Urine Dipstick Testing: Everything You Need to Know

BY JAMES R. ROBERTS, MD

Think of all the times you order urinalysis each shift. It seems to be a straightforward test, 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 can 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. When one considers the complexity of the UA, it is obvious that this is not a simple test. The intricacies and subtleties are actually quite amazing. This month’s column focuses on dipstick testing, and next month’s will review urine microscopy.

Urinealysis: A Comprehensive Review

Simerville J, Maxted WC, Pahira JJ
Am Fam Physician 2006;74(7):1096

The authors of this nifty review discuss the value of the standard UA for diagnosing many urinary tract conditions, including malignancy and metabolic issues. The review covers the correct method for performing 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: A midstream clean-catch technique is usually adequate for most men and women and in most ED situations. These authors say (and many would disagree) that the time-honored ritual of cleaning the external genitalia in women has little or no proven benefit, although it is commonly emphasized. Some reviews put the contamination rates as similar in specimens obtained with or without prior cleaning. (Arch Intern Med 2000;160(16):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 cloudy urine.

Urine clarity is a good but not infallible guide to the presence or absence of UTI. (Pediatrics 2000; 106(5):E60.) Many believe that odoriferous urine is a sign of infection; but it can only represent a concentrated specimen or a particular diet. Urine that has prolonged bladder retention time can develop an 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. Dipstick testing is quite helpful, serving as a screening test for some conditions and a definitive test for others. Dipstick testing in complicated cases or serious disease 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 include glycosuria and syndrome of inappropriate antidiuretic hormone secretion (SIADH). Osmolality is the more important parameter to measure in such cases. A decreased USG, also known as dilute urine, is associated with diuretic use, diabetes insipidus, adrenal insufficiency, aldosterone, or a plethora of conditions 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 filtrate. This is known as isosthenuria, a condition seen, for example, in patients with renal dysfunction because of sickle cell disease.

Urinary pH: The urine pH generally 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 metabolic activity, the generally accepted normal pH of urine is about 5.5 to 6.5. The kidney cannot acidify the urine in renal tubular acidosis (RTA), 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 ingesting fruits (hence the use of cranberry juice) that acidify the urine. Diets high in citrus and in citrus fruits, legumes, and vegetables can cause alkaline urine. Meat eaters tend to have more acidic urine, and vegetarians tend to have alkaline urine. Alkaline urine in the presence of a documented UTI may suggest infection with a urea-splitting organism (such as Proteus). Triple phosphate crystals (magnesium ammonium phosphate crystals) in alkaline urine 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 three or more red cells per high-powered field in two of three urine samples. The urine dipstick 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 of myoglobinuria or hemoglobinuria, not true hematuria.

The authors present a table listing 45 causes of hematuria; some rare ones, such as Fabry’s disease, will likely escape the detection and knowledge of the emergency physician, but 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.

RBC 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 cutoff 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 workup. Hematuria, in the absence of proteinuria or RBC 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 proteins include primarily albumin, but some serum globulins are detected. The actual definition of proteinuria is the excretion of more than 150 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.

Accuracy of Urinalysis for Disease Detection

<table>
<thead>
<tr>
<th>Condition</th>
<th>Test</th>
<th>Results</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microscopic hematuria</td>
<td>Dipstick</td>
<td>≥1 + blood</td>
<td>91-100</td>
<td>65-99</td>
</tr>
<tr>
<td>Significant* proteinuria</td>
<td>Dipstick</td>
<td>≥3 + protein</td>
<td>96</td>
<td>87</td>
</tr>
<tr>
<td>Culture-confirmed UTI</td>
<td>Dipstick</td>
<td>Abnormal leukocyte esterase</td>
<td>72-97</td>
<td>41-86</td>
</tr>
<tr>
<td></td>
<td>Dipstick</td>
<td>Abnormal nitrates</td>
<td>19-48</td>
<td>92-100</td>
</tr>
<tr>
<td></td>
<td>Dipstick</td>
<td>&gt;5 WBC/HPF</td>
<td>90-96</td>
<td>47-50</td>
</tr>
<tr>
<td></td>
<td>Microscopy</td>
<td>&gt;5 RBC/HPF</td>
<td>18-44</td>
<td>88-89</td>
</tr>
<tr>
<td></td>
<td>Microscopy</td>
<td>Bacteria (any amount)</td>
<td>46-58</td>
<td>89-94</td>
</tr>
</tbody>
</table>

* Defined as 3 + or greater on dipstick.

Source: Adapted from Am Fam Physician 2006;74(7):1096.

Glycosuria: Glucose is normally filtered by the glomerulus, but this substance is then almost completely absorbed in the proximal tubule. Glycosuria results when the amount of filtered glucose exceeds the kidney’s ability to resorb, 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. The dipstick will identify this condition when bacteria reduce urinary nitrates to nitrites. One needs the presence of bacteria for the dipstick to register a positive nitrite.

A positive nitrite test usually means infection. It generally requires more than 10,000 bacteria per ml to turn the dipstick positive, making it a specific but not a very sensitive test. A negative nitrite test does not rule out a UTI, but a positive one strongly suggests infection. Infection with non-nitrate-reducing organisms will result in a negative nitrite test. If the diet is deficient in nitrates, the test may also 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. WBCs anywhere in the genitourinary tract, including the vaginal tract, can cause a positive esterase test. LE is somewhat non-specific, 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. Bilary 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. This urobilinogen is reabsorbed into the portal circulation and eventually filtered by the kidney. Patients with hemolysis or other types of liver disease will have an elevated urobilinogen level.

The eyeball analysis of dipsticks has been replaced with machine reading. This device reads the dipstick and transfers the results directly to an electronic medical record.

