Urine Dipstick Testing: Everything You Need to Know

By James R. Roberts, MD

Emergency physicians routinely order urinalysis (UA) many times each shift. It's usually a straightforward issue, and most physicians think they are well versed in the interpretation of the results: You give it a glance, and make a decision. The dipstick analysis, the microscopic exam, and other information gleaned from a UA make their way into decision-making for a variety of diagnostic, therapeutic, and disposition issues. Like most things learned in detail many years ago, the interpretation of the UA should be revisited on a regular basis.

I find myself thinking I know everything about a certain test only to find that the guidelines have changed, technology has advanced, and previously held dogma is now relegated to the status of misconception. With that in mind, I’ll review the ins and outs of the urinalysis in emergency medicine. When one considers the complexity of the UA, it is obvious that this is not a simple test. The intracies and subtleties are actually quite amazing. This month’s column focuses on dipstick testing, and next month’s will review urine microscopy.

Urinalysis: A Comprehensive Review

Simerville J, et al
Am Fam Physician
2005;71(1):153

The authors of this nifty review discuss the value of the standard UA for the diagnosis of many urinary tract conditions, including malignancy and metabolic issues. The review discusses the correct method for performing a urinalysis and highlights the importance and diagnostic value of a number of abnormal results found on the dipstick and with microscopy. Information gained for the UA is termed invaluable by these urologists from Georgetown University.

Specimen Collection: For most men and women and in most ED situations, a midstream clean-catch technique is usually adequate. According to these authors (but many would disagree), the time-honored ritual of cleaning the external genitalia in women has little or no proven benefit, although it is commonly emphasized. In some reviews, contamination rates are similar in specimens obtained with or without prior cleaning. (Arch Intern Med 2000;160:2537.) Urine should be refrigerated if it cannot be examined for more than two hours because delayed analysis can produce unreliable results.

Physical Properties: A variety of foods, medications, metabolic products, and infections can cause abnormal urine colors and odors. Normal urine is clear and light yellow in color. Concentrated urine produces a darker color, a common finding in the morning after overnight water restriction. Cloudy urine can be normal, usually caused by precipitated phosphate crystals in alkaline urine. Significant pyuria also can cause clouded urine. Urine clarity is a good but not infallible guide to the presence or absence of UTI. (Pediatrics 2000;106(5):E60.) Although many believe that odoriferous ammonia-like odor. A fecal smell in the urine suggests a GI-bladder fistula. Certain foods such as asparagus or beets and a variety of medications can change the odor or color of urine. Myoglobin colors the urine brown, carrots can produce a deep yellow color, and pseudomonas infections, propofol, and amitriptyline may give a blue/green hue to the urine.

Dipstick Analysis: The accuracy of detecting microscopic hematuria, significant proteinuria, or urinary tract infection is a subject of much interest and practicality to emergency physicians. The urine dipstick has false-positive and false-negative results, and a list is presented in the table. It also should be noted that the commonly used urine dipstick has a finite lifespan, should be kept in a closed container, and should not be constantly exposed to air. Testing with outdated and improperly stored materials can lead to erroneous results. As an overview, dipstick testing is quite helpful, serving as a screening test for some conditions and a definitive test for others. In complicated cases or serious disease, dipstick testing must be correlated with microscopy and clinical parameters.

Urine Specific Gravity: Urine specific gravity (USG) generally correlates with the urine osmolality. The most useful information derived from the USG is insight into the patient’s hydration status and the concentrating ability of kidneys. The latter function is disrupted in a variety of diseases.

The normal USG ranges from 1.003 to 1.030. USG less than 1.010 is suggestive...
of relative hydration, and values greater than 1.020 indicate relative dehydration. Pathologic conditions that increase the USG without regard to hydration includ ed glycosuria and Syndrome of Inappro priate Antidiuretic Hormone Secretion (SIADH). In such cases, osmolality is the more important parameter to measure. A decreased USG, also known as dilute urine, is associated with diuretic use, diabetes insipidus, renal insufficiency, aldosteronism, or a plethora of condi tions causing impaired renal function. It should be noted that the purpose of the kidney is to concentrate urine when needed. Many renal diseases alter this concentrating function and result in a fixed specific gravity — about 1.010, the specific gravity of the glomerular fil trate. This is known as isosthenuria, a condition seen, for example, in patients with renal dysfunction due to sickle cell disease.

**Urinary pH:** In general the urine pH reflects the serum pH, but the primary and normal function of the kidney is to acidify the urine. Normal serum pH is 7.4, but the normal urinary pH ranges from 4.5 to 8. Because of normal meta bolic activity, the generally accepted normal pH of urine is about 5.5 to 6.5. In renal tubular acidosis (RTA), the kidney cannot acidify the urine, so the urine can be alkaline while the patient’s serum demonstrates a metabolic acidosis.

