

MINI REVIEW

How Swedish guidelines on urinary tract infections in children compare to Canadian, American and European guidelines

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Abstract

Urinary tract infections (UTI) are common in children and the guidelines focus on preventing kidney damage. We compared the 2013 national Swedish guidelines on UTIs in children with the guidelines from America, Canada, UK, Spain, Italy and European urologists. This showed that urinalysis and urine cultures are endorsed by all the guidelines, but sampling techniques and bacteria levels differ. They all recommend initial oral treatment and renal ultrasound to detect major anomalies in infants. The Swedish guidelines are more liberal on antibiotic prophylaxis.

Conclusion: Differences in diagnostic criteria, workup and accepted methods for urine sampling were noted and are discussed.

KEYWORDS

antibiotic prophylaxis, diagnostic criteria, guidelines, urinary tract infection, vesicoureteral reflux

1 | INTRODUCTION

It is common for children to have a urinary tract infection (UTI) and these affect 2% of children below two years of age.¹ Diagnoses are based on the child's symptoms, nitrite and, or, leucocytes in the urine and a positive urine culture. However, specific symptoms are difficult to identify if children are not toilet trained and the youngest children often present with a fever of unknown origin. In infants, failure to thrive or feeding difficulties can be the only signs of a UTI, as sometimes they do not have a fever and their general condition is unaffected.²

Upper urinary tract and kidney infections cause more severe symptoms and risk permanent renal damage. Renal involvement is suspected when there are signs of inflammation, with fever and increased C-reactive protein (CRP) or procalcitonin and the child's general condition is affected. The association between renal scarring and UTIs increases with the severity and number of infections

and if there are concomitant anomalies of the urinary tract, such as dilating vesicoureteral reflux (VUR) or an obstruction.³

Long-term complications from UTIs, and associated renal damage, are rare and of low clinical significance if UTIs are diagnosed promptly.⁴ Childhood UTI cohorts followed for more than 20 and 40 years only showed a moderate risk of preeclampsia during pregnancy and hypertension if bilateral or severe unilateral renal damage had occurred.⁵⁻⁷ The increased use of prenatal ultrasonography has shown that combined renal and urinary tract anomalies tend to be congenital, rather than acquired, especially in boys. Meanwhile, girls have more renal scarring from UTIs.⁸

A UTI is often the presenting symptom in children with congenital anomalies of the kidneys and urinary tract. Numerous childhood UTI guidelines have been published over the years. These aimed to protect children from developing renal damage, due to obstruction or recurrent UTIs, and support those with established renal congenital

Abbreviations: cfu, colony-forming units; CRP, C-reactive protein; DMSA, dimercaptosuccinic acid; MSU, mid-stream urine sample; RBUS, renal and bladder ultrasound; SPA, suprapubic aspiration; UTI, urinary tract infection; VCUG, vesico-cysto-urethrography; VUR, vesicoureteral reflux.

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hypodysplasia or acquired scarring. This mini review presents the national 2013 Swedish guidelines and compares them to six other national and international guidelines published, and in some cases updated, from 2007 to 2020.

2 | THE 2013 SWEDISH GUIDELINES ON CHILDHOOD UTI

The 2013 Swedish guidelines were the result of a national collaboration initiated by the Swedish Society of Paediatric Nephrology. They were based on published studies and presented, and implemented, nationwide in 2013. The working group comprised paediatric nephrologists from four of the country's five tertiary hospitals and paediatricians from county hospitals. They searched the literature for information on risk factors for renal damage and recurrent UTIs, acute and follow-up dimercaptosuccinic acid (DMSA) after UTIs, antibiotic treatment and prophylaxis and bladder and bowel function. The working group also relied on the thorough preparatory work that had been presented by the National Institute of Health and Care Excellence in the UK⁹ and by the American Association of Pediatrics.¹⁰ The aim was to harmonise the management of children with UTIs in Sweden and to reduce the number of investigations, without jeopardising the safety of children at risk. The Swedish guidelines focus on children below two years of age. However, they also provide advice on managing older children and provide separate recommendations for children with VUR (Figures 1-3). The algorithm for children under the age of two includes two different options for the timing of DMSA scintigraphy, to reflect different access to acute DMSA scans across the country. The main recommendation is an early DMSA scan within weeks of an acute UTI that has specific risk factors (Figure 1A). The alternative option is a late DMSA scan to detect permanent scarring (Figure 1B). This latter option is considered equally safe for children, but requires a longer follow-up period and more imaging with vesico-cysto-urethrography (VCUG). Before they were finally approved, the algorithms were tested against data from a previously published cohort of 209 infants with febrile UTIs. They had all been investigated with acute ultrasound, DMSA scintigraphy within two weeks of the UTI, VCUG within two months of the UTI. The cohort also underwent a follow-up DMSA scan if there were uptake defects on the acute scan or they had recurrent UTIs.^{11,12}

The definition of UTI presented here is for clinical purpose. In most scientific studies, the definition is more rigorous, to avoid confusing the results with ambiguous cases.

3 | DIAGNOSING UTI

3.1 | Urine sampling

Urine sampling for cultures should be as clean as possible, preferably with suprapubic aspiration (SPA) or catheterisation. If clean catch mid-stream urine (MSU) is used, two separate samples should be

Key notes

- This paper compared the 2013 national Swedish guidelines on urinary tract infections in children with American, Canadian, UK, Spanish, Italian and European guidelines.
- The guidelines all endorse urinalysis and urine cultures and recommend initial oral treatment and renal ultrasound to detect major anomalies in infants.
- However, the recommended sampling techniques and bacteria levels are not the same and this paper explores the differences and similarities.

sent for cultures. as two samples that produce the same bacteria increase the probability of true bacteriuria. However, one sample will suffice for girls with positive nitrite sticks. Urine collected from a urine bag or pad can be used for dipstick screening. If the dipstick is positive, another urine sample, collected using MSU, a catheter or SPA, should be sent for culture.

