

A practical approach to urine dipstick test abnormalities in relation to kidney and urinary tract disorders in children

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Abstract

The routine use of urine dipstick testing in the consulting room of the family physician has fallen into disfavour for several reasons. One of the arguments cited most often is that it is time consuming and not cost beneficial. This is particularly true with respect to small children, because of the difficulties experienced collecting urine from this group of patients. The aim of this review is to stress the important role that urine dipstick testing plays in the diagnostic work-up of any patient with a kidney or urinary tract disorder. A practical approach is provided on urine dipstick test abnormalities in relation to kidney and urinary tract disorders in children.

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Introduction

Routine urine dipstick analysis is not performed in children who attend primary healthcare clinics, because of the large number of relatively healthy patients who are seen there. It is only carried out when indicated by symptoms or signs that suggest kidney or urinary tract disorders. Also, many primary healthcare physicians have stopped conducting urine dipstick analysis in their consulting rooms, arguing that it is time consuming and not cost beneficial. The utility of screening urinalyses in asymptomatic children has also come into question, based on data from studies conducted in healthy children that revealed a very low positive yield for renal disease.^{1,2} The difference between the former-described scenario and the child whose parents consult the primary healthcare physician is that, in the latter case, the child is symptomatic.

The aim of this review is to describe the essential role of urine dipstick testing in the diagnostic work-up of a symptomatic child, regardless of the symptoms. An interpretation of positive or negative dipstick findings that are associated with disorders that affect the kidney and urinary tract specifically, as well as a practical approach to further management thereof, is provided.

What is the purpose of a routine urine dipstick test?

Urine collection in children is more cumbersome than in adults, and is often the Achilles heel of a missed diagnosis. It is common practice for many primary healthcare physicians

to only perform a urine dipstick test when a clinical indication is present. Unfortunately, this is where the problem arises. Unlike adults, small children with kidney and urinary tract disorders often have nonspecific symptoms. Even in older children with kidney disease, the presenting complaint may not appear to have any relationship with the kidneys or urinary tract. In these cases, a positive urine dipstick test may come as a complete surprise. Therefore, it is advised that routine dipstick tests are undertaken in children at every medical encounter. Importantly, however, a negative dipstick test does not rule out underlying kidney disease.

The collection of urine for routine dipstick testing

The purpose of urine testing determines the method of urine collection in children. Small children, especially little girls, are often shy and reluctant to void in the presence of strangers. Therefore, generally parents are given the task of obtaining a urine sample. A disposable specimen container is preferred, but if this is not available, the chosen container must be clean and dry. Boys who are older than four years of age, and who are continent, can be instructed to void the middle part of the urine sample directly into the urine container.

Collection of a clean, voided urine sample in small girls is more problematic. It is best to advise the mother to collect a sample while the child is sitting on the toilet facing backwards. This forces the child to separate her legs, resulting in a horizontal urine trajectory for a few seconds, before following gravity downwards.

Unfortunately, valuable information may be lost when urine collection is not carried out or observed by the practitioner. A sterile disposable plastic urine bag should be used in infants and children who have not yet been toilet trained. The bag should be attached over the genitalia after washing the perineum with tap water and drying it thoroughly, to allow it to adhere sufficiently until the urine is passed. Bag samples are unsuitable for culture purposes.

To obtain the best results, fresh urine should be tested, preferably no longer than 60 minutes after collection.

A practical approach to abnormalities in urine dipstick testing

Kidney and urinary tract disorders in a child may manifest in any of the following ways:

- The onset of discoloured urine, including urine that is turbid, pink, brown or bloody.
- Urinary symptoms that are associated with an abnormal urine dipstick test.
- Complaints that appear to be unrelated to the kidneys or urinary tract that are associated with an abnormal urine dipstick test.

Detection of discoloured urine

Usually, freshly voided urine is clear. Cloudy urine may be caused by pyuria, calcium phosphate crystals or a combination of calcium salts, uric acid, cystine or struvite (magnesium ammonium phosphates).

A pinkish turbidity indicates the presence of urates. Typically, it is seen in neonates who are nursed under overhead radiant warmers in high care settings. The pinkish urine causes a brown stain on the nappy after a while. The high uric acid excretion relates to the normal rapid physiological cell turnover in neonates. In these cases, the urine dipstick shows an alkaline pH and tests negative for blood.

