Urinalysis/Physical

The physical examination consists of assessing the **color** ***of the urine, its*** *odor*, its **foam** ***and its****turbidity*. An important part of the physical examination is the determination of pH, density and osmolality. For the purpose of functional examinations, it is necessary to measure the *volume* of urine for a precisely defined period of time.

Polyuria

By polyuria we mean an increase in daily diuresis above 2500 ml.

There are two types of polyuric states:

Polyuria caused by the so-called *water diuresis*.

> Water diuresis is given by a **reduction of tubular resorption of water'** in the distal segment of the nephron. Tubular resorption and excretion of osmotically active substances is within normal limits. Urine osmolality is lower than serum osmolality. It is always less than 250 mmol/kg H_2O. We encounter water diuresis physiologically when taking in a larger volume of water or, for example, when insufficient secretion of antidiuretinu (diabetes insipidus).

Polyuria due to the so-called "osmotic diuresis".

> It is caused either by increased filtration of osmotically active substances due to their increased osmotic concentration in ECT (e.g. hyperglycemia) or by their decreased tubular resorption. Unabsorbed osmotically active substances "bind" water to each other and the result is a decrease in their tubular resorption. Urine osmolality is higher than 250 mmol/kg H_2O. Osmotic diuresis is characteristic, for example, of diabetes mellitus or the polyuric phase of renal failure or is the result of diuretics.

Color

Fresh urine has an amber-yellow coloration attributed to certain bilirubinoids, particularly urobilinu. The intensity of the coloring depends on the concentration and amount of urine, which is determined by fluid intake and extrarenal output. First morning urine, which is more concentrated, tends to be darker. Some pathological conditions or ingestion of certain exogenous substances can cause a change in color (e.g. beetroot, rhubarb). Selected characteristic changes in the color of urine are shown in the table:

Characteristic changes in urine color

Color	Exciting substance	Occurrence
yellow to colorless		▪ increased diuresis with excessive fluid intake ▪ diuretics ▪ diabetes mellitus ▪ diabetes insipidus ▪ polyuric phase of renal failure
brown	bilirubin	▪ diseases of the liver and bile ducts
greenish brown	biliverdin – is formed from bilirubin by oxidation in air	▪ old urine ▪ diseases of the liver and bile ducts
yellow-orange	carotenoids, riboflavin	▪ exogenous income
pink to flesh red (*no turbidity*)	hemoglobin myoglobin porphyrins beetroot	▪ intravascular hemolysis ▪ burns ▪ muscle necrosis ▪ inflammation of the muscles ▪ porphyria ▪ exogenous income
pink to flesh red *with cloudiness*	blood in the urine - hematuria (microscopic hematuria, which can only be demonstrated by chemical or microscopic examination, will not affect the color of urine)	▪ kidney disease ▪ diseases of the urinary tract ▪ bleeding conditions
Dark brown (standing in the air the color deepens to black)	melanin homogentisic acid	▪ melanoma ▪ alkaptonuria
Light red	urates	▪ hyperuricosuria

Odor

We assess it in fresh urine, because exposure to light breaks down some components of urine and changes the smell. Certain diseases, listed in the table, cause a characteristic odor:

Odor of urine

Odor character	Cause	Occurrence
Ammoniacal	the presence of urease-producing bacteria, which catalyzes the breakdown of urea into ammonia and carbon dioxide	▪ old urine ▪ urinary tract infection ▪ diseases with chronic urinary retention (e.g. benign prostatic hyperplasia)
Acetone *(overripe apples)*	urinary acetone excretion in ketoacidosis	▪ diabetes mellitus ▪ starvation
Maple syrup or maggi seasoning	branched-chain carboxylic oxoacids (in particular 2-oxoisocaproic acid, 2-oxoisovaleric acid)	▪ leucinosis (maple syrup disease)
hydrogen sulfide to putrid	bacterial decomposition of proteins releases H_2S from sulfur-containing amino acids	▪ urinary tract infection associated with proteinuria ▪ cystinuria
Mouse	phenylacetate	▪ phenylketonuria

Foam

Normal urine foams little, the foam is white and disappears quickly. More abundant, colorless, more persistent foam occurs in proteinuria. In the presence of bilirubin, the urine foam is colored yellow to yellow-brown.

Turbidity

Fresh urine is usually clear. The turbidity that occurs after a longer period of standing is caused by epithelia and has no pathological significance. In fresh urine, turbidity can be caused by the presence of bacteria, leukocytes, lipids, phosphates, carbonates, uric acid, leucine, tyrosine and oxalates. It can be distinguished chemically or microscopically.

Density

In the literature, also '*specific gravity*.