3.2 | Urine analysis

UTI urine dipsticks are often positive for leucocyte esterase, but leukocyturia is also present in other febrile infections, with a sensitivity of 83% (range 67–94) for a UTI and specificity of 78% (range 64–92).¹⁰ A negative leucocyte esterase dipstick makes a UTI less likely, but does not exclude it completely.¹³ Urine microscopy can be used for a UTI diagnostic workup, but is not usually available as an emergency test in Sweden and is not included in the 2013 guidelines.

Nitrite sticks are negative in 50% of children with bacteriuria, due to short bladder incubation time or bacteria that do not produce nitrite, providing a sensitivity of 53% (range 15–82).¹⁰ A positive nitrite stick is strongly predictive of true bacteriuria, with a specificity of 98% (range 90–100).¹⁰ It can provide a false positive in boys, as bacteria under the prepuce can produce nitrite.¹⁴

3.3 | Urine culture

When a UTI is suspected, urine should be sent for culturing to establish the diagnosis. There is no safe lower limit to discriminate between contamination and true bacteriuria. Hence, the culture result must be interpreted in relation to the symptoms, age and sex of the child and to the results from the urine analysis and blood tests. *Escherichia coli* is the most common bacteria found in UTI studies. UTIs with other bacteria than *Escherichia coli* increase the probability of abnormalities or dysfunction of the bladder and urinary tract.¹⁵

(A)