Observation of dark-brown or red urine is a frightening experience for parents. Usually, it will prompt them to consult the family physician, even if the child is completely asymptomatic. There are several causes of discoloured urine, some of which have a physiological explanation, while others may herald pathology in or outside the kidney and urinary tract (Table I).

Usually, the medical history and physical examination provide the answer with regard to children who have red urine that is not caused by any illness. In most cases, the colour is due to ingestion of beetroot. The child is healthy and the urine dipstick test is negative.

The differential diagnosis of most children with disease conditions that cause dark red urine, and who have a positive

Table I: Causes of pink, red, reddish-brown or cola-coloured urine

Physiological
Urine dipstick and urine microscopy negative
Blueberries and berry juice (dark red)
Beetroot (pink to red)
Urates (pink to red)
Drugs, e.g. rifampicin (orange to red)
Porphyrin (port-wine colour after standing for a while)
Bile (amber to brown)
Pathological
Urine dipstick haemoglobin positive and urine microscopy negative
Intravascular haemolysis (dark red to brown)
Rhabdomyolysis (dark red colour)
Urine dipstick haemoglobin positive and red blood cells present on urine microscopy
Urinary tract disorders
Urinary tract infections (usually red)
Hypercalciuria and kidney stones (red)
Urinary tract abnormalities, e.g. pelvoureteric junction obstruction (red)
Trauma (red to brown)
Tumours of the urinary tract, e.g. rhabdomyoma of the bladder (red)
Kidney disorders or renal vasculature disease
Glomerulonephritis (postinfectious or other immune-mediated types)
Haemolytic uraemic syndrome or other microangiopathies
Acute tubular necrosis
Renal vein thrombosis
Congenital abnormalities of the kidneys, e.g. polycystic kidney disease
Tumours of the kidney, e.g. Wilm's tumour
Bleeding disorders
Haemophilia

urine dipstick test for haemoglobin, becomes apparent after taking a thorough history and examining the child. In such cases, it is mandatory to carry out urine microscopy on a fresh urine sample. If the urine microscopy reveals no red blood cells, the two main differential diagnoses are rhabdomyolysis or acute intravascular haemolysis. The clinician will undoubtedly be able to differentiate between these, based on clinical grounds. Additional confirmatory investigations, such as quantitative measurement of the blood myoglobin levels, or investigations to find the cause of acute intravascular haemolysis, will be necessary. These patients are usually very ill and need to be referred urgently as complications such as acute renal failure are likely to develop if management is delayed.

Unfortunately, urine microscopy is no longer carried out by clinicians in the diagnostic work-up of a patient. It is also not performed by family practitioners in private practice,

nor by doctors who work in public hospitals or in teaching hospitals. In the latter case, it is probably because of lack of the necessary functioning equipment, including centrifuges and microscopes. Consequently, a large number of inappropriate and unnecessary investigations are often carried out in search of a diagnosis. Urine microscopy is necessary to confirm the finding of haematuria. It also provides other important information, for example, the presence of crystals and casts (red cell, leukocyte, hyaline or granular casts) or schistosoma ova. Red cell morphology, conducted on a fresh urine sample, can be very helpful in differentiating between glomerular and nonglomerular haematuria.³ This test is available in private laboratories, but is hardly ever requested. The National Health Laboratory Service (NHLS) laboratories do not provide this investigation as the sample needs to be processed and examined within one hour. Although primary healthcare physicians can be excused for not having the necessary skills to conduct urine microscopy, they are certainly expected to be able to interpret a urine microscopy report correctly.

Macroscopic haematuria

Macroscopic haematuria is an uncommon finding in children. In the majority of such cases, there is an easily recognisable and apparent cause which is revealed by the history, including family history, and clinical examination of the child. The most common disorders that the clinician will encounter can be determined based on the symptoms described by the child. However, usually infants and small children are not able to describe their symptoms. The result is that parents provide their interpretation of the symptoms. In the latter case, the clinician will need to spend more time to obtain an accurate and complete history and will need to give attention to detail during the clinical examination.

The causes of macroscopic haematuria (positive urine dipstick test and red blood cells on microscopy) can be divided into two main categories, namely disorders of the renal parenchyma (glomeruli and tubuli) and urinary tract disorders (Table I). Generally, the presence of a large amount of proteinuria is indicative of glomerular disease, but in the case of macroscopic haematuria, the large amount of haemoglobin in the urine may cause false positive proteinuria on the urine dipstick test.

