Compendium

Urinalysis with Test Strips
**Important Information for Customers in USA and Canada**

The product names used in this brochure are different from the product names used in USA and Canada. The table shows the synonyms for the products available in USA and Canada only:

<table>
<thead>
<tr>
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<th>Product Name in USA</th>
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<tr>
<td>Combur-Test</td>
<td>Chemstrip</td>
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</tr>
<tr>
<td>Combur^2 Test UX</td>
<td>Chemstrip 10 MD</td>
<td>Chemstrip 10 A</td>
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<tr>
<td>Combur^2 Test M</td>
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<tr>
<td>Diabur-Test 5000</td>
<td>Chemstrip uG</td>
<td>Chemstrip uG</td>
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<tr>
<td>Keto-Diabur-Test 5000</td>
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<td>Chemstrip uG/K</td>
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<tr>
<td>Miditron <em>Junior II</em></td>
<td>Chemstrip Criterion II Urine Analyzer</td>
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History of urinalysis with test strips

In many cultures urine was once regarded as a mystical fluid, and in some cultures it is still regarded as such to this day. Its uses have included wound healing, stimulation of the body’s defences, and examinations for diagnosing the presence of diseases.

Modern medicine has at its disposal a variety of quick and hygienic test methods permitting safe and reliable analysis of urine test specimens. The starting point for diagnosing a wide range of pathological conditions is, however, simple visual examination of the urine, and a long path had to be travelled to the development of the modern test strips now used routinely for determining the urine status. Let us now take a quick look at this long development process.

It all started over 2000 years ago

The origin of visual urine diagnostics, the oldest method of examining body fluids, can be traced back to ancient Egypt, where polyuria and haematuria are mentioned as states of disease in old medical papyri. Hippocrates (ca. 400 BC) observed certain changes in the odour and color of urine in the presence of fever, and pointed out the importance of examining the patient’s urine. The Indian physician Caraka (ca. 100 AD) described ten pathological kinds of urine, including urines that contained sugar and bacteria.

No medical teaching of the past was, however, so important, and none had such lasting influence, as that of Claudius Galenus of Pergamum, also known as Galen, who in the second century AD combined the medicine of his day, divided into a number of groups, into one major system with his doctrine of humoral pathology: “It is not solid organs that are the seat of disease but the four body fluids or humours: blood, phlegm, black bile, and choler or yellow bile. Disease is due to an imbalance of these fluids, and the nature and site of the disease can be established from the composition and appearance of the humours. An illness
therefore also shows itself in the urine.” This doctrine dominated medical thinking up to the 16th century. In pathology the teaching of Galen of Pergamum was in fact abandoned only in the 19th century.

In the 10th century the Arab physician Isaac Judaeus, basing himself on Galen’s humoralism, developed a scheme of humours with which he raised the urine findings to the level of an almost infallible diagnostic criterion for all states of disease. The extreme consequence of this theory was so-called uromancy or uroscopy practiced in the Middle Ages (Fig. 1), which according to modern views was devoid of any scientific basis. Over 20 shades of color were distinguished in the urine (from crystal clear via camel hair white, blackberry red, and pale green to black), and corresponding conclusions were drawn about the patient’s illness (Fig. 2). The development went so far that all that was wrong with the human body was believed to be reflected as in a mirror in the urine specimen. This view served as a basis for the “urine fortune-telling,” which was so caustically criticized by humanistic physicians in the 16th century.

In the 16th century Paracelsus prompted examination of the urine by the methods of alchemy, but the thinking of his time, tinged by ideas of magic and astrology, prevented his proposals from developing into forerunners of medical and chemical analysis of the urine.

Fig. 2: A urine glass disc with 20 color nuances (1491 AD)
From uromancy to the idea of clinical chemistry of the urine

It was only towards the end of the 18th century that doctors interested in chemistry turned their attention to a scientific basis of urinalysis and to its use in practical medicine. Writing in 1797, the physician Carl Friedrich Gärtnер (1772–1850) expressed a wish for an easy way of testing urine for disease at the patient’s bedside.

In the same year a work appeared in Britain in which the chemist William Cruikshank (1745–1800) described for the first time the property of coagulation on heating, exhibited by many urines. This observation led English physician Richard Bright to speak of the “albuminous nature of urine” and to describe this clinical symptom of nephritis in 1827 in “Reports of Medical Cases.” This marked the breakthrough of qualitative urine chemistry into medicine.

In the decades that followed a number of chemical urinalyses were introduced into clinical general practice, such as examinations of the urine for protein, sugar, and acetone. However, these examinations were associated with considerable time and effort, and the results were not very specific, e.g. the reduction methods of Fehling or Nylander for the detection of sugar in urine.

With the arrival of chemical urine diagnostics the year 1840 marked a true boom for methods aimed at the detection of pathological urine constituents. Criticisms were voiced at the time that doctors active in general practice had to do too much chemistry, since the tests were all based on wet chemistry. The first “test strips” were developed by the Parisian chemist Jules Maumené (1818–1898) when, in 1850, he impregnated a strip of merino wool with “tin protochloride” (stannous chloride). On application of a drop of urine and heating over a candle the strip immediately turned black if the urine contained sugar. Despite its simplicity the test was not widely accepted, and it took another 70 years or so before the Viennese chemist Fritz Feigl (1891–1971) published his technique of “spot analysis.”

In the intervening years prominent physicians, above all in Britain, concerned themselves with the development of the forerunners of modern test strips. Thus, English physiologist George Oliver (1841–1915) marketed his “Urinary Test Papers” in 1883. The principle in this case was to fix the reagents required for the preparation of solutions in high concentrations on filter paper or cloth, to facilitate the work of the practitioner.

Reagent papers were already commercially obtainable at the beginning of this century from the chemical company of Helfenberg AG. A test for the presence of blood by a wet-chemical method using benzidine became known in 1904, and it was not long before an analogous benzidine paper test appeared on the market.
**Triumph of the test strips**

All these “dry reagents” still did not deserve the designation of “dry chemistry” in the modern sense of the term, but they must be regarded as rudimentary fore-runners of the modern test systems. Even if the basic principle of reagent drying for a time did not undergo any change, urine diagnostics made major progress in the 1930s. The informative power and the reliability in particular were distinctly improved, and test performance itself became progressively easier.

Urine test strips in the sense used today were first made on industrial scale and offered commercially in the 1950s. The company Boehringer Mannheim, today a top leader on the world market under the name of Roche Diagnostics, launched its first Combur test strips in 1964. Even though the test strips have changed their external appearance little since the 1960s, they now contain a number of revolutionary innovations. New impregnation techniques, more stable color indicators, and the steady improvement in color gradation have all contributed to the fact that the use of urine test strips has now become established in clinical and general practice as a reliable diagnostic instrument.

The parameter menu offered has steadily grown longer in the intervening decades. Today Combur-Test product line from Roche Diagnostics can be used for the recognition of the early symptoms of the following three major disease categories:

- diseases of the kidneys and the urogenital tract
- metabolic diseases (diabetes mellitus)
- liver diseases and haemolytic disorders

Diabetic and hypertension-determined nephropathies have been diagnosed early with the aid of Micral-Test in the presence of microalbuminuria.
Indications for urine test strips

Urine test strips are a central diagnostic instrument, their ease of use yielding quick and reliable information on pathological changes in the urine. Their significance lies primarily in first-line diagnostics. Routine testing of the urine with multiparameter strips, allowing a determination of the complete urine status, is therefore the first step in the diagnosis of a very wide range of disease pictures.

Indications for urine test strips:
- screening within the framework of routine examinations
- treatment monitoring
- self-monitoring by patients
- general preventive medicine

Screening within the framework of routine examinations

Within the framework of routine examinations urine test strips are used for screening both in hospitals and in general practice. The aim of screening is early identification of likely patients by examination of large groups of the population. No direct diagnoses are established on the basis of the screening results, which serve only as a basis for further microscopic, bacteriological, or clinicochemical examinations of the urine.

Urine test strips can satisfy all the requirements for effective screening:
- the result is obtained quickly
- the test is easy and inexpensive
- high sensitivity (diagnostic sensitivity)
- sufficiently high diagnostic specificity

A field study carried out in seven European countries with over 11,000 urine samples illustrates the value of screening with urine test strips (Fig. 3). A pathological urine finding (after checking for nitrite, protein, glucose, ketones, urobilinogen, and blood) was diagnosed in 16% of “normal healthy persons,” in 40% of outpatients, and in 57% of hospitalized patients.

With the aid of routine examinations early symptoms of the following three groups are identified:
- diseases of the kidneys and the urinary tract
- carbohydrate metabolism disorders (diabetes mellitus)
- liver diseases and haemolytic disorders

Diseases of the kidneys and urogenital tract

Screening parameters:
- leukocytes
- nitrite
- protein
- blood
- specific gravity
- pH
Indications for urine test strips

Diseases of the kidneys and the urogenital tract often remain asymptomatic for a long time. Renal function disturbances frequently lie dormant for many years, leading eventually to often irreversible severe late damage. Kidney failure as the terminal stage of various primary and secondary nephropathics (Fig. 4) can only be treated by renal substitution therapy such as dialysis or kidney transplantation. Effects are also possible on other organ systems, especially on the cardiovascular system. The cardinal symptom of a urinary tract infection is the detection of significant bacteriuria (nitrite positive) and leukocyturia (leukocytes positive) by means of test strips.

The following non-specific symptoms occur time and time again in patients with urinary tract infections or pyelonephritis and require further clarification to avoid possible late consequences such as uraemia, hypertension, and cardiovascular complications:
- tiredness and exhaustion
- chronic headaches
- persistent lack of appetite
- loss of weight
- nausea and vomiting
- intermittent rises in temperature and fever of unclear origin (in children some 50% of urinary tract infections are manifested by fever)
- pale yellow skin color, puffy appearance

Importance of urinalysis as a screening procedure

Frequency of pathological urine in different groups of people. Parameters: nitrite, protein, glucose, ketones, urobilinogen, blood

<table>
<thead>
<tr>
<th>Group</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>“normal” persons</td>
<td>16%</td>
</tr>
<tr>
<td>outpatients</td>
<td>40%</td>
</tr>
<tr>
<td>hospitalized patients</td>
<td>57%</td>
</tr>
</tbody>
</table>

A field study carried out in seven European countries with over 11,000 urine samples

Fig. 3: Frequency of pathological urines
The following characteristic symptoms are much more rare:
- proteinuria
- “weak bladder,” a “bladder cold”
- burning and pain during micturition
- polyuria, dysuria, pollakiuria
- bed-wetting in older children
- pains in the lumbar and kidney region.

In certain risk groups the danger of urinary tract infections and pyelonephritis is particularly high:
- in pregnant women 4–8%
- in hypertensive subjects approx. 14%
- in older people 8–18%
- in diabetics up to 20%
- in patients with urinary calculi approx. 50%
- in patients with congenital urological disorders approx. 57%
- in gout patients approx. 65%
- in patients after catheterization, instrumentation, and operations on the urinary tract

Regular checking for urinary tract infections and infectious kidney diseases, especially in women and elevated-risk patients, enables treatment to be started early as a result of diagnosis in an early state of the disease, with good prognosis of the otherwise serious conditions. After the end of the therapy further control checks are also necessary to catch any relapses in good time.
Carbohydrate metabolism disorders (inter alia diabetes mellitus)
Screening parameters:
- glucose
- ketones

Around 30–40% of type I diabetics and around 20% of type II diabetics suffer in time from a nephropathy, and early recognition of diabetes is therefore of major significance for the further state of health of these patients.

Liver diseases and haemolytic disorders
Screening parameters:
- urobilinogen
- bilirubin

In many liver diseases the patients often show signs of pathology only at a late stage. Early diagnosis allows appropriate therapeutic measures to be instituted in good time, avoiding consequential damage and further infections.

Treatment monitoring
Treatment monitoring with the aid of urine test strips allows the treating doctor to check on the results of the prescribed therapy, and if necessary to introduce any changes into the therapeutic strategy. An additional benefit of such monitoring is improved patient compliance.

Monitoring is particularly useful in two clinical conditions:
In diabetes mellitus combined checks for glucose and ketones are advisable for the purpose of early detection of any dietetic errors by changes in the metabolic status and for their correction.

Patients suffering from hypertension run an increased risk of developing kidney damage in the course of their condition. Micral-Test allows early detection of incipient nephropathy.

Self-monitoring by patients
Under their doctor’s instructions patients can benefit directly from the advantages of urine test strips. This applies particularly to diabetics, where the idea of self-monitoring of the metabolic status (determinations of glucose and ketones) is self-evident.

General preventive medicine
Spontaneous preventive monitoring at home has meanwhile become widespread in the population. For example, a check on the first morning urine for an asymptomatic urinary tract infection can be carried out without any problems on a day-to-day basis. The same applies to an examination of the urine 2 hours after a carbohydrate-rich main meal to check for the presence of diabetes mellitus. The whole family is often involved in such preventive monitoring.
Pre-analytical treatment and test performance

Reliable analytical results can only be obtained from a urine specimen that has been collected, transported and stored properly. To this day the diagnostic possibilities of urinalysis are often not utilized to the full because correct pre-analytical treatment cannot be ensured.

Sample collection
The urine collection and dispatch equipment should always comprise clean and sterile disposable containers, made as a rule from plastic. Important patient data (surname, first name, date of birth, sender, collection date and time) should be affixed to the container in a waterproof manner before the sample collection.

Depending on the time and nature of the urine specimen collection, a distinction is drawn between:
- spontaneous urine
- first morning urine (after a night’s rest)
- second morning urine (collected before noon)
- timed urine (usually 24-hour urine)
- midstream urine
- bladder puncture urine

The first morning urine has proved its worth for most test purposes. As a rule it ensures sufficiently long residence of urine in the bladder, and its composition is independent of the daily variations due to food and fluid intake and physical activity. For

![Fig. 5: Collecting a mid-stream urine sample](image-url)
checks on glucosuria it is best to use urine passed about 2 hours after a carbohydrate-rich meal.

Contamination is frequent in normal “spontaneous” urine collected without any special hygienic precautions, especially in the case of women, and consists of leukocytes in the presence of discharge and of erythrocytes in the presence of menstruation. For this reason no urine diagnostics should be attempted in women during and 2–3 days after menstruation.

Correct sample collection is made easier by leaflets with a detailed description of the procedure for patients and medical personnel.

Sample storage
Examination of the urine with test strips should be carried out at the latest 2 hours after micturition, since longer standing times can lead to false results owing to the following influences:
- disintegration (lysis) of leukocytes and erythrocytes
- proliferation of bacteria
- bacterial degradation of glucose
- a rise in pH due to ammonia formed as a result of bacterial degradation of urea
- oxidation of bilirubin and urobilinogen, especially in sunlight

These changes in the specimen can be slowed down if the urine is kept in a sealed container in a refrigerator.
### Pre-analytical treatment and test performance

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<td>Unstable</td>
<td>Unstable</td>
<td>Fluid intake, diuretics</td>
<td>pH &gt; 7</td>
<td>Precipitation changes the specific gravity</td>
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<td>pH</td>
<td>Unstable</td>
<td>Unstable</td>
<td>Diet (meat ↓, vegetarian ↑)</td>
<td></td>
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<td>Leukocytes</td>
<td>1–4 h</td>
<td>1–4 h</td>
<td>Vaginal secretion</td>
<td>Strong color of urine ↑</td>
<td>Fast lysis at specific gravity &lt; 1.010 and pH &gt; 7. Mix urine specimen well</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>High glucose and protein values ↓</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Certain antibiotics ↑ or ↓</td>
<td></td>
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<tr>
<td>Nitrite</td>
<td>8 h</td>
<td>4 h</td>
<td>Bacterial count</td>
<td>Strong color of urine ↑</td>
<td>Antibiotics inhibit nitrite formation</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ascorbic acid ↓</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Phenazopyridine ↑</td>
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<td>Protein (albumin)</td>
<td>7 days</td>
<td>1 day</td>
<td>Physical activity pregnancy</td>
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<td>Ejaculate ↑ Preservatives ↑</td>
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<tr>
<td>Glucose</td>
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<td>2 h</td>
<td>Pregnancy, fever, old age</td>
<td>Bacteria ↓</td>
<td>Test is more sensitive to acetooacetic acid than to acetone</td>
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</tr>
<tr>
<td>Ketones</td>
<td>6 h</td>
<td>2 h</td>
<td>Starvation, fasting, fever</td>
<td>Phenylketones ↑</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Phthaleins ↑</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SH compounds ↑</td>
<td></td>
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<tr>
<td>Urobilinogen</td>
<td>2 h</td>
<td></td>
<td>Light ↓ Strong color of urine ↑</td>
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<td>Oxidation in air</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phenazopyridine ↑</td>
<td></td>
</tr>
<tr>
<td>Bilirubin</td>
<td>2 h</td>
<td></td>
<td>Light ↓ Ascorbic acid ↓</td>
<td></td>
<td>Oxidation in air</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phenazopyridine ↑</td>
<td></td>
</tr>
<tr>
<td>Blood (erythrocytes)</td>
<td>1–4 h</td>
<td>1–4 h</td>
<td>Menstruation, strong physical activity</td>
<td>Oxidizing cleaning agents ↑</td>
<td>Fast lysis at specific gravity &lt; 1.010 and pH &gt; 7. Mix urine specimen well</td>
</tr>
</tbody>
</table>

**Tab. 1: Storage conditions, influencing factors and interference factors**
### Tab. 1 (Continued): Storage conditions, influencing factors and interference factors

<table>
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<td>In sediment:</td>
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<tr>
<td>Bacteria</td>
<td>24 h</td>
<td>Unstable hours</td>
<td>Urinary pH</td>
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<tr>
<td>Casts</td>
<td>1–4 h</td>
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<tr>
<td>Epithelial cells</td>
<td>1–4 h</td>
<td>1–4 h</td>
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<tr>
<td>Erythrocytes</td>
<td>1–4 h</td>
<td>1–4 h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukocytes</td>
<td>1–4 h</td>
<td>1–4 h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine culture</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low pH, antibiotics, infections outside the bladder (kidney stones, prostate), fastidious microorganisms</td>
<td></td>
<td>Results too low or false-negative results</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Indwelling catheter, collection technique (children, old persons), delayed working-up</td>
<td></td>
<td>Results too high or false-positive results</td>
</tr>
</tbody>
</table>

Cells are lysed in dependence on pH and osmolality. Osmolality < 300 mmol/L reduces storage stability.
Macrosopic assessment of urine specimens
Macroscopic assessment of the urine (its color and odour) is of little diagnostic value, but within the framework of visual examination of the specimens any striking color changes are usually reported as well.