Swedish Society of Paediatric Nephrology 2013

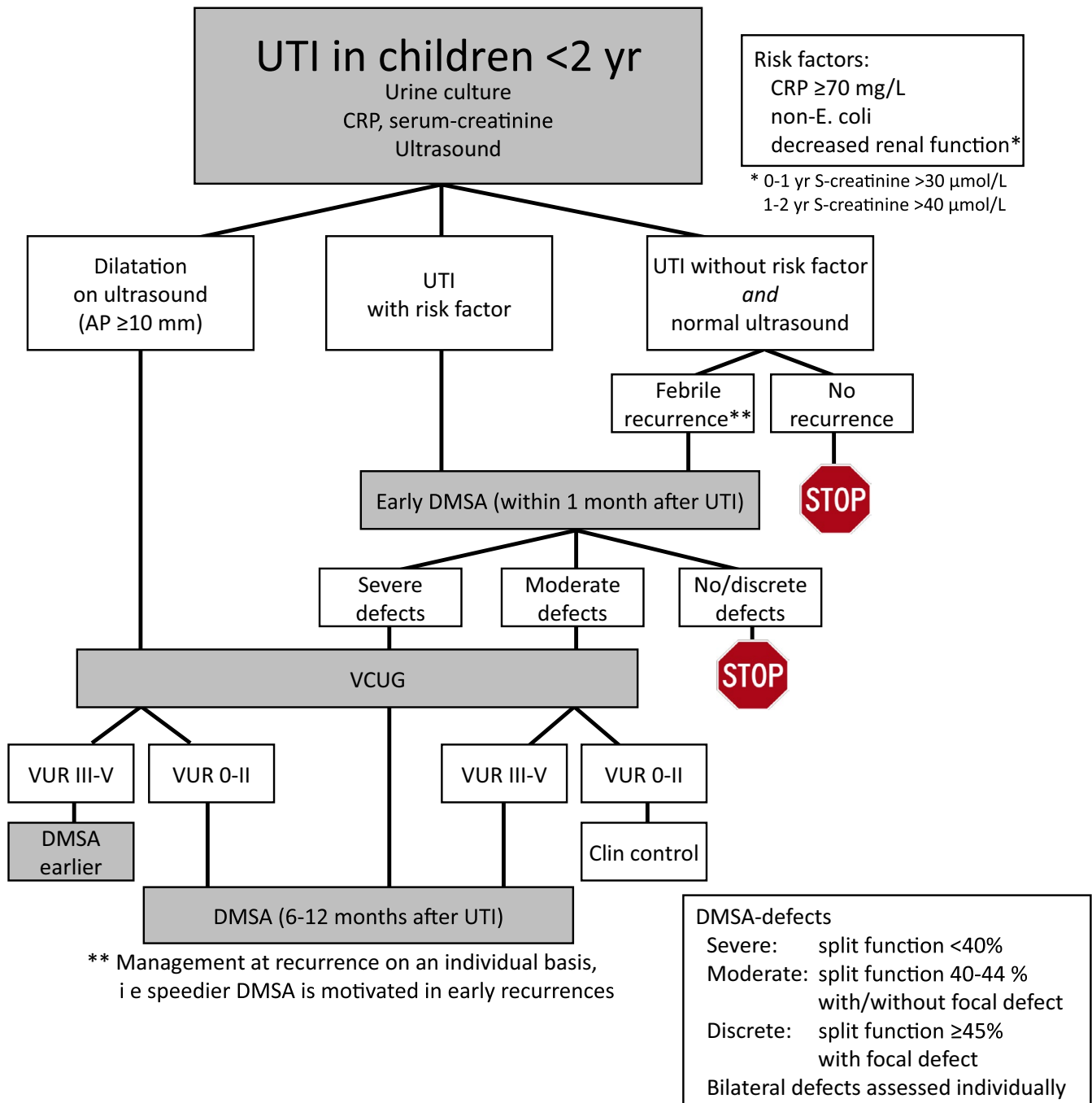


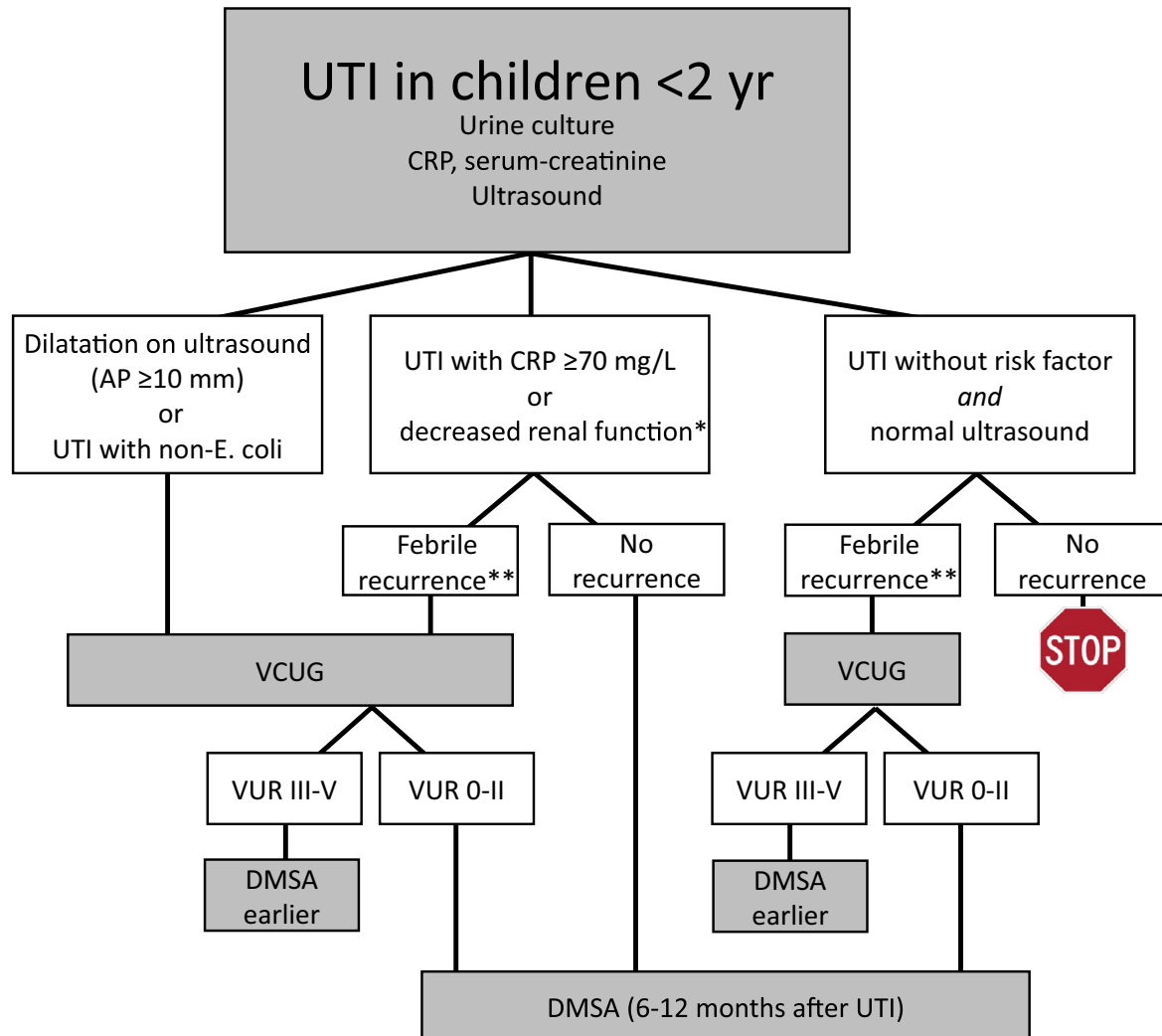
FIGURE 1 (A) UTI algorithm from Swedish guidelines for children below two years. UTI, urinary tract infection; CRP, C-reactive protein; AP, antero-posterior diameter; DMSA, dimercaptosuccinic acid scintigraphy; VCUG, vesico-cysto-urethrography; VUR, vesicoureteral reflux. (B) Optional algorithm for centres without access to acute DMSA scans. UTI, urinary tract infection; CRP, C-reactive protein; AP, antero-posterior diameter; DMSA, dimercaptosuccinic acid scintigraphy; VCUG, vesico-cysto-urethrography; VUR, vesicoureteral reflux.

(B)

Swedish Society of Paediatric Nephrology 2013**Optional algorithm**

where acute DMSA is not available

VCUG after dilatation on ultrasound, non-E. coli infection or febrile recurrence.
DMSA mainly as follow up after 6-12 months.



* 0-1 yr S-creatinine >30 $\mu\text{mol/l}$, 1-2 yrs S-creatinine >40 $\mu\text{mol/l}$

** Management at recurrence on an individual basis, i.e. speedier VCUG is motivated in early recurrences

DMSA-defects

Severe: split function <40%

Moderate: split function 40-44 %
with/without focal defect

Discrete: split function \geq 45%
with focal defect

Bilateral defects assessed individually

FIGURE 1 (Continued)

