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# Interpretation of Urinalysis Results

Urinalysis is used as a screening and/or diagnostic tool to detect substances or cellular material in the urine associated with metabolic disorders, renal dysfunction or urinary tract infections (UTI). Often, substances such as protein or glucose will begin to appear in the urine before patients are aware that they may have a problem.

Urine may be assessed both at the bedside (dipstick) and in the laboratory (microscopy, culture, sensitivity and urinary electrolytes). Urine for laboratory analysis must be transferred quickly and at the correct temperature otherwise it becomes a breeding ground for contaminants.

## Specific Gravity (1.002 – 1.035)

- Specific gravity of urine is a measure of the amount of solutes dissolved in urine as compared to water (1.000).
- Specific Gravity measures the ability of the kidney to concentrate or dilute the urine and is directly proportional to urine osmolality (solute concentration).
- Specific gravity between 1.002 and 1.035 on a random sample is normal **IF** kidney function is normal.

**Decreased**: **< 1.005**

- Inability to concentrate urine or excessive hydration (volume resuscitation with IV fluids).
- Nephrogenic diabetes insipidus, acute golmerulonephritis, pyelonephritis, acute tubular necrosis.
- Note: If specific gravity is not > 1.022 after a 12 hour period without food or water, renal concentrating ability is impaired and the patient either has generalized renal impairment or nephrogenic diabetes insipidus.
- Falsely low specific gravity can be associated with alkaline urine.

**Fixed**: **1.010**

- The glomerular filtrate in Bowman's space ranges from 1.007 to 1.010, any measurement below this range indicates hydration and any measurement above it indicates relative dehydration.
- In end stage renal disease, specific gravity tends towards 1.010.
- Chronic Renal Failure (CRF), Chronic glomerulonephritis (GN).

**Increased**: **>1.035**

- Increased specific gravity indicates a concentrated urine with a large volume of dissolved solutes.
- Dehydration (fever, vomiting, diarrohea), SIADH, adrenal insufficiency, pre-renal renal failure, hyponatraemia with oedema, liver failure, CCF, nephrotic syndrome.
- Elevation in specific gravity also occurs with glycosuria (*e.g.* diabetes mellitus or IV glucose administration), proteinuria, IV contrast, urine contamination, LMW dextran solutions (colloid).

## PH (4.5-8.0)

- The kidneys play an important role in acid-base regulation within the body to maintain a normal urinary pH range between 5.5 – 6.5 but it may vary from as low as 4.5 to as high as 8.0.
- The glomerular filtrate of blood plasma is usually acidified by renal tubules and collecting ducts from a pH of 7.4 to about 6 in the final urine.
- Control of pH is important in the management of several diseases, including bacteriuria, renal calculi, and drug therapy.

### High Urinary pH (Alkali Urine)

- Vegetarian diet, low carbohydrate diet or ingestion of citrus fruit (although citrus fruits are acidic – the digestion process leaves an alkali ash).
- Systemic alkalosis (metabolic or respiratory).
- Renal tubular acidosis (RTA I (distal)), Fanconi syndrome.
- Urinary tract infections (Bacteruria with urea splitting organisms).
- Drugs: Amphotercin B, carbonic anhydrase inhibitors (acetazolomide), NaHCO3, salicylate OD.
- Stale ammoniacal sample (left standing).

### Low Urinary pH (Acidic urine)

- High protein diet or fruits such as cranberries.

- Systemic acidosis (metabolic or respiratory).
- Diabetes mellitus, starvation, diarrhoea, malabsorption.
- Phenylketonuria, alkaptonuria, renal tuberculosis.

## Protein

- Normal daily protein excretion should not exceed 150mg/24 hours or 10mg/100mL. Proteinuria is defined by the production of >150mg/day with nephritic syndrome producing > 3.5 g/day.
- Dipstick urinalysis detects protein with Bromphenol blue indicator dye and is most sensitive to albumin and less sensitive to Bence-Jones protein and globulins. Trace positive results are equivalent to 10 mg/100 mL or about 150 mg/24 hours (the upper limit of normal).

