Urine Dipstick Analysis

Instructions

- All samples should be midstream and collected in a clean sterile container.
- Suprapubic aspiration or fresh catheter samples are ideal, but not always practical.
- The gold standard method of testing is to remove a small volume of urine from the sterile container with a fresh sterile syringe, and then apply the removed urine to the dipstick. In this way, the remainder of the collected sample contents remains untouched by a potentially unsterile dipstick and so can be sent for laboratory analysis if required.
- Hold the dipstick horizontally before reading.

Available tests include the likes of Multistix® (suitable for screening for glycosuria only), Micral-Test II® or Microalbumin® (detect microalbuminuria) and the more commonly used multiple combination strips - eg, five tests on each strip (detects blood, ketones, glucose, pH and protein), or seven tests on each strip (tests for blood, ketones, glucose, pH, bilirubin, urobilinogen and protein).

Costs vary depending on how many substances can be detected and on the supplier.

Physical examination

Colour

The colour of the urine can vary greatly. Normal urine varies from colourless to dark yellow. Various factors can affect urine colour.[1]

<table>
<thead>
<tr>
<th>Colour</th>
<th>Pathological causes</th>
<th>Food and drug causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown</td>
<td>Bile pigments, myoglobin</td>
<td>Levodopa, metronidazole, nitrofurantoin, some antimalarial agents, fava beans</td>
</tr>
<tr>
<td>Brownish-black</td>
<td>Bile pigments, melanin, methaemoglobin</td>
<td>Cascara, levodopa, methylclopa, senna</td>
</tr>
<tr>
<td>Green or Blue</td>
<td>Pseudomonal urinary tract infection (UTI), biliverdin</td>
<td>Amitriptyline, indigo carmine, IV cimetidine, IV promethazine, methylthioninium chloride, triamterene</td>
</tr>
<tr>
<td>Orange</td>
<td>Bile pigments</td>
<td>Phenothiazenes, phenazopyridine, rifampicin, hydroxocobalamin</td>
</tr>
<tr>
<td>Red</td>
<td>Haematuria, haemoglobinuria, myoglobinuria, porphyria</td>
<td>Beets, blackberries, rhubarb, phenolphthalein, rifampicin</td>
</tr>
<tr>
<td>Yellow</td>
<td>Concentrated urine (orange to gold in dehydration)</td>
<td>Carrots, cascara</td>
</tr>
</tbody>
</table>

Turbidity

Cloudy urine may be due to:

- Contamination with vaginal mucus or epithelial cells.
- Excess phosphate crystals precipitating in alkaline urine (no clinical significance).
- Pyuria secondary to infection.[2]
- Chyluria (presence of chyle/lymph in the urine - usually secondary to filariasis).[3]
- Hyperuricosuria secondary to a diet high in purine-rich foods.[4]
Odour\textsuperscript{[1]}

The normal odour is described as urinoid. In concentrated specimens this can be strong but does not imply infection, which has a more pungent smell. Alkaline fermentation causes an ammoniacal smell, and patients with diabetic ketoacidosis produce a urine that may have a sweet or fruity odour. Other causes of abnormal odours are cystine decomposition (a sulphuric smell), gastrointestinal-bladder fistulae (a faecal smell), medications (eg, vitamin B6), and diet (eg, asparagus).

Specific gravity

- Specific gravity (SG) <1.008 is dilute and >1.020 is concentrated.
- Increased SG is seen in conditions causing dehydration, glycosuria, renal artery stenosis, heart failure (secondary to decreased blood flow to the kidneys), inappropriate antidiuretic hormone secretion and proteinuria.\textsuperscript{[7, 8]}
- Some dipsticks give falsely high readings in the presence of dextran solutions and IV radiopaque dyes, but this varies, so check the manufacturer’s leaflet.\textsuperscript{[1]}
- The usefulness of SG in identifying dehydration in infants has been brought into question.\textsuperscript{[9]}
- Decreased SG is seen in excessive fluid intake, renal failure, pyelonephritis, and central and nephrogenic diabetes insipidus.\textsuperscript{[10]}
- False low readings are associated with alkaline urine (eg, a high-citrate diet).\textsuperscript{[1]}