Swedish Society of Paediatric Nephrology 2013

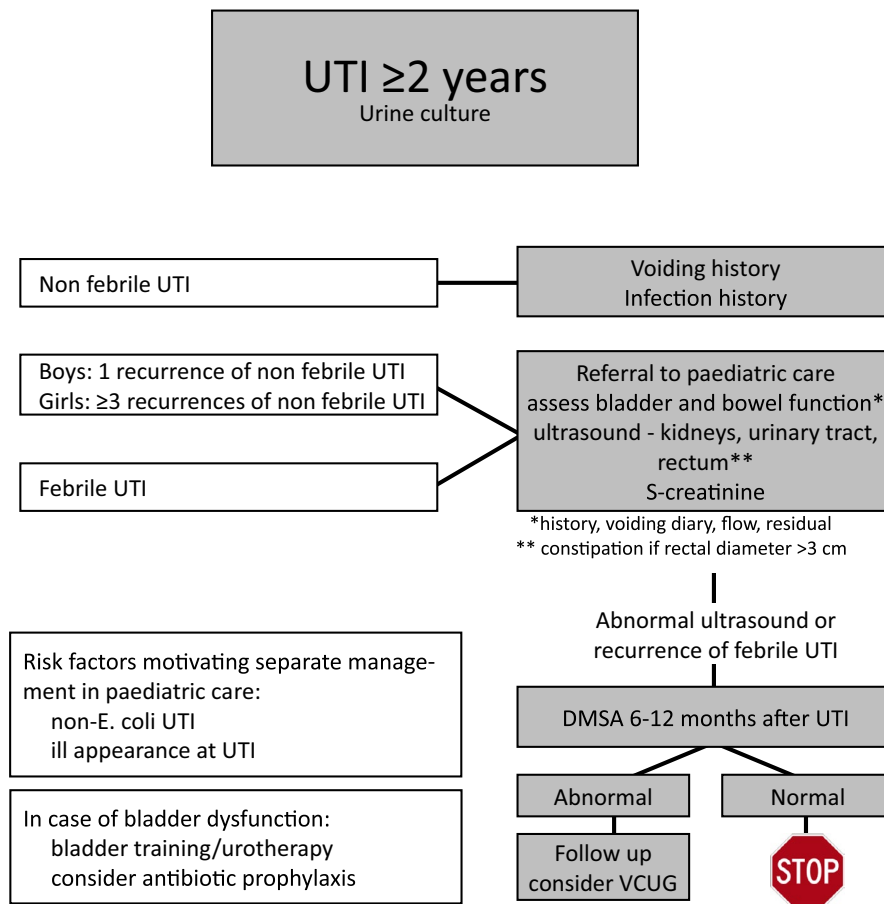


FIGURE 2 Algorithm from Swedish guidelines on UTI for children over two years of age. In the older children, imaging is reduced and there is more focus on bladder and bowel function. UTI, urinary tract infection; DMSA, dimercaptosuccinic acid scintigraphy; VCUG, vesico-cysto-urethrography.

3.4 | Level of infection

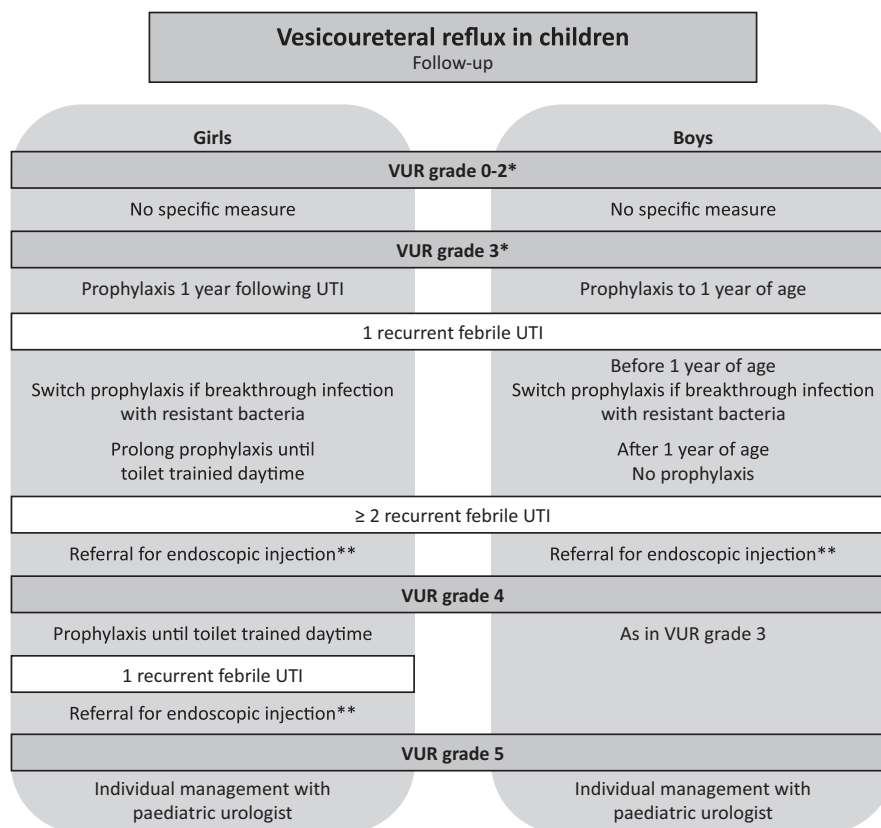
CRP, serum creatinine and temperature should be tested at presentation. UTIs with kidney involvement are usually associated with fevers at, or above, 38.5°C and a poor general condition. Raised inflammatory markers, such as CRP or procalcitonin have been associated with renal damage and dilating reflux.^{12,16,17} The chance of detecting reduced uptake on DMSA scintigraphy after a febrile UTI increases with the level of CRP. We recommend that a CRP that is above 70 mg/L should be seen as a risk factor and prompt further investigations.^{12,16} A CRP below 70 mg/L, which was tested within 24 hours of the start of the child's fever, should be retested the next day. Children below one month of age frequently present with lower fever and CRP levels. Thus, these children will need to be managed more intensely, regardless of the level of the infection. There is a small, but important,

percentage of patients, whose renal function is already impaired at the onset of the UTI. They often have congenital hypoplasia or dysplasia of one or both kidneys. That is why a serum creatinine that is above normal at presentation is a risk factor that requires further investigation.

