



The Febrile Infant with Urinary Tract Infection: An Evidence-Based Review from Emergency Diagnosis to the Prevention of Renal Scarring

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Abstract

Background: Urinary tract infections (UTIs) are a frequent cause of serious bacterial illness in febrile infants <24 months of age. They pose a formidable diagnostic challenge in the emergency department (ED) because of their non-verbal status and lack of specificity, and management dilemmas span acute treatment to prevention of long-term renal complications.

Aim: This systematic review integrates the evidence (2015-2024) to provide a clear framework for the management of febrile infant UTIs from ED diagnosis through preventing CKD, focusing on diagnosis, treatment, imaging controversies, and follow-up.

Methods: A systematic review of more recent literature was conducted, evaluating evidence regarding diagnostic accuracy of urinalysis and culture methods, effectiveness and resistance patterns of empiric antibiotic treatment, and outcomes with various imaging strategies and prophylactic measures.

Results: Evidence supports catheterization to diagnose for accurate urine culture. Empiric antibiotic choice must be based on local resistance patterns, often favoring cephalosporins. Imaging is risk-stratified; renal bladder ultrasound is non-specific, but voiding cystourethrogram is reserved for abnormal ultrasounds or recurrent infection. Prophylactic antibiotic administration is now restricted to high-risk cases, as it has little value in preventing renal scarring in most children.

Conclusion: An efficient, evidence-based pathway—from appropriate ED diagnosis and targeted treatment to selective imaging and nephrology follow-up of high-risk infants—is required for acute care and long-term renal function preservation, preventing unnecessary interventions while avoiding sequelae like hypertension and CKD.

Keywords: Febrile Infant, Urinary Tract Infection, UTI, Renal Scarring, Vesicoureteral Reflux, VUR, Emergency Department, Diagnosis, Antibiotic Prophylaxis, Pediatric Nephrology..

1. Introduction

Fever is an important reason for infants and young children to present to the emergency department (ED), and of the numerous potential causes, urinary tract infection (UTI) is a significant diagnostic consideration. Being the most common serious bacterial infection of this age group, UTI occurs in approximately 5-7% of febrile children under 24 months of age, more so in uncircumcised boys under 3 months and girls as a whole (Shaikh et al., 2008). Clinical presentation in non-verbal infants is famously non-specific, sometimes merely fever, irritability, vomiting, or feeding difficulties, thereby blurring with the presentation of viral infection and other bacterial infections. This diagnostic doubt

imposes a heavy responsibility on the ED physician to employ a formal, evidence-based approach so as not to underdiagnose, potentially causing urosepsis, or over-test, leading to undue worry and use of resources (Shaikh et al., 2022).

Management of a febrile infant with UTI is much more than the preliminary diagnosis and resolution of the immediate infection. Historically, the central interest has been in the relationship between UTIs, particularly those complicated by VUR, and the development of end-stage renal disease as reflux nephropathy. Renal scarring is a matter of public health concern due to its designation as a leading cause of childhood hypertension and CKD, and progression in severe cases to end-stage renal disease (Mattoo et

al., 2016; Murugapoopathy et al., 2020). Thus, the traditional paradigm of management has been aggressive, i.e., routine post-UTI imaging using renal bladder ultrasound (RBUS) and voiding cystourethrogram (VCUG), and then long-term antibiotic prophylaxis for diagnosed VUR.

The last decade (2015-2024), though, has witnessed a paradigm shift brought about by large randomized controlled trials and evolving guidelines. The efficacy of antibiotic prophylaxis in the prevention of recurrent UTI and renal scarring has come into question, and accordingly, a risk-stratified approach has been established. This has created controversy about the necessity and the timing of invasive imaging like VCUG. The ED doctor is therefore the gatekeeper who initiates a chain of treatment with significant implications for the child's renal function. This review will summarize the current evidence and offer a step-by-step guide from the initial steps of ED diagnosis to the controversy surrounding imaging and prophylaxis, through to long-term follow-up strategies for renal scarring prevention and its prevention.

