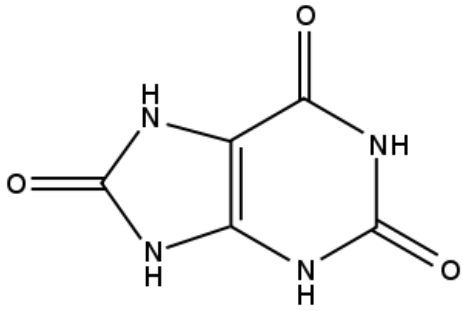
Uric acid

Uric acid is the end product of purine metabolism in humans. During catabolic processes, nucleic acids derived from the cell nuclei of the body and food are broken down into nucleotides, nucleosides and bases, which are partially converted by the **xanthine oxidase enzyme** into uric acid in the final phase. At this level, the degradation of purine bases in humans and primates is complete. In other mammals, uric acid is further converted by uricase to allantoin, which is more soluble in water than uric acid. Some of the purine bases are used for **nucleotide resynthesis** (salvage pathway) by the hypoxanthine guanine phosphoribosyltransferase (**HPRT**) and adenine phosphoribosyltransferase (**APRT**) enzymes.

The total amount of uric acid in the body is **approximately 1 g**.

Uric acid comes from **three** sources:

- from nucleotides
- from the breakdown of tissue nucleoproteins
- from own biosyntheis



Uric Acid

However, uric acid is not only a waste metabolite of purines - its **antioxidant effects** protect cells from the action of oxygen radicals. Most uric acid (75-80%) is excreted by the kidneys (see below). The remaining part of uric acid (20–25%) is eliminated by the gastrointestinal tract, where it can be further degraded by bacteria to NH_3 and CO_2.

Properties

Uric acid is a **poorly water-soluble** compound. At pH below 5.5, which is common in urine, most uric acid molecules are in **undissociated** and thus less soluble form. Uric acid can then form crystals or concretions. Lower temperature helps to reduce the solubility of uric acid. As the pH increases, its solubility increases.

At a physiological **pH of blood of 7.4**, it is present mainly in ionized form and with Na^+ and K^+ it forms sodium or potassium urate, which are more soluble in aqueous solution. Oxidative cleavage with concentrated **nitric acid** can be used to detect uric acid. The reaction opens the imidazole ring of purine and the two product molecules condense to purpuric acid, whose salts are colored. Addition of ammonia to the purpuric acid produces *murexide* (ammonium salt of the purpuric acid). **Murexide reactions** are used to detect uric acid in the analysis of urinary stones.

Serum uric acid

Serum uric acid The concentration of uric acid in plasma depends on the **intake of purines** by food, the intensity of self-production and its excretion. **Increased plasma concentrations** of uric acid - ie **hyperuricemia** - are clinicaly important. This occurs during overproduction or reduced uric acid excretion. In hyperuricaemia, urate concentrations may exceed their solubility.

Reference values

Serum uric acid concetrations:

- women: **120–340 µmol/l**
- men: **120–420 µmol/l**

Overproduction

- Overproduction of de novo purine synthesis associated with elevated uric acid levels is found in some genetic defects in purine metabolism, such as partial or complete hypoxanthine-guanine phosphoribosyltransferase deficiency (Lesch-Nyhan syndrome). It reduces the reuse of purine bases, which are therefore increasingly degraded to uric acid. Another genetic defect leading to increased uric acid production is increased phosphoribosyl diphosphate synthetase activity.
- Increased production of uric acid accompanies antitumor treatment (chemotherapy with cytostatics, irradiation), during which there is a more intense breakdown of cells. Purine bases released during nucleic acid degradation are metabolized to uric acid. Similarly, some haematological diseases associated with excessive neoplasia (polycythemia vera) or increased cell lysis (leukemia, haemolytic anemia) are accompanied by hyperuricaemia.
- Increased intake of a diet rich in purines (eg: offal, meat, legumes, to a lesser extent also chocolate, cocoa, coffee) leads to overproduction of uric acid. Healthy kidneys may not be able to compensate for the uric acid overload with more intense excretion, and uricemia then rises.
- Alcohol consumption increases uricemia by inhibiting uric acid secretion by the kidneys. Decreased uric acid excretion is later replaced by increased uricosuria.

Reduced excretion

Decreased uric acid excretion is one of the most common causes of hyperuricaemia.

- In patients with hyperuricemia, tubular uric acid secretion is often reduced; the cause is unknown.
- Decreased renal excretion of uric acid accompanies conditions associated with decreased glomerular filtration and tubular dysfunction (eg uric acid competition for tubular excretory mechanisms with lactate or keto acids - see below).

Uric acid in urine

Most uric acid is excreted by the kidneys (75-80%), where it is freely filtered by the glomerulus (it is minimally bound to proteins) and then most is reabsorbed in the proximal tubule. It is then secreted in the distal part of the proximal tubule and resorbed again by post-secretory reabsorption.

