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Dipstick analysis of urine chemistry: benefits and limitations of dry chemistry-based assays

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ABSTRACT
Urinalysis is a commonly utilized laboratory test, and analysis of urine has been studied and used since ancient times. Urine contains a wide array of metabolites that can provide information regarding the current physiologic state of the body and clinical manifestations of disease. In this review, we discuss the mechanics of the dry chemistry component of the urine dipstick such as the reaction principles underlying various assays and potential effects of collection and storage on results. Additionally, we discuss the benefits and limitations of the urine dipstick as it pertains to its use as a low-cost tool in point-of-care settings and the reasoning for a lack of its use as a broad screening tool.

Introduction
Urine is a biologically active fluid that uniquely reflects a multitude of complex physiologic activities of the kidneys, specifically, and the body, in general. Details of urine formation in health and disease are widely described in many physiology texts [1,2] and hundreds of review papers (not referenced here). Evaluation of urine composition is important because urine formation reflects metabolism in health and disease. In this sense, urine can act as a monitor of some aspects of the urinary tract.

The analysis of urine physical properties, chemical constituents, and suspended particulates (cells, crystals, and biological debris) has been an important medical diagnostic procedure for thousands of years [3,4]. Simple, inexpensive testing (visual observation of color and turbidity, odor detection, refractometry for determination of specific gravity, and dipstick analysis of common/diagnostically important chemical constituents) can and is often done by physicians and trained health-care professionals in point-of-care (POC) settings (offices and hospitals). Microscopic analysis of suspended particulates (‘urine sediment’) is best done by those trained in urine sediment analysis and typically occurs in the clinical laboratories. The evaluation of urine sediments is not discussed in this review.

Results of visual characterization and dipstick testing (in samples that have been properly collected [see below]) can be very helpful in triggering more rigorous patient evaluation. For example, gross turbidity invariably indicates a need for sample centrifugation and sediment evaluation. Intense, yellow-orange color and high urine specific gravity may be indicative of dehydration; the presence of chromogenic drug metabolites (rifampin [Rifadin®], phenazopyridine [Pyridium®], sulfasalazine [Azulfidine®], and isoniazid [Nydrazid®]), vitamin, and dietary plant metabolites; and a number of other normal and abnormal states of health and disease.

Therefore, an understanding of the value and limitations of dipstick evaluations of urine chemistry becomes important for timely patient care, in initiating further sensitive diagnostic evaluation, and assessing the value of such tests for ‘routine screening’ to detect incipient disease. The mechanics, value, and limitations of urine dipstick testing are the subjects of this review.

Body
Urine sample collection, handling, and storage
The quality of information derived from urinalysis is highly dependent on proper collection, handling, and storage prior to analysis [5–7]. Urine is sterile when formed by healthy kidneys. However, contamination of urine occurs by microorganisms that inhabit the urinary tract and external genitalia. Methods of urine collection include midstream clean-catch void, catheterization of the bladder, and cystocentesis (suprapubic aspiration). Each method varies in degree of invasiveness and ease of collection. Midstream clean-catch void is the most common method of urine collection [8]. While intended to minimize contamination without being invasive, some data suggest that midstream clean-catch samples do not necessarily decrease contamination rates when compared with free catch (no cleaning, no midstream) in patients with evidence of urinary tract disease [9]. A substantive body of literature, however, suggests that improvements in contamination rates
are associated with specific portions of the midstream clean-catch procedure such as spreading the labia or cleaning the perineum and that this improvement may be more pronounced in male patients performing midstream catch as opposed to free catch [7]. Additionally, this apparent lack of improvement in contamination rates across some groups may be due to a lack of proper education and explanation to patients as to properly perform the midstream clean-catch technique [10].

For purposes of chemical (dipstick) analysis, if uncontaminated urine samples are analyzed within 1–4 h, preservatives are usually not necessary. Virtually all clean-catch urine specimens that are not preserved either chemically or with a range of cold temperatures will have contaminant bacterial growth within 12–24 h, rendering them unsuitable for dipstick or other urinalyses [11,12]; however, the addition of some preservatives may affect chemical assays (elaborated below) [13]. In more rare cases where urine cannot be analyzed immediately or for the purposes of clinical research, it may be necessary to store samples for longer than 24 h.