Emergency Department Diagnosis: A Systematic and Evidence-Based Approach

Diagnostic consideration of urinary tract infection (UTI) in a non-verbal, febrile infant is an important clinical challenge in the emergency department (ED), which calls for a systematic approach married to a balancing act between clinical expertise and evidence-based assessment. While the American Academy of Pediatrics (AAP) guidelines are primarily concerned with children aged between 2-24 months, their model is frequently used as a template to guide care on younger infants in practice (Aronson et al., 2023). The system relies on a series of steps: first, the clinician must determine which babies are at risk enough to be tested; second, an obtainable urine sample must be gained; and third, the diagnostic tests must be properly interpreted to verify or eliminate infection.

Clinical Suspicion and Risk Stratification

Without the presence of suspicious symptoms such as dysuria or frequency, testing of a febrile infant for UTI is greatly dependent on determining pre-test probability by known risk factors. A number of important elements frame this clinical suspicion. Gender and status of circumcision are most important because women overall are at increased risk after the first month of life, and uncircumcised boys under one year of age have a greatly elevated risk, 5 to 10 times greater risk than circumcised boys (Morris et al., 2017). Age is also an issue, with the highest incidence of UTI in the first year. The character of the fever itself is also informative; a temperature of $\geq 39^{\circ}\text{C}$ or recurrent fever without a cause increases the likelihood of a UTI. A previous history of UTI is also one of the strongest predictors of recurrence (Hassan & Noori, 2021). While the lack of an alternative ready

source for the fever, e.g., otitis media or viral upper respiratory infection, does raise the suspicion, it should be kept in mind that UTI can occur concomitantly with other illnesses. Because of the non-specific nature of presentation, diagnosis is predominantly based on laboratory investigation, and use of clinical algorithms incorporating these risk factors has been shown to significantly improve testing efficiency and effectiveness (Gorelick & Shaw, 2000; Boon et al., 2021). Figure 1 summarizes the clinical decision-making process for diagnosing UTI in febrile infants.

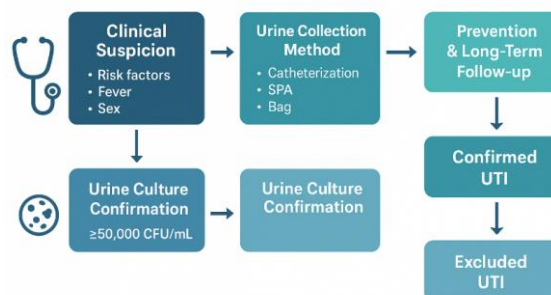


Figure 1: Evidence-Based Diagnostic Pathway for Febrile Infant UTI in the Emergency Department Walking the Fine Line between Accuracy and Invasiveness in Collecting Urine

How urine collection is performed is very important, as contamination may lead to false-positive results, inappropriate antibiotic exposure, and further invasive testing. The choice of technique is a balance between diagnostic yield and the invasiveness of the procedure. The hierarchy of preference is clearly established. SPA is the gold standard with nearly 100% specificity, but its invasiveness places it in reserve for very ill-appearing, young infants or in cases when other techniques fail. Transurethral catheterization is the most effective and commonly utilized method in the ED for non-toilet-trained patients, with a high specificity of approximately 95% when properly performed, and is usually less traumatic than SPA (Yang et al., 2023). The clean-catch bag specimen, though non-invasive, though, has an excessively high rate of contamination of up to 60%. A positive bag sample culture, therefore, cannot be utilized for the diagnosis of a UTI. Its utility is largely confined to ruling out infection with a negative result; all positive urinalysis from a bag must be confirmed by a specimen obtained with SPA or catheterization in an effort to ensure diagnostic reliability (Stein et al., 2015; A't Hoen et al., 2021).

Diagnostic Tests: Urinalysis and Culture

Diagnosis is founded upon the synergistic combination of the rapid urinalysis and definitive urine culture. The urinalysis is the ED's first-line test, and its main constituents provide valuable though not always reliable indicators (Table 1). Leukocyte esterase is an enzyme present in white blood cells, indicating pyuria, and is highly sensitive, though it

will be false in very recent infection. Nitrite is produced by most gram-negative bacteria, like *E. coli*, and is very specific but low in sensitivity, particularly in children who often empty their bladder. Microscopic examination adds its weight; the identification of any bacteria on a Gram-stained, non-centrifuged sample is highly predictive of a positive culture, and the presence of more than five white blood cells per high-power field in a centrifuged sample supports the diagnosis. Because no single component is infallible, the most accurate interpretive approach is to consider the urinalysis positive if any of the following are present: a positive nitrite, a positive leukocyte esterase, or pyuria on microscopy (Roberts & Pantell, 2021). A completely normal urinalysis, on the other hand, has a high negative predictive value

and can be used to discontinue empiric antibiotics if they were initiated pending results.