4 | BLADDER AND BOWEL DYSFUNCTION

Children with bladder dysfunction, in particular incomplete bladder emptying or infrequent voiding, have an increased risk of recurrent UTIs and a lower chance of resolving dilating VUR, spontaneously or after surgical intervention.¹⁸⁻²⁰ A detailed medical history is the most important tool to identify micturition difficulties. Parents should be asked if their child has demonstrated straining, postponing, holding manoeuvres, infrequent voiding, urgency and wetting. Toilet-trained

Swedish Society of Paediatric Nephrology 2013



* New VCUG only in case of DMSA deterioration or UTI recurrence

** Endoscopic injection considered without UTI recurrence if split function declines $\geq 10\%$ on repeat scintigraphy (DMSA or MAG-3)

FIGURE 3 Algorithm on management of VUR from Swedish guidelines on UTI in children. Antibiotic prophylaxis is used more often and for a longer time in girls due to their higher risk of recurrent UTIs. VUR, vesicoureteral reflux; UTI, urinary tract infection; VCUG, vesico-cysto-urethrography; DMSA, dimercaptosuccinic acid scintigraphy; MAG-3, mercaptoacetyl triglycine renography.

children can also be evaluated with micturition charts, uroflowmetry and residual urine assessment. Voiding observation can be performed in smaller children, to detect incomplete emptying.²¹ Invasive methods, such as cystometry, should be considered when neurogenic bladder dysfunction or bladder outlet obstruction is suspected.

Constipation and dysfunctional bowel elimination has been strongly associated with bladder dysfunction and an increased risk of recurrent UTI. It should always be addressed during the history taking, evaluated by the workup after a UTI in toilet-trained children and treated when present.²²

5 | Treatment

We recommend that symptomatic UTIs are treated with oral antibiotics. Initial intravenous treatment should be considered in children who are severely ill or unable to tolerate oral medication. A 10-day course is recommended for febrile infections, but a five-day course is sufficient if the child has a UTI without renal involvement.

The antibiotic used for febrile infections must be able to reliably penetrate the renal parenchyma. Due to the increasing antibiotic resistance of uropathogenic bacteria, we can no longer use trimethoprim-sulfamethoxazol as empiric treatment before the resistance pattern is established. The Swedish guidelines recommend ceftibuten as the first choice, with a switch to amoxicillin-clavulanate or trimethoprim-sulfamethoxazole if possible, as soon as the resistance pattern of the bacteria is obtained.

For intravenous treatment, we recommend cephalosporins, with the addition of an aminoglycoside in more severely affected children while they await the results of their culture report. If the infections include multi-resistant bacteria, the treatment should be tailored in collaboration with an infectious disease specialist.

6 | Asymptomatic bacteriuria

Bacteriuria without symptoms will not harm the kidneys.²³ If a non-virulent asymptomatic bacteriuria strain is eradicated by antibiotic

TABLE 1 General aspects and characteristics of the seven UTI guidelines.

Guidelines	UK	America*	Italy*	Canada	Europe	Spain	Sweden
Age	0–16 years	2–24 months	2–36 months	>2 months	0–18 years	0–18 years	0–18 years
Temp cut-off febrile UTI (°C)	≥38	≥38	≥38	-	≥38	-	Not defined ≥38.5 suggested
Advice on follow-up	Yes - general	-	-	-	-	'Individual'	Yes - detailed
Other	Defines 'atypical UTI'	Evidence grading	Evidence grading	-	Urologic approach	Evidence grading	Management of VUR

UTI, urinary tract infection; VUR, vesicoureteral reflux.

*Guideline only considers febrile UTIs.

treatment for any reason, there is a substantial risk of subsequent colonisation of the urinary tract with a more virulent strain, resulting in a symptomatic UTI. Hence, antibacterial treatment of asymptomatic bacteriuria should be avoided and prescribing antibiotics for other reasons should be restricted in children with asymptomatic bacteriuria.

7 | Follow-up procedures

To identify children at risk of recurrent UTIs, and those with established kidney damage, we recommend that all children under the age of two receive a renal and bladder ultrasound (RBUS) after their first UTI. The same approach should be adopted for older children after a febrile UTI or recurrent non-febrile UTIs. A DMSA scan is recommended within one month of a first UTI in children below two years of age, but only if the child has a risk factor or after a febrile UTI recurrence (Figure 1A). The risk factors are defined as dilatation on ultrasound, a serum CRP of ≥70 mg/L, the presence of other bacteria than *Escheria coli* and increased serum creatinine. Using VCUG, to detect and grade VUR and to identify any urethral obstruction, should be limited to children below two years of age with dilatation on ultrasound or with moderate to marked parenchymal defects on their DMSA scan, namely focal parenchymal uptake defects or split function <45%. VCUG should also be used in boys with impaired urine flow. A late DMSA scan should be performed after 6–12 months in those with abnormalities on the acute DMSA scan, to identify permanent renal damage.

In the alternative follow-up option, the acute DMSA scan is omitted and VCUG is used in children with dilatation on the ultrasound, evidence of other bacteria than *Escheria coli* or after a recurrent febrile UTI (Figure 1B). A late DMSA is recommended for children with any of the risk factors during their first UTI, as specified above, or after a recurrent febrile UTI.