Urine specimens kept at room temperature for greater than 4 h show significant growth of contaminating microorganisms [7]. Storing urine at cooler temperatures such as 4°C, −20°C, or −80°C can prevent degradation of the samples. The ideal temperature may vary depending upon the desired measurement. For example, osmolality of urine samples has been shown to be stable at room temperature and 4°C for 4 and 5 days, respectively, but for >14 days at −20°C [14]. Even cooler temperatures as low as −40°C and −80°C have been shown to be effective for preserving albumin-to-creatinine ratios (ACRs) in urine samples for as long as up to 6 months both with and without preservatives added [15]. Varying storage temperatures of urine samples affect urine metabolomic profiles which can be seen with results on mass spectroscopy. Investigators note variable decreases in the concentrations of branched-chain amino acids (valine, leucine, for example) and other metabolites (hexose H1, for example) attributable to the activity of enzyme complexes over a variety of temperature settings (−80°C, −40°C, 4°C, and 20°C) and multiple time points (0, 2, 8, and 24 h). This group recommended that urine should be transported at temperatures as low as −20°C to ensure the integrity of samples and to prevent excessive cycles of freezing and thawing, which was also shown to affect the metabolomic profile [16].

Specimens not appropriately preserved can have particles lyse due to low osmolality, low specific gravity, and higher pH. A variety of preservatives are used depending upon need. Boric acid affects various reactions on a test strip and can also inhibit the growth of some bacteria. In some cases, bacterial overgrowth may be undesirable and thus sodium azide may be used as for prevention of this. Formaldehyde use lowers specimen pH and provides false-positive results for leukocyte esterase, peroxidase reaction, and the presence of urobilinogen. Mercury salts, on the other hand, lead to false-negative results for leukocyte esterase [5]. Chlorhexidine solutions can be advantageous when urine is transported between health-care services, but samples are best kept at room temperature as decreased WBC counts and calcium oxalate can be found in samples kept on ice [17]. In summary, each preservative has specific situational uses but also comes with particular disadvantages.

**Overview of dipstick analysis of urine chemical composition and assay principles**

In practice, dipstick/dry chemistry analysis involves spotting urine onto different portions of a dipstick, allowing a timed reaction to take place, and then comparing an associated color change on the dipstick to a reference standard to determine a positive or negative result. The color change is typically triggered by the reaction of a chromogenic compound with another reaction product produced by the interaction of the sample and dipstick reagent. For example, heme (from hemoglobin) and glucose are detected by reaction of these compounds with peroxidases incorporated in the dipstick and subsequent generation of a chromogen end-product that can be evaluated [18]. Other common chemical reactions include binding of the dye compounds and enzymatic, immunologic, and catalysis of oxidation–reduction reactions [19] (Table 1).

Virtually all dipstick/dry chemistry analyses rely largely on colorimetry, with the intensity of color change proportional to the concentration of the analyte being measured. The color is then matched against a color reference chart to subjectively measure analyte concentration. These manual/visual evaluations may be imprecise, depending on the visual acuity and color vision fidelity of the observer.

Over the past 20 years, a variety of electronic technologies have significantly improved the interpretation of color reaction products on dipsticks. Portable (handheld) dipstick readers have become ubiquitous in primary care and hospital settings, as well as in the consumer market. They are convenient and economical and provide rapid, accurate results, depending on specimen handling, preservation, and quality. Such devices, based on electronics that convert photonic energy (from colored reaction products) to electronic signals (complementary metal oxide semiconductor devices), have reached a level of accuracy and precision that allows generation of semi-quantitative/quantitative data. This type of technology is also present in benchtop and larger laboratory-automated systems that use dipstick/dry chemistry, such as the Beckman Coulter IRICELL™ (Beckman Coulter Inc., Atlanta, GA), for example. Automated technologies increase specimen throughput, minimize specimen handling, reduce manual labor, and speed delivery of results to patient records and clinical databases but still employ the fundamental dry chemistry technologies that evolved decades ago. These electronic technologies, and their use in dipstick interpretation, have been the subject of several excellent papers and reviews; the interested reader is directed to them [20–25]. Recently, ‘lab on a chip’ dipstick readers, which can be used with smartphone technology, have been described in the literature [26].

Dipstick/dry chemistry analysis can also provide useful information about other physical and chemical properties of the urine sample. For osmolality, a complexing agent in the dipstick will release protons when in the presence of cations, which reacts with the dye indicator compound bromthymol blue, producing a color change [18]. Sample pH can be
determined within a range of 5.0–8.5, although deviations can occur toward the ends of this range (<5.5 and >7.5). The preferred and most accurate method to measure pH at those levels is the use of a glass electrode \[18\].