Relative density' (also *relative specific gravity*) is given by the **mass concentration of all dissolved substances** excreted in the urine. Unlike osmolality, it depends not only on the number of dissolved particles but also on their molecular weight. High molecular weight substances affect density to a greater extent than electrolytes. In the case of more pronounced glucosuria or proteinuria, the relative specific gravity rises. A protein concentration of 10 g/l increases the relative specific gravity of urine by 0.003 and a glucose concentration of 10 g/l by 0.004. The relative specific gravity of urine depends significantly on temperature.

By *relative density of urine* we mean the ratio of the density of urine to the density of water. The density of water is practically equal to 1 kg/l, so the difference between the density of water (in kg/l) and the relative density of urine is negligible. In the SI system, density has the dimension $kg \cdot m^{-3}$. The density of the sample in relation to the density of water is a relative quantity and is therefore given by a dimensionless number.

Determination of density of urine

The density of urine is estimated indirectly by the concentration of cations using diagnostic strips. The indicator zone of the strip contains a suitable polyelectrolyte as an ion exchanger and the acid-base indicator bromothymol blue. The principle of diagnostic strips is based on the exchange of cations from urine, especially Na^+, K^+, NH_4^+, for the H^+ ions of the polyelectrolyte in the indication zone. The released H^+ acidifies the weakly buffered acid-base indicator, which is in alkaline form. Acidification is accompanied by a change in color to bromothymol blue. The disadvantage is that examination with diagnostic strips does not take into account substances of a non-electrolyte nature such as glucose, proteins, urea, creatinine and some others.

Under physiological conditions, the density of urine ranges from 1.015–1.025. Extreme values of 1.003-1.040 can be achieved with dilution trial and concentration trial.

As a general rule, the larger the volume of urine, the lower its density (diluted urine) and vice versa, with a smaller volume of urine (concentrated urine) it is higher. Conditions in which osmotic diuresis occur deviate from this rule: for example, in diabetes mellitus, the volume of urine is larger with a higher specific gravity.

Determination of the density enables an approximate estimation of the concentration capacity of the kidneys. Values above 1.020 and above are indicative of good renal function and the ability of the kidneys to excrete excessive amounts of solutes. Highly concentrated urine indicates a substantial reduction in circulating plasma volume.

When the kidneys are unable to concentrate urine, poorly concentrated urine with a low specific gravity is excreted; we are talking about **hypostenuria**. The patient excretes the same amount of solids while consuming more water. Extremely dilute urine may be a symptom of impaired concentrating ability of the kidneys, such as in diabetes insipidus, or as a result of side effects of certain medications. The combination of hyposthenuria with polyuria indicates damage to the renal tubular system.

A serious symptom of kidney damage is **isostenuria**. The kidneys lose the ability to concentrate (and dilute) urine and excrete urine with the same density as the glomerular filtrate. The relative density of urine remains consistently low, around 1.010. The simultaneous finding of isosthenuria with oliguria is an indicator of severe renal insufficiency.

dehydration, proteinuria or glycosuria contributes to the increase in relative relative density - **hyperstenuria**.

Changes in the relative density of urine

Designation	Relative density	Causes
Eustenuria	1.020–1.040	
Hyperstenuria	> 1.040	▪ dehydration ▪ glycosuria ▪ proteinuria
Hyposthenuria	< 1.020	▪ diabetes insipidus ▪ hyperhydration ▪ kidney failure ▪ diuretics
Isosthenuria	1,010	▪ kidney damage

Osmolality

Urine osmolality depends on the **amount of osmotically active particles** excreted in the urine, regardless of their weight, size or electric charge. Osmolality is expressed in mmol/kg. It is only approximately dependent on urine density. Its measurement is more accurate compared to density, has a greater informative value and is preferred.

If we compare the two quantities, the osmolality reflects **the total mass concentration of all solutes**, while the density reflects their total mass concentration. Therefore, we can simply say that osmolality will be more affected by changes in the concentration of low molecular weight substances (in practice, especially sodium, glucose and urea), while density will be more significantly affected by the presence of protein in the urine.

Normal osmolality values at normal fluid intake are 300-900 mmol / kg. Urine osmolality depends on the dilution and concentration of the kidneys. The extreme values of osmolality at maximum dilution or maximum concentration are in the range of 50-1200 mmol / kg. If the osmolality of the urine is approximately the same as the osmolality of the blood, it is **isoosmolar** urine. **Hypoosmolar** urine has a lower osmolality than blood, i.e. less than about 290 mmol/kg. **Hyperosmolar** urine is urine with a higher osmolality than blood.

Theoretically, we can imagine that definitive urine arises from isoosmolar glomerular filtrate, to which pure, so-called solvent-free water is added or resorbed in the renal tubules.