The urine pH can be related to diet. Acid urine can be the result of ingestion of fruits (hence the use of cranberry juice) that acidify the urine. Diets high in citrate and in citrus fruits, lemons, and vegetables can cause alkaline urine. Meat eaters tend to have more acidic urine, and vegetarians tend to have alkaline urine. In the presence of a documented UTI, alkaline urine may suggest infection with a urea-splitting organism (such as Proteus). In alkaline urine, triple phosphate crystals (magnesium ammonium phosphate crystals) can form a staghorn calculus. Uric acid stones form in an acidic urine.

### Hematuria: The strict definition of hematuria by the American Urological Association is the presence of 3 or more red cells per high-powered field in two of three urine samples. The urine dip stick is used to test for the peroxidase activity of erythrocytes, not for the actual presence of the physical RBC. Of course, myoglobin and hemoglobin produce a positive dipstick for hematuria because these substances also will catalyze this reaction; these are the end products of hemolyzed RBCs or muscle breakdown. High doses of vitamin C will inhibit this process, and can invalidate the dipstick for this test. This also holds true for stool guaiac testing; vitamin C can produce a false-negative occult blood in stool. It has always been standard that a positive dipstick for blood in the absence of RBCs by microscopy is indicative myoglobinuria or hemoglobinuria, not true hematuria.

The authors present a table listing 45 causes of hematuria. Although some rare ones, such as Pahby’s disease, will likely escape the detection and knowl edge of the emergency physician, it is important to know that hematuria can be associated with malignant hypertension, numerous urinary tract cancers, infections, nephrolithiasis, nephritis (lupus) and vasculitis, tuberculosis, and a variety of drugs, including the obvious, heparin and warfarin.

**RB casts are classic for acute glomerulonephritis.** Hematuria also can be associated with TTP, renal vein thrombosis, sickle cell trait, or merely running a marathon. Contrary to popular belief, significant hematuria will not elevate the protein concentration to the required cut-off deemed positive, 3 plus or more on the dipstick. The authors note that up to 20 percent of patients with a gross hematuria have a urinary tract malignancy, so this condition requires a full work-up. Hematuria, in the absence of proteinuria or RB casts, suggests a pure urologic cause (stones/malignancy) for hematuria.

**Proteinuria:** Healthy kidneys limit the protein permeability of the glomerular capillaries, but diseased kidneys allow more protein to be filtered so proteinuria is a hallmark of a variety of renal diseases. Blood proteins are normally filtered and then reabsorbed by the proximal tubule cells. Urinary pro teins include primarily albumin, but some serum globulins are detected. The

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**Urine Dipstick Testing: Causes of False-Positive and False-Negative Results**

<table>
<thead>
<tr>
<th>Dipstick test</th>
<th>False-positive test</th>
<th>False-negative test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin</td>
<td>Phenazopyridine (Pyridium)</td>
<td>Chlorpromazine (Thorazine), selenium</td>
</tr>
<tr>
<td>Blood</td>
<td></td>
<td>Dehydration, exercise, hemo-globinuria, menstrual blood, myoglobinuria, semen in urine, highly alkaline urine, oxidizing agents use to clean perineum</td>
</tr>
<tr>
<td>Glucose</td>
<td>Ketones, levadopa (Larodopa), dipstick exposed to air</td>
<td>Elevated specific gravity, urobilinogen</td>
</tr>
<tr>
<td>Ketones</td>
<td>Acidic urine, elevated specific gravity, some drug metabolites, (e.g., levadopa)</td>
<td>Delay in examination of urine</td>
</tr>
<tr>
<td>Leukocyte</td>
<td>Contamination, nephrolithiasis</td>
<td>Elevated specific gravity, glycosuria, ketonuria, proteinuria, cephalexin (Keflex), nitrofurantoin (Furadantin), tetracycline, gentamicin, vitamin C</td>
</tr>
<tr>
<td>Esterase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrites</td>
<td>Contamination, exposure of dipstick to air</td>
<td>Elevated specific gravity, elevated urabolinogen levels, nitrite reductase-negative bacteria, pH&lt;6.0, vitamin C</td>
</tr>
<tr>
<td>Protein</td>
<td>Alkaline or concentrated urine, quaternary ammonia compounds, isolated radiocontrast agents</td>
<td>Acidic or dilute urine, primary protein is not albumin, such as Bence-Jones protein</td>
</tr>
<tr>
<td>Specific gravity</td>
<td>Dextron solutions, IV radiopaque dyes, proteinuria</td>
<td>Alkaline urine</td>
</tr>
<tr>
<td>Urobilinogen</td>
<td>Elevated nitrate levels, Phenazopyridine</td>
<td></td>
</tr>
</tbody>
</table>

1. Test depends on peroxidase activity of RBC. Tests will be positive with intact or lysed cells. This test is very sensitive and may be positive in normal urine (1-2 RBC/HFP).
2. Especially vaginal contamination.
4. Not clinically significant unless 3 plus or greater. Detects mainly albumin and requires protein excretions of 300-500 mg/day.
5. Accurate analysis for osmolality requires osmometer.