**True protein elevation:**

- **Renal**: Increased renal tubular secretion,increased glomerular filtration (glomerular disease), nephrotic syndrome, pyelonephritis, glomerulonephritis, malignant hypertension.
- **CVS**: Benign HT, CCF, SBE.
- **Functional proteinuria (albuminuria)**: fever, cold exposure, stress, pregnancy, eclampsia, CHF, shock, severe exercise.
- **Other**: Orthostatic proteinuria, electric current injury, hypokalaemia, Cushing's syndrome.
- **Drugs**: Aminoglycosides, gold, amphotericin, NSAID, sulphonamides, penicillins.

  **Note**: Bence Jones globulin associated with multiple myeloma, lymphoma and macroglobulinaemia is **NOT** detected by dipstick urinalysis.

- **False Positive:** Concentrated urine (UO < 2.5 L/day), alkaline urine (pH > 7.5), trace residue of bleach, aceazolomide, cephalosporins, $NaHCO_3$.
- **False Negative:** Dilute urine (UO > 5.0 L/day) or acidic urine (pH < 5).

| Dipstick Protein Reading | Protein excreting (m/24 hours) | Protein excretion (mg/dL) |
|---|---|---|
| Negative | < 0.1 | < 10 |
| Trace | 0.1 – 0.2 | 15 |
| 1+ | 0.2 – 0.5 | 30 |
| 2+ | 0.5 – 1.5 | 100 |

| | | |
|---|---|---|
| 3+ | 2.0 – 5.0 | 300 |
| 4+ | > 5.0 | > 1000 |

## Leucocytes (White Cell Count (WCC))

- Determines the presence of whole or lysed white cells in the urine (pyuria) by detecting leucocyte esterase activity.
- A positive leucocyte esterase test correlates well with pyuria. However, the diagnosis may be missed in up to 20% of cases if a negative urinalysis dipstick is used to exclude UTI.

  - **False positive:** Contaminated specimen, trichomonas vaginalis, drugs or foods that colour the urine red.
  - **False negative:** Intercurrent or recent antibiotic therapy (especially gentamicin, tetracycline and cephalosporins), glycosuria, proteinuria, high specific gravity. Low bacteria count UTI (especially in women).

## Nitrites

- Nitrates in the urine are converted to nitrites in the presence of Gram-negative bacteria such as E.coli and Klebsiella.
- A positive nitrite test is a surrogate marker of bacteruria.
- Positive test strongly suggests infection but negative test does not exclude it (PPV 95% and NPV 25 – 70 %).
  - **False negative:** Drugs or foods that colour the urine red. Certain bacteria such as *S. saprophyticus*, *acinetobacter* and most *enterococci*.

| | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|
| **Dipstick** | | | | |
| Leucocyte esterase | 75 – 90 | 95 | 50 | 92 |
| Nitrite | 35 – 85 | 95 | 96 | 27 – 70 |
| Nitrite and leucocyte esterase | 75 – 90 | 70 | 75 – 93 | 41 – 90 |
| **Microscopy** | | | | |
| WCC > $8 \times 10^6$ | 91 | 50 | 67 | 83 |
| **Culture** | | | | |
| >$10^5$ bacteria/L | 95 | 85 | 88 | 94 |

| | | | | |
|---|---|---|---|---|
| $>10^8$ bacteria/L | 51 | 59 | 98 | 94 |

## Blood (Erthrocytes)

- Dipstick urinalysis is able to detect haemolysed and non-haemolysed blood in the urine.
- The pseudoperoxidase reaction of erythrocytes, free haemoglobin or myoglobin catalyses chromogen oxidation on the dipstick to produce a colour change.
- A positive result may be indicative of haematuria from trauma, infection, inflammation, infarction, calculi, neoplasia, clotting disorders or chronic infection.
- Haemaglobinuria may be associated with intravascular haemolysis, burns, sudden cold, eclampsia, sickle cell crisis, multiple myeloma, alkaloids (mushrooms) and transfusion reactions.