The transport of solute-free water expresses its clearance. We will explain what this quantity means using the following considerations: First, let us define the **clearance of osmotically active substances**. It is a quantity analogous to the commonly used clearance of endogenous creatinine: the clearance of osmotically active substances represents the theoretical volume of blood plasma, which is completely deprived of all osmotically active particles in the kidneys per unit time. The following will apply (derivation is similar to endogenous creatinine clearance):

$$Cl_{osm} = \frac{U_{osm} \cdot V}{P_{osm}},$$

where Cl_{osm} is the osmolar clearence in ml/s,
V is diuresis in ml/s
U_{osm} is the osmolar urine concentration in mmol/kg of water,
P_{osm} is the osmolar plasma concentration v mmol/kg of water.

If the primitive urine has the same osmolality as the plasma and we neglect the contribution of proteins to the total osmolality of the plasma, the volume of filtered primitive urine must be the same as the clearance of the osmotically active Cl particles .

Solvent-free water clearance is the difference between the actual volume of definitive urine excreted per unit time and osmolar clearance:

$$Cl_{H_2O} = V - Cl_{osm}$$

where	Cl_{H_2O}	is the clearence of solute-free water in ml/s,
	Cl_{osm}	is the osmolar clearence in ml/s,
	V	is diuresis in ml/s.

If the clearance of solute-free water is **negative**, it means that part of the solute-free water has been resorbed from the primitive urine, so that the definitive urine is more osmotically concentrated. Conversely, if the clearance of solute-free water were **positive**, hypoosmolar urine would form, against blood plasma diluted with solute-free water. Physiological values range between ,00.027 and ,000.007 ml / s.

The kidneys are able to excrete large amounts of solute-free water to prevent hyponatremia. Conversely, in the absence of water, its excretion is limited and particles are excreted in a smaller volume of water.

Determination of the urine osmolality

With osmometer

Osmometers are used to accurately determine osmolality. They take advantage of the fact that dissolved particles affect some properties of the solution:

- they reduce the freezing point of the solution (**cryoscopic** principle);
- they increase the boiling point of the solution (**ebulioscopic** principle);
- they reduce the solvent vapor pressure above the solution.

The magnitude of the change in the above quantities depends on the concentration of osmotically active substances in the measured solution, and osmometers record these changes with great accuracy. A lowering of the freezing point is usually detected. It is true that 1 mol of particles of a substance dissolved in 1 kg of water lowers its freezing point by 1.86 °C.

Roughly by calculation based on the substance concentration values of Na^+, K^+, NH_4^+ and urea in urine

$$\text{Urine osmolality} = 2([Na^+] + [K^+] + [NH_4^+]) + [\text{urea}]$$

This calculation fails if the urine contains a high concentration of other substances, which are physiologically present in orders of magnitude lower amounts - for example, with significant glycosuria or ketonuria.

Roughly calculated from the relative density value

If the urine does not contain protein or sugar

we multiply the last two digits of the relative density value by a factor of 33.

Relative density of urine = 1,019 → Estimation of osmolalit: 19 · 33 = 627 mmol/kg.

If the urine contains protein or sugar

we must first correct the relative density value

- in the presence of protein, we subtract 0.003 from the relative density value for every 10 g/l;
- in the presence of glucose, we subtract 0.004 from the relative density value for every 10 g/l.

Examination of kidney concentration ability

Kidney concentration test

pH

The kidneys are the organ where the adjustment of the acid-base balance is carried out by the elimination (or retention) of H^+. In the glomerular filtrate, the pH is the same as in plasma. Urine acidification occurs when passing through the renal tubular system.

The concentration of free protons in urine is negligible compared to other ions; we can therefore say that H^+ is eliminated by the kidneys in two forms:

- bound to the anions present, e.g. to phosphates (conversion of hydrogen phosphate to dihydrogen phosphate)

  $$H^+ + HPO_4^{2-} \rightarrow H_2PO_4^-$$

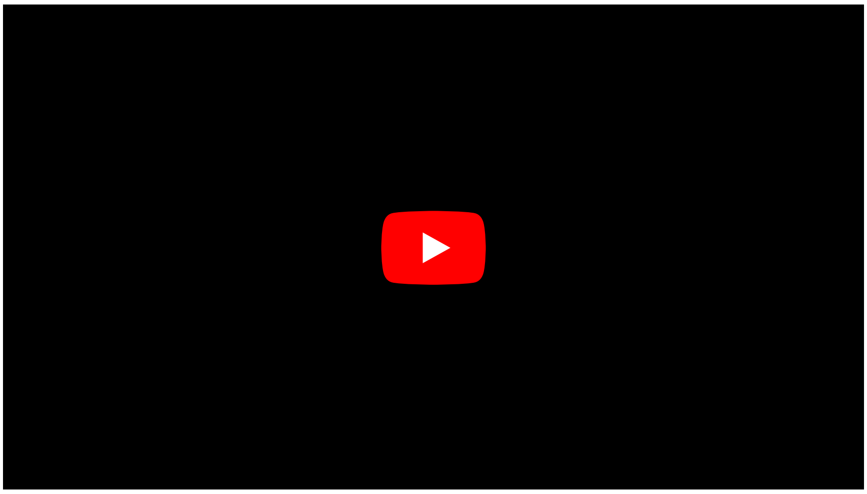
  or to the anions of some organic acids. This proportion is referred to as the so-called titratable acidity, which under normal conditions represents 10-30 mmol/24 hours. It can be determined by titration with sodium hydroxide.