pH

- The range is 4.5 to 8, but urine is commonly acidic (ie 5.5-6.5) due to metabolic activity.
- Acidic urine (low pH) may be caused by diet (eg, acidic fruits such as cranberries)\textsuperscript{[10]} and uric acid calculi.\textsuperscript{[11]}
- Urine pH generally reflects the blood pH but in renal tubular acidosis (RTA) this is not the case. In type 1 RTA (distal) the urine is acidic but the blood alkaline. In type 2 (proximal) the urine is initially alkaline but becomes more acidic as the disease progresses. Alkaline urine (high pH) is seen in the initial stages of type 2 RTA and also with infection with urease-splitting organisms, and may be associated with the formation of stag-horn calculi.\textsuperscript{[12]}

Haematuria

See also the separate article Haematuria.

- A positive test indicates either haematuria, haemoglobinuria or myoglobinuria.
- Dipstick tests for the presence of haemoglobin with the degree of colour change directly related to amount present.
- Free haemoglobin or myoglobin causes field change, whereas intact red blood cells (RBCs) are broken down on contact with the reagent pad and release local haemoglobin, producing a dot. These coalesce when >250 RBCs/ml.
- False positive readings are most often due to contamination with menstrual blood; they are also seen with dehydration which concentrates the number of RBCs produced, and exercise.
- False negative readings: captopril, vitamin C, proteinuria, elevated SG, pH less than 5.1 and bacteriuria.\textsuperscript{[1, 13]}
- Dipstick testing for haematuria is at best a screening tool which needs the support of microscopy to make a definitive diagnosis.\textsuperscript{[14]} Haematuria is defined as >3 RBC/high power field (hpf) of centrifuged sediment under the microscope.
- Prognostic significance of a positive test is very controversial - rates ranging from 0.5-6% of patients with a positive test have been found to have underlying significant pathology.

Proteinuria

See also the separate article Proteinuria.
Healthy adults normally excrete 80-150 mg protein in urine daily. Normal urinary proteins include serum globulins, albumin, and proteins secreted by the nephron.

Proteinuria is defined as albumin:creatinine ratio >30 mg/mmol or albumin concentration >200 mg/L. Clinical proteinuria is indicated at greater than 0.5 g of protein per day (greater or equal to 250 mg/L on a test strip).

Detectable proteinuria may be the first sign of renovascular, glomerular or tubulo-interstitial renal disease. Alternatively, it may be caused by overflow of abnormal proteins in diseases such as multiple myeloma.

Most dipstick tests will pick up albumin but may not detect low concentrations of Bence Jones’ protein or gamma-globulins. Bence Jones’ protein can be detected by a specific antibody test on a midstream sample, whilst urine gamma-globulins can be detected by urine electrophoresis.

False negatives: alkaline or dilute urine or when primary protein is not albumin. A more accurate method is to precipitate urinary proteins with 3% sulfosalicylic acid (detects at 2.5 mg/L and detects other proteins). If urine is negative on dipstick but strongly positive with sulfosalicylic acid, suspect multiple myeloma.

Persistent significant proteinuria detected by dipstick requires further assessment with 24-hour urinary protein excretion, urinary protein:creatinine ratio, microscopic examination of the urinary sediment, urinary protein electrophoresis, and assessment of renal function.[15]

Microalbuminuria can be detected with Micral-Test II® or Microbumintest® but this should be followed by confirmation in the laboratory, since false positive results are common.

**Glucose**

See also the separate article Glycosuria.

- Nearly all glucose filtered by the glomeruli is reabsorbed in the proximal tubules and only undetectable amounts appear in urine in healthy patients. Above the renal threshold (10 mmol/L) glucose will appear in urine. The test relies upon reaction of glucose with glucose oxidase on dipstick to form hydrogen peroxide which causes colour change. This is specific to glucose and no other sugar.
- Useful screen for diabetes mellitus.
- False positive results: seen when high levels of ketones are present. Also seen in patients taking levodopa.[16]
- False negatives: seen where SG is elevated, in uricosuria and in patients taking ascorbic acid.