The normal urine volume of an adult is some 700–2000 mL/day. An output of more than 2500 mL/day is classified as polyuria, an output of less than 500 mL/day as oliguria, and an output of less than 100 mL/day as anuria.

Color of the urine
The color of normal urine is due to the presence of porphyrins, bilirubin, urobin, uroerythrin, and some other, still unidentified, compounds. Striking changes should be reported in terms of definite colors: “red,” “brown,” “green,” etc.

Color changes are caused most often by drugs and their metabolites. A brick-red sediment is usually due to precipitation of urates in acidic urine (test: the precipitate redissolves on gentle warming). Haematuria is recognized by the presence of brown-red turbidity with a red-brown sediment. Darkening can also occur in the presence of substances other than those listed in the table below.

White turbidity can be due to:
- phosphates precipitating in alkaline urine (test: the precipitate redissolves on acidification with acetic acid)
- pyuria in massive bacterial or fungal infections (microbial count > 10⁷/mL)
- lipiduria in the presence of a nephrotic syndrome or on contamination with ointments
- massive proteinuria

Odour of the urine
Striking odour changes of clinical significance include:
- odour of fresh fruit or of acetone in the presence of ketonuria (sign of possible presence of metabolic acidosis, most often due to fasting or uncontrolled diabetes mellitus)
- “fetor hepaticus,” a musty odour of urine and breath in the presence of hepatic encephalopathies
- odour of alcohol in the presence of intoxication due to ethanol
- odour of ammonia in urinary tract infections due to urea-splitting bacteria; odour of hydrogen sulfide in urinary tract infections with proteinuria due to putrefacient bacteria
- a wide range of various odours due to intoxications and after certain foods

Pneumaturia
Pneumaturia (presence of fine gas bubbles) is a rare symptom pointing to the presence of a fistula between the urinary tract and the intestine.
<table>
<thead>
<tr>
<th>Color/ appearance</th>
<th>Endogenous causes</th>
<th>Suspicion of Drug</th>
<th>Exogenous causes Drug</th>
<th>Foods</th>
<th>Intoxications / infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorless</td>
<td>Polyuria</td>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yellow-brown</td>
<td>Bilirubin</td>
<td>Bilirubinaemia</td>
<td>Quinine</td>
<td>Anthrone (rhubarb)</td>
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<tr>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td>Methylidopa</td>
<td>Vitamin B₂</td>
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<td></td>
<td>Nitrofurantoin</td>
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<td>Phenytoin</td>
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<td>Sulfamethoxazol</td>
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<td>Porphyrin</td>
<td>Deferoxamine</td>
<td>Betanin (beetroots)</td>
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<td>Phenazopyridine</td>
<td>Rhodamine B</td>
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<td>(darkening)</td>
<td></td>
<td>(orange)</td>
<td>(ice cream)</td>
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<td>Bile</td>
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<td>Amitriptyline</td>
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<td>Evans blue</td>
<td>Pseudomonas</td>
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<td></td>
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<td>Resorcinol</td>
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<td></td>
<td>(darkening)</td>
<td>in malaria</td>
<td>(darkening)</td>
<td>Phenols</td>
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<td>Melanoma</td>
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<td>Homogentisate</td>
<td>Alkaptionuria</td>
<td>(darkening)</td>
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</tbody>
</table>

Tab. 2: Color changes in urine
Pre-analytical treatment and test performance

**Test performance**

1. Collect the urine specimen in a clean sterile container (preferably a disposable container).
2. Dip the test strip in the urine for no longer than 1 second.
3. On drawing the strip out of the sample run its edge over the rim of the container to remove excess liquid.
4. After 60 seconds (60–120 seconds for leukocytes) compare the reaction color in the test area against the color scale on the label.

Colors occurring only on the edges or ones that develop only after more than 2 minutes are not relevant for diagnostic purposes.

**Points to note**

- Urine examinations with test strips should be carried out within 2 hours at the latest
- The urine specimen should be mixed thoroughly prior to the test
- The specimens must always be kept in a refrigerator (at +4°C) if the tests cannot be done within 2 hours of the urine collection
- At the time of testing the samples must be at room temperature
- The test strip tubes must be stoppered again immediately after the removal of a test strip
- Remember to label the urine container

**Points to avoid at all times**

- Residues of cleaning agents or disinfectants falsify the results (false-positive findings for blood, protein and glucose)
- Freezing of the urine specimen will destroy leukocytes and erythrocytes and hence make the specimen unusable for subsequent microscopic examinations
- Specimens must not be centrifuged prior to test strip analysis
- Specimens must not be exposed to direct sunlight

**Quality assurance**

Quality assurance in urinalysis includes in addition to the analysis itself the operations of sample collection, preservation, preparation and transport. It is therefore necessarily interdisciplinary and requires involvement of the patient.
**Characteristics of urine test strips from Roche Diagnostics**

**Safe and hygienic handling**
The reagent paper and the underlying absorbent paper are covered over with a thin porous nylon mesh and fixed to a stable white carrier foil (Fig. 6).

**The nylon mesh**
- protects the reagent pad from contamination
- fixes the reagent pad reliably to the carrier foil
- ensures uniform color development through uniform penetration of the urine into the test area
- prevents falsification of the color by glue

The absorbent paper layer takes up excess urine and stops the test area colors from running.

**Semiquantitative results**
In the event of a pathological finding a color change occurs in the respective test area. The color intensity allows a semiquantitative evaluation of the result.

**Unequivocal color scale**
Special colorfast printing colors on the vial label allow easy and reliable evaluation of the results.

---

**Fig. 6: Structure of test strips from Roche Diagnostics**

- Nylon mesh
- Reagent paper
- Absorbent paper
- Carrier foil
**Long storage life**
A drying agent in the cap of the plastic tube protects the sensitive test strips from atmospheric humidity. The test strips are stable up to the expiry date specified on the package when stored and used according to the directions.

**High sensitivity**
An important evaluation criterion for the quality of urine test strips is the practical detection limit (Fig. 7), i.e. the concentration of the substance determined at which the test gives a positive result in 90 out of 100 different samples. The lower the detection limit, the more sensitively can pathological changes be identified by the test strip in question.

The practical detection limit is made such that even slight pathological changes in the urine are made visible by a clear color change in the test area.

---

**Fig. 7: Practical detection limit**

<table>
<thead>
<tr>
<th>% positive results</th>
<th>concentration of the analyte</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
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</tr>
<tr>
<td>90</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>
Protection against interference due to vitamin C
Vitamin C (ascorbic acid) inhibits the oxidation reactions for blood and glucose in the test area and can therefore lead to false-negative results in the presence of haematuria and glucosuria.

The test strips of the Combur-Test product line are protected against this interference by incorporation of iodate. Any vitamin C present in the urine sample is thus eliminated by oxidation. If the very wide use of ascorbic acid in the food industry is taken into account, and the numbers of people putting their faith in vitamin supplements, it obviously makes a decisive difference in haematuria and glucosuria diagnostics whether the urine test strip used is protected from vitamin C interference.

Significance of vitamin C
Vitamin C is added to many foods and beverages on account of its outstanding antioxidant and preservation activity; for example it is added to flour, bread, cakes and pastries, to sausages, cereal flakes, fruit and vegetable juices, to beer, and even to champagne. Many people in addition take pure vitamin C prophylactically in the form of vitamin tablets. All this can lead to elevated vitamin C levels in the urine and to interference in urinalysis when using test strips.

In a study published in 1992 Brigden et al.\(^1\) showed that an oral dose of as little as 100 mg vitamin C per day, or even a single glass of fruit juice, may already produce ascorbic acid concentrations of some 10 mg/dl in the urine. With conventional urine test strips these concentrations may be high enough to provoke interference. Combur-Test strips from Roche Diagnostics remain stable even in the presence of high concentrations of vitamin C, and false-negative reactions to blood and glucose are hardly ever observed.

Risks of ascorbic acid interference
It must be borne in mind that over 20% of all urine specimens may contain sufficient ascorbic acid concentrations to involve a risk of interference in testing for blood and glucose. The risk of false-negative results increases particularly sharply in the flu season, when people turn in large numbers to vitamin supplements, affecting the diagnosis of the following clinical pictures:

- **Blood:** glomerulonephritis, pyelonephritis, lithiasis, tumours
- **Glucose:** diabetes mellitus, glucosurias determined by kidney damage
Additional test areas for ascorbic acid on strips not protected from vitamin C interference will reveal an excessive vitamin C concentration in the patient’s urine, and the urine examination must then be repeated at a later time. On account of their potential falsification, the results are not used.

Reference
Specific gravity

Test principle
The test determines the ion concentrations in urine by reaction with a complex former and detection of the released protons.

Non-ionic constituents of the urine such as glucose or urea are not determined.

Sources of error
In the presence of small amounts of protein (100–500 mg/dL) there is a tendency to read off high values. The same occurs in the case of ketoacidotic urine.

An increase in urine specific gravity due to glucose concentrations >1000 mg/dL (>56 mmol/L) is not determined by test strips.

At pH 7 or higher the test result obtained has to be increased by 0.005 g/mL.

Influencing factors
The specific gravity of urine depends primarily on the amount of fluids drunk by the patient, but factors such as heavy sweating, the effect of low temperatures, or increased urine output provoked by diuretically active agents (e.g. coffee or certain medicines) also exert an influence, so that even in healthy persons the values can vary from 1.000 to 1.040 g/mL.

Clinical significance
The diagnosis of kidney function disturbances (e.g. a reduced concentration capacity) by determining the specific gravity of urine is today only of subordinate importance. Besides, controlled conditions are a prerequisite, such as fluid deprivation for 12 or 24 hours.

The diuresis factor can be used in the assessment of other urine parameters by means of the specific gravity; slightly elevated analyte values, e.g. the levels of protein, are more meaningful in samples having a low specific gravity than in concentrated urine.

Specific gravity is also significant in analysis of the urine for narcotics or for prescribed drugs in athletes, as it may point to manipulation of the specimen.

Values below 1.010 g/mL are of analytical significance, because in such urine erythrocytes and leukocytes undergo rapid lysis. This may explain negative sediment results with a positive test strip reaction.
**Test principle**
The pH test relies on a combination of three indicators, methyl red, bromthymol blue and phenolphthalein. In the pH range of 5–9 this gives a color gradation going from orange to yellow-green and to blue.

**Sources of error**
If the specimen is allowed to stand for too long, the urine may become alkaline (pH >7) as a result of bacterial decomposition of urea. The pH is then diagnostically meaningless.

**Reference ranges**
Course over the day: pH 4.8–7.4  
Morning urine: pH 5–6  

---

**Fig. 8: Principle of the urine pH test**

Acidic urine: mixed color orange  
Alkaline urine: mixed color green
Influencing factors
- Nutrition
- Animal protein leads to acidic urine, a vegetarian diet to strong alkalization
- Metabolic status
- Various diseases
- Medicines

Clinical significance
Persistently acidic or alkaline urine points to the possibility of a disturbance of the acid-base balance. Persistently alkaline pH values are evidence of an infection in the urogenital tract. High pH values are also of analytical significance because erythrocytes and leukocytes are lysed faster in such urine, which can explain the combination of negative sediment results with a positive test strip reaction.

Acidosis (pH <7) and alkalosis (pH >7) can also be due to the following causes:

Metabolic acidosis
- diabetic acidosis
- fasting
- medicines and toxins
- kidney failure
- renal tubular acidosis (pH rarely below 6.0)

Respiratory acidosis
- retention of CO₂ (emphysema)

Metabolic alkalosis
- severe potassium deficiency
- excessive intake of alkalis
- diuretics
- vomiting

Respiratory alkalosis
- infections
- fever
**Test principle**

The leukocytes excreted in the urine are almost exclusively granulocytes, whose esterase activity is detected in the test strip reaction. The test zone contains an indoxyl ester, which is cleaved by the granulocyte esterase. The free indoxyl released reacts with a diazonium salt to form a violet dye.

**Practical detection limit**

10–25 leukocytes/µL

**Reference ranges**

- Normal: <10 leukocytes/µL
- Borderline: 10–20 leukocytes/µL
- Pathological: >20 leukocytes/µL

**Specificity**

- The test detects the esterase activity of granulocytes and histiocytes (histiocytes are also produced in the presence of inflammatory processes and in microscopic examinations they are usually not distinguished from leukocytes)
- Not only intact but also already lysed leukocytes are detected, which are not found by urine sediment microscopy
- The test does not react to urine-pathogenic bacteria and trichomonads
- Epithelia, spermatozoa, and erythrocytes do not have any effect in the concentrations in which they can occur in urine

---

Fig. 9: Principle of the leukocyte test
Leukocytes

- pH values in the range of 4.5–9, nitrite in the presence of urinary tract infections, ascorbic acid, and ketones do not exert any influence

**Sources of error**
- If the urine is strongly colored, this intrinsic color could mask the color formed by the strip reaction
- Protein excretion in excess of 500 mg/dL and glucose excretion of over 2 g/dL could lead to a weaker color development, as could high doses of cephalaxin and gentamicin
- Preservatives falsify the test result (false-positive reading in the case of formaldehyde, false-negative in case of boric acid). Medication with imipenem, meropenem and clavulanic acid) could lead to false-positive results.

**Clinical significance**
Leukocyturia is an important guide symptom of inflammatory diseases of the kidneys and efferent urinary tract, e.g.
- bacterial infections: cystitis, urethritis, acute and chronic pyelonephritis
- abacterial infections due to yeasts, fungi and viruses
- parasite infestations, e.g. schistosomiasis
- glomerulopathies
- analgesics nephropathies
- intoxications
- urine-voiding disturbances

Leukocyturia occurs substantially more often in women than in men. This is explained on the one hand by the more frequent occurrence of urinary tract infections in women and on the other by the risk of contamination of the urine specimens by leukocytes from a vaginal discharge. One must therefore reckon with a positive leukocyte test in 30–40% of spontaneous urine specimens from women.

**The great majority of positive leukocyte findings is due to the presence of a bacterial urinary tract infection.**

If an inflammation is chronic or healed up, in particular, it is not rare to obtain a positive leukocyte reaction and yet fail to find any bacteria in the urine. This condition is known as “abacterial” leukocyturia. In chronic pyelonephritis leukocyturia is often the only symptom in the intervals between the acute episodes – the additional symptoms associated with the acute course, such as fever, kidney pains, proteinuria and erythrocyturia, are absent.

Abacterial leukocyturia can in addition constitute important evidence for the presence of tuberculosis or tumours.