Extensive parenchymal reduction from renal scarring, or a generally small hypoplastic kidney, have been associated with an increased risk of reduced renal function and hypertension, especially in those with severe or bilateral damage.^{6,24} That is why children with parenchymal defects should be followed up during childhood, at intervals of up to two years, with the focus on the early detection and treatment of hypertension and proteinuria.

Children who need a more individualised treatment and follow-up approach should be identified during multi-disciplinary conferences. The local paediatrician should be responsible for their care, often in

collaboration with specialists at tertiary centres, including paediatric nephrologists, urologists, radiologists and nuclear medicine specialists.

8 | VESICoureTERAL REFLUX

Studies have shown a strong association between dilating VUR and the risk of recurrent UTI and congenital or acquired renal damage.^{25,26} That is why identifying children with dilating VUR, and providing advice on their management, is an important objective of the Swedish guidelines. However, this association has been reported to be much lower in non-dilating reflux,²⁷ and consequently, children with low-grade reflux (VUR 1–2) are treated in a similar way to those with no VUR. We also primarily recommend conservative management in dilating VUR, due to its high rate of spontaneous resolution,²⁸ while surgical correction should be considered in children with frequent recurrences of febrile UTI or deteriorating renal total or split function (Figure 3). A more detailed elaboration of the surgical interventions that are available is beyond the scope of this paper.

9 | ANTIBIOTIC PROPHYLAXIS

Long-term antibiotic prophylaxis moderately reduces the risk of recurrent UTIs in all children with all grades of VUR, especially girls with dilating reflux.^{29–31} We recommend prophylaxis for children with dilating reflux: for boys, this should be up to one year of age, and for girls, it should be for a period of one year or until they are toilet trained, as girls have a much higher risk of recurrent UTI. We also recommend antibiotic prophylaxis for children with frequent recurrences of febrile UTIs, and for toilet-trained children with frequent UTIs, combined with urotherapeutic interventions. For antibiotic prophylaxis, we recommend nitrofurantoin (1 mg/kg once a day) or trimethoprim (0.5–1 mg/kg once a day).

10 | IMPLEMENTATION AND ADHERENCE

The Swedish guidelines were presented at the 2013 annual meeting of the Swedish Paediatric Society. Their implementation was facilitated by the longstanding collaboration between the Swedish paediatric nephrology centres, who attended the same educational

TABLE 2 Diagnostic recommendations.

Diagnostic procedure/ test	UK	America	Italy	Canada	Europe	Spain	Sweden
Urine collection in non-toilet trained	1. MSU 2. Pad 3. Cath/SPA	Cath/SPA MSU for screening	Hospital-toxic: Cath/SPA Not toxic: MSU Bag for screening	Cath/SPA MSU for screening	Cath/SPA/ MSU Bag for screening	Cath/SPA/MSU Bag for screening	1. SPA if <1 year 2. MSU (x2) 3. Cath
Significant bacteriuria	-	Cath/SPA $\geq 5 \times 10^4$	Cath/SPA $\geq 10^4$ MSU $\geq 5 \times 10^4$	SPA all growth Cath $\geq 5 \times 10^4$ MSU $\geq 10^5$	SPA all growth Cath $\geq 10^3$ MSU $\geq 10^5$ (10^4 if sympt)	SPA all growth Cath $\geq 10^4$ MSU $\geq 10^5$ (10^4 if sympt)	-
Blood test recommended	CRP should not be used for differentiating upper/lower UTI	-	<3 months and hospitalised: CRP, procalcitonin, FBC, creat	Creat if 'complicated' UTI	< 1 year: CRP/procalcitonin, FBC, creat, electrolytes	Optional If <3 months blood culture	CRP, creat, blood culture if iv
Urine handling	Culture within 4 h Otherwise cooled	Urinalysis (dipstick or microscopy) within 1 h				Kept cool for max 24 h culture	

MSU, mid-stream urine; cath, catheter; SPA, suprapubic aspiration; CRP, C-reactive protein; UTI, urinary tract infection; FBC, full blood count; creat, creatinine; iv, intravenous

meetings and took part in the same multicentre studies. They are now being evaluated by an ongoing, nationwide, multicentre study of adherence to the guidelines, which also examines the quality of care that is provided for infants with UTIs.

11 | DIFFERENCES AND SIMILARITIES BETWEEN THE PAEDIATRIC UTI GUIDELINES

There are differences, but also many similarities between the 2013 Swedish guidelines, and the guidelines published by six other countries and regions. These include the UK National Institute of Health and Care Excellence guidelines, published in 2007 and updated in 2018,³² and the American Academy of Pediatrics guidelines, published in 2011 and reaffirmed in 2016.^{10,33} They also include the 2019 Italian Society of Pediatric Nephrology guidelines,³⁴ the Canadian Paediatric Society guidelines, published in 2014 and reaffirmed in 2020^{35,36} the 2015 European Association of Urology/European Society for Paediatric Urology guidelines³⁷ and the 2019 Spanish Association of Paediatrics guidelines.³⁸

11.1 | General aspects of the guidelines

Most of the paediatric UTI guidelines focus on the younger age group (Table 1). This is due to the challenges in diagnosing UTIs in preverbal, non-toilet-trained children and the possibilities of underlying abnormalities in the urinary tracts of very young children with UTIs. The American and Italian guidelines exclusively consider children with febrile infections who are under the ages of 24 and 36 months, respectively. The UK, Canadian, European, Spanish and Swedish guidelines also include older children and those with non-febrile UTIs, making these guidelines more general. The American and Italian guidelines narrow the age span further by excluding infants who are under two months of age, stating that this age group requires special consideration and that the scientific evidence is generally derived from studies on children who are older than two months.

