Childhood urinary conditions

BACKGROUND Urinary abnormalities are commonly detected in children and can be due to a wide range of conditions.

OBJECTIVE This article provides an overview of common urinary abnormalities presenting in childhood to assist general practitioners in planning further investigation and management.

DISCUSSION An initial assessment based upon a comprehensive history, examination and urinalysis should ensure that serious conditions are not overlooked and that unnecessary laboratory studies are not performed. Urinary dipstick testing should not be used to diagnose a urinary tract infection, but can often be used as a screen to exclude one. Isolated microscopic haematuria is only rarely a sign of significant kidney or urinary tract disease and nonpostural proteinuria is a more important diagnostic and prognostic finding that requires specialist assessment. In the majority of cases, the family can be reassured that the risk of significant kidney disease in asymptomatic children with minor urinary abnormalities is small.
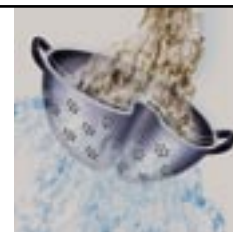
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Many general practitioners will encounter a child with either symptomatic kidney disease or an asymptomatic urinary abnormality that has been detected incidentally during investigation of an unrelated illness. For both symptomatic and asymptomatic kidney disease, the urinalysis forms an integral part of the initial diagnostic work-up, together with a complete history and physical examination. Dipstick urinalysis provides an immediate result, is versatile, simple and ideally suited to children as urine specimens in most cases can be obtained noninvasively. The results of the urinalysis, along with clinical signs and symptoms, can help direct further management by either aiding in establishing the diagnosis or directing further investigation.

Urinary tract infection

Urinary tract infections (UTIs) are one of the most common bacterial infections in children, with a cumulative incidence of ~8% for girls and ~2–3% for boys.[1] The incidence of first time UTI is highest during the first year of life – most marked for boys, but also occurs for girls. Symptomatic recurrence has been reported to occur in 32% of girls and 35% of boys in the first year of life,[2] while after 1 year of age, recurrences and repeated infections in boys without underlying structural abnormalities are unusual. *Escherichi coli* cause 80–90% of initial UTIs in children, while other common organisms include klebsiella and proteus. Enterococci and pseudomonas are more commonly seen in patients with underlying structural urinary abnormalities.

Clinical presentation

The symptoms of a UTI depend on the level of infection (cystitis or pyelonephritis) and the age of the patient. Symptoms in infants are nonspecific and include high fever, poor feeding and vomiting. Other nonspecific signs of sepsis such as apathy, anorexia, poor peripheral

perfusion may also be present. In contrast, symptoms localised to the kidneys and urinary tract become more common as children get older, although high fever may also be the only sign of acute pyelonephritis in a young child. Children cannot usually report back or loin pain until they are 3–4 years of age or over, but renal tenderness can sometimes be found in young children who cooperate well with the physical examination. While children over 2 years of age are able to complain of dysuria and frequency, these symptoms are generally nonspecific. Studies in adolescent and adult women show that as many as 50% of patients with these symptoms won't have a UTI.[3]

Diagnosis

Urinary dipstick testing for leukocytes and nitrite are commonly used as part of the initial evaluation of a child that presents with fever or urinary symptoms. The high negative predictive value of the dipstick test (*Table 1*) means that a UTI is unlikely when these tests are negative, especially in otherwise asymptomatic children. Of note, bacteria require about 4 hours to produce nitrite, so this test may be falsely negative in children with urinary frequency and is best performed on a first morning specimen. The nitrite test may also be falsely negative in the case of a UTI caused by pseudomonas, enterococci and streptococci, as these bacteria do not convert nitrate to nitrite.