**Clarification of leukocyturia**
The following procedure is recommended for further differential diagnostics:
- clarification of proteinuria, haematuria, nitrituria
- determination of the microbial count
- microscopic examination of the sediment for leukocyte casts
**Test principle**

Nitrite is detected by the same principle as that of Griess’ test. Any nitrate present in the urine is converted by bacterial reduction into nitrite:

Nitrate $\rightarrow$ bacterial reduction in urine $\rightarrow$ nitrite

The aromatic amine sulfanilamide reacts with nitrite in the presence of an acid buffer to form a diazonium compound, which is coupled with 3-hydroxy-1,2,3,4-tetrahydrobenzo-(h)-quinoline to form an azo dye. The intensity of the red color is a measure of the nitrite concentration present, but says nothing about the severity of the infection.

**Practical detection limit**

11 µmol/L (0.05 mg/dL).

**Reference range**

Bacteria-free urine does not contain any nitrite.

**Specificity**

The nitrite detection is specific for the presence of bacteriuria; the reaction is independent of the pH.

A single negative test does not exclude a urinary tract infection, because the microbial count and the nitrate content of the urine can vary. Absence of color on repeated testing is also not reliable evidence for the absence of a urinary tract infection.

---

**Fig. 10: Principle of the nitrite test**

![Chemical reaction and structures](image)
infection, since a pathogenic microorganism that does not form nitrite could be present. If there is clinical suspicion of an infection, therefore, it is advisable to go on in all cases to a determination of the microbial species and the microbial count.

**Sources of error**
False-negative results may occur as a result of:
- strong diuresis with frequent voiding of urine (the incubation time of the urine in the bladder is too short)
- fasting states
- parenteral nutrition
- vegetable-free diet
- specimens that have been left standing for too long (test done more than 4 hours after the specimen collection)

False-positive results may be due to:
- bacterial contamination of urine left to stand for too long
- treatment with medicines containing phenazopyridine

**Clinical significance**
Presence of nitrite in the urine is one of the most important symptoms of a bacterial urinary tract infection. A positive test strip result in the nitrite field is a reliable pointer to the presence of an acute infection.

After respiratory tract infections, urinary tract infections are the most common bacterial diseases. Their spread in the population varies with age and sex, increasing strongly with advancing age (Fig. 11). Women are particularly affected by this condition. During pregnancy, regular checking for urinary tract infections is indispensable. Men suffer from these infections increasingly after the age of 60. Recognition and early treatment of urinary tract infections is of decisive importance, because a progressive infection may lead to chronic kidney failure, pyelonephritic atrophic kidneys, and uraemia.

Normal urine does not contain any nitrite. The ingestion of even large amounts of nitrite or nitrite-containing therapy does not result in nitrite excretion. Any nitrite excreted through the urinary tract can therefore be attributed exclusively to bacterial reduction of nitrate.

Normal nutrition as a rule ensures a sufficiently high content of nitrate in the urine for the detection of bacteria. The most frequent pathogen responsible for urinary tract infections, E. coli, and most of the other urine-pathogenic organisms (Klebsiella, Aerobacter, Citrobacter, Salmonella, and to some extent also enterococci, staphylococci, and Pseudomonas) reduce urinary nitrate to nitrite and can therefore be detected indirectly with test strips.
On average about 50% of urinary tract infections can be identified by the nitrite test, but under the following conditions the recognition rate can be improved to more than 90%:

- Repeated checking of the first morning urine. Being a biological process, nitrite formation requires a reasonably long residence time of the urine in the bladder, at least 4–6 hours.
- Normal vegetable-containing nutrition on the preceding day. A normal vegetable-containing diet generally ensures a urinary nitrate level sufficient for performance of the test.
- Exclusion of antibacterial therapy.
- In the presence of antibiotic treatment or chemotherapy the enzyme metabolism and the microbial population are suppressed, so that not enough nitrite is formed for the test. All antibacterial therapy must therefore be discontinued at least 3 days before the urinalysis.

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<th>41–50</th>
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<td>♂ 9.9</td>
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<tr>
<td>Inpatients</td>
<td>♂ 17.1</td>
<td>♂ 17.2</td>
<td>♂ 17.2</td>
<td>♂ 16.0</td>
<td>♂ 13.5</td>
<td>♂ 20.6</td>
</tr>
</tbody>
</table>

*Fig. 11: Relative frequency of positive nitrite findings in urine samples*
Protein (Albumin)

Test principle
The detection reaction relies on the so-called protein error of pH indicators.

The protein test area contains a buffer mixture and an indicator which undergoes a color change from yellow to green in the presence of protein, even though the pH is held constant.

Reference range
Below 10 mg/dL (for total protein).

Specificity
The indicator reacts particularly sensitive-ly to albumin excreted in the presence of kidney damage. The sensitivity to other proteins (e.g. γ-globulins, Bence-Jones protein, proteoses, peptones, mucoproteins) is lower.

Medicines such as quinine, quinidine, chloroquine, sulfonamides, and penicillin have virtually no effect on the color reaction. The same applies to pH values of 5–9 and to various urine specific gravity.

Practical detection limit
A clear color reaction is obtained at a concentration of 6 mg/dL albumin and above, situated somewhere between the negative color field and 30 mg/dL on the comparison scale.

Evaluation
30 mg/dL was selected as the first positive comparison color, because pathological proteinurias are normally above this value. Color changes that do not unequivocally reach the value of 30 mg/dL are normally assessed as negative. In patients with clini-

![Fig. 12: Principle of the test for protein](image-url)

Fig. 12: Principle of the test for protein
Protein (Albumin)

cally manifest kidney damage, who often have only low-grade proteinuria, this finding cannot, however, be used for controlling the course of their illness.

**Sources of error**
False-positive results are obtained under the following conditions:
- infusion of polyvinylpyrrolidone (a blood substitute)
- presence of residues of disinfectants containing quaternary ammonium groups or chlorhexidine in the urine container
- phenazopyridine medication

**Clinical significance**
Proteinuria is a frequent symptom in renal diseases, but it is also non-specific. It is not proof of nephropathy, nor does its absence exclude nephropathy. Detection of protein in the urine should therefore always be followed by differential diagnostics.

**Benign proteinuria**
In persons with healthy kidneys proteinurias are observed predominantly up to the age of 30, and account for up to 90% of the proteinurias observed in this age group. The causes of these benign proteinurias are in particular physical stress (sport), emotional stress, orthostatism and lordosis. Proteinurias associated with hypothermia, heat, pregnancy, or the use

![Daily course of urinary protein excretion](image)

Fig. 13: Daily course of urinary protein excretion
of vasoconstrictively acting drugs are also as a rule benign. Benign proteinuria has been observed in 20% of women during pregnancy.

Benign proteinurias occur intermittently. While in the morning urine the protein excretion is normal, values reaching 500 mg/dL may be observed in the course of the day. On the basis of this property benign proteinuria is relatively easily distinguished from the pathological form by repeated testing of the first morning urine (Fig. 13).

Additional examinations of the urine for nitrite, blood, and leukocytes, and measurement of the blood pressure, give normal findings if the proteinuria is benign. If a benign proteinuria is diagnosed, however, it should be monitored in order to detect the development of a kidney disease in good time.

**Extrarenal proteinuria**

Protein is detected in the urine in many mostly acute clinical pictures, such as colics, epileptic fits, infarcts, strokes, head injuries, and postoperative states. These proteinurias disappear after the extrarenal cause has been eliminated. Proteinurias due to fever are usually harmless, but they do require clinical supervision and course monitoring.

**Renal proteinuria**

An increase in the permeability of the glomerular capillaries due to pathological processes leads to the development of renal proteinuria.

Renally determined proteinurias are as a rule persistent and are observed in both nocturnal and daytime urine. In general the level is in excess of 25 mg/dL, the most pronounced proteinurias being observed in nephroses. In glomerulonephritis the protein excretion is usually 200–300 mg/dL, but lower values must be reckoned with in the event of glomerulonephritis associated with few symptoms. This proteinuria is usually accompanied by microhaematuria.

Tubular proteinuria can be due to lesions of the tubule cells and/or to a disturbance of the tubular uptake of proteins from glomerular filtrate. This proteinuria is encountered e.g. in the presence of pyelonephritis, cystic kidneys, and gouty kidneys.

Intermittent protein excretion is often found in chronic pyelonephritis.

**Postrenal proteinuria**

Postrenal proteinuria can occur following inflammation of the bladder or prostate and on bleeding in the urinary tract.
Glucose

Test principle

The detection of glucose is based on a specific glucose-oxidase-peroxidase reaction in which D-glucose is oxidized enzymatically by atmospheric oxygen to δ-D-gluconolactone. The hydrogen peroxide formed oxidizes the indicator TMB under peroxidase catalysis, to give a blue-green dye which on the yellow test paper causes a color change to green.

Practical detection limit

For ascorbic-acid-free urine the practical detection limit is around 2.2 mmol/L (40 mg/dL), so that even slightly pathological glucosurias can be detected with high reliability. The upper limit of physiological glucosuria in the first morning urine is around 0.8 mmol/L (15 mg/dL).

Specificity

The enzymatically catalyzed reaction sequence ensures that glucose is the only urinary constituent that will react and give a positive test result.

Reference range

<table>
<thead>
<tr>
<th>Type</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting morning</td>
<td>&lt;1.1 mmol/L (&lt;20 mg/dL)</td>
</tr>
<tr>
<td>Daytime urine</td>
<td>&lt;1.7 mmol/L (&lt;30 mg/dL)</td>
</tr>
</tbody>
</table>

Test principle

Fig. 14: Principle of the glucose test
Ketones do not interfere, and the pH of the urine similarly does not exert any influence on the test result. However, before its analysis with test strips the urine must not be acidified.

**Sources of error**
The best known interference factor for enzymatic glucose detection in urine, the presence of ascorbic acid (vitamin C), has been largely eliminated in this test. At glucose concentrations of 5.5 mmol/L (100 mg/dL) and higher even high ascorbic acid contents practically never lead to false-negative test results.

Other metabolic products and drug metabolites which have a reducing action and can exert an influence on the reaction, such as the degradation products of salicylates, normally occur only in small amounts in the urine and cause interference only in their sum.

False-positive results can occur as a result of the presence of residues of peroxide-containing or other strongly oxidizing cleaning agents in the urine container.

**Clinical significance**
The determination of glucose in urine has a high diagnostic value for early detection of diabetes mellitus and for course control.
Glucose higher than in healthy persons. In older patients in particular the renal threshold is often so high that no glucose appears in the urine despite diabetic blood glucose levels.

In spite of all these restrictions, detection of urinary glucose is of major significance for early detection, control, and self-monitoring of diabetes.

The following conditions are seen as risk factors for diabetes mellitus:
- obesity
- hyperlipoproteinaemia
- hyperuricaemia
- gout
- hypertension
- coronary, cerebral, and peripheral blood flow disorders
- diseases of the liver and the bile tract
- chronic urinary and respiratory tract infections
- chronic skin diseases

Further risk factors are:
- Age over 40
- Familial predisposition to diabetes
- Mothers of children with a large weight at birth (over 4.5 kg)

Renal glucosuria
If the renal threshold is significantly lowered owing to reduced glucose reabsorption in the renal tubules, increased glucose excretion will be found in the urine even if the blood glucose is normal, below the diabetic range. The frequently
observed glucosuria in the course of pregnancy (in 5–10% of cases) is also due normally to a lowering of the renal threshold. After the woman has given birth this kind of glucosuria is no longer observed.

**Alimentary glucosuria**
This can occur after an extremely large ingestion of carbohydrates.

**Glucosuria in the presence of kidney damage**
Symptomatic renal glucosuria occurs when kidney function falls to 30% or less of normal renal performance. This renal diabetes mellitus is also observed in acute renal failure.

**Diabur-Test 5000**
**Keto-Diabur-Test 5000**
These two test strips have been designed especially for monitoring the urinary glucose level in diabetes mellitus. The measurement range of the glucose field, extended compared with the multitest strips, permits an exact differentiation of the urine’s glucose content from 0 to 5%.

The glucose test in (Keto-)Diabur-Test 5000 is also based on the glucose-oxidase-peroxidase reaction and is specific for glucose. Other sugars, like fructose or galactose, do not react.
Ketones

**Test principle**
The detection of ketones is based on the principle of Legal’s test. Acetoacetate acid and acetone react with sodium nitroprusside and glycine in an alkaline medium to give a violet color complex. The reaction is specific for these two ketones. β-hydroxybutyric acid does not react.

**Reference range**
Below 0.5 mmol/L (below 5 mg/dL) for acetoacetic acid.

**Practical detection limit**
The test is substantially more sensitive for acetoacetic acid (detection limit 5 mg/dL = 0.5 mmol/L) than for acetone (detection limit about 40 mg/dL = 7 mmol/L).

**Specificity**
Glucose, protein, and ascorbic acid do not interfere.

**Sources of error**
Phenylketones and phthalein compounds produce red colors on the test patch. These are, however, quite different from the violet colors produced by ketone bodies. Captopril, mesna (2-Mercaptoethanesulfonic acid sodium salt) and other substances containing sulfhydryl groups may produce false-positive results.

**Clinical significance**
Ketones (acetoacetic acid, β-hydroxybutyric acid, and acetone) occur in the urine when an increased fat degradation takes place in the organism owing to

---

**Ketones**

<table>
<thead>
<tr>
<th>Test principle</th>
<th>Ketones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na₂[Fe(CN)₅NO] + CH₃C-R + NaOH → Na₃[Fe(CN)₅N=CHC-R] + H₂O</td>
<td>Sodium nitroprusside Ketone Color complex (violet)</td>
</tr>
</tbody>
</table>

Fig. 16: Principle of the ketone test
insufficient supply of energy in the form of carbohydrates.

Predominance of lipolysis over lipogenesis leads to increased free fatty acid levels in serum, and on their breakdown in the liver more acetyl-coenzyme A is formed than can be utilized by other metabolic processes, e.g. the tricarboxylic acid cycle. This excess is converted into acetoacetic acid, which in turn is partly transformed into β-hydroxybutyric acid and to a smaller degree into acetone.

**Ketonuria in diabetes mellitus**
Detection of ketones in the urine (acetoacetic acid and acetone) is particularly important in diabetes mellitus for checking metabolic decompensation.

Precomatose and comatose states in diabetes are almost invariably accompanied by ketoacidosis, with the exception of hyperosmolar comas. Relative or absolute insulin deficiency causes reduced glucose utilization in fat and muscle cells and triggers increased lipolysis. The resulting ketones in combination with other pathophysiological changes of the dysregulated metabolism (dehydration, electrolyte shifts) can lead to diabetic coma.

Diabetic coma is a life-threatening event, and ketonuria is an early symptom of the metabolic dysequilibrium.

All diabetics should check their urine for ketones on a regular basis. In juvenile and insulin-dependent diabetics in particular, in whom coma may develop within a few hours, a check for ketones in urine should therefore always form part of self-monitoring, side by side with the checks on urinary glucose.

Progressive ketoacidotic metabolic dysregulation may occur if the diabetic patient is not sufficiently well managed with insulin. The condition is characterized by ketone excretion in urine, an odour of acetone on the breath, and increased urinary levels of glucose.

**Ketonuria of non-diabetic origin**
Ketones are also found in the urine in the following situations:
- Fasting states
- Slimming diets low in carbohydrates, or protein-rich nutrition, or total starvation diets. The acid-base turnover, however, remains fully compensated if good kidney function is ensured by sufficient intake of fluids. Checking for ketones also serves in such cases as a control of compliance with the diet
- Acetonaemic vomiting in small children
- Fever, especially in the presence of infectious diseases
- Pernicious vomiting in pregnancy
- Congenital metabolic diseases
Complete absence of urobilinogen in the urine, perhaps on complete obstruction of the common bile duct, cannot be detected.

**Specificity**
The test is specific for urobilinogen and does not react with other diazo-positive substances. It is also not subject to the interference known in the Ehrlich test. No red color is formed in the presence of porphobilinogen, indican, p-aminosalicylic acid, sulfonamides, sulfonylureas, and other substances occurring in the urine.

**Test principle**
p-methoxybenzenediazonium fluoroborate, a stable diazonium salt, forms a red azo dye with urobilinogen in an acid medium.

**Reference range**
Below 17 µmol/L (below 1 mg/dL).

**Practical detection limit**
The practical detection limit is around 7 µmol/L (0.4 mg/dL), at which level the urobilinogen also present in normal urine gives a pale pink color. Differentiation between normal and pathological urine is possible by means of color comparison.