Source: Adapted from Am Fam Physician 2005;71:1153.
DIPSTICK TESTING

Continued from previous page

actual definition of proteinuria is the excretion of more than 100 mg of protein per day. Patients with early renal disease may have microalbuminuria. Early diabetic nephropathy may not be detected by dipstick testing, so it is not a good screening test for this condition. The dipstick test is sensitive almost entirely to albumin; it will not detect low concentrations of globulins or the Bence-Jones proteins associated with multiple myeloma.

The dipstick is actually quite sensitive for proteinuria, and produces false-positive results by reacting to minor proteinuria that would not be considered clinically significant. Concentrated early morning urine may give the false impression of significant proteinuria. The authors state that the dipstick must be 3 plus or greater for protein to be considered significant. Interestingly, prolonged standing can produce proteinuria, termed orthostatic (postural) proteinuria. Ionized radiographic agents and a high alkaline urine may turn the dipstick falsely positive.

Glycosuria: Glucose is normally filtered by the glomerulus, but this substance is then almost completely absorbed in the proximal tubule. When the amount of filtered glucose exceeds the kidney's ability to resorb, glycosuria results, making glycosuria an abnormal finding. The blood glucose is usually at least 180 mg/dL to be detected by the dipstick.

Ketonuria: It is not normal to find ketones in the urine. Ketones are the product of fat metabolism that is commonly encountered in uncontrolled diabetes. Some ketonuria can occur normally in patients on a carbohydrate-free diet (high-protein weight loss diets), and occasionally with starvation or a prolonged fast.

Nitrites: There is a difference between nitrates and nitrites. Although nitrates are excreted by the kidney, nitrites are not normally found in urine. When bacteria reduce urinary nitrates to nitrites, the test also may be falsely negative in the presence of infection. The nitrite reagent on the dipstick is quite sensitive to environmental air, so this test is the one that is most affected when out-of-date dipsticks or those kept in an open container are used. Improperly stored dipsticks are the most common cause of a false-positive test for nitrites.

Leukocyte Esterase: LE is an enzyme produced by neutrophils. It may signal pyuria associated with UTI. However, WBCs anywhere on the GU tract, including the vaginal vault, will produce LE. The dipstick should be allowed to sit for at least 30 to 60 seconds before reading the LE test. LE is somewhat nonspecific, and will be positive in patients with chlamydia infections, urethritis, tuberculosis, bladder tumors, viral infections, nephrolithiasis, foreign bodies, and corticosteroid use.

Bilirubin and Urobilinogen: Urine does not usually contain bilirubin. Any bilirubin found in the urine is conjugated bilirubin because unconjugated bilirubin cannot pass through the glomerulus. Biliary obstruction or liver disease will cause an elevated urine bilirubin. There can normally be small amounts of urobilinogen in the urine. Urobilinogen is the end-product of conjugated bilirubin after it passes through the bile duct and has been metabolized in the intestines. There is a direct correlation from the portal circulation and eventually filtered by the kidney. Patients with hemolysis or other types of liver disease will have an elevated urobilinogen level. If the bile duct is obstructed, less bilirubin enters the intestine, and therefore less urobilinogen is detected in the urine.

Comment: This article is humbling, and makes the clinician yearn for the memory and recall prowess he had in medical school. One marvels at how the interpretation of the lowly UA dipstick has morphed into a very sophisticated science. The main take-home point from this discussion is that dipstick testing is not an exact science.

Although physicians may think that they are well versed in the interpretation of a dipstick urinalysis, a periodic review is helpful. It might not be a bad idea to carry this article in your briefcase because the information is difficult to find in general textbooks. I particularly like the tables (45 causes of hematuria and 37 causes of proteinuria), widening one's differential from just a kidney stone and cancer to such bizarre things such as Ig nephropathy and Goodpasture's disease. No normal individual can possibly remember all these conditions during a busy shift.

Trace-positive dipsticks often confuse the clinician, and those done in the ED don't always match the lab tech's report. There is no totally agreed-upon standard about how to use the dipstick in the ED. Most clinicians use the dipstick to screen for problems, and eschew sending the UA to the lab for repeat testing or microscopy if the dipstick is totally negative. This seems reasonable. ([Clin Neph 1994;41[3]:167].)

Post-Vermont, Kidney stones, for example, can be associated with a 10 percent to 20 percent incidence of a negative dipstick for blood. Don't rule out a kidney stone solely on the basis of a negative dipstick. And hematuria is common with endocarditis and aortic dissection.