Continued on next page
Urine Testing
Continued from previous page

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.

Physicians may think that they are well versed in the interpretation of a dipstick urinalysis, but 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 liked the tables (45 causes of hematuria and 37 causes of proteinuria), which widen one’s differential from disease.

The main take-home point from this discussion is that dipstick testing combines dipstick testing with microscopy and clinical information. 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.

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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>Blood¹</td>
<td>Dehydration, exercise, hemoglobinuria, menstural blood, myoglobinuria, semen in urine, highly alkaline urine, oxidizing agents use to clean perineum</td>
<td>Captopril (Capoten), elevated specific gravity, pH &lt;5.1, proteinuria, vitamin C, dipstick exposed to air</td>
</tr>
<tr>
<td>Glucose</td>
<td>Ketones, levodopa (Larodopa), dipstick exposed to air</td>
<td>Elevated specific gravity, uric acid, vitamin C</td>
</tr>
<tr>
<td>Ketones</td>
<td>Acidic urine, elevated specific gravity, some drug metabolites (e.g., levodopa)</td>
<td>Delay in examination of urine</td>
</tr>
<tr>
<td>Leukocyte esterase³</td>
<td>Contamination² nephrolithiasis</td>
<td>Elevated specific gravity, glycosuria, ketonuria, proteinuria, cephalaxin (Keflex), nitrofurantoin (Furadantin), tetracycline, gentamicin, vitamin C</td>
</tr>
<tr>
<td>Nitrites</td>
<td>Contamination, exposure of dipstick to air</td>
<td>Elevated specific gravity, elevated urobinogen levels, nitrate reductase-negative bacteria, pH &lt;6.0, vitamin C</td>
</tr>
<tr>
<td>Protein⁴</td>
<td>Alkaline or concentrated urine, quaternary ammonia compounds, iodinated radiocontrast agents</td>
<td>Acidic or dilute urine, primary protein is not albumin, such as Bence-Jones protein</td>
</tr>
<tr>
<td>Specific⁵ gravity</td>
<td>Dextran 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/HPF).

² Especially vaginal contamination.

³ Sterile pyuria seen with interstitial nephritis, TB, and nephrolithiasis.

⁴ Not clinically significant unless 3 + or greater. Detects mainly albumin and requires protein excretions of 300-500 mg/day.

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Adapted from Am Fam Physician 2006;74(7):1096.
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Learning Objectives for This Month’s CME Activity: After participating in this CME activity, readers should be better able to interpret dipstick urinalysis results to aid decision-making for a variety of diagnostic, therapeutic, and disposition issues.

In Brief

Trainee Consultants Leaving Scottish ED

Consultant trainees at the Royal College of Physicians and Surgeons of Glasgow (RCPG) in Scotland are leaving to enter other specialties after witnessing the pressure put on their certified counterparts. The issue, according to the president of RCPG, needs to be addressed as a matter of urgency, according to the Scottish newspaper, The National (25 March 2015, http://bit.ly/1x1rJzl.)

Consultants are already overextended without adding the component of properly and thoroughly training their successors. That leads trainees, after seeing consultants constantly struggling, to decide it’s not for them. This decision ultimately puts a damper on trainee retention.

In another effort to retain trainees, the RCPG has backed the Royal College of Emergency Medicine (RCEM) of Scotland in its campaign, Step, to help improve the quality and safety of emergency care in hospitals across Scotland. “We have continued to drive increased recruitment within our emergency departments,” said Shona Robison, Scotland’s Secretary of Health.

“Since September 2006, the number of emergency medicine consultants has risen from 75.8 whole-time equivalent staff to 205 — an increase of 170.6 per cent — and we are committed to working with the RCEM on this issue.”

No Benefit of Nicotine Patches After Six Months

Patients do not receive any added benefit of wearing nicotine patches beyond 24 weeks of treatment, according to a study published in JAMA. (http://bit.ly/7Jl5a7G).

Researchers compared the standard eight-week treatment, an extended 24-week treatment, and a 52-week maintenance treatment for promoting tobacco abstinence. More than 500 treatment-seeking smokers participated in a randomized clinical trial that took place from June 2009 through April 2014 at two universities.

Twenty-one percent of participants in the standard treatment group were abstinent at the end of 24 weeks, compared with 27 percent of participants in the extended and maintenance treatment groups. Participants in the extended and maintenance treatment groups reported significantly greater abstinence rates at 24 weeks, compared with participants in the standard treatment group who had a longer duration of abstinence until relapse, and reported more abstinent days.

At 52 weeks, participants in the maintenance treatment group did not report significantly greater abstinence rates, compared with participants in the standard and extended treatment groups.

Feds Speed Plans for Value-Based Payments

The U.S. Department of Health and Human Services said it would fundamentally reform how it pays providers for treating Medicare patients in the coming years.

“Today, for the first time, we are setting clear goals — and establishing a clear timeline — for moving from volume to value in Medicare payments. We will use benchmarks and metrics to measure our progress; and hold ourselves accountable for reaching our goals,” said HHS Secretary Sylvia Mathews Burwell in an official announcement.

Those goals are for 30 percent of all Medicare provider payments to be in alternative payment models that are tied to how well providers care for their patients, instead of how much care they provide and to do it by 2016 and for virtually all Medicare fee-for-service payments to be tied to quality and value (at least 85 percent in 2016 and 90 percent in 2018).

HHS announced the creation of a Health Care Payment Learning & Action Network to facilitate the public-private sector partnership, and they plan to hold the first meeting in March. The announcement marks the Obama administration’s biggest effort yet to shape how physicians are compensated across the health care system, according to a Washington Post article. Read more: http://wapo.st/1HhNhuc & http://usa.gov/1zK2YJx.