SUMMARY

Background: Urinalysis is the most commonly performed biochemical test in infancy and early childhood. The urine sample should be correctly obtained, age-specific aspects should be considered, and age-dependent reference values should be used.

Method: This review is based on a selective literature search in electronic databases, textbooks, and guidelines from Germany and abroad on the acquisition of urine samples and the performance of urinalysis in infancy and early childhood.

Results: The timing and mode of acquisition of the urine sample affect the assessment of hematuria, proteinuria, leukocyturia, nitrituria, and the uropathogenic bacterial colony count in the urine culture. Dipstick tests can be used for targeted screening for these features. The test results should be interpreted together with the findings of urine microscopy, the medical history, and the physical examination. Proteinuria should be quantified and differentiated; both of these things can be done either from collected urine or (especially in infants and young children) from a spontaneously voided urine sample, by determination of the protein/creatinine quotient. Orthostatic proteinuria in an adolescent requires no further evaluation or treatment. Hematuria should be characterized as either glomerular or non-glomerular erythrocyturia. Asymptomatic, isolated microhematuria in childhood is not uncommon and often transient; in the absence of a family history, it usually does not require an extensive work-up. Proteinuria combined with hematuria should arouse the suspicion of glomerulonephritis.

Conclusion: Urinalysis in infancy and early childhood is a simple and informative diagnostic test as long as the urine sample has been obtained properly and the results are interpreted appropriately for this age group.

D iagnostic assessment of the urine is a basic component of the evaluation of diseases of the kidneys and urinary tract, along with the history, physical examination, and other tests. Urinalysis is most commonly performed to diagnose a urinary tract infection or to rule out renal disease. Abnormal findings in urinalysis can be seen in 1–14% of healthy schoolchildren (1, 2, e1, e2).

We selectively searched the PubMed database for articles from the last ten years containing the key words “dipstick urine analysis,” “leukocyturia,” “bacteriuria,” “nitrituria,” “hematuria,” “proteinuria,” and “pediatric.” We also considered older publications cited in these articles, textbooks and current guidelines from Germany and abroad on urinary diagnosis in infancy and childhood.

Learning objectives

After reading this article, the reader should be able to list the main principles of urine sample acquisition in infancy and childhood and critically assess dipstick test findings. The reader will also learn the basic principles of the age-appropriate interpretation of hematuria, proteinuria, and leukocyturia.

Urine sample acquisition

Single urine samples

Midstream urine – Midstream urine can be obtained from any child that has achieved urinary continence. Cleaning the genitals and perineum with soap and water before voiding has been shown to lessen contamination of the urine with periurethral organisms and leukocytes (3, 4).

Acquisition of urine samples from infants and toddlers – There are four ways to obtain urine samples from small children who cannot yet control their voiding:

- **Bag urine:** The genitals are inspected, thoroughly cleaned, and dried, and a self-adhesive urine
**TABLE 1**

| Proteinuria in collected urine and determination of the protein/creatinine quotient in spontaneously voided urine (10, 28–30, e4) |
|---|---|---|
| 24-hour urine collection | Protein/creatinine quotient in spontaneous urine | Albumin/creatinine quotient in spontaneous urine |
| Physiological | ≤ 4 mg/m² BSA/hr (≤100 mg/m² BSA/d) | ≤ 0.2 mg/mg (children 6-24 mo ≤ 0.5 mg/mg) | ≤ 30 mg/g |
| Proteinuria | > 4 mg/m² BSA/hr (> 100 mg/m² BSA/d) | > 0.2 mg/mg (children 6-24 mo > 0.5 mg/mg) | 30 – 299 mg/g, microalbuminuria |
| Marked proteinuria | > 40 mg/m² BSA/hr (> 1 g/m² BSA/d) | > 2.0 mg/mg | > 300 mg/g, macroalbuminuria |

BSA, body surface area

A sample from the first voiding of the morning is most suitable for biochemical testing (10, 11), but the second voiding is more practical in the outpatient clinic (10). Urine should always be obtained at the same time of day from each patient, so that the findings will be comparable across tests. Spontaneously voided urine should not be kept before testing for any longer than 1–2 hours at room temperature, or 4 hours in a refrigerator (at 4 °C), or else the cells will disintegrate, the bacterial count will increase, and the pH will rise (e5).