**Hemoglobin**

Dipsticks can detect hemoglobin due to the heme moiety, which has pseudo-peroxidase activity that catalyzes the reaction of peroxide and a chromogen molecule to produce a colored reaction product. The oxidation of a benzidine compound via reduction of a buffered organic peroxide provides a positive result \[27\]. This test thus can detect hematuria, hemoglobinuria, or myoglobinuria, as all involve the heme moiety reaction \[28\].

Pseudo-peroxidas are hemoproteins that have active sites that can catalyze the $\text{H}_2\text{O}_2$ reduction to water. Molecules that meet specific criteria can be considered to have peroxidase-like activity and could theoretically trigger a false-positive result. These criteria include molecules that have iron in the ferric form (Fe (III)), five coordination bonds and an $\text{H}_2\text{O}$ molecule on the distal side of the heme molecule that is replaced with $\text{H}_2\text{O}_2$, and specific arrangements of amino acids (conserved histidine–arginine couple) \[29\]. There does not seem to be extensive documented evidence in the literature of porphyrin molecules or patients with porphyrias triggering ‘positive’ results for hematuria; however, if a molecule in the pathway of hemoglobin synthesis was to meet the pseudoperoxidase criteria, then it could theoretically trigger a positive result.
False-positive results for hematuria may be produced in instances of hemoglobinuria and myoglobinuria and from exogenous pseudo-peroxidases produced by contaminating bacteria such as *Lactobacillus* species [27]. Strong reducing agents such as ascorbic acid can also cause false-negative results [18]. In combination with a microscopic urinalysis for RBC count, a dipstick result for ‘blood’ (hematuria) can provide insight and guidance to whether a patient’s macroscopically discolored urine may be the result of hematuria, hemoglobinuria, myoglobinuria, and pseudo-hematuria (drugs, dyes, etc.) [30].

**Glucose**
For glucose detection, it is the interaction of glucose with glucose oxidase that forms D-glucono-1,5-lactone and hydrogen peroxide. A peroxidase then catalyzes the reaction of hydrogen peroxide with a reduced chromogen. Ascorbic acid (a reducing agent) and some bacteria may cause a false-negative result, while oxidizing agents and hydrochloric acid can cause false-positive results [18].

**Proteinuria**
Dipsticks are commonly used to test for proteinuria. They can give a general estimate of the amount of protein present in a sample. This is because the concentration of protein in a buffer will cause a proportional change in pH. The dipstick method is most sensitive to albumin and less sensitive to other proteins. The color of the dipstick can change from pale green, to green, to blue and offers an approximate quantification that is noted as 0 to plus-3 (+++) or plus-4 (++++) depending upon the color [18].

In the absence of protein, the dipstick will remain yellow. Protein will disrupt the dye and buffer on the dipstick and cause a green color to develop. Causes for a false-positive result can include alkaline urine (pH >7.5), overly length time of urine immersion, highly concentrated urine (less hydrated states), gross hematuria, pus, semen, vaginal secretions, or some drugs such as penicillin. False-negative results can occur if the urine is extremely diluted such that the protein is not adequately detected by the dipstick or if the protein is significantly lower in molecular weight (light chains) and other non-albumin proteins [31].

While glomerular disease is more common, tubular pathology can also result in proteinuria. This occurs when proteins, of lower molecular weight, are unable to be reabsorbed from the filtrate due to a tubulointerstitial pathological process. This proteinuria is generally less than 2 g in 24 h and may result in a false-negative dipstick result [31].

Protein light chains such as Bence-Jones proteins (kappa and lambda light chains) are not detected by dipstick and require additional testing. If there is suspicion for these smaller protein chains, a sulfosalicylic acid test may be performed; however, the definitive test for monoclonal light chains would be electrophoresis [32,33].

**Leukocytes – esterase activity**
Dipsticks can provide insight into the presence of leukocytes in urine by means of indoxyl esterase activity. This enzyme is released in the lysis of neutrophils and macrophages. Samples that have an alkaline pH or low densities due to the favored lysis of leukocytes in those environments will result in false positives, while conversely, high-density samples will decrease sensitivity to leukocytes. High levels of glucose and protein, as well as some drugs (e.g. tetracyclines), can provide false-negative results for leukocytes. Leukocytes will lyse and release indoxyl esterase, which will catalyze reactions involving indoxyl or pyrrole carboxylic acid esters, and result in a product that interacts with a diazonium salt to produce color [34].