While dipstick testing can be useful in excluding infection, the positive predictive value of dipstick tests is generally low (*Table 1*). This indicates that a positive test does not signify a UTI in a significant proportion of cases and should always be confirmed by urinary culture. A properly collected urine specimen is required for both initial dipstick screening and subsequent quantitative urine culture. Adhesive perineal bags are the most convenient method of urine collection in children less than 2 years of age, and in combination with urinary dipstick testing can be used as a screening test to exclude UTIs in young children. The perineal area should be washed before applying the bag with plain water or sterile saline only, as the use of antiseptics can produce false negative results. The bag should be removed as soon as possible after the child has urinated and ideally should be changed if the child has not passed urine within 60–90 minutes. Urine collected in this way can be used for dipstick testing but should not be sent for culture because of unacceptably high rates of false positive results due to contamination.[4] If the urinalysis from a bag specimen is positive, a suprapubic aspirate or transurethral catheter specimen should be obtained for definitive culture.

A clean catch specimen can be used in children aged 2–3 years who are not toilet trained. The preparation is the same as for a perineal bag, but a sterile container is used to catch the urine once the child starts to urinate. Midstream collection is recommended for older cooperative children but specific instruction (separation of labia in girls, retraction of foreskin in uncircumcised boys) is required to avoid contamination.

The management of UTIs and subsequent investigation to determine the presence of underlying structural urinary tract abnormalities is beyond the scope of this article but has been discussed in a number of excellent reviews (see *Resources*).

Haematuria

Routine screening urinalysis of asymptomatic children is not generally recommended due to the high cost to benefit ratio.[5] Thus children with haematuria will present in one of three ways:
- onset of gross haematuria
- onset of urinary or other symptoms with incidental finding of microscopic haematuria, or
- the inadvertent discovery of microscopic haematuria during a visit where a urinalysis is required (eg. pre-sport physical).

In each case, the initial step in evaluation is to confirm haematuria by microscopy, as a number of nonrenal conditions can cause discolouration of the urine or

Table 1. Predictive values for the diagnosis of UTI by urinary dipsticks

	Positive predictive value (%)		Negative predictive value (%)	
	<1 year age	>1 year age	<1 year age	>1 year age
Leukocyte +	11–21	7–25	99	98–100
Nitrite +	47–65	34–70	98	96–99
Nitrite and leukocytes +	21–35	13–40	96–98	95–99

produce a false positive dipstick reading (*Table 2*).

Macroscopic haematuria

Gross haematuria is uncommon in unselected populations of children. A retrospective North American study of children attending an emergency clinic[6] reported an incidence of 0.13%, and in over half (56%) of these children there was a readily identifiable cause for haematuria that could be elicited by a detailed history (including family history), examination, and a limited panel of investigations. Urine microscopy to determine the character of red cells is commonly used to differentiate renal from urological causes of haematuria. Normal doughnut shaped red blood cells are generally due to lower urinary tract bleeding. In contrast, dysmorphic urinary red blood cells show variation in size with an irregular or distorted outline, and if present in large numbers, are considered to indicate a glomerular origin of the haematuria. The common causes of macroscopic haematuria are shown in *Table 3*, suggested investigations are shown in *Table 4*. If the cause of the gross haematuria is not readily apparent from these investigations, the child should be referred to a paediatrician or paediatric nephrologist for further assessment.

Macroscopic haematuria with a predominance of dysmorphic red cells and the presence of red cell casts, hypertension, and renal insufficiency are characteristic features of glomerulonephritis (GN). Poststreptococcal GN typically follows 10–14 days after infection with Group A ß-haemolytic streptococci and is the most common form of acute GN seen in children. While pharyngitis and pyoderma are the common antecedents, 20% of asymptomatic school children are carriers of streptococci, therefore acute GN may be seen in the absence of identifiable prodromal illness. Treatment of acute streptococcal pharyngitis does not prevent the occurrence of GN.

