
   - B. Brown
   - C. Pink
   - D. Black
   - E. Orange

2. **The normal amount of glucose in the urine is...**
   - A. ...less than or equal to 140 mg/dl.
   - B. ...less than or equal to 30 mg/dl.
   - C. ...less than or equal to 1.30 mg/dl.
   - D. ...less than or equal to 13 mg/dl.
   - E. ...less than or equal to 130 mg/dl.

3. **Coffin lid shaped crystals are a characteristic feature of...**
   - A. ...calcium oxalate stones.
   - B. ...uric acid stones.
   - C. ...cystine stones.
   - D. ...struvite stones.
   - E. ...calcium phosphate.
References


Urinalysis via emedicine.medscape.com
Urinalysis via nlm.nih.gov
Urinalysis via mayoclinic.org

Correct answers: 1A, 2E, 3D

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Notes