---

**Fig. 17: Principle of the urobilinogen test**

\[
\begin{array}{c}
\text{Urobilinogen} \\
\begin{array}{c}
\text{Acid medium} \\
\end{array}
\end{array}
\]

\[
\begin{array}{c}
\text{Diazonium salt} \\
\text{BF}_4^- + \text{Urobilinogen} \rightarrow \text{Azo dye (red)}
\end{array}
\]
**Sources of error**

False-negative results occur under the following conditions:
- prolonged standing of the urine specimen, especially in direct sunlight, leads to oxidation of urobilinogen
- formaldehyde preservation with concentrations in excess of 70 mmol/L (200 mg/dL) in the urine

False-positive results:
- may be due to drugs that color the urine red or that are red in an acid medium (e.g. phenazopyridine)

A momentary yellow coloration of the test paper points to the presence of large amounts of bilirubin, but the reading is not impaired. In rare cases a green or blue color may develop slowly about 60 seconds after immersion in the urine.

**Clinical significance**

Urobilinogen is formed by bacterial reduction from bilirubin secreted into the intestine with the bile. It is then reabsorbed into the bloodstream and is subsequently broken down in the liver and partly excreted in the urine.

Detection of urobilinogen in the urine is indicative of two possible causes:
- a disturbance of liver function due to a primary or secondary liver disease
- an increased degradation of haemoglobin due to a primarily haemolytic disease or secondarily to other disease pictures

Urobilinogen is excreted in increased amounts in the urine when in the entero-hepatic circulation of the bile pigments the functional capacity of the liver is impaired or overloaded, or when the liver is bypassed.

**Overloading of the functional capacity of the liver**

If large amounts of bilirubin, and therefore also of urobilinogen, are formed as a result of increased degradation of haemoglobin, the functional capacity of the liver may be exceeded even though the liver can deal with 2–3 times the normal amounts of urobilinogen. The urobilinogen not processed further in consequence of such overloading of the liver’s capacity passes into the bloodstream and is finally excreted in the urine via the kidneys.

The causes of overloading of the functional capacity of the liver may be listed as follows:
- Increased degradation of haemoglobin in:
  - haemolytic anaemia
  - pernicious anaemia
  - intravasal haemolysis, e.g. as a result of intoxications, infectious diseases, or transfusion accidents
  - polycythaemia
  - reabsorption of large extravasations of blood
Increased formation of urobilinogen in the intestine due to:
- pronounced constipation
- enterocolitis
- ileus
- increased fermentation processes

Increased urobilinogen formation and reabsorption in bile tract infections, e.g. in cholangitis.

Incomplete obstructions of the bile ducts (depending on the degree of parenchyma cell damage)

In viral hepatitis in particular urobilinogenuria is very often encountered, while the cardinal symptom proper, namely jaundice, is mostly absent.

**Bypassing of the liver**

In certain pathological conditions, e.g. in liver cirrhosis, the influx of portal vein blood and therefore also of urobilinogen to the liver is reduced. Part of the urobilinogen then bypasses the liver and is excreted in increased amounts in the urine.

The causes of liver bypass include the following conditions:
- liver cirrhosis with portal hypertension
- portal vein thrombosis
- occlusion of the hepatic vein

**Impairment of the functional capacity of the liver**

Liver diseases exert an adverse effect on its functional capacity. The urobilinogen coming in through the portal vein can no longer be completely processed and appears in increased amounts in the urine.

The functional capacity of the liver may be reduced in the following situations:
- Viral hepatitis (except in very severe forms or for a short time at the peak of the illness)
- Chronic hepatitis and liver cirrhosis (depending on the degree of damage to the parenchyma cells)
- Toxic liver damage (e.g. due to alcohol, fungal poisons, organic solvents, medicines, and toxins produced in the course of infections or sepsis)
- Congestion of the liver (e.g. after a cardiac infarct, acute heart failure, or cardiac insufficiency)
- Liver hypoxia (e.g. after severe anaemias or intoxications with carbon monoxide)
- Liver tumours (depending on their size and location)
Absence of urobilinogen in the urine

Urobilinogen is absent in the urine in situations comprising failure of bile production in the liver cells, disturbances of bile secretion into the intestine, and absence of bilirubin reduction in the intestine, even though a severe disease may be present.

Possible causes of failure of urobilinogen formation:
- complete obstruction of the common bile duct in the absence of a bile tract infection
- complete stoppage of bile production in the liver (very severe viral hepatitis, severe toxic liver damage)
- absence of intestinal flora (physiological in newborn babies, rarely observed after intensive antibiotic therapy)
Bilirubin

Test principle
The test reaction is coupling of the bilirubin with a stable diazonium salt (2,6-dichlorobenzenediazonium fluoroborate) in an acid medium of the test paper. A red-violet azo dye is formed, causing a color change to violet.

Reference range
Adults below 3.4 µmol/L (below 0.2 mg/dL).

Practical detection limit
The practical detection limit in urine free from ascorbic acid lies at 9 µmol/L (0.5 mg/dL). In favourable cases as little as 3–7 µmol/L (0.2–0.4 mg/dL) may give a positive reaction.

Sources of error
The sensitivity is degraded by large amounts of ascorbic acid in the urine specimen.

False-negative results:
- Prolonged standing of the urine, particularly in direct sunlight, leads to oxidation of the bilirubin.

False-positive results:
- Medicines that color the urine red or that are themselves red in an acid medium, e.g. phenazopyridine.

Clinical significance
As a result of conjugation (esterification) with glucuronic acid bilirubin becomes water-soluble and therefore susceptible to excretion by the renal route. The bilirubin present in urine is always conjugated (direct) bilirubin.

In all pathological processes that increase the concentration of conjugated bilirubin in plasma, the excretion of bilirubin in urine can reach considerable levels. Conjugated bilirubin is found in the following

\[
\text{Diazonium salt} + \text{Bilirubin} \xrightarrow{\text{Acid medium}} \text{Azo dye (red-violet)}
\]

Fig. 18: Principle of the bilirubin test
situations as a result of its increased passage from the liver into plasma:

- increased intracanalicular pressure due to an extrahepatic or intrahepatic obstruction
- periportal inflammation or fibrosis
- swelling or necrosis of the liver cells

Bilirubinuria can be encountered in the following clinical conditions:

**Damage to the liver parenchyma**
This is the commonest cause of bilirubinuria. The cell membrane permeability increases and conjugated bilirubin appears in the blood and via the kidneys in urine:

- acute and chronic viral hepatitis
- alcoholic hepatitis
- fatty liver hepatitis
- liver cirrhosis
- toxic liver cell damage

**Bilirubin excretion disturbances**
When conjugated bilirubin can no longer be secreted into the bile ducts as a result of an excretion disturbance of the liver, various amounts of it pass through the cell membranes or via the lymph into blood, depending on the severity of the hepatic disturbance, and escape via the kidneys into urine:

- the Dubin-Johnson syndrome
- Rotor’s syndrome
- intrahepatic cholestasis and drug icterus
- icterus of pregnancy
- cholestasis occurring after infectious diseases

**Impedance of bile flow**
If bile flow is impeded within or outside the liver or interrupted altogether, the result is cholestasis and with it a rise in conjugated bilirubin in the serum and bilirubin excretion in urine:

- cholangitis
- cholangiolitis
- cholecystitis
- intrahepatic bile duct carcinoma
- extrahepatic obstructive jaundice due to stone occlusions, tumours, and strictures

**Absence of bilirubinuria in hyperbilirubinaemia**
Diseases in which only unconjugated bilirubin is increased in the serum proceed without bilirubinuria, because unconjugated bilirubin is not excreted by the renal route. The cause may be an oversupply of bilirubin in the liver cells or a disturbance of uptake or conjugation:

- haemolytic jaundice
- jaundice of the newborn
- Gilbert-Meulengracht disease
- Crigler-Najjar syndrome

On account of the differentiated liver diagnostics in serum, detection of bilirubin in urine has now lost much of its former significance.
Blood (erythrocytes/hemoglobin)

**Test principle**
The test is based on the peroxidative action of haemoglobin or myoglobin which catalyzes the oxidation of the color indicator TMB by an organic hydroperoxide (2,5-dimethylhexane-2,5-dihydroperoxide) to give a blue-green dye which on the yellow test paper causes a colour change to green. High sensitivity is achieved by the addition of an activator to the reagent mixture.

The risk of interference from ascorbic acid known for this oxidation reaction has been eliminated; the test area has an iodate-impregnated mesh laid over the actual reagent paper, which oxidizes any ascorbic acid present. Even high ascorbic acid concentrations have virtually no influence on the test result.

Intact erythrocytes are lysed on the test paper and the haemoglobin released sets off the color reaction. Visible green points are formed. In contrast, haemoglobin dissolved in the urine (erythrocytes in lysed form) leads to the development of a uniform green color.

**Reference range**
0–5 erythrocytes/µL.

**Detection limit**
The practical detection limit for intact erythrocytes is about 5 erythrocytes/µL and for haemoglobin the amount corre-

![Fig. 19: Principle of the test for blood (erythrocytes/hemoglobin)](image-url)
Blood (erythrocytes/hemoglobin)

...sponding to around 10 erythrocytes/µL. The practical detection limit of the test reaches the limit of the normal range.

**Specificity**

The test is specific for haemoglobin and myoglobin. Other cellular constituents of the urine, such as epithelia, leukocytes, and spermatozoa, have no effect. The rarely encountered green coloration of leukocyte-containing urine specimens is probably attributable to haemoglobin.

**Sources of error**

- In test strips from Roche Diagnostics the interference due to ascorbic acid (vitamin C) in the detection of blood has been widely eliminated so that ascorbic acid has virtually no influence on the test results.
- False-positive results can be obtained if the urine contains residues of strongly oxidizing cleaning agents from the container.

**Evaluation**

**Erythrocytes**

The observation of individually separated to closely set green dots on the test paper points to the presence of intact erythrocytes.

At higher concentrations the dots may be so close together that the test area appears almost uniformly green. Dilution of the urine 1:10 or 1:100 with 0.9% (physiological) saline and repetition of the test with another strip then makes it possible to decide whether intact erythrocytes or free haemoglobin is present.

A finding of 5–10 erythrocytes/µL requires repeated checks on the urine, and if it is obtained again must be clinically clarified.

**Haemoglobin**

A homogeneous green color of the test area points to the presence of free haemoglobin or lysed erythrocytes, or to the presence of myoglobin.

A weaker green color, as a first sign of a positive reaction, requires a repetition of the test with a fresh urine specimen. This second test may reveal, inter alia, intact erythrocytes which at the time of the first test had already become haemolyzed. Persistence of the finding requires a clinical clarification in all cases.
Blood (erythrocytes/hemoglobin)

In the event of a weakly positive haemoglobin reaction the cause may also be simply heavy physical exertion. This can be easily excluded from the anamnesis.

**Partial haemolysis**
Partial haemolysis of erythrocytes present in the urine leads to the appearance on the test area of individual green dots against a diffuse green background. An exact assignment of the comparison color is then impossible, because the degree of haemolysis can be very variable as a function of age, concentration, and pH of the urine. A repeat test with a fresh urine specimen is indicated.

**Clinical significance**
Haematuria, excretion of erythrocytes in the urine, is encountered in many pathological conditions, and careful clarification of its cause is therefore absolutely necessary.

This applies both to microhaematuria and to macrohaematuria, red coloration of the urine perceptible to the naked eye due to the presence of more than 0.5 mL blood per litre of urine, corresponding to approximately 2500 erythrocytes per µL.

The principal causes of haematuria are conditions relating to the kidneys and the urogenital tract (Fig. 20).

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**Fig. 20: Important renal and postrenal causes of haematuria**

- Glomerulonephritis
- Renal tumour
- Kidney stone
- Pyelonephritis
- Ureteral tumour
- Ureteral stone
- Bladder carcinoma
- Cystitis
- Bladder stone
- Prostata adenoma
Stone formation
Approximately 1–3% of the population suffers from urolithiasis or is at a risk of urolithiasis. Oxalate-containing stones (about 60%), phosphate-containing stones (about 20%), and uric acid calculi (about 25%) are particularly frequent. Most of these patients also exhibit hyperuricaemia. Men are affected by the condition much more often than women. Stones in the efferent urinary tract as a rule provoke acute colic-like pains, though the initial stage of stone formation may be completely painless. Detection of haematuria is then often the first symptom.

Tumour
The possibility of a tumour should always be suspected until the cause of the haematuria has been clarified.

Microhaematuria is decisive for early detection of malignant tumours in the kidneys, the efferent urinary tract, and the bladder. Determination of this symptom is therefore very important, since tumours often remain painless for a long time.

Glomerulonephritis
In the presence of glomerulonephritis haematuria acts as a detectable leading symptom in approximately 90% of the cases. Proteinuria and hypertension are also often observed in addition. Glomerulonephritis is mostly encountered in children and in adults under the age of 30.

Most forms of glomerulonephritis can be attributed directly or indirectly to an earlier infection. The important forerunner diseases of glomerulonephritis and other glomerular damage may be listed as follows:

- sore throat, chronic tonsillitis
- colds, influenzal infections, pneumonia
- scarlet fever, diphtheria, measles, mumps
- sinusitis, otitis
- skin infections, particularly in children
- lupus erythematosus
- relapsing dental foci
- chronic appendicitis
- endocarditis lenta
- polyarteritis nodosa

Elimination of these typical forerunner conditions is necessary to prevent the subsequent development of glomerular damage. The possibility of a renal involvement is checked most easily by the determination of microhaematuria.

Pyelonephritis
According to clinical data the incidence of pyelonephritis is estimated at 5–8%. The population groups affected most often are women and older men. Haematuria is present in one-third of these patients.
Blood (erythrocytes/hemoglobin)

Haemorrhagic diatheses
The following causes of haemorrhagic diatheses come into consideration:
- treatment with anticoagulants
- haemophilia
- coagulopathies
- thrombocytopenia

Further diseases
- urinary tract infections (cystitis, urogenital tuberculosis)
- toxic and hypoxic damage and degenerative changes in the glomeruli
- papillary necrosis
- trauma to the kidneys and urinary tract
- renal infarct
- renal cysts
- gouty kidney
- renal congestion in the presence of right-ventricular failure
- hypertension in the presence of vascular renal involvement
- diabetes mellitus
- lupus erythematosus

Haemoglobinuria and myoglobinuria
In contrast to haematuria, in which intact erythrocytes are excreted, in haemoglobinuria the urine contains free haemoglobin. This appears in the urine when erythrocytes have been broken down within the vascular system. Following intravasal haemolysis the haemoglobin passes into the urine as soon as the haptoglobin-binding capacity of the plasma and the tubular reabsorption capacity for haemoglobin have been exceeded. This occurs as a rule from plasma haemoglobin concentrations of around 60 µmol/L (100 mg/dL).

Myoglobinuria is generally due to muscular injury or muscular necrosis, when the myoglobin level in plasma exceeds 9–12 µmol/L (15–20 mg/dL).

Since haemoglobin and myoglobin are difficult to distinguish in a urine specimen, some of the positive test results obtained after heavy physical exertion must be attributed to myoglobinuria.

The causes of haemoglobinuria or myoglobinuria are as follows:
- severe haemolytic anaemia
- severe intoxications
- severe infectious diseases
- burns
- intensive physical exertion, e.g. in training athletes
- muscle injuries
- progressive muscle diseases
**Principle of test strip sieve**
Several comparison studies have shown that pathological changes in the urine can be detected more reliably with the aid of multitest strips than by examinations of the sediment. This led to the development of the “test strip sieve” concept, a stepwise procedure in which the two examination methods are efficiently combined.

The urine specimen is first routinely investigated with test strips for leukocytes, blood, protein, nitrite, and a pH greater than 7. If at least one of these parameters is found to be positive, the urine is designated as “microscopically relevant.” These specimens are then immediately checked for sediment constituents important for differential diagnostics or subjected to a bacteriological examination.

If the test strip results turn out to be negative and there is nothing in the patient’s medical history or clinical picture to raise suspicion of a pathological process, the laborious and time-consuming microscopy and bacteriology need not be carried out.

On average every other sample is thus excluded from subsequent examination of the sediment, resulting in an appreciable rationalization of the urinalyses.

The reliability of the “test strip sieve” in picking out pathological specimens is

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**Fig. 21: Rational urine diagnostics according to the “test strip sieve” concept**

- **Leukocyturia**
- **Haematuria**
- **Proteinuria**
- **Nitrituria**
- **pH > 7**

All results negative, no suspicious signs in the medical history or the clinical picture: no further urinalysis necessary. Microscopic examination of the urine can thus be avoided in about half of the cases.

One or more of the test strip results are positive: indication for targeted microscopic and/or bacteriological examination of the urine.
approximately 95%, while in the case of sediment analyses only about 80–85% of relevant urine specimens can be recognized as conspicuous.