The typical presentation of poststreptococcal GN is of a school aged child with macroscopic haematuria, oedema due to fluid retention, and possibly a headache due to hypertension. Investigation shows elevation of urea and creatinine, a normocytic anaemia, elevated streptococcal markers (ASOT/anti-DNase B) and a depressed complement (C3) level. These clinical and biochemical findings can also be seen following illness with a wide range of other infectious agents. In these cases the streptococcal serology will be negative and the disease is usually referred to as postinfectious GN. Management involves treatment of fluid overload with diuretics, and control of hypertension. Milder cases that do not have oliguria, renal impairment

Table 2. Selected causes of red-brown urine discolouration

Medications
- Chloroquine, iron, isoniazid, melanin, metronidazole, nitrofurantoin, rifampin, salicylates, sulfa drugs

Foods
- Beets, blackberries, rhubarb, food colouring

Pigments/toxins
- Hameoglobinuria*, myoglobinuria*, bile, lead, porphyria, urates

* Produce false positive dipstick reading

or hypertension can be managed on an outpatient basis, with twice weekly reviews. The prognosis is excellent with almost all children making complete recovery. While microscopic haematuria may persist for 1–2 years after the initial illness, it does not indicate a worse prognosis but warrants ongoing follow up to document its disappearance.

If there are atypical clinical features, a renal biopsy is usually required to differentiate postinfectious GN from other primary glomerular diseases such as IgA nephropathy, membranoproliferative GN and crescentic GN. Glomerulonephritis may also been associated with systemic disorders such as Henoch-Schonlein purpura and systemic lupus erythematosis. These conditions can often be identified on history and examination.

Microscopic haematuria with clinical symptoms

Children in this category may have general clinical symptoms (eg. fever, malaise, abdominal pain), nonurinary signs and symptoms (eg. rash, purpura, arthritis), or specific urinary symptoms (eg. dysuria, urgency, frequency). The list of possible diagnosis is extensive and includes infections, both generalised and renal, rheumatological or immunological conditions, glomerular and interstitial disease, lower urinary tract disease, kidney stones, and tumours. Therefore, this is the most difficult category for which to make recommendations regarding further investigation and management. Evaluation should be directed toward the clinical manifestations with the haematuria considered as but one sign. It is recommended that children with clinical features that cannot be clearly differentiated into a category of illness should be referred for further assessment.

Isolated microscopic haematuria

Asymptomatic isolated microscopic haematuria is common, with screening studies in children of all ages showing a prevalence of 0.5–2%.[7] However, persistent

Table 3. Causes of macroscopic haematuria

Common
Urinary tract infection
Perineal irritation
Trauma
Meatal stenosis with ulceration

Uncommon
Glomerulonephritis
Renal calculi
Coagulation abnormalities
Tumours

Table 4. Investigation of macroscopic haematuria

Urine
Dipstick urinalysis
Microscopy and culture/red blood cell morphology
Calcium/creatinine ratio

Blood
Electrolytes including creatinine, full blood count
Antistreptolysin titre (ASOT)/anti-DNase B
Complement (C3)

Imaging
Renal ultrasound

microscopic haematuria is less common (<0.5%) indicating that investigation of isolated microscopic haematuria should only be instigated once persistence has been established in at least 3 different specimens taken over a period of 2–3 weeks. Investigation of persistent microscopic haematuria is the same as for gross haematuria, although complement levels are not required. Dipstick assessment of first degree relatives for the presence of haematuria should also be undertaken to identify benign familial haematuria (also known as thin basement membrane disease), a nonprogressive autosomal dominant condition that does not require any specific treatment. Significant renal disease is very unlikely if all investigations are normal, but periodic review for at least 5 years is warranted to assess new features on history, examination and urinalysis. The appearance of macroscopic haematuria or proteinuria requires referral for further evaluation (eg. renal biopsy).

Proteinuria

As with haematuria, proteinuria is likely to present either as symptomatic disease (ie. nephrotic syndrome), an incidental finding during assessment of either renal or nonrenal symptoms, or detected on urinary screening in asymptomatic patients.