**Nitrites**
Dipstick tests for nitrites can be used as a proxy test for some gram-negative bacteria that utilize the nitrate reductase to reduce nitrates into nitrites. In order for this test to detect nitrites, there first must be sufficient nitrates, typically from a vegetable-rich diet. The nitrites first react with p-arsanilic acid on the dipstick to create a diazonium compound which then couples with a quinolone compound on the dipstick to produce a pink color [34].

**Ketones**
The dipstick test to detect ketones such as acetoacetate and acetone involves their reaction with nitroprusside or nitroferrocyanide and glyceine [28]. Most test strips will detect acetoacetate, which is the first ketone body created from acetyl-CoA, and some brands will detect acetone; however, none detect beta-hydroxybutyric acid [34]. Ketostix® reagent strips (Siemens Healthcare Diagnostics Inc./Bayer Diagnostics, Tarrytown, NY) were first demonstrated to be more effective than test tube methods of ketone detection in 1958 [35]. Most modern test strips will detect acetoacetate, which is the first ketone body created from acetyl-CoA, and some brands will detect acetone; however, none detect beta-hydroxybutyric acid. Beta-hydroxybutyric acid is the predominant ketone body present and is best tested with its own assay using capillary blood [36]. Due to the predominance of beta-hydroxybutyric acid, the nitroprusside test may be weakly positive in some cases of increased ketones such as alcoholic ketoacidosis [37]. In diabetic ketosis and ketoacidosis, capillary blood ketone testing was found to have fewer false-positive and false-negative results than dipstick urine ketone testing [38].

**Bilirubin and urobilinogen**
Only bilirubin that is conjugated with glucuronic acid can pass through the glomerulus. Bilirubin is also converted by bacterial enzymes into urobilinogen in the intestines, which can then be oxidized into urobilin, which has a brown-pigmented color. These compounds can be present in the urine. Bilirubin is normally not present in urine in any significant quantity; however, urobilinogen can be present normally [34].

Many dipsticks that screen for bilirubin make use of a coupling reaction that occurs in the presence of acid between bilirubin and a diazonium salt; however, the specific salt used and resulting color can vary between manufacturers. These sticks are ready after 30–60 s, and the typical resulting
colors range from shades of tan to purple. Common diazo-
nium salt indicators used by different dipsticks include
2,6-dichlorobenzene-diazonium-tetrafluoroborate in the
Chemistrip® (Hoffmann-LaRoche Ltd., Basel, Switzerland) and
2,4-dichloroaniline diazonium salt (Siemens Healthcare
Diagnostics, Tarrytown, NY) [34].

For urobilinogen dipstick screening, the Ehrlich aldehyde
reaction is utilized. In this reaction, an aldehyde (p-dimethyla-
minobenzaldehyde) or diazonium salt compound is used in an
acid condition to react with urobilinogen to produce a red or
pink colored azo dye product. The dipstick is read after 30–60
s [34]. Urobilinogen may be elevated in situations of increased
hemolysis and hepatocellular disease. It may also be
decreased with antibiotic use due to a change in the micro-
biota [28]. Since a positive result on this test may be normal,
the screening of bilirubin is more useful for the early detection
of pathology than urobilinogen.

Benefits – why are dipsticks used?

Urine dipsticks are widely used for a number of reasons. As
depicted above in the section on assay principles, dipsticks
can be used to test for a variety of factors that can help with
clinical decision-making and trigger further testing or investi-
gation. Urine dipsticks are well poised to be used in point-of-
care settings due to their ease of use. This type of testing, as
opposed to traditional central laboratory testing, has some
advantages.

Point-of-care testing (POCT) can improve efficiency and
metrics in primary care clinics by allowing for faster commu-
nication with patients prior to them leaving the clinic, as well
as saving costs on more expensive tests that may not be
necessary [39]. While initially more expensive than central
laboratory testing, POCT can reduce costs over time by redu-
cing turnaround time and reducing patient time spent in the
emergency department (ED) or hospital depending upon the
situation [40]. The use of a point-of-care comprehensive meta-
bolic panel has been shown to reduce ED length of stay in
patients either admitted to the hospital or discharged to home
as compared to central laboratory testing [41].