**Collected urine**

Common indications for urine collection include the determination of endogenous creatinine clearance, the quantification and differentiation of proteinuria (Table I), and the measurement of fluid and electrolyte excretion. The most important determinant of test validity is the accuracy, rather than the overall duration, of urine collection (10, 12, e6). Urine should be collected in a clean vessel that is stored in a cool place. The starting point of collection is considered to be the time of the last spontaneous voiding before collection, and its endpoint is the time of the last collected voiding. The duration and total volume of urine collection are documented, and 10–20 mL of the mixed urine are analyzed. Accurate urine collection in infants or incontinent children is possible only through an indwelling bladder catheter. In such cases, the single-void urine samples should be reported as a quotient of the parameter in question and the creatinine concentration and compared with age-specific norms (13, e7–e10).

**Leukocyturia**

Leukocyturia makes a urinary tract infection likely; as an isolated finding, it is highly sensitive (83%), but not very specific (Table 2, [14]). The authors recommend microscopic analysis of a freshly obtained, native urine sample, because, in our opinion, the leukocyte esterase reaction of urinary dipsticks is not a fully adequate substitute for microscopy, although there is some debate on this point in the literature (14, 15, e11). The leukocyte esterase test can be made positive by lysed leukocytes or subreptitious material even when microscopy does not reveal any leukocytes; it can also be negative despite positive microscopic findings if the urine is highly concentrated or contains “collapsed” leukocytes (e6).

Whatever is being tested, the instructions for use of the dipstick should be followed conscientiously. The leukocyte count per unit volume is affected by collection bag is securely attached. Ideally, the child should void after being given fluids, and the urine sample should be processed immediately. Bag urine is unsuitable for culture, because contamination frequently causes false-positive findings (5–7).

- **Clean-catch urine:** For the acquisition of a fresh vesical urine sample, the child is held on an adult’s lap with the genitals exposed; urine that is spontaneously voided after drinking is caught in a sterile vessel. This method yields false-positive findings in 5–26% of cases (7, 8).

- **Catheter urine:** A suitable urine sample for culture can be obtained from a female infant or toddler by one-time catheterization (i.e., not from an indwelling bladder catheter). In boys, suprapubic bladder puncture should be performed instead of transurethral catheterization (9).

- **Suprapubic bladder puncture:** This is a simple (though rarely performed), relatively noninvasive means of acquiring a urine sample if pyelonephritis is suspected, particularly when the patient is an infant. Vesical puncture is indicated whenever bag urine can be expected to be contaminated, e.g., in patients with vulvovaginitis, anogenital dermatitis, or phimosis. The puncture is most likely to be successful if the degree of filling of the bladder is assessed beforehand by ultrasonography: in neonates and infants, ultrasonography increases the likelihood of an adequate urine sample from 60% to nearly 97% (e3, e4).

**Urine acquisition for reliable microbiological testing**

In infants and toddlers, urine must be obtained by clean catch, catheterization, or bladder puncture; spontaneously voided urine is likely to be contaminated.

**Isolated leukocyturia or bacteriuria**

Isolated leukocyturia does not imply a urinary tract infection.
the variable amount of urine in each voiding. This can alter the findings not only of dipstick tests, but also of counting chambers and other cell-counting methods. A leukocyte count of 5–10/μL is considered abnormal in boys over age 3; in girls, counts in the range of 20–50/μL are suspect for a urinary tract infection, and counts above 50/μL are considered clearly abnormal (Table 3).

The microscopic demonstration of leukocyte cylinders in the urine sediment, together with marked bacteriuria, is pathognomonic for pyelonephritis.