Diagnosis gold standard is the urine culture, providing definitive evidence. The positive culture is defined as growth of $\geq 50,000$ colony-forming units (CFU) per milliliter of a single uropathogen from a catheterized urine specimen, or any growth from a suprapubic aspirate. The role of culture goes beyond the simple confirmation; it is mandatory for causative organism identification—*Escherichia coli* being held accountable for 75-90% of community-acquired UTIs among children—and performing antibiotic susceptibility testing, which is indispensable in informing targeted definitive therapy and meeting the difficulty of antimicrobial resistance (Hewitt et al., 2023; Ohnishi et al., 2021).

Table 1: Diagnostic Approach to Febrile Infant with Suspected UTI in the Emergency Department

Component	Key Considerations	Evidence-Based Threshold/Interpretation	Clinical Utility in ED
Clinical Suspicion	Non-specific signs (fever, irritability, vomiting).	High risk: Female, uncircumcised male, fever $\geq 39^{\circ}\text{C}$, no source.	Determines pre-test probability and need for testing.
Collection Method	Catheterization is preferred for the balance of accuracy/invasiveness.	SPA (Gold Standard), Catheter (High Specificity), Bag (Rule-out only).	Critical to avoid false-positive diagnoses.
Urinalysis (UA)	Rapid screening test.	Positive if: Nitrite+ OR (Leukocyte Esterase+ OR >5 WBC/HPF).	High NPV is completely normal. Guides empiric therapy.
Urine Culture	Definitive diagnostic test.	$\geq 50,000$ CFU/mL from catheter specimen; any growth from SPA.	Confirms diagnosis, identifies organism, and guides targeted therapy.
Blood Tests	Not routinely required for diagnosis.	CBC: May show leukocytosis. CRP/Procalcitonin: Can indicate upper UTI/systemic involvement.	Useful in ill-appearing infants or for assessing severity.

Acute Infection Management: Empiric and Definitive Antibiotic Therapy

Prompt initiation of effective antibiotic therapy is a critical measure to eradicate the pathogen, to alleviate acute symptoms, to prevent ascending infection, renal parenchymal invasion, and bacteremia. The treatment plan is segmented into an empiric initial stage, on the basis of presumptive pathogens and local resistance patterns, and then a definitive stage on the basis of culture and sensitivity reports.

Empiric Choice of Antibiotics and the Problem of Resistance

Empiric choice of antibiotics relies on the clinical status of the infant and on local epidemiological data. In healthy-appearing, non-toxic infants who are tolerating oral feeds, therapy most often can be initiated with oral agents. Cephalosporins such as cefixime or cefdinir are first-line options, while amoxicillin-clavulanate is an alternative option,

but with high rates of increased resistance. Conversely, in those ill-appearing infants, with recurrent vomiting, or with any of the signs suggesting urosepsis, parenteral therapy from the beginning is required (Roberts, 2011). Third-generation cephalosporins like ceftriaxone or cefotaxime, or an aminoglycoside like gentamicin, are common intravenous choices. A consideration of highest priority in empiric selection is the global issue of antimicrobial resistance. The growing prevalence of extended-spectrum beta-lactamase (ESBL)-producing *E. coli* and other resistant bacteria requires the utilization of local antibiogram results. In regions of elevated resistance, empiric therapy using amoxicillin or the first-generation cephalosporins is now avoided, and local trends will decide on a beginning with a broader-spectrum drug like ceftriaxone right from the start, or even carbapenems in complex, severe infections (Korbel et al., 2017; Daniel et al., 2023).