POCT urine analyzers can be used to read the results of
dipstick dry chemistry, which can appear very shortly after
exposure to urine, with accuracy comparable to or exceeding
visual analysis [42]. This automation can further improve the
efficiency of point-of-care urinalysis. Automated dipstick tools
have been shown to be sensitive for diagnosing urinary tract
infection (UTI) and can provide further justification to move
forward with urine culture, although flow cytometry may pro-
vide even better predictions [43]. As stated in the section on
assay principles, a standard urine dipstick can be used to
assess for a variety of enzymes and the presence of particles.

Further, regardless of automation, dipsticks themselves are
relatively straightforward to use in the clinic and can be
utilized in settings with fewer resources and technology [18].
Automated dipstick analysis has been combined with flow
cytometry to construct devices that can cross-check for dis-
crepancies between tests, thus reducing the turnaround time
necessary to check samples manually in which results may be
incorrect [44]. As noted previously, there is robust literature
describing the benefits accrued from both handheld and auto-
mated systems that use electronic technologies to interpret
chemical reactions on dipsticks.

Economically, urine dipsticks are among some of the most
affordable and least expensive laboratory tests available. The
cost to a primary care clinic of running a test including speci-
men collection, processing, labor costs, personal protective
equipment (gloves), and the physical dipstick itself can be
estimated to total $3.05 [45]. The retail price of a packet of 100
Chemistrip® dipsticks costs $57.45 at the time of this
writing, amounting to less than $0.60 per stick [46]. The esti-
imated cost of the automated urinalysis test at the Veterans
Affairs Medical Center in Salem, VA, including the cost of labor
for technicians, phlebotomy, and bundled cost of a
microscopic analysis, is less than $5.00. Average combined
time for collection and analysis is approximately 6 min
(April 2019 e-mail from S.T. Stoneman, Laboratory
Information Manager, MT to Varun Kavuru [VA urine dipstick
cost]; unreferenced).

Dipsticks themselves are fairly inexpensive tests, but
a positive result for proteinuria will result in further confirma-
tory, quantitative testing such as a 24-h urine collection or an
ACR [31]. The National Kidney Foundation also supports the
use of ACR or albumin-specific dipsticks after a positive dip-
stick for proteinuria in its information for patients [47]. In
addition to the above quantitative tests, a positive proteinuria
dipstick result can trigger further microscopic analysis of urine
sediment which may provide further findings of casts that can
provide further insight into a pathologic process [31]. In the
cases of false positives, this will result in more cost as tests are
ordered with no true need to calculate protein loss; however,
a negative screening dipstick result would not trigger the
further more expensive testing and provides a quick less
expensive POC option for testing.

Limitations – why should not dipsticks be used

As noted, dipstick/dry chemistry tests can be useful POC
screening tests to trigger more definitive diagnostic evaluation
but are not useful for providing a definitive diagnosis alone.
While a single, dipstick/dry chemistry measurement of
a suitable urine specimen at a single time point may provide
temporally useful information, the results are not intended to
be diagnostic. Dipstick/dry chemistry testing is not generally
accepted as a means to screen large populations for the
presence/absence of disease (see below).

The limitations of such dipstick/dry chemistry tests
(whether at a POC or in an automated laboratory setting) are
well known and include:

- They may be inaccurate in quantifying important indica-
tors of disease including glucose, protein, albumin,
hemoglobin (see examples and discussion, below),
although recent advances in the analysis of dipstick
reactions (colors) with electronic technology can pro-
duce semi-quantitative/quantitative data for further
interpretation,
Their use in determining the presence/absence of common conditions such as UTIs may be problematic and is considered debatable (especially in urgent POC settings) [10,48–54], They are not diagnostic for any particular disease and may only provide a simple, suggestive result for a variety of simple or more complex pathologies, Interfering compounds, including therapeutic drugs, vitamins/supplements, chemical preservatives, and detergents (used during sample collection), may invalidate test results, Values obtained by dipstick/dry chemistry measurement need to be interpreted in the context of urine concentration, measured as urine specific gravity, and time of sample collection [55], Values obtained by dipstick/dry chemistry measurements need to be interpreted in the context of urine pH since dipstick chemical reactions may be suboptimal at the extremes of urine pH, Re-testing of individual samples (i.e. repeated dipstick tests on the same sample) is rarely done, Proximately timed, serial samples from the same individual are rarely tested, False-positive test results clearly may mislead and channel diagnostic thinking among health-care providers and may create needless anxiety for patients, False-negative results may discourage further diagnostic evaluation, POC interpretation (visual inspection) is subjective, based on color vision acuity of the observer, lighting conditions, and correct timing of test interpretation (at the chemical reaction maximum), and, The use of dipstick/dry chemistry test strips that are nearing expiration or which have been improperly stored is problematic due to the possibility of false positives.