### Nitrite Test

Most urinary pathogens (with the important exception of enterococci) can reduce nitrate to nitrite; thus, nitrite in the urine indicates bacteriuria. The nitrite dipstick test may be falsely negative if the urine is held for too short a time in the bladder (less than 4 hours). As a result, the sensitivity of nitrite dipstick testing for clinically significant bacteriuria is no higher than 30–50% in infants, who generally urinate every 1–4 hours. On the other hand, its sensitivity in girls at least 3 years of age is 98% (9, 14, 16). The simultaneous demonstration of nitrituria and leukocyturia is 93% sensitive for a urinary tract infection (Table 2, [14]).

### Bacteriuria

For urine culture, a fresh urine sample should be obtained and kept at 4–8°C until and during its transport to the laboratory. Alternatively, the sample can be pre-incubated in culture media and sent directly at 36°C. The bacterial count per milliliter is determined; its interpretation depends on the mode of acquisition of the sample. The diagnosis of a urinary tract infection requires the demonstration of at least 10^5 organisms/mL (17); more recent studies call for a minimal count of 10^5 or 10^6/mL (18). Lower counts in catheterized urine may be pathological, and any number of demonstrated organisms is pathological in urine obtained by bladder puncture (Table 3). Depending on the mode of acquisition, urine culture often has false-positive rates up to 25%, and the false-positive rate of bag urine culture ranges from 30% to 63%. Bladder puncture is superior to clean catch and thus provides a far more suitable sample than bag collection of the urine (5, 6, 17, 18).

In children of school age, the typical clinical manifestations of urinary tract infection are pain on urination, increased voiding frequency, and difficulty voiding; pyelonephritis is characterized by flank pain and fever. Whenever there are discrepant findings, urinalysis should be repeated before any further, possibly inappropriate diagnostic or therapeutic measures are taken. A recurrent or complicated urinary tract infection or a history of recent treatment with antibiotics should arouse the suspicion of a fungal or viral infection or of a pathogen whose detection requires special culture media (Chlamydia, Trichomonas, Ureaplasma).

One should ask critically whether the demonstrated organism is typical for the patient’s age and sex. At any age, and in both sexes, the most common pathogen is Escherichia coli. In boys at least 1 year of age, Proteus species account for up to 30% of urinary tract infections, while Staphylococcus species are found in about 30% of urinary tract infections in girls aged 9 to 15 (1, 19–24). Indications of possible contamination include a low cell count, mixed flora in a single culture, different pathogens in serial studies, and organisms that are not usually found in urinary tract infections.

Routine screening occasionally reveals significant bacteriuria without leukocyturia in apparently healthy children (0.2–2%). This is called asymptomatic bacteriuria (25, 26, e12) and does not require antibiotic treatment. Urethritis is common in sexually active adolescents (e13, e14).

### Urinary Tract Infections

Urinary tract infections are classified as either asymptomatic (bacteriuria and leukocyturia without

### Table 2

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (range), %</th>
<th>Specificity (range), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte esterase test</td>
<td>83 (67–94)</td>
<td>78 (64–92)</td>
</tr>
<tr>
<td>Nitrite test</td>
<td>53 (15–82)</td>
<td>98 (90–100)</td>
</tr>
<tr>
<td>Leukocyte esterase or nitrite test positive</td>
<td>93 (90–100)</td>
<td>72 (58–91)</td>
</tr>
<tr>
<td>Microscopy, leukocytes</td>
<td>73 (32–100)</td>
<td>81 (45–98)</td>
</tr>
<tr>
<td>Microscopy, bacteria</td>
<td>81 (16–99)</td>
<td>83 (11–100)</td>
</tr>
<tr>
<td>Leukocyte esterase or nitrite test or microscopy positive</td>
<td>99.8 (99–100)</td>
<td>70 (60–92)</td>
</tr>
<tr>
<td>Hematuria (peroxidase test)</td>
<td>86.1 (73–89)</td>
<td>85 (81–93)</td>
</tr>
</tbody>
</table>
clinical symptoms) or symptomatic (with symptoms, possibly but not necessarily including fever). They can also be classified as uncomplicated or complicated on the basis of the patient’s urinary tract anatomy (malformations of the urinary tract), vesical and renal function, and immune competence. In complicated urinary tract infections, culture often reveals multiple pathogens. Colony counts and resistance testing should be obtained for each pathogen.