The valuable role of urine microscopy is demonstrated by the following three examples: the presence of *Schistosoma* ova, a large number of bacteria and pus cells, or the presence of red cell casts and dysmorphic red blood cells. In each of these cases, the microscopic findings are diagnostic of totally different conditions that streamline the special investigations that are necessary to confirm the diagnosis. Finally, only a few of the following special investigations will

be necessary to confirm the diagnosis: urine culture, urinary calcium-creatinine ratio, complete blood count (including platelet and reticulocyte count), serum creatinine, C3 and renal ultrasound. If the cause of the gross haematuria is not readily apparent from these investigations, the child will benefit from further evaluation by a paediatrician or paediatric nephrologist.

Urine pH

Normal kidneys are capable of producing urine with a pH that can vary from 4.5-8.0, depending on the time of the day and the intake of food and water. During fasting and when eating a high-protein diet, urine often becomes acidic, whereas alkaline urine is frequently excreted after meals or is present when a diet high in fruit and vegetables and dairy products is consumed. This wide normal range for urine pH is a reason why clinicians tend to pay little attention to it.

Urine pH may provide a valuable clue when diagnosing acid-base disturbances in infants. Most infants with renal tubular disease present with feeding difficulties, which can range from vomiting and constipation to polyuria and dehydration. Very often, the underlying renal disease is not recognised. A series of milk formulas, one after the other, is tried, and is often accompanied by an inappropriate prescription of antiemetics, laxatives and antispasmodics. The correct diagnosis will only be made if the clinician recognises the inappropriately high urine pH in an infant who presents with dehydration, failure to thrive and tachypnoea caused by metabolic acidosis. Infants with distal renal tubular acidosis are unable to acidify their urine, despite being acidotic. Distal renal tubular acidosis has a wide range of causes and is associated with hypercalciuria and kidney stones.^{4,5} Such children need to be referred to a paediatrician for further investigation and management.

Children with persistent alkaline urine and recurring urinary tract infections are likely to have *Proteus* infections, occurring in a morphologically abnormal urinary tract. *Proteus* organisms have the ability to split urea to ammonia and thus alkalise the urine, which increases the risk of forming phosphate stones. In this case, the clue to the diagnostic problem lies in the persistent alkaline urine, which should prompt referral of the child to a paediatrician or paediatric urologist.

Microscopic haematuria

Microscopic haematuria is defined as five or more red blood cells per high-power field.⁶ Persistent microscopic haematuria is similarly defined, but in addition requires that this finding be present in three fresh urine specimens collected over a few weeks.

The dipstick test for haematuria is extremely sensitive, capable of detecting five to 20 red blood cells/ μ l, or 0.015-0.060 mg free haemoglobin/dl. Therefore, if isolated microscopic haematuria is present in an asymptomatic patient, the general rule is to confirm it on at least three consecutive occasions, over a period of three months. Significant renal disease is almost nonexistent in the child who remains asymptomatic and has a normal physical examination and urine dipstick test that reveals haematuria only. These patients need to be followed up at regular intervals. A complete systematic history should be obtained at each visit, with an emphasis on the family background and the development of symptoms. Physical examination and microscopic analysis of the first urine that is passed on rising in the morning are essential elements of the long-term follow-up.

Idiopathic hypercalciuria and hyperuricosuria should be excluded in children with persistent microscopic haematuria. It is usually, but not invariably, associated with a positive family history of urolithiasis. The urinary sediment should be examined for crystalluria. The presence of uric acid crystals may focus the work-up. A random urine sample to determine urate, calcium and creatinine levels should be collected for investigation (Table II).

There are many causes of hypercalciuria and hyperuricosuria. These may have serious long-term complications. Children with these conditions require metabolic evaluation and are best referred to a paediatrician for further management.⁸

Microscopic haematuria that is associated with a positive family history of kidney disease, with clinical symptoms and signs or proteinuria, may be caused by a vast number of conditions, either benign nonprogressive or progressive serious renal disease. Unless the patient falls into a clear category of illness that is easily identified and manageable, it is best to refer him or her to a paediatrician or paediatric nephrologist for further management rather than to a urologist, because microscopic haematuria is almost always a medical problem.