Two examples illustrate some of these limitations.

Both macroscopic and microscopic hematuria can be detected with dipstick/dry chemistry testing. There is a multitude of common and uncommon causes of hematuria, including UTI, normal menstruation, abnormal menstruation, urinary tract calculi, glomerulonephritis, pyelonephritis, and genitourinary tract neoplasms, to name a few. Clearly, the dipstick test was not designed to and cannot differentiate among these and many other causes.

Dipstick testing is rarely needed or used when macroscopic hematuria is seen. When accompanied by pain, UTI or the presence of calculi is common, suspected etiologies. When pain is not present, there is suspicion of primary glomerular disease or the presence of urinary tract neoplasia. Further diagnostics may follow such as urine microscopy and cytology followed by referral to a urologist if no clear etiology is determined. This may lead to further more testing such as CT intravenous pyelogram and cystoscopy [56]. In the setting of macroscopic hematuria in the ED, use of dipsticks may still provide utility in evaluating the presence of infection as a possible cause and can be considered part of the workup [57].

However, the detection of asymptomatic microscopic hematuria in routine urinalysis specimens is common (seen in up to 18% of specimens) with dipstick testing [58,59]. Given a positive test result, the patient and physician must then decide how to proceed, including (1) whether to repeat the urinalysis, including urinary cytology, and/or (2) pursue diagnostic imaging, and/or (3) consider cystoscopy for occult lesions (such as bladder cancer). The diagnostic path to be followed has been the subject of considerable debate [60,61]. In a recent study, Matulewicz and coworkers considered the use of dipsticks to detect microhematuria a useful diagnostic procedure for the detection of bladder cancer [62]; however, there is no widely accepted algorithm that is followed when ‘dipstick hematuria’ is found in routine screening urinalyses [63–65].

The presence of protein in urine is a significant indicator for further diagnostic evaluation if incidental specimen contamination is ruled out (i.e. from secretions and cells in free-catch specimens). While protein in urine may indicate renal disease, it is difficult to discern early stages of disease (i.e. before albumin appears in urine), and free-catch specimens may be contaminated with proteins and secretions from other tissues in the urinary and genital tracts [66].

In the past, regular measurement of urine glucose (for the purposes of adjusting insulin dosage) allowed incidental measurement of urine protein. With the widespread acceptance of blood glucose monitoring for the management of diabetes, routine collection of urine from diabetics has decreased. It is, however, well established that the development of microalbuminuria (defined here as the presence of small amounts of albumin in the urine) is a harbinger of renal dysfunction in diabetes mellitus and that regular screening of the urine of diabetics for the presence of albumin is both necessary and standard-of-care [67,68].

It is apparent that an economical, home-based test (i.e. dipstick/dry chemistry assay) could be useful in early detection of diabetes-associated renal dysfunction. In a home-testing-based study of a cohort of patients with type 2 diabetes, Nagrebetsky and coworkers found that dipstick-based testing did not reliably detect microalbuminuria compared to laboratory-based testing of urine albumin–creatinine ratio [69]. Using systematic literature review and data meta-analysis, Wu and coworkers found that laboratory-based testing of urinary albumin concentration and albumin–creatinine ratio, although more expensive and less convenient than dipsticks, were more reliably sensitive and specific tests for diabetes-associated microalbuminuria [70].