Leukocyturia without bacteriuria may represent sterile leukocyturia; its differential diagnosis includes urolithiasis, renal tubular acidosis, interstitial nephritis, cystic renal diseases, tuberculous, appendicitis, vaginitis, irritation of the meatus/urethra, and dehydration (14).

Proteinuria—excessive elimination of protein in the urine—is a feature of tubular or glomerular dysfunction. It is assessed on the basis of a midstream urine sample in school-age children or a bagged urine sample in infants and toddlers. The second voiding of the day is often used; the first voiding of the day is the most concentrated, but often cannot be obtained in outpatients (e7–e9).

Dipstick tests provide only semiquantitative findings because they do not take the renal filtration rate into account. The degree of blue staining in the test field is correlated, in particular, with the strength of the albumin reaction with tetrabromophenol. False positive findings can arise because of mucus, pus, blood, or highly alkaline (pH > 8) and highly concentrated urine; false negative ones, because of diluted urine (27). Proteinuria is present by definition when the protein concentration is at least 30 mg/dL (e6). Microalbuminuria at lower concentrations is present in as many as 5–12% of asymptomatic children (e7).

Ideally, urinary protein should be quantified on the basis of a 24-hour urine collection (Table 1). Collected urine samples are considered the gold standard of diagnosis. For infants and toddlers, in whom the collection of urine samples over time is especially problematic, the protein/creatinine and albumin/creatinine quotients in spontaneously voided urine can be measured instead. These values are independent of the urine volume, because the amount of creatinine excreted per day is stable. For the quotient to be reliable, the urinary creatinine concentration should be no lower than 10 mg/dL; lower values in neonates (including premature ones) and in children with polyuria may lead to misinterpretation. A low albumin fraction in the total amount of excreted protein may indicate an extrarenal cause of proteinuria, e.g., hemoglobin, myoglobin, light chains (very rare in children), amyloid, and other causes.

**TABLE 3**

Reference ranges for leukocyte and bacteria counts (per µL and mL, respectively) in uncentrifugated urine (14, 22, e30)

<table>
<thead>
<tr>
<th></th>
<th>Spontaneously voided urine</th>
<th>Midstream or catheterized urine</th>
<th>Urine obtained by bladder puncture</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Leukocyte count</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>physiological</td>
<td>&lt; 20</td>
<td>&lt; 15</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>suspect</td>
<td>20–50</td>
<td>15–50</td>
<td>5–10</td>
</tr>
<tr>
<td>pathological</td>
<td>&gt; 50</td>
<td>&gt; 50</td>
<td>&gt; 10</td>
</tr>
<tr>
<td><strong>Bacteria count</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>physiological</td>
<td>&lt; 10⁴</td>
<td>&lt; 10⁴</td>
<td>&lt; 10⁴</td>
</tr>
<tr>
<td>suspect</td>
<td>10⁴</td>
<td>10⁴ to 5 × 10⁴</td>
<td>10⁴ to 5 × 10⁴</td>
</tr>
<tr>
<td>pathological</td>
<td>&gt; 10⁵</td>
<td>&gt; 5 × 10⁴</td>
<td>&gt; 5 × 10⁴ any detection of bacteria</td>
</tr>
</tbody>
</table>

Utility of dipstick tests for proteinuria
The extent and type of proteinuria cannot be judged from a dipstick test alone. Further tests are needed so that proteinuria can be quantified and categorized.