Some guidelines provide definitions to help readers to interpret some of the statements that are used. For example, the American, Italian, UK and European guidelines define the cut-off temperature for febrile UTI at ≥ 38 degrees Centigrade, signalling kidney involvement, while others leave the definition of fever to the readers.

In contrast to the other guidelines, the Swedish and UK guidelines provide some specific advice on how to follow up children with renal parenchymal defects and the Swedish guidelines also include how to manage dilating VUR.

11.2 | Diagnostic recommendations

The optimal method of collecting urine in children is controversial and Table 2 covers the diagnostic recommendations. All the

TABLE 3 Treatment recommendations.

Treatment	UK	America	Italy	Canada	Europe	Spain	Sweden
Route of administration in febrile UTI	<3 months: refer to hospital <1 month: iv <3 months and toxic: iv >3 months oral	Iv if toxic/unable to retain oral fluid. Otherwise oral	Iv if toxic/unable to retain oral fluid. <3 months: iv Otherwise oral	Iv if toxic/unable to retain oral fluid. Otherwise oral	7-14 (toilet trained, uncomplicated 7)	Iv if toxic/unable to retain oral fluid. <3 months: iv Otherwise oral	Iv if toxic/unable to retain oral fluid. Otherwise oral
Length of treatment (days) in febrile UTI	10	7-14	10	7-10	7-14	7-10	10
Prophylactic antibiotics recommended	No	No	Not routine. Consider if: VUR grade 4-5 >3 febrile UTIs/1 year	Not routine. VUR grade 4-5 and anomalies: discuss with urologist	Consider if <1 year and in non-toilet-trained girls	No Consider if obstructive uropathy	VUR≥grade 3 Recurrent UTI
Comments on BBD attention	Yes	Yes	Yes	No	Yes	Yes	Yes

UTI, urinary tract infection; iv, intravenous; VUR, vesicoureteral reflux; BBD, bladder and bowel dysfunction.

guidelines conclude that bags and urine pads should not be used for cultures, due to the high risk of contamination, but some guidelines suggest they could be used for dipstick screening. A UTI is unlikely when the dipstick or microscopic analysis on a urine bag sample is negative, but it cannot be ruled out with certainty.

All the guidelines recognise that the invasive methods of urine collection, namely using SPA or a catheter, carry the lowest risk of contamination. These are the recommended methods for cultures in several guidelines. However, using SPA and catheters are not plausible methods in all healthcare settings and the difference in the guidelines are, at least partially, a reflection of differences between local healthcare systems. In the UK, for example, a child with a UTI is very likely to be seen by its family doctor in a primary care setting and the UK guidelines recommend non-invasive methods in the first instance. On the other hand, in America, Spain, Sweden and Italy, the guidelines are mainly directed towards clinicians working in specialist paediatric care, where SPA and catheters are more readily used in younger children.

Clean catch or MSU is recommended by all the guidelines, but primarily for screening. This is because it is difficult to obtain clean catch or MSU sample from a child who has not been toilet trained, making the risk of contamination high. However, the UK guidelines generally recommend MSU as the preferred method. The Swedish and European guidelines argue that the risk of contamination in an MSU specimen is acceptable and recommend this as an alternative method. An MSU sample is accepted also by the Italian guidelines, provided the child is in a good clinical condition.

The guidelines differ with regard to the diagnostic threshold for significant bacteriuria. The recommendations on blood tests also differ between guidelines. This is due to the lack of evidence for specific biomarkers or cut-off levels of inflammatory markers to differentiate UTI from other infections or to decide the level of a UTI with certainty. Some guidelines have chosen to recommend inflammatory markers in blood as part of the diagnostic workup, while others provide no such recommendations. In the Swedish guidelines, CRP is used for risk stratification.

11.3 | Treatment

The recommendations on antimicrobial agents are not considered in this paper, because they depend considerably on the availability of drugs, local traditions and regional differences in bacterial susceptibility. The treatment recommendations are summarised in Table 3. When it comes to the length of treatment for a febrile UTI, the guidelines are in general agreement and a 10-day course (range 7-14 days) is the most common recommendation. All the guidelines acknowledge that oral administration is as effective as intravenous administration, except for when the child is severely ill or unable to retain oral fluid.

Recommendations on antimicrobial prophylaxis remain controversial, but there is agreement on their restrictive use. However, compared to the other guidelines, the Swedish guidelines are more

TABLE 4 Follow-up imaging.

Imaging	UK (UK)	American (America)	Italian (Italy)	Canadian (Canada)	European Europe, urology	Spanish (Spain)	Sweden
RBUS	<6 months: all children >6 months if atypical or recurrence	All children	All children	<2 years all children	All children	<6 months: all children >6 months if atypical or recurrence	<2 years: all children >2 years: febrile UTI or recurrent cystitis (boys one, girls three)
VCUG	<6 months if atypical or recurrence 6–36 months: Consider if [atypical or recurrence] +risk factor*	If abnormal RBUS or complicated UTI. Consider if recurrence	If abnormal RBUS, recurrence or non-E Coli infection	If abnormal RBUS <2 years if recurrence	<1 year: all children >1 year: non-toilet-trained children (boys only if recurrence) Alternative: DMSA (top-down model)		<2 years if dilatation on RBUS or DMSA pathology >2 years if [recurrent febrile UTI or abnormal RBUS] +DMSA pathology
DMSA	<3 years if atypical or recurrence >3 years if recurrence	Not recommended	If VUR grade 4–5	Only if UTI diagnosis is in doubt (acute scan)	Alternative to VCUG (top-down) within 1–2 months from infection	If atypical or recurrence If UTI diagnosis is in doubt	<2 years if abnormal RBUS, risk factor** or recurrence >2 years if abnormal RBUS or recurrence

RBUS, renal and bladder ultrasonography; VCUG, voiding urethra-cystography; DMSA, dimercaptosuccinic acid scintigraphy; UTI, urinary tract infection; VUR, vesicoureteral reflux.