Zeller et al. conducted a study in which they assessed the diagnostic accuracy of transferrinuria and an albumin-specific dipstick for detecting microalbuminuria in hypertensive non-diabetic patients. These albumin-specific dipsticks such as MicrAl® (Hoffmann-LaRoche Ltd., Basel, Switzerland) strips were found to be less sensitive and specific than transferrin-to-creatinine ratios. The authors noted that prior studies of this type of dipstick had largely been done in diabetic patients. They found the test to have more false positives than false negatives but deemed this acceptable for the screening purposes of the test. They found the negative predictive value of the albumin-specific dipsticks to be high (92%) and concluded that the test provides a simple, useful, and cost-effective method of screening for microalbuminuria in hypertensive patients in a primary care setting [71].
The presence of albumin (and other proteins) in urine is an accepted indicator of the presence and severity of chronic kidney disease (CKD), and regular monitoring of the urine of patients in early stages of CKD may be quite useful in detecting responses to medical/lifestyle management, as well as detecting progression of disease. Although economical and convenient (see above), dipstick/dry chemistry testing for the presence of protein is unlikely to be either sufficiently sensitive or specific in the management of CKD. Abnormalities in the composition of urine sediments (hematuria, pyuria, casts, and other changes) also are considered potential indicators of CKD and may be of greater value than single spot measurements of urine proteins with dipstick assays. Other molecular indicators of CKD, including the presence of complex metabolic by-products collectively termed ‘uremic solutes,’ are not measured routinely in serum or urine, either by dipstick/dry chemistry assays or standard laboratory automated urinalysis, but may become important diagnostic biomarkers since they are important in the pathogenesis/progression of CKD and systemic comorbidities such as cardiovascular disease [72].

A 2014 systemic review of guidelines for the use of urinary dipsticks for screening across 67 organizations in 9 countries found a lack of agreement in guidance among organizations for the use of dipsticks for screening for some assays. Regarding screening for hemoglobin with dipsticks, United Kingdom (UK) organizations of nephrology and urology and the UK National screening committee recommended against screening while some organizations made no comment or recommendation. Regarding screenings for leukocyte esterase and nitrites, all organizations recommended against screening asymptomatic non-pregnant patients. Additionally, regarding screening for proteinuria, the UK National Screening Committee and Canadian Society of Nephrology recommended against screening with dipsticks. The National Kidney Foundation K/DOQI guideline recommends screening patients at high risk for CKD but recommended the use of albumin–creatinine ratios or albumin-specific dipsticks. Overall, this study found a lack of clear consensus among guidelines across multiple organizations and countries for the use of dipsticks for screening purposes [73].

Conclusion

In summary, urine dipstick dry chemistry is easy to use and inexpensive and has the ability to assess a variety of assay principles in a short period of time, making it ideal for a POCT setting. It is critical that careful attention is paid to the storage conditions of urine samples that are stored for longer than 2 h. The use of preservatives and cold temperature ranging from −80°C to 4°C can extend the shelf life of urine and prevent the overgrowth of microorganisms, breakdown of metabolites, and subsequent test results on a dry chemistry dipstick. However, one must note that no one preservative substance is capable of perfectly preserving urine samples and without effect on sample composition.

Urine dry chemistry is capable of assessing a wide array of assays such as pH, osmolality, hemoglobin/myoglobin/hematuria, leukocyte esterase, glucose, proteinuria, nitrites, ketones, and bilirubin. These findings can then provide a basis for further testing based upon clinical suspicion. Examples include UTIs, diabetes mellitus (as well as diabetic ketoacidosis), glomerular damage, metabolic defects, and even hepatic dysfunction.

Other benefits of dipsticks include their ability to be automated to reduce human error and labor as well as their ability to be utilized in a point-of-care setting. The simple and fast nature of the test, dripping urine onto the test strip, or dipping the test strip into a urine sample and allowing the relevant reaction to occur lends itself able to be done very close to the patient’s bedside. These factors allow for the potential for the test result to be returned to the patient very early and may prevent the need for a second visit. In an emergent care setting, it can allow for faster discharge or admission and facilitate decision-making between provider and patient.

Despite its advantages, dipstick dry chemistry presents a number of limitations to its use as a broad screening tool. Dipstick dry chemistry alone is often not sufficient for decisions regarding clinical management and often prompt or discourage further testing, depending upon dry chemistry results. Limitations include a lack of quantifiable results, subject to false positives and negatives due to various confounding factors in the patient’s diet or contamination of sample, and dipstick interpretation variability. Another example of the limitation of dipsticks is the lack of a widely accepted diagnostic algorithm for asymptomatic hematuria. Furthermore, dipsticks have not been shown to exhibit sufficient sensitivity for albumin in a routine home testing setting, and other markers such as ACR have been shown to be more effective for the detection of diabetes-associated microalbuminuria. In conclusion, despite the benefits of their ease of use, low economic cost, and wide assay, urine dipsticks face a number of limitations in their use as broad screening tools.

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