Orthostatic proteinuria
Orthostatic proteinuria is diagnosed on the basis of a daytime urine sample and the first voided urine of the morning.
The protein/creatinine quotient in single, spontaneously voided urine samples is closely correlated with the amount of protein in 24-hour urine collections and is therefore suitable for the quantification of proteinuria, including for follow-up over time (Table 1 [10, 28–30, e4]). Just as in the determination of the glomerular filtration rate, the amount of proteinuria may be under- or overestimated if the urinary creatinine concentration is very high (> 2.5 g/L, e.g., among adolescent body-builders) or very low (< 0.2 g/L, e.g., in muscular dystrophy). A 24-hour urine collection is needed if proteinuria is to be assessed precisely without any interference from circadian fluctuations (11). These fluctuations are due, in part, to changes in body position over the 24-hour period.

Large protein molecules, such as immunoglobulins, do not cross the glomerulus, while smaller ones do. In addition to this selectivity with respect to size, there is also selectivity with respect to charge: strongly negatively charged proteins are retained, including more than 99% of albumin. Neutral or positively charged molecules the size of albumin pass more freely through the glomerular filter. Low-molecular-weight proteins normally cross the basal membrane but are then reabsorbed by endocytosis in the proximal tubule in amounts up to 96% (e15).

The above considerations account for the typical patterns of abnormal urinary protein findings. In selective glomerular proteinuria, medium-sized protein molecules—mainly albumin—cross the basal membrane. If the IgG/albumin quotient exceeds 3%, nonselective glomerular proteinuria is present. In tubular proteinuria (e.g., after chemotherapy or in hereditary or acquired tubulopathy), low-molecular-weight proteins are reabsorbed from the urine in the proximal tubule in less than normal amounts.

Urinary dipstick tests mainly disclose the presence of albumin, in semiquantitative fashion, and thus cannot reveal tubular proteinuria. In contrast, the Biuret reaction gives a quantitative measure of all urinary proteins. To quantify further proteins in the urine, other methods are needed, e.g., SDS-PAGE (sodium dodecyl sulfate—polyacrylamide gel electrophoresis).

Asymptomatic proteinuria is present as an isolated finding in 0.6% to 6.3% of children. In a cohort of 9000 children, significant proteinuria was found in a single sample in 10.7%, but was present in two samples from the same child in only 2.5% and in four samples in only 0.1% (31). Clearly, urinalysis should always be repeated if proteinuria is found before any further testing is done for renal or systemic disease.

Proteinuria can be transient or functional. In general, proteinuria is not indicative of renal disease in the following situations (32, e8):

- hyperthermia
- fever
- physical exertion
- emotional stress
- congestive heart failure
- seizures
- hyperthyroidism.

Orthostatic proteinuria is characterized by moderate, nonselective proteinuria of up to 1.0 mg/mg creatinine in the daylight hours, and physiologic protein excretion during nighttime sleep. It is diagnosed by separate analysis of daytime and nighttime urine samples. It mainly affects obese adolescents and accounts for 20–60% of all cases of asymptomatic proteinuria. Its overall prognosis is favorable, as it does not seem to be associated with renal disease of any kind (11, e16).

If an isolated finding of mild proteinuria persists (< 1 g/m²/day, or an albumin/creatinine quotient of 0.17–2 mg/mg [exception: orthostatic proteinuria]), a

<table>
<thead>
<tr>
<th>Causes of dark urine (e5)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Endogenous</strong></td>
</tr>
<tr>
<td>erythrocytes</td>
</tr>
<tr>
<td>hemoglobin</td>
</tr>
<tr>
<td>myoglobin</td>
</tr>
<tr>
<td>metabolic products</td>
</tr>
<tr>
<td>homogentisic acid (alcaptonuria), porphyrins</td>
</tr>
<tr>
<td>amorphous urates (brick-dust sediment)</td>
</tr>
<tr>
<td><strong>Exogenous</strong></td>
</tr>
<tr>
<td>foods</td>
</tr>
<tr>
<td>red beets (betanidine), rhubarb (anthrone derivatives), blackberries, food coloring (e.g., aniline)</td>
</tr>
<tr>
<td>drugs</td>
</tr>
<tr>
<td>chloroquine, deferoxamine, ibuprofen, metronidazole, nitrofurantoin, rifampicin, phenolphthalein, phenothiazines, phenytoin, imipenem/cilastatin</td>
</tr>
<tr>
<td>bacteria</td>
</tr>
<tr>
<td>Serratia marcescens</td>
</tr>
</tbody>
</table>
Hematuria