The “test strip sieve” does not detect various types of crystalluria and hyaline casts, but the diagnostic informative power of these parameters is low.

**Microscopy/test strip comparison**
Test strips allow a direct or indirect detection of the microscopic elements listed in Fig. 22.

For red and white blood cells the two methods are in good agreement, as long as the cells are still intact and microscopically detectable.

With increasing lysis low or false-negative results are obtained in the microscopic examination.

Cell lysis is accelerated by the following conditions:
- low specific gravity or osmolality of the urine
- high pH (pH > 7)
- long standing time of the urine (> 2 hours)
- high room temperature

In contrast, the haemoglobin from erythrocytes and the esterase from leukocytes are still detectable with urine test strips after several hours. Moreover, the centrifugation of the urine specimen necessary for subsequent microscopy leads to an appreciable loss of the cells.

The concentration values on the test color scales and the reflectance photometric printouts of the results (erythrocytes/µL, leukocytes/µL) for test strips are based on comparisons with chamber counting. The conversion into numbers of cells per high power field is inexact, because sediment examination has still not been standardized and its result is influenced by various factors such as the sample volume or the duration of centrifuging.

<table>
<thead>
<tr>
<th>Test strips</th>
<th>Microscopic elements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>Erythrocytes, erythrocyte casts</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>Leukocytes, leukocyte casts</td>
</tr>
<tr>
<td>Protein</td>
<td>Granular casts, waxy casts</td>
</tr>
<tr>
<td>Nitrite</td>
<td>Bacteria</td>
</tr>
</tbody>
</table>

Fig. 22: Microscopic clarification of pathological test strip findings
Microscopic assessment of the sediment

Urinalysis with test strips often requires an additional microscopic examination of the sediment in order to support the diagnosis. In the following indications additional examination of the sediment is necessary to supplement the test strip result:
- one or more pathological test strip findings
- the patient exhibits symptoms of a kidney or efferent urinary tract disease
- course control of a kidney or efferent urinary tract disease
- determination of a suspicious result.

A cell atlas showing the most important urinary sediment constituents is included in the Appendix to this brochure.

Principle
Sediment analysis consists of a microscopic examination of the precipitate of a centrifuged specimen of native urine, as a rule using ×10 and ×40 objectives. The elements investigated are cells, casts, and individual microorganisms. It should be noted that sediment analysis is not standardized and does not yield valid quantitative results.

Test material
Midstream urine collected not more than 2 hours earlier, without the use of preservatives. The concentrated morning urine is optimal, because erythrocytes and leukocytes are readily haemolyzed in hypotonic urine.

Working up
- 10 mL volumes of well-mixed urine are filled into centrifuge tubes with a tapered bottom and centrifuged for 5 minutes at about 400 g (1500 revolutions per minute with a radius of 15 cm)
- The supernatant is decanted in a single operation, without swirling up the sediment or entraining it into the liquid phase
- The sediment is then resuspended in urine running back down the tube walls

Performance of the examination
- A small droplet (about 20 µL) of the sediment is placed in the middle of a clean microscope slide.
- A cover slip is then placed on it, avoiding the formation of air bubbles.
- Using a ×10 objective, the sample is checked for casts parallel to the edges of the cover slip.
- Using a ×40 objective, at least 10 fields are inspected.
- The results are documented as follows:

<table>
<thead>
<tr>
<th>Cells</th>
<th>Description</th>
<th>Corresponding Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+)</td>
<td>0–1 per field</td>
<td>0–1 per field (corresponds to about 0,3 µL)</td>
</tr>
<tr>
<td>+</td>
<td>1–5</td>
<td>1–5 µL</td>
</tr>
<tr>
<td>++</td>
<td>6–15</td>
<td>6–15 µL</td>
</tr>
<tr>
<td>+++</td>
<td>16–50</td>
<td>16–50 µL</td>
</tr>
<tr>
<td>Abundant</td>
<td>&gt;50</td>
<td>&gt;50 µL</td>
</tr>
</tbody>
</table>
Microscopic assessment of the sediment

Result
If urinalysis with test strips was carried out at the same time, the results are interpreted in combination and documented as a joint finding.

Erythrocytes
Round discs without nuclei (diameter 7–8 µm), without granules, with a doubly-contoured margin; in hypertonic urine they are shrunken into a thorn apple form; after emergence of their haemoglobin they fade to pale shadows. Deformed (dysmorphic) erythrocytes are of glomerular origin and are indicative of the presence of a kidney disease.

Sources of error: Possible confusion with fat droplets or yeast cells (smaller, oval, often germinating).

Reference interval: 0–5 per field of view, >30% of dysmorphic erythrocytes points to their glomerular origin.

Leukocytes
Almost exclusively granulocytes (diameter 10–12 µm).

Sources of error: In the case of women spontaneous urine gives up to 40% of false-positive results due to vaginal contamination.

Reference interval: 0–5 per field of view.

Epithelial cells
Pavement or squamous epithelium cells always originate from the urethra or the external genitals and are regarded as contamination.

Transitional epithelium cells are smaller than pavement epithelium cells, often have tail-like processes, and come from the efferent urinary tract.

Renal epithelium cells are the only ones of diagnostic significance. They come from the tubules and resemble leukocytes; they are distinguished by their large round nuclei.

Casts
Protein-containing cylindrical casts from the renal tubules, with a diameter of 15–50 µm.

Hyaline casts are transparent, colorless, and structureless formations of Tamm-Horsfall protein, a mucoprotein secreted by the distal tubules. They often appear in the urine following physical exertion, prolonged standing, or fever, and they have no diagnostic significance.

Granular casts are observed most often in the presence of chronic glomerulonephritis. Droplets of plasma proteins or fragments of lysed cells are included in the matrix.
**Microscopic assessment of the sediment**

**Erythrocyte casts** are made up of erythrocytes embedded in a homogeneous matrix. They point to a renal origin of the haematuria.

**Leukocyte casts** similarly point to a renal origin of the leukocyturia, which can be differentiated from a leukocyturia due to cystitis or a vaginal discharge.

**Epithelial casts** consist of desquamating tubular epithelium and are indicative of ischaemically or toxically determined tubule cell necroses. With time they degenerate to granular and finally wax-like casts.

**Renal insufficiency casts** are 2–6 times as wide as the other cylindrical casts. They are formed in dilated tubules or in collecting tubules when the flow of urine has been strongly slowed down.

**Microorganisms**

**Bacteria** can only be detected and the result documented as a “yes” or “no.” Simultaneous observation of leukocyturia is indicative of an infection, otherwise the possibility of contamination should be considered.

**Trichomonads** (diameter 10–30 µm) are best observed live in very fresh urine by their erratic motion.

**Worm eggs** or **echinococcal constituents** are rarely observed in the urine in Central Europe, in contrast to the tropical countries.

**Artefacts**

Recognition of artefacts is essential if incorrect interpretations are to be avoided.

**Fat droplets** are as a rule due to contamination with ointments, residues of suppositories, or catheter lubricants.

**Crystals** are usually treated as artefacts because they are only formed pH-dependently in cooled urine on standing. Diagnostic significance is attributed only to the extremely rare crystals of cystine (colorless hexagonal plates), leucine (yellow-brown spheres with radial banding), and tyrosine (clusters of fine, colorless, shiny needles).

**Fungi** (most often yeasts) are usually the result of contamination; fungal infections are rare.

**Starch grains** are round to oval, variable in size, and exhibit concentric layering. They originate from cosmetic powders.

**Fibres** are frequently observed as contaminants.

**Pollen grain** may be confused with worm eggs.
Urine is normally a virtually sterile body fluid, but it may serve as a very good nutrient medium for many bacteria.

**Diagnostics**
The evidence for a urinary tract infection can be based on a test strip reaction (a positive nitrite test or leukocyturia) or on the outcome of microscopic examination of the sediment (leukocytes, bacteria).

Pre-packed immersion nutrient media are suitable for primary culture and for microbial count determinations of gram-positive and gram-negative bacteria, and also as a medium for transport between the doctor and the test laboratory. CLED agar can be used for growing all organisms, and it is particularly good for urinary tract pathogens. MacConkey agar largely suppresses the growth of gram-positives with the exception of enterococci. Proliferation of Proteus is largely suppressed on both these agars. Other nutrient media are also available, e.g. for selective growth of Pseudomonas. Gono-cocci, mycobacteria, and other relevant organisms do not grow.

**Sample material**
Midstream first morning urine.

**Analysis**
The nutrient medium carrier is dipped in fresh urine in a sterile container to a depth such that the agar layer is completely moistened. If the sample volume is small, the agar layer is carefully moistened all over.

- The excess urine is allowed to flow off the medium carrier; the last few drops on the lower edge of the carrier held vertically are removed by suction using a swab.
- The nutrient medium carrier is next placed back in its tube and incubated for 16–24 hours at 35–37°C.
Urine culture

Fig. 23: Microbial counts on MacConkey agar

(Midstream urine) Catheter or bladder puncture urine: a count of less than 10,000 bacteria per mL can already be indicative of an infection in this case.

Repetition of the test is recommended because these counts occur in chronic urinary tract infections, but they can also appear in midstream urine as contaminants.

The urine sediment must be examined. In women high microbial counts can sometimes be due to external contamination, e.g. due to vaginal discharge or vaginitis, and the urine sediment can then show increased numbers of pavement epithelia without an increase in leukocytes. A diagnosis of infection is therefore reliable only when the test urine has been obtained by catheterization or by bladder puncture. Subsequent identification of the organism and a determination of its antibiotic sensitivity are necessary.
**Interpretation**

- If each side of the nutrient medium carrier shows <10,000 organisms/mL, the specimen has most probably been contaminated and the result is not significant.
- The bacteriuria is significant when both sides of the carrier give a count of over 100,000 organisms/mL.
- This reference value applies when only one organism is present; if there are two or more species the bacteriuria is again usually due to contamination.

**Remark**

- The nutrient medium carriers must be kept in unopened tubes at 15–25°C until the expiry date. They must not be frozen. Carriers showing signs of mould or bacterial growth must not be used. Water of condensation does not interfere as long as the nutrient layer is not appreciably shrunken.

**Further procedure**

- The nutrient medium carriers must be dispatched to the test laboratory within 24 hours.
- As a rule the frequently encountered local pathogens such as enterobacte-riaceae, non-fermenting gram-negative bacilli, staphylococci, streptococci, and fast growing Candida strains are routinely cultured. Less frequent microorganisms, such as Mycoplasma, Mycobacteria, and anaerobes are cultured only when this is specially requested. Resistance tests are done in the usual way.
Urine cytology with Testsimplets

Testsimplets*) are ready-to-use stain-coated microscope slides which produce excellent color differentiation of cells in body fluids for microscopy and in cytological screening of urine. Testsimplets permit rapid differential staining of suspected cancerous cells in urinary sediment and replace the time-consuming Papanicolaou and Pappenheim staining procedures.

The simple, clean procedure and rapid staining with standard stains make Testsimplets easy to use in the doctor’s office or hospital.

**Procedure**
The method of working up the urine is similar to that used when preparing normal urinary sediment:
1. Centrifuge the urine at 3000 rpm for approx. 10 minutes
2. Carefully decant all the supernatant
3. Resuspend the sediment in 3 drops of physiological saline
4. Put 1 drop of this suspension in the middle of one of the enclosed cover slips and lay it on the color field
5. The staining process is complete after 5–10 minutes
6. The preparation can then be examined

The preparation can be evaluated up to 5 hours after staining if kept at room temperature.

**Evaluation**
It is best to start screening the preparations at ×100 magnification and then to assess specific suspect cells or cell clusters at ×200 to ×400 magnification or at ×1000 magnification using oil immersion.

The vital staining means that stained cells appear at their natural size, so – by contrast to other techniques – details such as the nuclear structures and nuclear membranes in particular are extremely clear.

**Clinical significance**
Testsimplets permit extraordinarily good differentiation and classification of nuclear structures, nuclear membranes, chromatin networks, and nucleoli as well as structures in the cytoplasm.

Urinary cytodiagnosis is helpful in:
- all forms of micro- and macrohaematuria
- treatment-resistant cystitis
- cystalgia
- dysuria of unclear origin
- follow-up after urothelial tumour operations
- early identification and follow-up of bladder cancer

Assessment of the degree of malignancy is carried out in exactly the same way as with conventional staining techniques.

*) Distributed by: Diagonal GmbH & Co. KG
Havixbecker Straße 62, D-48161 Münster
www.diagonal.de, info@diagonal-online.com
Automated Urinalysis

Instrumental urinalysis
Because of their ease of use, high sensitivity and specificity, Combustest urine test strips permit rapid and reliable conclusions about pathological changes in the urine. However, it is not really possible to standardize visual evaluation of urine test strips, and a number of environmental factors such as
- differences in light conditions at the workplace
- strongly colored urine samples
- individual differences in color differentiation ability of users
- declining concentration when examining long series of samples, and
- differences in the accuracy of compliance with the specified test strip reaction time
can have a negative effect on the quality of the result.

Instrumental evaluation of urine test strips virtually eliminates the above factors and guarantees a rapid, standardized measurement and immediate reliable documentation of the result.

Urinalysis systems can be divided into 3 categories:

**Instruments intended for single measurements**
One test strip is inserted at a time, manually. The test strip is measured automatically, and the result is delivered after about 1 minute. The test strip then has to be removed manually.

**Semi-automatic urinalysis systems**
Test strips can be inserted manually at short intervals. Transport, measurement, and disposal of the used test strips into an

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Urisys 1100</th>
<th>Miditron Junior II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specific gravity</td>
<td>610 nm</td>
<td>620 nm</td>
</tr>
<tr>
<td>pH</td>
<td>610 nm / 565 nm</td>
<td>620 nm / 557 nm</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>565 nm</td>
<td>557 nm</td>
</tr>
<tr>
<td>Nitrite</td>
<td>565 nm</td>
<td>557 nm</td>
</tr>
<tr>
<td>Protein</td>
<td>565 nm</td>
<td>557 nm</td>
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<tr>
<td>Glucose</td>
<td>565 nm</td>
<td>557 nm</td>
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<tr>
<td>Ketone</td>
<td>565 nm</td>
<td>557 nm</td>
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<tr>
<td>Urobilinogen</td>
<td>565 nm</td>
<td>557 nm</td>
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<tr>
<td>Bilirubin</td>
<td>565 nm</td>
<td>557 nm</td>
</tr>
<tr>
<td>Erythrocytes</td>
<td>610 nm</td>
<td>620 nm / 557 nm</td>
</tr>
<tr>
<td>Compensation</td>
<td>565 nm</td>
<td>557 nm</td>
</tr>
</tbody>
</table>

Table 3: Wavelengths
in-built container are automatic. The results are automatically saved in the memory and printed out.

**Fully automatic urinalysis systems**

Manual dipping and insertion of the test strips is not necessary. The urine samples are applied from sample tubes using a rotor or rack. Sample identification, the test procedure and disposal of the used test strips into an in-built container are fully automatic. The results are automatically saved in the memory and printed out.

Urinalysis systems evaluate test strips by reflectance photometry using selective light-emitting diodes with a wavelength and measurement time tailored exactly to the chemical reaction and color development of the test field concerned. Compared with visual assessment, this produces improved accuracy near the limit of detection.

In calculating the result, a correction for interference by the intrinsic color of the urine is made by measuring a blank field on the test strip (compensation field). In addition, the result of the Specific Gravity test is automatically corrected if the pH is high.

Although urinalysis systems using reflectance photometry evaluate the test field color changes with high precision, it is not possible to completely eliminate all differences in the composition of the sample material which could have an effect on color development, so urinalysis systems – unlike instruments for the measurement of blood glucose or Reflotron – only yield semi-quantitative results.

<table>
<thead>
<tr>
<th>Urisys 1800</th>
<th>Urisys 2400</th>
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</thead>
<tbody>
<tr>
<td>620 nm</td>
<td>650 nm</td>
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<tr>
<td>620 nm / 555 nm</td>
<td>620 nm / 555 nm</td>
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<td>555 nm</td>
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<td>555 nm</td>
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</table>
As well as correct determination of the test strip result with the objective of achieving a high level of standardization, urinalysis systems must fulfill the data-processing requirements of the laboratory environment. The urinalysis systems supplied by Roche Diagnostics can be connected to bar-code scanners for automatic sample identification and to external printers to print the findings, and the results of the measurements can be transferred to the laboratory computer system or PC. Fully automatic urinalysis systems such as Urisys 2400 and semi-automatic systems such as Miditron M and Miditron Junior II have already proved themselves over a period of years in the hospital laboratory. As a logical development of Miditron M a new system, Urisys 1800, will be launched in 2004.