The dipstick for blood is probably the test result of greatest utility to the ED, but this is a very sensitive test that has a number of false-positives. The few RBCs that normally inhabit the urine (2-3) can give a trace reading.

The dipstick does not identify RBCs, it essentially detects the presence of RBC peroxidase activity, whether these cells are intact, or if there is merely free hemoglobin in the specimen. Even if the patient is on heparin or warfarin, gross hematuria has always prompted a consideration for malignancy. This is similar to finding occult blood in a stool sample in a patient on iron or aspirin. It may well be related to the drug, but you just can't say for sure. Dehydration and exercise will give a false-negative dipstick for true hematuria, and vitamin C (blocks peroxidase activity), captopril use, a pH less than 5.1, and proteinuria may produce a false-negative dipstick analysis for blood.

I frequently encounter trace to 1 plus protein via dipstick testing. It is rarely important in the ED. Trying to track down trace or 1 plus proteinuria is auseless task in the ED and probably in general medicine. The reason that this test detects albumin, the sulfosalicylic acid test (SSA) detects all proteins in the urine. The SSA test would pick up a myeloma kidney (Bence-Jones light chain immunoglobulin).

With regard to specific gravity, one reason sickle cell patients often go into crisis when there is no good reason to be...
dehydrated is that they cannot concent-
trate their urine. Finding an USG of 1.010 in a patient with advanced sickle cell disease does not mean they are well hydrated. They may be quite dehydrated and unable to concentrate their urine. While USG usually corresponds to osmolality, large molecules in the urine, such as glucose or IV dye, can produce large changes in USG with relatively minimal changes in osmolality. It has been shown that there is no clear or consistent relationship between USG and osmolality (Arch Dis Child 2001;86:155) so when osmolality deter-
minations are important, an osmometer should be used.

With regard to urinary pH (normal 4.5-8.0), there are many causes of alka-
line urine, and not all patients with this finding have uro-genital organisms. The kidney’s task is to acidify urine, and normally a serum pH of 7.4 produces a urine pH of about 6.0. Interestingly, in the presence of urinary tract obstruc-
tion by a stone, the kidney loses its ability to secrete acid, and obstruction alone can produce alkaline urine. (Pedi-
atr. Nephro 1988;2:24.) Patients with a significant metabolic acidosis would be expected to produce an acidic urine, usually below 5.0. Higher pH would sug-
gest RTA.

In my experience, finding a trace or 1 plus leukocyte esterase (LE) is com-
monly a falsely abnormal test. This is likely mostly due to contamination. Interestingly, nephrolithiasis alone, in the absence of infection, can produce a dipstick positive for LE. This may lead the clinician to suspect infection in the stone former when it is not present. With regard to the ability of the dipstick to diagnose UTI (confirmed by culture), the specificity for a positive LE test can be as low as 41%.

While many organisms are capable of converting nitrates and nitrites, non-
nitrate-reducing organisms also can cause false-negative nitrite results. Of course, patients who consume a low-
nitrate diet will not have the nitrate sub-
strate for the bacteria to convert.

The nitrite test is much more sensi-
tive for infection than the LE, although it takes a while for the bacteria to reduce the nitrates to nitrites. The urine must remain in the bladder for some time, and I could not determine the exact specifics. Importantly, if your dipsticks are scattered around the ED lab in an open container for more than two weeks, about three-quarters of them will give a false-positive result for nitrites. Perhaps the lab is better at protecting dipsticks than the ED, but I rarely see the top put back on the container in my ED’s stat lab. Everyone has difficulty with quality control with dipstick testing in the ED. We all now use machines to read the dipstick rather than relying on a nurse’s eyeball, and a printout has replaced the pen. Nonetheless, our hos-
pital lab often disagrees with the ED reading for leukocyte esterase and the degree of hematuria.

Like most things in medicine, the dipstick urinalysis is not as straightfor-
ward as one would like. It is clearly not foolproof nor a gold standard for many things. A plethora of conditions pro-
duce positive or false-negative results. It can serve as a useful guide to the emergency physician as a screening test or as a diagnostic test, but there are times when the dipstick must be corre-
lated with other testing and clinical information.

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June 2007

Questions:

1. The accuracy of urine dipsticks can deteriorate and give incorrect results if the dipsticks are old, exposed to air, or otherwise improperly stored.  
   - True  - False

2. Dipsticks define the presence of intact RBCs in the urine specimen.  
   - True  - False

3. A dipstick test will be positive for blood will result if the patient has myoglobinuria.  
   - True  - False

4. Leukocyte esterase positive dipsticks have a near 100% specificity for bacterial infection.  
   - True  - False

5. The most sensitive dipstick test for infection is the nitrite test.  
   - True  - False

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   - Yes  - No

2. On a scale of 1 to 5, with 5 being the highest, how do you rank the overall quality of this educational activity?  
   - 1  - 2  - 3  - 4  - 5

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