## Ketones

- Ketones (acetone, aceto-acetic acid, beta-hydroxybutyric acid) are the end-point of incomplete fat metabolism. They accumulate in the plasma and are excreted in urine.
- Ketonuria is associated with low carbohydrate (high fat/protein) diets, starvation, diabetes, alcoholism, eclampsia and hyperthyroidism.
- Ketonuria also associated with overdose of insulin, isoniazid and isopropyl alcohol.
- Most urinalysis reagent tests utilise the nitroprusside test which is most sensitive to aceto-acetic acid, less sensitive to acetone, and not sensitive to beta-hydroxybutyric acid.

  - **False positive**: Heavily pigmented urine. Drugs such as captopril, L-dopa, salicylates, phenothiazines.
  - **False negative**: Negative nitroprusside tests for ketonuria underestimate the presence of ketonemia due to increased beta-hydroxybutyric acid concentrations.

## Glucose

- Glucose is not normally present in the urine with < 0.1% of glucose normally filtered by the glomerulus appears in urine (< 130 mg/24 hr).
- Glycosuria occurs in patients with elevated serum glucose levels (e.g. diabetes mellitus see chapter on hyperglycaemia) or in the presence of a reduced renal threshold and reduced glucose reabsorption in renal tubular disease and pregnancy.

- Glycosuria also associated with certain drugs such as cephalosporins, penicillins, nitrofurantoin, methyldopa, tetracycline, lithium, carbemazepine, phenothiazines, steroids and thiazides.

  - **False positive**: Hydrogen peroxide or bleach.
  - **False negative**: Ascorbic acid (vitamin C) or fruit juices. Some dipsticks are affected by increased specific gravity and ketonuria.

    **Note**: Dipsticks employing the glucose-oxidase/peroxidase reaction for screening are specific for glucose but can miss other reducing sugars (e.g. galactose and fructose) and are not suitable for testing newborn and infant urine. (Instead use a modified Benedict's copper reduction test.

## Bilirubin

- Bilirubin is not present in the urine of normal healthy individuals. The presence of bilirubinuria may be an early indicator of liver disease and occur befor the clinical signs of jaundice develop.
- Bilirubin is formed as a by-product of red blood cell degradation in the liver, and then conjugated with the solubilising sugar, glucuronic acid and excreted in bile. Within the intestine, the bilirubin is converted into stercobilin (exrcreted in faeces) and urobilinogen (excreted by the kidneys).
- Failure of conjugated bilrubin to reach the intestines (e.g. biliary obstruction) will result in bilirubinuria. *Note*: Only conjugated bilrubin can be excreted as bilirubinuria. A positive test for urine bilirbin confirms conjugated hyperbilirubinaemia.
- Raised conjugated bilirubinaemia (with bilirubinuria) is associated with hepatocellular disease, cirrhosis, viral and drug induced hepatitis, biliary tract obstruction (e.g. choledocholithiasis), pancreatic causes of obstructive jaundice (e.g. carcinoma of the head of the pancreas) and recurrent idiopathic jaundice of pregnancy.

  - **False positive:** Phenothiazines.
  - **False negative:** Ascorbic acid (vitamin C), aged sample (conjugated bilirubin hydrolses to unconjugated bilirubin at room temperature), rifampicin and exposure to UV light (converts bilrubin to biliverdin).

## Urobilinogen

- Urobilinogen is normally present in the urine in low concentrations (0.2 – 1.0 mg/dL or < 17 μmol/L). Bilirubin is converted to urobilinogen by intestinal bacteria in the duodenum. Most urobilinogen is excreted in the faeces or transported back to the liver and converted into bile. The remaining urobilinogen (< 1 %) is excreted in the urine.
- Urobilinogen is present in increased concentrations in the urine in patients with cirrhosis, infective hepatitis, extravascular haemolysis, haemolytic anaemia, pernicious anaemia, malaria, and hepatitis secondary to infectious mononucleosis
- Very sensitive but non-specific test to determine liver damage, haemolytic disease and severe infections. Urobilinogen levels are decreased or absent in obstructive jaundice and elevated levels of bilirubinuria.

| **Dipstick Urinalysis** | **Normal** | **Biliary obstruction** | **Hepatic disease** | **Haemolytic disease** |
|---|---|---|---|---|
| Bilirubin | Negative | Positive | Positive | Negative |
| Urobilinogen | Positive | Negative/ Decreased | Increased | Increased |