Serial studies reveal hematuria in 1.5–2% of all children and adolescents (34). Macrohematuria arises in 1.3/1000 children (35). The prevalence of microhematuria in routine school medical examinations was found to be 41/1000 in a sample of 8954 children aged 8–15. In another study, girls were found to have microhematuria more commonly than boys (incidence 32/1000 versus 14/1000 in a sample of 12 000 children) (34).

Hematuria is the abnormal excretion of blood or erythrocytes in the urine (34). It is subcategorized as erythrocyturia (red blood cells in the urine) or hemoglobinuria (hemoglobin in the urine). Microhematuria is diagnosed either indirectly with a dipstick test (1 to 2 times positive testing, due to the peroxidase-like activity of hemoglobin) or directly by light microscopy (> 5–10 RBC/µL) in a counting chamber; macrohematuria (> 1000 RBC/µL) is grossly visible as a reddish discoloration of the urine (34). Even 1 mL of blood in a liter of urine produces macrohematuria (ca. 25 000 RBC/µL). Microhematuria is usually an incidental finding, while macrohematuria often leads patients to consult a physician. Microhematuria should always be confirmed by multiple urinalyses. A positive urinary dipstick test is 73–89% sensitive and 81–93% specific for hematuria (Table 1 [38, e17]). Hematuria combined with proteinuria indicates renal disease and calls for further diagnostic evaluation.

Reddish discoloration of the urine is not, however, synonymous with macrohematuria, as it may also be due to hemoglobinuria, myoglobinuria (dipstick test positive, microscopy negative), or medications or foods (dipstick test and microscopy both negative) (Table 4, [e5]). The basic diagnostic evaluation of macrohematuria for its further differentiation always includes microscopic analysis of the urine.

Erythrocyturia can be of either glomerular or postglomerular (non-glomerular) origin. Postrenal sources of bleeding may be located anywhere in the urinary pathway, from the calyces to the urethral opening. Macrohematuria of postrenal origin causes bright red discoloration of the urine, while macrohematuria of glomerular origin is rusty brown. Centrifugation of fresh blood-tinged urine yields a clear fluid if hematuria is postrenal, a brownish fluid if hematuria is renal, and an unchanged reddish fluid in case of hemoglobinuria or myoglobinuria. This test alone is insufficient for clinical evaluation; microscopy is essential for diagnostic purposes, ideally phase-contrast microscopy of the urine sediment, as the demonstration of dysmorphic erythrocytes (acanthocytes or “Mickey Mouse” cells) of erythrocyte cylinders may indicate glomerular damage. A fraction of dysmorphic erythrocytes above 5% is 52% sensitive and 98% specific for a glomerular source of erythrocyturia, such as glomerulonephritis or congenital glomerulopathy [29]. The sensitivity can be increased to 80% by repeated microscopy of at least three different urine samples (40). The demonstration of erythrocyte cylinders proves that the source of the erythrocytes is glomerular, as the cylinders arise by compaction of glomerular-derived...
erythrocytes in the renal tubules and collecting ducts (e18). Blood clots are not found in glomerular hematuria (Table 5).

**Transient hematuria**

Transient hematuria is often not of any pathological significance. It can accompany fever or arise with exercise (“jogger’s hematuria” [e19]), but it may also be due to a urinary tract infection, urolithiasis, a renal tumor (Wilms tumor), or interventions in the urinary tract. In girls, the urine sample may contain blood from vaginal secretions (menstruation) or after sexual intercourse.