The compact Urisys 1100 system enables even the medical practice, the small hospital laboratory or hospital ward to make use of the advantages of instrumental urinalysis.

Fig. 24: Measuring Head (schematic)
Automated Urinalysis

(reflectance values that are programmed in the analyzer for each parameter) and outputs a semi-quantitative result (6). Results can be printed out or transferred to the laboratory computer system.

Before each measurement the optical system is tested and corrected for variations in LED brightness and detector sensitivity using internal reference settings. The correct positioning of the test strip under the optical system is checked during the measurement. If the strip is not in the correct position the result is not printed out, and the instrument instead asks for the measurement to be repeated.

The LED (1) emits light of a defined wavelength on to the surface of the test pad (2) at an optimum angle. The light hitting the test zone is reflected from the surface more or less intensely depending on the color produced on the test pad, and is picked up by the detector (3), a phototransistor positioned directly above the test zone. The phototransistor sends an analogue electrical signal to an A/D converter (4), which changes it to digital form. The microprocessor (5) then converts this digital reading to a relative reflectance value by referring it to a calibration standard.

Finally, the system compares the reflectance values with the defined range limits (reflectance values that are programmed in the analyzer for each parameter) and outputs a semi-quantitative result (6). Results can be printed out or transferred to the laboratory computer system.

Fig. 25: Reflection photometry (schematic)
Urisys 1100

Urisys 1100 is a compact, time-saving urinalysis system for reflectance-photometric measurement of individual test strips of the Combur-Test line. The system test strip for Urisys 1100 is ComburUX with 10 urine parameters and an additional field for compensating for the color of the urine. Urisys 1100 can also measure ComburTest and ComburTest urine test strips without compensation pad.

Operation of Urisys 1100 is perfectly simple: Just dip the test strip in the urine sample, place it on the movable loading tray, and press the start button. The system does the rest. After 55 seconds it reads the individual fields on the test strip one after the other and prints out the result on the integrated low-noise thermal printer. There is the option of sending the results through a serial port to a PC or laboratory computer system. The whole measuring cycle takes about 70 seconds, so it is possible to measure approx. 50 samples per hour.

When carrying out the measurements, Urisys 1100 automatically assigns each sample a serial number, but there is also the option of inputting patient numbers using a bar-code scanner or a PC keyboard. The printout of the results includes a heading, the serial number, the date and time, and patient ID. Abnormal results are flagged and are thus immediately recognizable. The results can be printed out in conventional, SI, or arbitrary units. The number and sequence of the parameters on the printout can be selected at will and, even when printing out immediately after the measurement, it is possible to choose between one and two copies. Urisys 1100 can store up to 100 readings with patient data. There are also various options available for later or multiple printouts.

All system settings are accomplished using the function keys in association with text shown on the display, which is available in 5 languages. The user instructions are clear and self-explanatory. Inbuilt checking functions inform the user of any operating or system errors. When ComburUX Test UX strips are used, Urisys 1100 automatically requests a weekly calibration with Control-Test M. Calibration is just as quick and easy to carry out as the measurement itself.

When a strongly alkaline urine sample is being measured, Urisys 1100 automatically corrects the result of the specific gravity test field. When the urine sample has a strong intrinsic color, automatic color compensation is performed. Measurement sensitivity can be fine-tuned by gradually adjusting the factory set limits to suit the user’s individual requirements.

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1) In some countries ComburTest and ComburTest are not available or are not offered for use with Urisys 1100.
2) not available in the U.S. version.
3) only when ComburUX Test UX is used.
Inserting a new roll of paper and cleaning the device is simplicity itself. Just remove the loading tray and clean it under running water. Load the roll of paper and close the printer cover – Urisys 1100 is ready to perform the next measurement.

Urisys 1100 can evaluate the well-proven Combur-Test urine test strips. The procedure is easy, user-friendly, time-saving and standardized. Because the system is so simple to operate and provides a number of software options, it is ideal for medical practices, small laboratories and hospital wards.

The benefits at a glance

- Handy, compact instrument for measuring individual test strips. Urisys 1100 delivers standardized results and virtually excludes sources of error associated with visual evaluation.
- Easy to use: Place the test strip on the loading tray and press the start button. The system does the rest – quietly and efficiently.
- Optimized procedure: Immediate automatic documentation of results – option of printing or sending them to a PC or laboratory computer system.
- Reliable results: Can measure the high-quality Combur®Test UX test strip.
- Useful computer interface: Urisys 1100 has a serial interface for connection to a PC or laboratory computer system. An optional bar-code scanner or PC keyboard may also be used to input patient data.
- Efficient in daily routine: Very simple operation, fast results, reliable documentation, changing paper and cleaning done in a matter of seconds.
- Interactive user guide on CD-ROM: Videoclips explain procedures from first-time startup to maintenance.
Miditron Junior II

Miditron Junior II is a compact semi-automatic urinalysis system for reflectance-photometric evaluation of Combur® Test M and Combur® Test M urine test strips. It is extremely easy to operate using the six programme keys and user instructions shown on the display.

An optical and acoustic signal tells the operator to get a test strip ready for the measurement and then to lay it on to the insertion area of the instrument. From there it is automatically carried to the measurement position and measured. The test strip tray includes a waste container which can hold up to 75 measured test strips. Up to 100 test strips can be measured per hour in normal mode. Higher operating speeds are available for processing short series of measurements. The memory can store up to 150 results. Calibration has to be carried out only every 2 weeks.

When carrying out the measurements Miditron Junior II automatically assigns each sample a serial number, but there is also the option of inputting a sample number via the in-built key-pad or a barcode scanner. The sample numbers can be stored in the instrument memory in advance and printed out in the form of a work-list, or they can be input at the same time as the measurements, after insertion of the test strip.

The results can be printed out in conventional, SI, or arbitrary units. Combinations of units can also be used. Positive results on the printout are indicated by an asterisk. The associated thresholds can be set individually. The limits of the reflectance/concentration ranges can be adjusted to the individual needs of the user.

The results of the test strip evaluation are printed out on the integral thermal printer. Three standard RS 232 C ports permit connection to a bar-code scanner, external printer, PC, or bidirectional connection to the laboratory computer system.

Miditron Junior II combines ease of use and high-quality results with economy and small size, so it is particularly suitable for the smaller laboratory handling an average of 50 urine samples per day.
The benefits at a glance

- Semi-automatic urinalysis system for measurement of Combur Test M and Combur Test M
- Hygienic and simple operation
- 3 optional operating speeds:
  Normal mode: Cycle time approx. 36 seconds, max. 100 tests/hour
  Accelerated mode: Cycle time approx. 20 seconds, max. 180 tests/hour
  Fast mode: Cycle time approx. 12 seconds, max. 300 tests/hour
- Includes connectors for bar-code scanner and external printer
- Bidirectional connection to the laboratory computer system
- Numerous setting options for optimal adjustment to the individual operating situation and laboratory environment
Urisys 1800

Urisys 1800 is a semi-automatic urinalysis system for reflectance-photometric evaluation of Combur\textsuperscript{1} Test M and Combur\textsuperscript{2} Test M urine test strips.

Measuring urine samples with Urisys 1800 is perfectly simple: Dip test strips in urine and place them on the insertion tray. The system will detect their presence and transport them to the measuring position on a 6-second work cycle. Following an incubation time of approx. 60 seconds each test strip is measured and then placed in the inbuilt waste container. The high throughput of max. 600 strips per hour means that even large numbers of samples can be processed quickly and efficiently. System memory can accommodate up to 1000 complete test data records.

Urisys 1800 has a large intuitive LCD touch-screen that grants direct access to various software features, enabling the user to call up various system functions and adjust settings quickly and conveniently. Urisys 1800 supports quality control of test strip readings by allowing the name, batch number and standard values of control urines to be input and saving the results in a separate 300-position memory reserved for controls (100 per control level).

Sample and control results can be printed out via the integral thermal printer with optimized paper format (112 mm wide), sent to a laboratory computer system via the integral port (ASTM standard interface protocol) or saved to disk. For users who have previously worked with Miditron M or Miditron Junior II systems, these interface protocols are also provided for convenience. In addition, the inbuilt disk drive can be used to save calibration results and laboratory-specific system settings.

Ports are provided for connecting a barcode scanner and Miditron ST Sediment Terminal. Miditron ST allows sediment findings to be input in parallel to the test strip measurements, so that a second person can carry on with time-intensive microscopic examinations at the sediment workstation while the other samples are being measured in the Urisys 1800 system. The complete urinalysis finding is documented as already stated above.

Thanks to its extreme user-friendliness and superior data management, Urisys 1800 is the right choice to carry out efficient routine urinalysis in laboratories with a urine sample throughput of 50–100 samples per day and more.
The benefits at a glance

- Semi-automatic urinalysis system for measuring Combur™ Test M and Combur™ Test M
- Continuous loading of dipped test strips without the need to keep to a strict timing regime
- Easy user guidance through large LCD touch screen
- Separate data handling for quality control measurements
- Ports for bar-code scanner and bidirectional connection to the laboratory computer system
- Miditron ST Sediment Terminal connectivity for inputting microscopic findings
- Inbuilt disk drive for optionally saving sample results and calibrations to disk
- Numerous setting options for optimal adjustment to the individual operating situation and laboratory environment
**Urisys 2400**

Urisys 2400 is a fully automated urinalysis system for reflectance-photometric evaluation of Urisys 2400 Cassette test strips including the parameters pH, leukocytes, nitrite, protein, glucose, ketones, urobilinogen, bilirubin, erythrocytes and color, as well as specific gravity (refractometry) and clarity via physical determination.

Urisys 2400 provides enhanced walk-away capability for medium to high volume laboratories with typically > 100 urine samples per day.

It is the first urinalysis system with an innovative cassette providing the users with highly convenient reagent handling, and with Roche Diagnostics standard racks for common sample handling. Because all steps in the operation, from pipetting the urine sample onto the test strip to output of the test results, are completely automatic, manual handling of the samples and test strips is reduced to a minimum.

The samples are placed on the standard racks and the racks are loaded via the tray with a capacity of 15 racks = 75 samples. Continuous loading of single racks is also possible. Sample and rack identification is done via an integrated bar-code reader.

Automatic level control in the sample tubes by a liquid level sensor and precise dosing volume ensures sufficient urine sample to be pipetted onto each single pad of the test strip. In addition, all samples are automatically mixed immediately before the measurement, so that any components which have precipitated are detected correctly.

The ready-to-use Urisys 2400 Cassette with 400 test strips allows high convenience together with an on-board stability of 2 weeks and long calibration interval of one month.

The high throughput of 240 samples per hour in combination with the large on board supply of 400 test strips ensures that even large numbers of samples can be processed rapidly. High result memory capacity allows data storage for 1000 routine samples, 200 STAT samples and 300 control samples (100 per control level). Controls are automatically identified via user definable control racks.

The results of samples or controls can be printed on an external printer, send to a host (ASTM standard interface protocol) or can be stored on a diskette.

Abnormal or edited results are indicated by different flags on the print out.

The limits of the reflectance/concentration ranges can be adjusted to the individual needs of the user.
Automated Urinalysis

The benefits at a glance

- Fully automated chemical urinalysis by measurement of Urisys 2400 Cassette test strips
- The innovative, ready to use Urisys 2400 Cassette provides quick and convenient one-grip loading of cassettes and large on board supply of 400 test strips in a humidity safe compartment
- High throughput of 240 samples per hour
- Automatic volume control via liquid level detection and mixing of sample before measurement
- Integrated bar-code reader for automatic sample and rack identification
- User-friendly, intuitive software ensures easy system operation via color touch screen
- Ports for connection to external printer and Host (ASTM)
- Various setting options for optimal adjustment to the individual operating situation and laboratory environment
Detection of microalbuminuria with Micral-Test

**Test principle**
Micral-Test allows a specific detection of human albumin in the urine by a combination of chromatographic and immunological processes; human albumin migrates from a liquid reservoir into a layer of conjugate fleece. Here in an immune reaction it is bound specifically to a soluble antibody-gold conjugate. The resulting antigen-antibody complex migrates into the actual reaction field.

Excess antibody-gold conjugate is bound by immobilized albumin in a capture zone, so that the detection field is reached only by conjugate molecules charged with the urinary albumin. Depending on the albumin concentration, the detection field assumes a color ranging from white to red.

**Specificity and sensitivity**
With a cut-off at 20 mg/L for microalbuminuria, the sensitivity is 97% and the specificity 71%.

On the basis of the immunological reaction, Micral-Test measures human albumin specifically. Cross-reactions with other human proteins such as IgG, IgA, leukocytes, and erythrocytes are below 0.5%.

---

![Fig. 26: Structure of Micral-Test strip](image-url)
Test material
The use of the first morning urine collected in midstream is recommended, because at that time the albumin concentration is not falsified by physical activity or the intake of fluids. Since albuminuria is subject to physiological variations, the morning urine should preferably be tested on 3 days in a week.

Test performance
NOTE: Since the reaction of this urine test strip is based on chromatographic and immunological principles, the procedure is not the same as that with conventional test strips.

1. The test strip is dipped for 5 seconds in the urine sample to a depth such that the liquid level is between the two black lines. It is then withdrawn. Neither during the dipping nor during the withdrawal may the strip touch the container wall (possibility of interference effects during chromatography).

2. The test strip is now laid on a non-absorbent horizontal substrate or on the urine container.

3. After 1 minute the reaction color is compared against the colors on the label. The color predominating over the area is decisive. Any smaller spots of a different color are disregarded in the evaluation.

Evaluation
The result is positive if at least 2 of the 3 morning urine samples give a concentration of 20 mg or more albumin per litre.

Sources of error
Interference with the test result may be due to a number of factors: immersion depth too large, immersion time too short, reading after an insufficient time, and contact between the test strip and the wet container wall.

The following findings restrict the informative power of microalbuminuria:
- acute diseases and infections of the urinary tract
- positive urine findings for protein, nitrite, leukocytes, or blood
- pregnancy
- severe metabolic dysregulation, for example in diabetics
- physical exertion at the time of urine collection in the bladder (physiological albuminuria)
- albumin of postrenal origin

Influence of drugs
Interference due to medicinal drugs has not been observed so far, but the effects of medicines and/or their metabolites on Micral-Test are not all known. In cases of any doubt, therefore, if this is medically acceptable, the medication should be discontinued and the test carried out once again.
Clinical significance

Patients with diabetes mellitus or with hypertension often suffer from a nephropathy as a late complication. Some 30–40% of type I diabetics develop a renal disease after 10–15 years, and recent studies have shown that nephropathies also occur in around 20% of type II diabetics. In hypertensive patients the corresponding figure is around 25%. If both conditions are present simultaneously, their organ-damaging potential on the cardiovascular system and on the kidneys is compounded.

Once an advanced stage with manifest proteinuria, elevated serum urea and creatinine, and morphological changes in the kidneys has been reached, the process can only be slowed down, but no longer arrested, even with good management of the underlying disease.

Both diabetic and hypertension-determined nephropathies should therefore be detected as early as possible, in order to be able to act on their progressive course in the direction of terminal kidney failure.

The most important factor in early recognition of a nephropathy is microalbuminuria, defined as albumin concentrations between 20 and 200 mg/L urine. Values below 20 mg/L are normal. Early diagnosis of microalbuminuria allows glomerular damage to be caught at a time at which appropriate therapeutic measures can still exert an influence on the glomerulopathy and at which the progression towards renal failure can still be avoided.

Regrettably, not many doctors take advantage of this possibility of improving their therapeutic effectiveness by checking their patients for microalbuminuria.

The potential indications include, for example, metabolic optimization, early institution of antihypertensive therapy (preferably with ACE inhibitors), and a low-protein diet in the case of diabetics. In hypertensive subjects general measures and an effective drug therapy to lower the blood pressure are indicated.
Detection of microalbuminuria with Micral-Test

**Scheme of the reaction**

**Micral-Test**

\[
\begin{align*}
\text{Antibody-gold conjugate (red)} & \quad \text{Albumin (antigen)} & \quad \text{Antigen-antibody complex} \\
+ & \quad \rightarrow \\
\end{align*}
\]

Free albumin from the urine is bound into an antibody-gold conjugate. An antigen-antibody complex is formed.

**Scheme of the reaction**

**Micral-Test**

\[
\begin{align*}
\text{Excess antibody-gold conjugate} & \quad \text{Fleece} & \quad \text{Immobilized albumin} & \quad \text{Immobilized antigen-antibody complex} \\
+ & \quad \rightarrow \\
\end{align*}
\]

Excess conjugate molecules are bound in the capture zone by immobilized human albumin.