Table II: Normal urinary values in children, based on random urine⁷

Parameter	Age	Normal values (mg/mg)
Calcium/creatinine	0-6 months	< 0.8 mg/mg
	6-12 months	< 0.6 mg/mg
	2-8 years	< 0.2 mg/mg
Uric acid/GFR calculated as: U-uric acid* x S-creatinine* U-creatinine ⁻¹	≥ 3 years	< 0.56 mg uric acid/dl GFR

* All values in same units: mg/dl or mmol/l
GFR: glomerular filtration rate, S: serum, U: urine

Proteinuria

Dipstick analysis is not a good quantitative test for proteinuria because of the effect of urinary concentration. (More concentrated urine will show a higher protein content). Approximate estimates of urine protein concentration, according to the dipstick result, are shown in Table III.

False-positive proteinuria may be caused by concentrated or alkaline urine, gross haematuria or contamination with antiseptics. Therefore, proteinuria should always be confirmed quantitatively. Because of the inherent difficulties in collecting a 24-hour urine sample to measure protein excretion in children, the test has been replaced by the measurement of the urine protein:creatinine ratio in a spot urine sample. By calculating a ratio, one can correct for the variation in urine concentration. The test is best performed on the first urine sample that is passed in the morning.

The presence of proteinuria strongly suggests glomerular disease, even though tubulointerstitial disease may also present with proteinuria. Urine dipsticks do not test for tubular proteinuria. This implies that the urine dipstick test may be negative in a patient with renal tubular disease. Microalbuminuria will also not be detected by dipstick testing.

Patients with proteinuria and haematuria are more likely to have significant renal disease, for which there is a wide range of possible causes. It is in this group of patients that primary healthcare practitioners tend to overutilise laboratory investigations in search of a diagnosis. These patients should be referred to a specialist for further investigation and management.

Nitrites

A nitrite test is of limited value in isolation. The nitrite test is an indirect method to detect significant bacteriuria. Normally, nitrates are excreted in the urine as a result of protein metabolism. Common uropathogens, including *Enterobacter*, *Escherichia*, *Klebsiella*, *Pseudomonas* and *Proteus* spp., all produce reductases, which convert nitrates to nitrites. Therefore, a positive nitrite test is indicative of significant bacteriuria. A false-negative test can be the result of urine that has been in the bladder for a short while only.

Table III: Approximate estimates of urine protein concentration according to dipstick result⁹

Dipstick result	Approximate urine protein concentration
Trace	0.15 g/l
1+	0.3 g/l
2+	1 g/l
3+	3 g/l

Urine needs to be in the bladder for at least one hour for the conversion of nitrate to nitrite to occur. This test has a high specificity, but a low sensitivity, for the diagnosis of urinary tract infections, and is best used in combination with a leukocyte esterase test. To confirm a urinary tract infection, urine culture remains necessary.

Leukocyte esterase

This test detects the esterase that is released from white blood cells in the urine and is an indirect test for urinary tract infections. The presence of white blood cells in the urine alone is not diagnostic of a urinary tract infection. It may be present in children with fever without a urinary tract infection, with interstitial nephritis or kidney stones, or it may be the result of contamination during the collection of the sample, especially in girls. A positive dipstick test for both leukocyte esterase and nitrites is in favour of a urinary tract infection (specificity of 98% and sensitivity 45%),¹⁰ but is not diagnostic. When an infant or small child presents with fever of unknown origin, unexplained dehydration, feeding intolerance or failure to thrive, a urine screening test is mandatory. If the urine sample then tests positive for leukocytes and nitrites, a urine sample for culture should be collected aseptically, in other words, either with suprapubic aspiration or with catheterisation of the bladder. In the older child, a midstream clean-catch urine sample for culture is acceptable practice.

Conclusion

Most children with a urinary tract infection can be managed by the general practitioner. The most common error in the management of urinary tract infections in children, and especially in infants, is failure to establish the diagnosis properly in the first place. The failure does not lie in the knowledge to diagnose a urinary tract infection, but in the collection of the urine sample.

For a price of R14.49 (NHLS quote tariff code 3525), the urine dipstick test is available as an invaluable diagnostic tool, either to confirm or exclude kidney disease. Primary healthcare physicians should give this simple, old-fashioned test the time and the place that it deserves to do just that.

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