**Persistent hematuria**

Rare but serious causes of glomerular hematuria include hereditary defects of the glomerular basal membrane, as in Alport syndrome (e20, e21) and the thin basement membrane disease (benign familial microhematuria) (e22). These diseases are due to defects in the synthesis of type 4 collagen; they have different inheritance patterns and overlapping clinical manifestations. They are often associated with sensorineurial hearing impairment and ocular changes. Isolated asymptomatic microhematuria requires long-term follow-up, as it may indicate the presymptomatic stage of a renal disease (e23). Glomerular (micro-)hematuria needs further evaluation if other family members also have this finding, or if there is a family history of chronic renal disease or hearing impairment. The evaluation should include audiometry, ophthalmologic and molecular-genetic testing, and/or renal biopsy.

Tubulointerstitial causes of erythrocyturia include the following:
- cystic renal diseases
- pyelonephritis (of bacterial or, rarely, other origin, e.g., adenovirus [e24], malaria, toxoplasmosis)
- nephrocalcinosis
- medications
- toxins or tumors (e25).

As these diseases do not involve the glomerulus, the erythrocytes in the urine are eumorphic.

The same holds for hematuria of vascular origin, i.e., microthrombosis in sickle-cell anemia, renal venous thrombosis, or renal artery embolism (e25, e26).

Postrenal causes of hematuria include trauma, urinary tract infections, urolithiasis, hypercalciuria, and anatomical lesions (obstruction, hydronephrosis, tumor). A tumor causing postrenal hematuria in childhood is almost always a nephroblastoma (Wilms tumor); such tumors can be visualized by ultrasonography (e27, e28). In some of the cohorts studied, 30–35% of children with isolated microhematuria were found to have hypercalciuria (i.e., a calcium excretion of more than 4 mg/kg BW/24 hours; age-dependent calcium/creatinine ratio in spontaneously voided urine, [e29]).

As findings such as proteinuria, hematuria, leukocyturia, and bacteruria/nitrituria can arise either in isolation or in combination, they should always be interpreted in the light of the history and physical examination, and a differential diagnosis should be generated. In this article, which focuses on basic nephrologic testing, we cannot provide a complete diagnostic algorithm and instead give only a rough guide to the relevant clinical situations.

A thorough history, physical examination including blood pressure measurement (obligatory), ultrasonography of the kidneys and urinary tract, and the urinary evaluation described above may need to be supplemented by further laboratory tests depending on the clinical situation (complete blood count, C-reactive protein [CRP], creatinine, and, if indicated, cystatin C, electrolytes, blood-gas analysis, albumin, IgA, C3 complement, anti-neutrophile cytoplasmic antibodies [ANA], p-/c-ANCA, anti-streptococcal antibodies, clotting tests). Other diagnostic tests that may be indicated in the further evaluation of hematuria/proteinuria include threshold audiometry, ophthalmologic examination for retinal changes (fundus hypertonicus), echocardiography (to evaluate possible hypertrophy), chest x-ray (infiltrates, hemorrhage, pleural effusion); in patients with urinary tract infections, a reflux study (micturition cystourethrography); and, in patients with hydronephrosis, dynamic (MAG3) renal scintigraphy.

**Overview**

The basic prerequisites for the interpretation of urinalysis findings are the correct acquisition of the sample and the correct performance of the tests in question. Dipstick tests can be used to detect leukocyturia, nitrituria, proteinuria, and hematuria; their findings are best interpreted together with the findings of urine microscopy and in view of the

**Localizing the source of erythrocyturia**

In children and adolescents with hematuria, an underlying nephrologic disease should be ruled out. The erythrocyte morphology should be evaluated early to localize the source of erythrocyturia.

**Isolated erythrocyturia**

Although isolated erythrocyturia may be a clinically irrelevant finding, it nonetheless requires comprehensive nephrologic evaluation and follow-up.
clinical situation, sometimes with targeted further testing.

Leukocyturia should be evaluated in connection with the presence or absence of any clinical signs of a urinary tract infection, a systemic inflammatory reaction, and a clearly identified pathogen.