**Scheme of the reaction**

**Micral-Test**

The red antibody-gold conjugate charged with albumin from the urine causes a white to red coloration of the detection field, depending on the albumin concentration in the specimen.

*Fig. 27: Scheme of the reaction in Micral-Test*
The urinary apparatus is made up of:
- two kidneys
- two ureters
- the urinary bladder
- and the urethra

The kidneys are the most important excretion organ in the human organism. Every 24 hours around 1500 L of blood flow through the kidneys, which filter off daily 170 L of primary urine from this blood volume. Primary urine is a blood “ultrafiltrate” and consists of water, salt, and dissolved low-molecular blood constituents. The water is largely reabsorbed, and all substances needed by the organism are taken up again. The remaining “worthless” substances are conveyed drop-wise to the renal pelvis as urine. The urine then passes into the ureters and through them into the bladder. The bladder is a muscular hollow organ in which urine is collected. The amount of urine finally excreted daily through the urethra is approximately 1.5 L.

**Function and importance of the urinary organs**
The organs of the efferent urinary tract comprise:
- the renal calices
- the renal pelvis
- ureters
- bladder
- the urethra

---

**Anatomy of the urinary apparatus**

![Anatomy of the urinary apparatus](image)

*Fig. 28: Anatomy of the urinary apparatus*
Renal calices/renal pelvis
The renal calices are individual funnel-like tubular structures which open into the renal pelvis, the expansion at the upper end of the ureters.

Ureters
The ureters have a length of 24 to 34 cm as measured from the renal pelvis to the point at which they enter the bladder. Urine is conveyed down into the bladder by peristaltic contractions of the ureters.

Bladder
The bladder is an elastic muscular hollow organ in which the urine is collected. Urine is voided by muscular contractions of the bladder wall, the abdominal wall, and by the muscle tone of the elastic system.

Urethra
The urethra is the final excretion channel for urine. The female urethra is shorter than the male, and this is the reason why urinary tract infections are more common in women than in men.
The Kidneys and the Efferent Urinary Tract

The Kidneys

The principal functions of the kidneys are as follows:

- Filtration of blood for the purpose of excretion of toxic products and degradation products (metabolic end products and toxins, for example urea).
- Regulation of:
  - the acid-base equilibrium of the organism
  - the water and electrolyte balance
  - the intracellular and extracellular fluid
  - blood pressure (secretion of the hormone renin) and erythropoiesis (secretion of the hormone erythropoietin)
- Excretion of blood constituents (e.g. glucose) when their concentration exceeds a certain limit.
- Production and degradation of hormones (prostaglandins) and hormone-like substances which exert an effect on the metabolism and the circulation.

Fig. 29: Longitudinal section through a kidney
Nephrons
The kidney consists of 1–3 million tubular structures known as nephrons. The nephrons can be subdivided further into glomerular and tubular sections. They are closely packed and form the renal parenchyma (the cortex and the medulla).

Structure of the nephron
- renal corpuscle with a glomerulus and Bowman’s capsule
- proximal convoluted tubule
- Henle’s loop
- the distal convoluted tubule and the collecting tubule

Fig. 30: The nephron with its glomerular and tubular sections
The Kidneys and the Efferent Urinary Tract

**Renal corpuscles**

Blood enters the glomerulus via a blood vessel and undergoes filtration through the membrane (semipermeable basal membrane) of the glomerular capillaries into Bowman’s capsule. The renal corpuscle acts as a “point of contact” between the blood vessel and the place where primary urine is filtered out. The gap between the two walls of Bowman’s capsule serves as a container for primary urine glomerular filtrate and enables the passage of primary urine through the open end into the proximal tubule.

**Proximal convoluted tubules**

In the proximal convoluted tubule all substances that can be utilized by the organism are actively reabsorbed out of the glomerular filtrate and taken up again into the metabolism, while others are concentrated and excreted with the urine. The utilizable substances include, for example, sodium, potassium, amino acids, phosphates, and glucose (glucose should not be present in the urine).

The urine volume is drastically reduced here – 99% of the primary urine volume is reabsorbed.

The proximal tubule connects the glomerulus with Henle’s loop.

**Henle’s loop**

The residual filtrate passes into Henle’s loop. Water is removed in the descending part by osmosis, and sodium and chloride are reabsorbed in the ascending part. Excessive reabsorption of water in the ascending part is prevented by impermeability of the walls to water. This selective reabsorption process – the countercurrent principle – maintains the osmotic gradient of the renal medulla, which is decisive for final concentration of the filtrate when it reaches the collecting tubule.

**Distal convoluted tubule and the collecting tubule**

In the terminal section of the nephron (the distal convoluted tubule and the collecting tubule) the composition of the urine is further modified by continuing reabsorption of sodium and potassium and by secretion of hydrogen ions. The hormones adiuretin and aldosterone exert an influence on the water-absorption process, changing the wall permeability (loss or retention of water) and regulating the chemical equilibrium via ion exchange. This equilibrium is the actual end determinant for urine volume and urine concentration.
Epithelial cells

Fig. 1: Group of pavement epithelium cells (×1000). These are the largest cells encountered in urinary sediment (30–50 µm).

Fig. 2: Pavement epithelium cells, transitional epithelium cells (urothelial cells) (×450).

Fig. 3: Binuclear transitional epithelium cells (×1000). Urothelial cells measure about 20–30 µm, easily take up water, and are usually the plumpest structures encountered.

Fig. 4: Group of transitional epithelium cells (×1000). Exfoliation of urothelial cells may be indicative of a pathological process in the lower part of the urinary tract.

Fig. 5: Group of suspicious urothelial cells (×1000).

Fig. 6: Group of about 15 urothelial cells (×1000). In addition to various signs of malignancy the cells show a dysplastic vacuolated cytoplasm.
Urine sediment

Tubular epithelium cells

Fig. 7: Epithelial cells probably of tubular origin (×1000). Identification of renal epithelial cells is often difficult.

Fig. 8: Three epithelial cells probably of tubular origin (×1000). The characteristic cell clustering and the cylindrical form point to tubular origin.

Fig. 9: Tubular epithelium cells, dysmorphic erythrocytes, and a leukocyte (×1000). The cylindrical cells have eccentric nuclei and a weakly expressed brush border.

Fig. 10: Tubular epithelium cells (×450). The occurrence of tubular epithelium cells in large clusters is unusual.

Fig. 11: Degenerating tubular epithelium cells (×1000). Phagocytosis of considerable amounts of urine constituents leads to cell overloading and degeneration. The non-functional epithelial cells are then excreted in urine.

Fig. 12: Tubular epithelium cells (“fat granule cells”) (×1000). As a result of excessive lipid storage these cells are clearly larger than other tubular epithelium cells and point to a severe renal function disturbance.
Eumorphic erythrocytes

Morphologically normal so-called eumorphic subrenal erythrocytes show that a disorder of the efferent urinary tract is present.

Eumorphic biconcave erythrocytes (×1000).
Eumorphic erythrocytes not showing the cell membrane alterations typical in erythrocytes of renal origin.

Eumorphic erythrocytes (×400).

Juvenile erythrocytes with typical biconcave form; some of the cells show a transition to a crenated form.

Eumorphic erythrocytes (×1000).
In alkaline or hypotonic urine erythrocytes swell up and undergo haemolysis. The cell-membrane residues are called erythrocyte shadows.
Dysmorphic erythrocytes

**Fig. 19:** Dysmorphic erythrocytes (×1000). Erythrocytes that have undergone morphological changes in the kidneys are designated as "dysmorphic."

**Fig. 20:** Dysmorphic erythrocytes (×1000). Morphological abnormalities of the erythrocyte membrane are probably attributable to sustained changes in pH and osmolality in the tubule system.

**Fig. 21:** Various kinds of dysmorphic erythrocytes (×1000). Erythrocytes of glomerular origin can point to the presence of a very wide range of morphological abnormalities.

**Fig. 22:** Dysmorphic erythrocytes (×1000). Erythrocyte shadows of glomerular origin (see Fig. 18, subrenal erythrocyte shadows).

**Fig. 23:** Dysmorphic erythrocytes (×1000). Erythrocyte shadows of glomerular origin (see Fig. 18, subrenal erythrocyte shadows).

**Fig. 24:** Dysmorphic erythrocyte (×1000). Blue field: interference contrast microscopy; brown field: light-field microscopy.
**Leukocytes**

Fig. 25: Neutrophilic polymorphonuclear granulocytes (×1000).
These are easily recognizable by their segmented nuclei and, when present in large numbers, point to an inflammatory disease in the urogenital tract.

Fig. 26: Leukocytes, yeast cells (×400).
An opportunistic infection with Candida albicans is a relatively frequent finding.

Fig. 27: Leukocytes, pavement epithelium cells (×1000).
In women large numbers of pavement epithelium cells and granulocytes in the sediment of spontaneous urine may be due to a vaginal contamination.

Fig. 28: Leukocytes, erythrocytes, bacteria (×1000).
Signs of cytolysis are evident in both erythrocytes and leukocytes (alkaline reaction of the urine in bacterial infections).

Fig. 29: Leukocytes, urothelial cells (×400).
Urinary sediment with characteristic signs of an acute or chronic urinary tract infection.

Fig. 30: Leukocytes, triphosphate, bacteria (×400).
Triphosphate crystals are often encountered in infected alkaline urine, but they can be indicative of obstructed urine flow.
Fig. 31: Hyaline cast (×400). Hyaline casts, which can also occur in the urine of healthy persons, are often overlooked because of their low refractive index.

Fig. 32: Small leukocyte cast (×1000). Leukocyte casts are pathognomonic for pyelonephritis.

Fig. 33: Leukocyte cast (×400). A prerequisite for the formation of leukocyte casts is increased intrarenal excretion of leukocytes in pathological proteinuria.

Fig. 34: Erythrocyte cast (×1000). Erythrocyte casts are pathognomonic for glomerulonephritis.

Fig. 35: Erythrocyte cast (×1000). The erythrocytes are partly embedded in a matrix of a hyaline cast and partly attached to a finely granulated surface.

Fig. 36: Mixed erythrocyte cast (×1000). Hyaline cast with dysmorphic erythrocytes, tubular epithelium cells, and granular material on the cast surface.
Fig. 37: Epithelial cast (×400). Epithelial casts occur very rarely in sediment. They consist of desquamated tubular epithelium cells bound into the matrix of a hyaline cast.

Fig. 38: Finely granular cylindrical cast (×400). Granular casts are encountered in nearly all forms of specific kidney diseases.

Fig. 39: Coarsely granular cast (×400). Helically twisted cylindrical cast with coarsely granular material (weakly discernible cell structure).

Fig. 40: Granular cast (×400). Extended granular cylinder with many embedded dysmorphic erythrocytes.

Fig. 41: Extended waxy cast (×400). A number of dysmorphic erythrocytes adhere to the “waxy” surface of the cast, which is surrounded by abnormal sediment structures.

Fig. 42: Waxy cast (×100). Cylindrical waxy casts are always indicative of severe chronic kidney diseases (advanced renal failure).
Urine sediment  **Histiocytes, bacteria, carcinoma cells**

**Fig. 43:** Histiocyte (× 1000).
Histiocytic exhibit substantial variations in size. They usually contain numerous vacuoles, granules and other phagocytic material.

**Fig. 44:** Bacteria on a pavement epithelium cell (×1000).
Bacteria are often encountered on the surface of large epithelial cells. If neither inflammation sources nor protein can be found, the bacteria are usually due to contamination.

**Fig. 45:** Group of yeast cells (×1000).
Free-swimming yeast cells are easily confused with erythrocytes or fat droplets. Attention should be paid to branching hyphae and to clumps of budding yeast cells.

**Fig. 46:** Urothelial carcinoma cells (×1000).
In the presence of large groups of urothelial cells there is always a suspicion of a tumour in the region of the efferent urinary tract.

**Fig. 47:** Cells of a poorly differentiated bladder carcinoma (×1000).
Characteristic features of malignancy: anisocytosis and nuclear polymorphism, disturbed nucleus/cytoplasm ratio, hyperchromatism of the cell nuclei or the cell walls, multiple nucleoli.

**Fig. 48:** Group of urothelial carcinoma cells (×1000).
Characteristic features of malignancy: complete loss of cytoplasm in some cells, anisocytosis and nuclear polymorphism, thick cell nucleus membrane.
Urine Cytology

Normal urothelial cell surrounded by erythrocytes

Bladder carcinoma G3, dedifferentiated cells with large nuclei, vacuoles, and nucleoli

Bladder carcinoma G2, hyperchromatic nuclei, numerous nucleoli, destructive changes in the cytoplasm, several leukocytes in the surrounding region

Bladder carcinoma G3, some hyperchromatic nuclei, small cells, multiple nucleoli, hyperchromatism of the nucleus walls