Nephrotic syndrome

Nephrotic syndrome is defined by the occurrence of generalised oedema, heavy proteinuria (+++ or ++++ on dipstick), hypoalbuminaemia and hypercholesterolaemia and occurs most commonly in young children, with peak incidence for the initial episode at 2 years of age. Children with steroid responsive nephrotic syndrome usually have no nephritic features such as haematuria, hypertension or raised serum creatinine. However, microscopic haematuria is occasionally seen (15–30%) and clears before or with remission of proteinuria. The majority of children will have minimal change disease (80%) or focal segmental GN (5–10%), while mesangial proliferative GN, membranoproliferative GN and membranous GN are all rare.

Children with their first episode of nephrotic syndrome should be referred for admission to hospital. The mainstay of treatment is prednisolone and children will usually respond with a diuresis and complete clearance of proteinuria within 3 weeks of starting treatment. Children not responding after 4 weeks of an appropriate dose of steroids require a renal biopsy. In those that do respond, the initial course of prednisolone is slowly tapered over a number of months and eventually ceased. Relapses occur in 75% of children and generally these children can be managed as outpatients with further courses of prednisolone. Children with more than two relapses in 6 months or ≥4 relapses in 12 months are classified as frequent relapsers and should be referred to a paediatric nephrologist for further management.

Proteinuria with clinical symptoms

In as many as 30–50% of children, proteinuria is transient and resolves over 1–2 weeks. Transient proteinuria is common during febrile illnesses and can also occur with strenuous exercise, emotional stress and following seizures or abdominal surgery. In all of these circumstances, proteinuria resolves spontaneously after the cessation of the causal factor and an extensive work-up is generally not necessary.

Isolated proteinuria

Proteinuria in a single urine specimen is relatively common in children with a reported prevalence of 1–10%,[8] while persistent proteinuria is much less common. A screen of 9355 South Australian school children reported a low prevalence of proteinuria (0.25%),[9] but

one-third of these children were found to have significant renal disease indicating the importance of persistent proteinuria as a marker of renal disease.

The initial assessment of proteinuria detected on dipstick urinalysis involves laboratory quantitation. It is recommended that total protein, rather than albumin, should be measured for all children except diabetics. This recommendation is based on the fact that congenital structural abnormalities and tubular disorders occur more commonly in children than in adults and are characterised by significant excretion of low molecular weight proteins that would not be detected by testing exclusively for albumin.

In young children, accurate timed collections are difficult to obtain and the protein/creatinine ratio (PCR) on an untimed urine specimen has been the accepted standard for many years. For ease of collection, a random urine specimen is acceptable as the PCR on both first/early morning and random urine specimens correlates well with the 24 hour protein excretion.[10] However, abnormally elevated values should be confirmed with a first morning urine sample to exclude the diagnosis of postural (orthostatic) proteinuria. Postural proteinuria accounts for up to 60% of all cases of asymptomatic isolated proteinuria in children, and has an even higher incidence in adolescents.[11] Diagnosis can be confirmed by performing a 24 hour urine collection and two additional urine samples, one collected on the first morning void and another taken during the day after a period of usual activity. In patients with postural proteinuria, the 24 hour protein excretion is usually less than 1 g per day, and first morning specimen protein will be within the normal range, while the protein level in the afternoon sample may be elevated. A number of long term follow up studies strongly suggest that this is a benign condition with an excellent prognosis.[12,13] Nevertheless, a single follow up 12 months later with assessment of any new features on history and examination and protein quantitation on a first morning urine specimen is recommended to exclude significant renal disease.

Conclusion

Urinary abnormalities are common in children and present in a number of different guises. Classifying children according to the mode of presentation and clinical and urinalysis findings facilitates a structured approach to subsequent investigation and management that helps to avoid unnecessary and potentially expensive testing. In many cases, parents can be reassured that minor urinary abnormalities detected incidentally during investigation of an unrelated illness will resolve upon recovery from the primary illness.

Resources

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