**Ketones**

See also the separate article Urinary Ketones.

- Ketones are not normally found in urine.[1, 18]
- Dipstick tests for the presence of acetoacetic acid at 5-10 mg/dL but not acetone or beta-hydroxybutyric acid.
- A positive test is associated with uncontrolled diabetes, pregnancy without diabetes, carbohydrate-free diets and starvation.
- False trace results may be seen in highly pigmented urine and in patients taking levodopa.[1]
- Delay in testing a sample may result in a false negative result.[1]

**Bilirubin and urobilinogen**

See also the separate article Bilirubinuria.

- Unconjugated bilirubin is water-insoluble and not normally present in the urine.
- Conjugated bilirubin only appears in urine in the presence of liver disease or obstruction of the bile ducts.
- A small amount of urobilinogen is normally found in urine, but significant amounts suggest that further assessment for haemolytic and hepatocellular disease is indicated.[1]
- Urobilinogen levels can be increased in conditions associated with elevated nitrite levels (eg, UTIs).[1]

**Leukocyte esterase and nitrite test**
Nitrites
- This test relies on the breakdown of urinary nitrates to nitrites, which are not found in normal urine.
- Many Gram-negative and some Gram-positive bacteria are capable of producing this reaction and a positive test suggests their presence in significant numbers (i.e., more than 10,000 per ml). A negative result does not rule out a UTI.\[1, 19\]
- The reagent is highly sensitive to air exposure, which may cause a false positive response.\[20\]
- False negative results may be seen where:
  - Bladder incubation time is shortened (less than four hours).
  - There is absence of dietary nitrate.
  - There is presence of nitrate reductase-negative organisms (e.g., some mycobacteria strains).\[21\]
  - Urine SG is elevated.\[1\]
  - The pH is less than 6.0.\[1\]
  - There is presence of urobilinogen and urinary vitamin C.

Leukocyte esterase
- This relies on the reaction of leukocyte esterase produced by neutrophils and a positive result suggests pyuria associated with UTI.\[1\]
- Isolated trace results may be of questionable significance, but repeated ones should not be ignored.
- False positive results may be caused by contamination with vaginal discharge.\[1\]
- Elevated urine glucose or oxalic acid concentrations may reduce sensitivity, and this may also be seen in patients taking tetracycline or cefalexin.\[1\]

Efficacy
Nitrites
There have been many studies evaluating the accuracy of dipsticks tests. These are mostly in relation to their role detecting bacteriuria and UTI. A meta-analysis of 26 studies in children, showed wide differences in diagnostic accuracy across studies. This could not be fully explained by differences in age, or by differences in the definition of the criterion standard.\[22\] The lack of an adequate explanation for the heterogeneity of the dipstick accuracy stimulates an ongoing debate.

Overall, the sensitivity of the urine dipstick test for nitrites in testing for a UTI has been found to be low (45-60% in most situations) with higher levels of specificity (85-98%).\[23\] The test for nitrites has its highest accuracy in specific populations such as pregnant women, urology patients and elderly people. The test for nitrites may perform better in asymptomatic patients and in patients who are not on antibiotics.

Leukocyte esterase
When testing for urinary tract infections, the sensitivity of the urine dipstick test for leukocyte esterase has been found to be, in general, slightly higher than for the dipstick test for nitrites (48-86%), while the specificity was slightly lower (17-93%).\[23\] Generally, this results in a lower accuracy, compared to the test for nitrites, lower predictive values of positive test results and similar predictive values of negative test results.

The leukocyte esterase test has been found to have a much higher accuracy in urology patients. Sensitivity is highest in primary care, but requires further investigations because of the high rates of false positives. In primary care, negative results do not exclude the presence of infection.

Further reading & references
7. Urine Specific Gravity; Medline Plus, 2008
10. Urine pH; Rnceus, 2008
23. Walter LJM Devill et al; The urine dipstick test useful to rule out infections. A meta-analysis of the accuracy, June 2004

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