About **0.6 g of uric acid per day** (3.6 mmol / day) is normally excreted in the urine with a purin-free diet, and values are higher with a normal diet - around 0.8 g / day (5.0 mmol / day). Tubular uric acid secretion may be inhibited by concomitant increased excretion of other organic acids such as acetoacetic acid, β-hydroxybutyric acid, lactic acid and some drugs.

Uric acid in the urine is a significant risk factor for both the urinary tract and the renal parenchyma.

Due to the poor solubility of uric acid, there is a risk of **urate urolithiasis** with increased urinary excretion. Individuals with permanently more acidic and concentrated urine pose a special risk. Urate stones are most often formed by pure uric acid, sometimes sodium urate. Ammonium urate stones may form in slightly alkaline urine, which is usually in the presence of a urinary tract infection associated with the breakdown of urea.

Sodium urate crystals can also **precipitate in the renal interstitium** and cause an inflammatory reaction (chronic interstitial nephritis).

Acute renal failure is relatively rare, which may occur with a sudden rise of uric acid in the blood (eg cytostatic therapy in patients with leukemia) when urine is concentrated (acidic dehydration) at an acidic pH. These circumstances create the conditions for the formation of **uric acid crystals in the distal renal tubules and renal collecting ducts**, and these can block the outflow of urine (acute urate nephropathy).

Urine uric acid testing is important especially in patients with elevated serum uric acid levels and in patients with urolithiasis.

The amount of uric acid in urine can be expressed in several ways:

1. **by measuring the concentration in the morning urine sample.** According to the results, the concentration of uric acid in the morning sample adjusts the drinking regime in patients with urolithiasis in order to reduce its concentration in urine during this period.
2. **as the amount of uric acid excreted in 24 hours.** It is analyzed in a urine sample taken from a mixed all-day collection. Examination of uric acid waste in 24 hours is useful for distinguishing hyperuricemia from uric acid overproduction and decreased excretion;
3. as the ratio of uric acid / creatinine in a randomly collected urine sample that does not require all-day urine collection (**Kaufman index - IK**);
4. **uric acid clearance.** Examination of uric acid clearance helps to distinguish whether the cause of hyperuricaemia is a metabolic disorder or a change in its renal excretion. We use the formula for the calculation:

   $$\mathrm{Cl_{KM}\ [ml/s]} = \frac{\mathrm{U_{KM} \cdot V}}{\mathrm{P_{KM}}},$$

   where Cl_{KM} is uric acid clearance, U_{KM} is uric acid concentration in urine (mmol/l), P_{KM} is plasma uric acid concentration (mmol/l), V is diuresis (ml/s);

5. **by determining the fractional excretion of uric acid.** There is summary information about transport processes in the renal tubules. The fraction of uric acid excretion suggests the role of renal tubular cell dysfunction in hyperuricemia. It can be tested in a randomly taken urine and blood sample, in which we examine the concentration of uric acid and creatinine. We calculate it according to the formula:

   $$\mathrm{FE_{KM}} = \frac{\mathrm{U_{KM} \cdot P_{kreat}}}{\mathrm{U_{kreat} \cdot P_{KM}}},$$

   where FE_{KM} is the fractional excretion of uric acid, U_{KM} concentration of uric acid in urine in mmol/l, P_{KM} concentration of uric acid in serum (plasma) in mmol/l, P_{kreat} concentration of creatinine in serum (plasma) in mmol/l, U_{kreat} concentration of creatinine in urine in mmol/l

Reference values

- Urinary acid loss in 24 hours:

  3,5 mmol/24 h (purine-free diet)

5,0 mmol/24 h (normal diet)

- Uric acid clearance:

  0,07–0,22

Methods of determination

Most modern methods for determining the concentration of uric acid use the enzyme **uricase**, which converts uric acid to allantoin, hydrogen peroxide and carbon dioxide. The decrease in uric acid concentration in the reaction mixture can be determined directly by measuring the loss of absorbance at 290-293 nm. This method is based on different absorption spectra of allantoin and uric acid. Unlike uric acid, allantoin formed in the uricase reaction does not show an absorption peak at 290–293 nm. Another possibility is an indirect determination using the resulting hydrogen peroxide for another peroxidase-catalyzed coupled reaction. **Oxidative coupling**[† 1] of usually 4-aminoantipyrine with a suitable phenol derivative [(in our case N-ethyl-N- (2-hydroxy-2-sulfopropyl) -m-toluidine)] produces a quinone imine dye whose color intensity is proportional to the concentration of uric acid. in the sample. Ascorbic acid interferes with the determination. Its effect is suppressed by the presence of ascorbate oxidase in the reaction mixture.

Links

- ws:Kyselina močová

Related articles

- Non-protein nitrogen (NPN)

Source

- With the consent of the authors taken from https://el.lf1.cuni.cz/p45355481/

Notes

1. Oxidative coupling, which is used as an indicator reaction, is a special type of coupling between aromatic amines and phenols. The hydrogen peroxide formed in the previous reaction is used for the peroxidase catalyzed oxidation. Oxidative coupling is the essence of the determination of other important analytes in biological material such as glucose, cholesterol or triacylglycerols.

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