Bladder carcinoma G2, distinct variance in nucleus size, multiple nucleoli, nucleus/cytoplasm ratio shifted in favour of the nuclei
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acidosis</td>
<td>A metabolic disturbance associated with a shift of the acid-base balance to the acid side (pH &lt; 7.0)</td>
</tr>
<tr>
<td>Adenoma</td>
<td>Mostly benign epithelial tumour derived from glandular epithelium</td>
</tr>
<tr>
<td>Adiposity</td>
<td>Obesity</td>
</tr>
<tr>
<td>Agar</td>
<td>A polysaccharide obtained from various marine algae and used, among others, for the preparation of nutrient media for bacterial cultures</td>
</tr>
<tr>
<td>Alimentary</td>
<td>Due to nutrition</td>
</tr>
<tr>
<td>Alkalosis</td>
<td>A metabolic disturbance associated with a shift of the acid-base balance to the alkaline side (pH &gt; 7.0)</td>
</tr>
<tr>
<td>Alkaptonuria</td>
<td>Excretion of homogentisic acid in the urine causing a dark to black discoloration of the specimen in air due to alkalization</td>
</tr>
<tr>
<td>Anaemia</td>
<td>“Blood deficiency,” a collective term for diseases based on a reduction in the amount of haemoglobin and usually also of erythrocytes in the blood</td>
</tr>
<tr>
<td>Anamnesis</td>
<td>Complete medical history of the patient (including earlier illnesses and diseases running in the family); the anamnesis is the first diagnostic step and is of major significance</td>
</tr>
<tr>
<td>Anisocytosis</td>
<td>Occurrence of erythrocytes of various sizes in blood, a feature of a number of blood diseases</td>
</tr>
<tr>
<td>Apoplexy</td>
<td>Stroke</td>
</tr>
<tr>
<td>Appendicitis</td>
<td>Inflammation of the vermiform appendix, a wormlike diverticulum of the caecum</td>
</tr>
<tr>
<td>Ascorbic acid</td>
<td>Vitamin C</td>
</tr>
<tr>
<td><strong>Glossary of Specialist Medical Terms</strong></td>
<td></td>
</tr>
<tr>
<td>----------------------------------------</td>
<td></td>
</tr>
<tr>
<td><strong>Bacteriuria</strong></td>
<td>Excretion of bacteria in urine</td>
</tr>
<tr>
<td><strong>Benign</strong></td>
<td>Not malignant</td>
</tr>
<tr>
<td><strong>Cast</strong></td>
<td>Cylindrical protein-containing structure formed within renal canaliculi and detected in urinary sediment; casts are differentiated according to their constituents</td>
</tr>
<tr>
<td><strong>Catalysis</strong></td>
<td>Acceleration of a chemical reaction by a material (catalyst) which lowers the activation energy for the process</td>
</tr>
<tr>
<td><strong>Cerebral blood flow disturbance</strong></td>
<td>Circulation disturbance in the brain</td>
</tr>
<tr>
<td><strong>Cholangiolitis</strong></td>
<td>Inflammation of the fine terminal elements of the bile duct system</td>
</tr>
<tr>
<td><strong>Cholangitis</strong></td>
<td>Inflammation of the bile duct</td>
</tr>
<tr>
<td><strong>Cholestasis</strong></td>
<td>Bile congestion in the gallbladder</td>
</tr>
<tr>
<td><strong>Cholecystitis</strong></td>
<td>Inflammation of the gallbladder</td>
</tr>
<tr>
<td><strong>Chyle</strong></td>
<td>Milky turbid fluid contained in the intestinal lymph vessels</td>
</tr>
<tr>
<td><strong>Chyluria</strong></td>
<td>Excretion of chyle in the urine</td>
</tr>
<tr>
<td><strong>Cirrhosis</strong></td>
<td>Cicatricial shrinkage of an organ</td>
</tr>
<tr>
<td><strong>Coagulopathy</strong></td>
<td>Blood coagulation (clotting) disturbance due to a plasma factor deficiency in blood</td>
</tr>
<tr>
<td><strong>Colic</strong></td>
<td>Acute spasm-like pains in the abdominal region</td>
</tr>
<tr>
<td><strong>Congenital</strong></td>
<td>Present at and usually before birth</td>
</tr>
<tr>
<td><strong>Constipation</strong></td>
<td>Infrequent or difficult evacuation of the faeces</td>
</tr>
<tr>
<td>Term</td>
<td>Description</td>
</tr>
<tr>
<td>----------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Contamination</td>
<td>Soiling, pollution</td>
</tr>
<tr>
<td>Cystalgia</td>
<td>Pain in the bladder</td>
</tr>
<tr>
<td>Cystitis</td>
<td>Inflammation of the bladder</td>
</tr>
<tr>
<td>Dehydration</td>
<td>Withdrawal of water</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Chronic metabolic disturbance with delayed or incomplete utilization of glucose in the organism</td>
</tr>
<tr>
<td>Diabetic coma</td>
<td>Life-threatening disturbance of consciousness due to a diabetic metabolic dysregulation</td>
</tr>
<tr>
<td>Dilated</td>
<td>Expanded</td>
</tr>
<tr>
<td>Discharge</td>
<td>Excretion of a fluid from the female sex organs</td>
</tr>
<tr>
<td>Diuresis</td>
<td>Excretion of urine</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Drugs promoting urine excretion</td>
</tr>
<tr>
<td>Dysmorphic</td>
<td>Morphologically altered (malformed)</td>
</tr>
<tr>
<td>Dysuria</td>
<td>Urine evacuation disturbance</td>
</tr>
<tr>
<td>E. (scherichia) coli</td>
<td>Gram-negative bacteria in human large intestine; E. coli can also provoke urinary tract infections, diarrhoea, sepsis, various inflammations, etc.</td>
</tr>
<tr>
<td>Electrophoresis</td>
<td>Movement of electrically charged particles in a carrier material under the influence of an electric field (used in medicine for analytical purposes)</td>
</tr>
<tr>
<td>Emphysema</td>
<td>Accumulation of air in tissues, inflation of organs or body parts</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
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<tr>
<td><strong>Encephalopathy</strong></td>
<td>Brain disease</td>
</tr>
<tr>
<td><strong>Endocarditis lenta</strong></td>
<td>Bacterial inflammation of the endocardium, the lining membrane of the heart cavities</td>
</tr>
<tr>
<td><strong>Enterocolitis</strong></td>
<td>Inflammation of the small and large intestine</td>
</tr>
<tr>
<td><strong>Enterohepatic</strong></td>
<td>Relating to the intestine and the liver</td>
</tr>
<tr>
<td><strong>Enterococci</strong></td>
<td>Gram-positive bacteria normally forming part of the intestinal flora; outside the intestine they may, however, act as pathogens (e.g. of urogenital infections)</td>
</tr>
<tr>
<td><strong>Enuresis</strong></td>
<td>Involuntary passage of urine, bed-wetting</td>
</tr>
<tr>
<td><strong>Epithelial cells</strong></td>
<td>Cells of the topmost tissue layers; urogenital epithelial cells are a constituent of urinary sediment</td>
</tr>
<tr>
<td><strong>Erythrocytes</strong></td>
<td>Red blood corpuscles; haemoglobin-containing cells responsible for the transport of oxygen and carbon dioxide in blood</td>
</tr>
<tr>
<td><strong>Eumorphic</strong></td>
<td>Morphologically unchanged (showing a normal form)</td>
</tr>
<tr>
<td><strong>Excretion</strong></td>
<td>Elimination of waste metabolic products from the body</td>
</tr>
<tr>
<td><strong>Exfoliation</strong></td>
<td>Gradual peeling of dead tissue and bone components</td>
</tr>
<tr>
<td><strong>Extrarenal</strong></td>
<td>Outside the kidneys</td>
</tr>
<tr>
<td><strong>Extravasate</strong></td>
<td>Fluid such as blood or lymph escaping from a vessel into the surrounding tissue</td>
</tr>
<tr>
<td><strong>Filariasis</strong></td>
<td>A disease state caused by the presence of nematode worms in the body</td>
</tr>
<tr>
<td><strong>Glomerulonephritis</strong></td>
<td>Renal inflammation affecting mainly the glomeruli</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
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<td>--------------------</td>
<td>---------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Glomerulopathy</strong></td>
<td>Pathological alteration of the glomeruli</td>
</tr>
<tr>
<td><strong>Glomerulus</strong></td>
<td>A capillary vessel cluster in the kidneys, site of the first phase of urine formation</td>
</tr>
<tr>
<td><strong>Glucosuria</strong></td>
<td>Excretion of glucose in urine</td>
</tr>
<tr>
<td><strong>Gonococci</strong></td>
<td>Gram-negative bacterial species responsible inter alia for gonorrhoea</td>
</tr>
<tr>
<td><strong>Gram-negative</strong></td>
<td>Assuming a red color on Gram staining</td>
</tr>
<tr>
<td><strong>Gram-positive</strong></td>
<td>Assuming a blue color on Gram staining</td>
</tr>
<tr>
<td><strong>Gram stain</strong></td>
<td>The most important differential-diagnostic stain in bacteriological examinations</td>
</tr>
<tr>
<td><strong>Granulocyte</strong></td>
<td>A large white blood corpuscle, the leukocyte species encountered most frequently in pathological urine</td>
</tr>
<tr>
<td><strong>Haematuria</strong></td>
<td>Excretion of destroyed (lysed) red blood corpuscles with the urine</td>
</tr>
<tr>
<td><strong>Haemoglobin</strong></td>
<td>The pigment of red blood corpuscles</td>
</tr>
<tr>
<td><strong>Haemoglobinuria</strong></td>
<td>Presence of dissolved haemoglobin in urine as a result of erythrocyte lysis</td>
</tr>
<tr>
<td><strong>Haemolysis</strong></td>
<td>Destruction of red blood corpuscles by release of haemoglobin</td>
</tr>
<tr>
<td><strong>Haemophilia</strong></td>
<td>“Blood disease,” a genetically determined blood clotting disturbance</td>
</tr>
<tr>
<td><strong>Haemorrhagic diathesis</strong></td>
<td>Abnormal tendency towards bleeding</td>
</tr>
<tr>
<td><strong>Heart failure</strong></td>
<td>Myocardial weakness, insufficient functional performance of the heart</td>
</tr>
<tr>
<td><strong>Hepatic</strong></td>
<td>Relating to the liver</td>
</tr>
<tr>
<td>-------------------</td>
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</tr>
<tr>
<td><strong>Hepatitis</strong></td>
<td>Inflammation of the liver</td>
</tr>
<tr>
<td><strong>Hyperchromatism</strong></td>
<td>Increased staining capacity of cell nuclei</td>
</tr>
<tr>
<td><strong>Hyperemesis gravidarum</strong></td>
<td>Abnormally severe vomiting during pregnancy</td>
</tr>
<tr>
<td><strong>Hyperglycaemia</strong></td>
<td>Elevated blood glucose level</td>
</tr>
<tr>
<td><strong>Hyperosmolar coma</strong></td>
<td>Increased osmolarity of the serum due to pronounced hyperglycaemia in so-called hyperosmolar form of diabetic coma</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>High blood pressure, a disease of the circulatory system characterized by elevated arterial blood pressure</td>
</tr>
<tr>
<td><strong>Hyperuricaemia</strong></td>
<td>Uric acid concentration in blood exceeding 6 mg/dL</td>
</tr>
<tr>
<td><strong>Hyphae</strong></td>
<td>Thread-like fungal cells</td>
</tr>
<tr>
<td><strong>Hypoglycaemia</strong></td>
<td>Strongly reduced glucose content in blood</td>
</tr>
<tr>
<td><strong>Hypotension</strong></td>
<td>Chronic low blood pressure</td>
</tr>
<tr>
<td><strong>Hypoxia</strong></td>
<td>Oxygen deficiency in tissue due to a low oxygen content in blood (reason: respiration impairment or circulation disturbance)</td>
</tr>
<tr>
<td><strong>Icterus</strong></td>
<td>Jaundice, a symptom of various liver diseases and of bile duct obstruction</td>
</tr>
<tr>
<td><strong>Ileus</strong></td>
<td>Constriction or obstruction of a part of the intestine</td>
</tr>
<tr>
<td><strong>Insulin</strong></td>
<td>A blood-glucose-lowering hormone formed in the pancreas</td>
</tr>
<tr>
<td><strong>Intermittent</strong></td>
<td>Occurring from time to time</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
</tr>
<tr>
<td>---------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Intoxication</td>
<td>Poisoning</td>
</tr>
<tr>
<td>Intrahepatic</td>
<td>Occurring within the liver</td>
</tr>
<tr>
<td>Intracanicular</td>
<td>Situated within an extremely fine tubular passage or channel (canaliculus)</td>
</tr>
<tr>
<td>Intrarenal</td>
<td>Situated within a kidney</td>
</tr>
<tr>
<td>Intravasal</td>
<td>Situated within a blood vessel</td>
</tr>
<tr>
<td>Ketoacidosis</td>
<td>Metabolic disturbance in which there is a shift of the acid-base balance, provoked by increased formation of ketones</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>A gram-positive bacterial species</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>White blood corpuscles; a collective term for all nucleus-containing colorless blood cells</td>
</tr>
<tr>
<td>Leukocyturia</td>
<td>Excretion of leukocytes in urine</td>
</tr>
<tr>
<td>Lipogenesis</td>
<td>New formation of fats in fat tissue and in the liver</td>
</tr>
<tr>
<td>Lipolysis</td>
<td>Enzymatic cleavage of fats</td>
</tr>
<tr>
<td>Lordosis</td>
<td>Physiological curvature of the cervical and lumbar spine</td>
</tr>
<tr>
<td>Lupus erythematosus</td>
<td>Inflammatory skin disease with bluish-red skin flecks</td>
</tr>
<tr>
<td>Lymph</td>
<td>The fluid content of the lymph vessels, of major significance for material exchange in tissues</td>
</tr>
<tr>
<td>Lysis</td>
<td>Destruction of cells, e.g. erythrocytes or bacteria</td>
</tr>
<tr>
<td>Malignant</td>
<td>Tending to become progressively worse and resulting in death</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
</tr>
<tr>
<td>--------------------</td>
<td>-------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Metabolite</td>
<td>A low-molecular substance formed or transformed in the course of metabolic processes</td>
</tr>
<tr>
<td>Metaphylaxis</td>
<td>Treatment of a patient after recovery from a disease as a preventive measure to avoid possible relapses</td>
</tr>
<tr>
<td>Micturition</td>
<td>Voiding of urine</td>
</tr>
<tr>
<td>Morphology</td>
<td>Science of the form and structure of organisms and their organs</td>
</tr>
<tr>
<td>Mycobacteria</td>
<td>Gram-positive bacteria responsible for tuberculosis and leprosy</td>
</tr>
<tr>
<td>Necrosis</td>
<td>Death of cells, tissues, or organs</td>
</tr>
<tr>
<td>Nephritis</td>
<td>Inflammation of the kidneys, mostly in the form of pyelonephritis</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>General designation for kidney damage</td>
</tr>
<tr>
<td>Nucleolus</td>
<td>Small strongly staining corpuscle often occurring in large numbers in cell nuclei</td>
</tr>
<tr>
<td>Obstruction</td>
<td>Occlusion of cavities and vessels</td>
</tr>
<tr>
<td>Orthostasis</td>
<td>Upright position of the body</td>
</tr>
<tr>
<td>Osmolality</td>
<td>Molar concentration of all osmotically active molecules in solution, expressed in weight units</td>
</tr>
<tr>
<td>Osmolarity</td>
<td>Molar concentration of all osmotically active molecules in solution, expressed in volume units</td>
</tr>
<tr>
<td>Osmosis</td>
<td>Migration of water molecules through a semi-permeable membrane separating two solutions of different concentrations until the concentrations have become equal</td>
</tr>
</tbody>
</table>
**Otitis**  
Ear inflammation

**Oxidation**  
Combination of a chemical substance with oxygen

**Papillary necrosis**  
Necrosis of renal papillae

**Parenchyma**  
Tissue serving for the specific function of an organ (in contrast to connective or supporting tissue)

**Parenteral**  
Bypassing the gastrointestinal tract

**Pathogenic**  
Provoking disease

**Pathognomonic**  
Characteristic of a disease picture

**Pathological**  
Caused by a morbid condition

**Periarteritis nodosa**  
Rare vascular disease; inflammation of the wall layers of smaller arteries with nodule-like outgrowths

**Periportal**  
In the neighbourhood of the portal vein

**Permeability**  
Penetrability (of a membrane) by fluids

**Persistent**  
Continuing to exist, persevering

**Phagocytosis**  
Destruction of foreign substances in an organism and making them innocuous by “ingesting cells”

**Pneumonia**  
Inflammation of the lungs

**Pollakiuria**  
Frequent urge to pass water, though only a small amount of urine is voided each time

**Polycythaemia**  
Abnormal proliferation of erythrocytes, leukocytes, and platelets, which leads, among others, to swelling of the liver and spleen
**Porphyria**  
A metabolic disturbance with increased excretion of porphyrins in the urine

**Postrenal**  
Occurring functionally downstream of the kidneys

**Precipitation**  
Flocculation or settling out in coagulation processes

**Predisposition**  
Tendency or sensitivity of the organism to certain diseases

**Progressive**  
Increasing, advancing

**Prophylaxis**  
Measures serving for the prevention of diseases

**Proteinuria**  
Excretion of proteins in urine

**Proteus**  
Genus of gram-negative, actively mobile, organisms occurring in various distinct forms (putrefaction bacterium, causative agent of urinary tract infections)

**Pyelonephritis**  
Simultaneous bacterial inflammation of the renal pelvis and the kidneys; the most common causative agents are E. coli, Klebsiella, Proteus, and enterococci

**Pyuria**  
Excretion of pus in the urine

**Reflectance photometry**  
Method of photometric evaluation of urine test strips

**Renal**  
Relating to the kidneys

**Renal failure**  
Pronounced impairment of kidney function

**Renal threshold**  
Maximum reabsorption capacity of the kidneys

**Resorption**  
Uptake of food constituents after their digestion through the intestinal mucosa, especially in the small intestine

**Respiratory**  
Referring to breathing (respiration)
| **Retention** | Physiological: holding of a substance in the organism e.g. as a result of increased tubular reabsorption in the kidneys |
| **Relapse** | Recurrence (of a past illness) |
| **Rupture** | Traumatic or spontaneous tearing or disruption of organs |
| **Screening (test)** | Investigation of large groups of the population for the purpose of early detection of probable carriers of the target condition; in screening no diagnosis is established, and positive test results must be followed by further differential diagnostics |
| **Semi-permeable** | Semi-penetrable |
| **Sepsis** | Blood poisoning |
| **Sinusitis** | Acute or chronic inflammation of paranasal sinuses |
| **Stricture** | Narrowing of a body organ by scarring |
| **Suppository** | Medicated mass intended for introduction into the rectal, vaginal, or urethral orifice |
| **Test-strip screening** | Stepwise screening method in urine diagnostics in which only the urine samples with relevant positive test strip results are investigated further microscopically or bacteriologically |
| **Thrombo(cyto)penia** | Blood-platelet deficiency |
| **Tonsillitis** | Inflammation of tonsils |
| **Transient** | Temporary |
| **Traumatic** | 1. Producing a wound  
2. Produced by a lesion  
3. Leading to psychological shock |
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td><strong>Uraemia</strong></td>
<td>Urine intoxication (presence of urea in blood) as a terminal stage of renal failure; the only effective methods of treatment are dialysis and kidney transplant</td>
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<tr>
<td><strong>Urethritis</strong></td>
<td>Inflammation of the urethra</td>
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<tr>
<td><strong>Urine cytology</strong></td>
<td>Evaluation of the cell alterations in a stained smear of urine sediment</td>
</tr>
<tr>
<td><strong>Urine status</strong></td>
<td>Result of examinations carried out on freshly voided mid-stream urine with multitest strips</td>
</tr>
<tr>
<td><strong>Urobilinogenuria</strong></td>
<td>Excretion of urobilinogen in the urine</td>
</tr>
<tr>
<td><strong>Urolithiasis</strong></td>
<td>Formation of urinary stones (calculi) and the resulting pathological condition</td>
</tr>
<tr>
<td><strong>Vacuole</strong></td>
<td>Hollow cavity in cell nucleus or cytoplasm, filled with a watery or thick-flowing substance</td>
</tr>
<tr>
<td><strong>Vasoconstrictive</strong></td>
<td>Vessel-narrowing</td>
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</tbody>
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Further Reading

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