- as the ammonium cation, which represents the most important system.

  $$H^+ + NH_3 \rightarrow NH_4^+$$

  The amount of NH_4^+ excreted in the urine varies between 30-50 mmol/24 hours.

RTA:



Urine pH depends on: on the composition of the diet

In a healthy person, the pH of urine is most influenced by the composition of the diet. A lacto-vegetarian diet causes alkalinization of the urine. Conversely, a diet rich in protein (meat) is accompanied by acidification.

on the state of acid-base balance

Under pathological circumstances, urine pH reflects disturbances in acid-base balance. Changes in urine pH are a manifestation of the compensatory and corrective activity of the kidneys. Aciduria is the result of metabolic correction and respiratory acidosis compensation, alkaliuria is at the beginning of respiratory compensation and metabolic alkalosis correction. However, the excretion of acidic urine in acidosis and alkaline in alkalosis applies only to mild disorders and well-functioning kidneys. The simultaneous finding of aciduria and ketonuria indicates starvation. A combination of aciduria, ketonuria and glycosuria is common in diabetes mellitus decompensation.

The most common factors affecting urine pH

Acid pH	Basic pH
protein diet	vegetarian diet
dehydration	renal tubular acidosis
diabetic ketoacidosis	respiratory and metabolic alkalosis
metabolic and respiratory acidosis	bacterial urinary tract infection
starvation	

Persistently *alkaline* urine pH can signal:

- '*Infection* of the kidneys or urinary tract with urease-producing bacteria. Enzymatic hydrolysis of urea produces ammonia, which alkalizes the urine. A similar situation exists with bacterially contaminated urine, in which bacteria have multiplied over a longer period of storage.

$$H_2N\text{-}CO\text{-}NH_2 + H_2O \xrightarrow{ureáfor} 2NH_3 + CO_2$$
$$NH_3 + H_2O \rightarrow NH_4^+ + OH^-$$

- **Renal tubular acidosis of the distal type**, which is a renal tubular cell disorder characterized by the inability of the distal tubule to excrete H^+.

The main benefit of urine pH testing is in **diagnosis and treatment of urinary infection and urolithiasis'**. Permanent variations in urine pH can be one of the factors contributing to the formation of urinary stones.

- Calcium oxalate stones are common in ``acidic *urine. At an acidic pH, uric acid stones are easily formed. Urine alkalinization above a pH value of 7.0 can, under favorable circumstances, slowly dissolve uric acid stones and prevent their formation. Cystine also precipitates more easily in acidic urine.*
- In ""alkaline"" urine, phosphates are poorly soluble, and at pH above 7, ammonium-magnesium phosphate falls out of the solution (struvite - $MgNH_4PO_4$·6H< sub>2O) and a mixture of phosphate and calcium carbonate ["carbonate apatite" - $Ca_{10}(PO_4CO_3OH)_3(OH)_3$].

Urine pH determination

Urine pH must always be tested in ``fresh *urine. It is usually determined by **diagnostic strips'**. Accurate determination of pH can be done pH-meter.*

The physiological pH of urine is in the range of 5.0–6.5, extreme values are 4.5–8.0. Extreme values in the acidic or alkaline range raise suspicion of non-compliance with urine collection instructions.

Examination of kidney acidification activity

The basic test to assess the acidifying activity of the kidneys is the pH test of the morning urine sample. The pH determination needs to be done immediately and it is recommended to use a pH-meter. In a healthy adult, the pH of a morning sample is less than 6.0. With a higher value, there is a suspicion of a disorder of the acidification ability, and if there are no contraindications (e.g. significant limitation of kidney function), it is possible to perform an **acidification test** after a load of NH_4Cl or $CaCl_2$ (in patients with impaired liver function). We give the patient ammonium chloride (2 mmol per kg of body weight). 3 hours after ingestion of the test substance, urine is collected in 3 one-hour intervals, and immediately after collection, the acidity in the urine samples is measured with a pH meter. If the acidifying function of the kidneys is intact, the pH of the urine should fall below 5.5.

The acidification capacity is impaired in patients with renal tubular acidosis of the distal type.

In the event of an ambiguous result of the acidification test, the alkalizing capacity of the kidneys is investigated after an oral or intravenous sodium bicarbonate load.