*UK risk factors, specified in the guidelines as: dilatation on ultrasound, poor urine flow, the presence of bacteria other than *Escheria coli* and a family history of VUR.

**Swedish risk factors, specified in the guidelines as: dilatation on ultrasound, a serum CRP of ≥ 70 mg/L, the presence of other bacteria than *Escheria coli* and increased serum creatinine.

liberal about the use of prophylactic antibiotics. They recommend prophylaxis for children with dilating VUR, in girls for a period of one year and in boys up to one year of age.

11.4 | Investigations and follow-up

Table 4 summarises the recommended investigations and follow-ups. In previous clinical practice, VCUG was a standard investigation following a febrile UTI. However, the most recent guidelines aim to reduce the discomfort of procedures and burden of radiation. They all omit VCUG in the primary workup for children without risk factors or signs of underlying uropathies.

All the guidelines agree on a RBUS following the first febrile UTI. However, the Spanish and UK guidelines only recommend this in children over the age of six months if they have an atypical or recurrent UTI.

VCUG is recommended by all the guidelines when dilatation or renal abnormalities are seen on the RBUS and after recurrences of febrile UTIs. However, for children aged between six and 36 months, the UK guidelines only recommend considering VCUG after a recurrent UTI when another risk factor is present. The UK guidelines state that the risk factors are as follows: dilatation on ultrasound, poor urine flow, the presence of bacteria other than *Escheria coli* and a family history of VUR.

Recommendations on imaging differ between the guidelines, in particular when it comes to investigations for detecting renal parenchymal infection, scarring or damage. The American guidelines do not recommend a DMSA scan and the Canadian only recommend a DMSA scan if the diagnosis of acute or repeated UTIs is in doubt. The UK and Spanish guidelines recommend DMSA if the child has atypical or recurrent UTIs. The Italian guidelines recommend a DMSA scan when VUR grade 4–5 is detected. The European guidelines provide two options. The first is a top-down approach, namely a DMSA scan followed by a VCUG if it is positive. The second is a bottom-up approach of a VCUG in the first instance, followed by a DMSA scan if there is dilating VUR.

The Swedish guidelines comprise a top-down model with an early DMSA, for children with one or more risk factors, recurrent UTIs or abnormal RBUS. A second scan is recommended after 12 months if significant uptake defects are detected. The guidelines also provide recommendations for the long-term follow-up of children with permanent kidney scarring or damage.

12 | DISCUSSION

The different national and local guidelines we reviewed are based on the same scientific information. They are similar in their approach, but differ when it comes to the details, as they often reflect different healthcare systems and traditions between nations and specialties. There is a need for experts from different nations and specialties to work together to create future guidelines. The ongoing collaboration

within the European Society for Paediatric Nephrology on common European guidelines for UTI in children is a good example of such an initiative.

One area of disparities is the number of colony-forming units (cfu) that is significant in a urine culture and what impact the sampling technique has. This uncertainty reflects the lack of evidence in the literature. There is a risk of underdiagnosing UTIs with a fixed high threshold and the opposite is true when there are low limits. The literature sometimes refer to 100,000 cfu/mL in MSU as a lower limit for symptomatic UTI, which stems from the 1960 Kass study of women with UTIs,³⁹ and 10,000 cfu/mL for a catheter sample. Most of the guidelines consider any growth significant in an SPA sample. However, the number of bacteria in a urine sample also depends on the bladder incubation time and the type of bacteria. Studies that have carried out simultaneous sampling of MSUs and SPAs have indicated that there is a risk of underdiagnosing true bacteriuria by up to 20% if commonly used fixed limits are applied.^{40,41}

The more liberal use of antibiotic prophylaxis in the Swedish guidelines is a reflection of the results from the Swedish reflux trial, where we found that prophylaxis had a convincing protective effect on girls aged 1–4 years with dilating VUR.³¹ This was also seen in the Prevention of Recurrent Urinary Tract Infection in Children with Vesicoureteric Reflux and Normal Renal Tracts study³⁰ and the Randomized Intervention for Children with Vesicoureteral Reflux trial.²⁹ There was lack of evidence in the younger age group, and we decided to keep a conservative approach and also recommend prophylaxis for children below one year of age.

The main option in the Swedish guidelines is an acute DMSA after a UTI with specified risk factors. The aim of this is to identify children with kidney involvement who warrant further follow-up during childhood. By limiting the use of VCUG to those with kidney involvement, observed on DMSA or dilatation on RBUS, we could halve the number of VCUGs. One concern about this strategy is the increased radiation burden for children exposed to repeated scans, which should be weighed up against the risk of lost opportunities to prevent or reduce the long-term consequences of kidney damage.

13 | CONCLUSION

The current UTI guidelines that we studied focus on children who face a risk of renal damage. There is also increasing awareness of the large number of children with UTIs, without any future risk of kidney malfunction, who should be protected from unnecessary, painful and potentially harmful investigations. Guidelines have to be balanced, with a limited approach to imaging that does not jeopardise the health of children who face the risk of progressing renal damage. The Swedish guidelines use CRP, RBUS and DMSA to identify these children. As there are new indicators for risk assessment on the horizon, we can expect guidelines to be revised, hopefully as a result of international collaboration. These should ideally result in less demanding, and more individualised, management of children with UTIs.

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CONFLICTS OF INTEREST

The authors have no conflict of interest to disclose.

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