Proteinuria should be quantified and subcategorized by type. Orthostatic proteinuria is of no pathological significance. Proteinuria combined with hematuria and/or edema calls for a nephrological evaluation for possible glomerulonephritis and/or glomerulopathy (respectively).

The detection of erythrocyturia should be followed by urine microscopy to determine whether its origin is glomerular or non-glomerular. The further diagnostic evaluation depends on which of these is the case. Microhematuria, if it is an isolated finding, may be of no pathological significance. Hematuria accompanied by other abnormal urinary findings or clinical manifestations may be a sign of nephritis or of a systemic disease with renal involvement.

Conflict of interest statement
Prof. Klaus and PD Dr. Utsch declare that they have no conflict of interest.

References

Red discoloration of the urine
Even a small amount of blood can cause macro-hematuria. The finding of red discoloration of the urine provides no information about its cause (glomerular or non-glomerular hematuria, other).


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For eReferences please refer to:
www.aerzteblatt-international.de/ref3714

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“The Diagnosis and Graded Treatment of Atopic Dermatitis” (issue 29–30/2014) until 12 October 2014,
Please answer the following questions to participate in our certified Continuing Medical Education program. Only one answer is possible per question. Please select the answer that is most appropriate.

**Question 1**
What method of obtaining a urine sample is most suitable for reliable biochemical testing?
- a) the first voided urine of the day
- b) the second voided urine of the day
- c) a 12-hour urine collection
- d) a 24-hour urine collection
- e) the nocturnal portion of collected urine

**Question 2**
Which of the following statements about the interpretation of findings of urinary dipstick tests is true?
- a) The time the urine spent in the bladder does not affect the result of the nitrite dipstick test.
- b) Fluctuations of urine volume do not affect the leukocyte count per unit volume.
- c) The sensitivity of dipstick testing for clinically significant bacteriuria in an infant is roughly 90%.
- d) In infants, the nitrite dipstick test is rarely falsely negative.
- e) The nitrite dipstick test can be falsely negative if the voided urine has been in the bladder for too short a time (less than 4 hours).

**Question 3**
What symptoms and signs are characteristic of pyelonephritis in school-aged children?
- a) insomnia and hematuria
- b) pleuritic pain and dysuria
- c) arthritis and pain on urination
- d) flank pain and fever
- e) vomiting and sepsis

**Question 4**
Which of the following is the most likely underlying cause of a bacterial urinary tract infection in an infant?
- a) an anatomical malformation of the urinary tract
- b) nephroblastoma
- c) diaper dermatitis
- d) a virus or fungus
- e) neoplasia

**Question 5**
Which of the following testing methods in urinalysis in childhood has the highest specificity?
- a) the peroxidase test
- b) the leukocyte esterase test
- c) the nitrite test
- d) microscopy for bacteria
- e) microscopy for leukocytes

**Question 6**
Which of the following foods can darken the urine?
- a) potatoes
- b) strawberries
- c) asparagus
- d) carrots
- e) rhubarb

**Question 7**
What is the reference range for an abnormal leukocyte count in midstream urine from a girl under 3 years of age?
- a) 1 – 10/µL
- b) 10 – 20/µL
- c) 20 – 30/µL
- d) 30 – 40/µL
- e) > 50/µL

**Question 8**
Which of the following is a tubulo-interstitial cause of erythrocyturia?
- a) surgery on the urinary tract
- b) hepatitis
- c) urolithiasis
- d) toxoplasmosis
- e) Alport syndrome

**Question 9**
What type of malignant tumor is the cause of nearly all cases of postrenal hematuria in childhood?
- a) adenocarcinoma
- b) nephroblastoma
- c) choroid plexus carcinoma
- d) myelodysplastic lymphoma
- e) osteosarcoma

**Question 10**
What conditions are often associated with type 4 collagen mutations?
- a) sensorineural hearing impairment and ocular changes
- b) rheumatoid arthritis and Crohn’s disease
- c) varicocele and hepatitis
- d) reflux esophagitis and arrhythmia
- e) atopic dermatitis and dysphagia