Conversion to Definitive Therapy and Duration of Treatment

Upon receipt of urine culture and sensitivity results, usually within 48 hours, there ought to be a significant transition from empiric to definitive, specific antibiotic therapy. Truncating the spectrum to the most selective, best agent maintains the microbiome and reduces selection pressure for resistance. The complete course of antibiotics for an established febrile UTI in an infant is usually 7 to 10 days. While shorter treatment durations of 5-7 days can be administered to some of the lower-risk patients, the standard practice to this day is a treatment duration of 7-10 days to ensure total eradication (Strohmeier et al., 2014). Early oral route switch, also known as sequential therapy, should be performed in infants started on intravenous therapy once they have been afebrile for 24-48 hours and demonstrate apparent clinical improvement.

The Imaging Conundrum: RBUS, VCUG, and DMSA Scans

Following diagnosis and treatment of a febrile UTI, the focus is on the identification of predisposition to recurrent infection and renal injury, most importantly vesicoureteral reflux (VUR). The imaging approach to this indication has undergone a dramatic and evidence-driven shift away from routine, blanket testing to more selective, risk-stratified evaluation.

Renal Bladder Ultrasound (RBUS): The Universal First Step

The renal bladder ultrasound (RBUS) is a radiation-free, safe imaging study that forms the basis of the post-UTI study. It provides invaluable anatomic details that assess for renal size, parenchymal echogenicity, dilated collecting system, and congenital abnormalities such as hydronephrosis or duplex systems and complications like abscesses. Although globally accepted, the limitation of RBUS is established; a typical study does not rule out VUR, as 50% of children with VUR have a normal urinary tract on sonography (Mori et al., 2007). Its highest value is in identifying structural abnormalities that may qualify for further evaluation, irrespective of VUR status. Current recommendations suggest the implementation of an RBUS, though time—whether acute illness stage or after treatment—appears to have little impact on outcomes if the child is well on antibiotics (Birnie et al., 2017).

The Voiding Cystourethrogram (VCUG) Controversy: A Paradigm Shift

The voiding cystourethrogram (VCUG) is the diagnostic and grading gold standard of VUR. But its invasiveness, attendant radiation exposure, and patient and family distress have fueled an ongoing controversy regarding its appropriate use. The traditional approach was to give a VCUG after every first febrile UTI. This has been supplanted in large part by a modern, risk-stratified approach, founded upon

the landmark studies like the RIVUR trial. These investigations demonstrated that the majority of low-grade VUR (Grades I-III) resolved spontaneously and that the efficacy of antibiotic prophylaxis to prevent recurrent UTI or new renal scarring is, at best, moderate (Hoberman et al., 2014; Autore et al., 2023). Thus, current guidance by prominent organizations like the AAP and the National Institute for Health and Care Excellence (NICE) is for selective use, saving VCUG for those children whose RBUS demonstrates hydronephrosis, scarring, or other significant abnormality, or for those with unusual or repeated febrile UTIs (Peal et al., 2018; guideline NG217, 2022). This more focused approach does a great job of catching at highest risk children with clinically significant, high-grade VUR (Grades IV-V) without risking unnecessary intervention on most.

Dimercaptosuccinic Acid (DMSA) Scan: A Niche Role

The dimercaptosuccinic acid (DMSA) renal scan is the most sensitive for the diagnosis of acute pyelonephritis and, by proxy, for established renal scarring. An acute scan within the initial two weeks of the infection might determine renal parenchymal involvement, while follow-up at 6-12 months can mark permanent scarring. DMSA scanning for a routine purpose in a first febrile UTI is controversial and not recommended. It is ideally suited for challenging clinical cases, such as in the evaluation of infants with recurrent UTIs, those with fixed high-grade VUR, or as a baseline study in severe acute illness to predict and quantify the long-term risk of scarring (Chishti et al., 2010; Muir et al., 2021).

Prevention of Renal Scarring: Prophylaxis and Follow-up Roles

The ultimate objective of long-term management of febrile UTIs in infants is the preservation of renal function through prevention of renal scarring. This is achieved through a keen re-evaluation of antibiotic prophylaxis and emphasis on structured, multi-disciplinary follow-up.

Controversy of Antibiotic Prophylaxis

Antibiotic prophylaxis, the long-term use of low-dose antibiotics to forestall recurrent infection, has been a cornerstone of pediatric UTI treatment for decades. But its benefit was being drastically reassessed in the light of robust evidence. The seminal RIVUR trial, though demonstrating a modest reduction of recurrent UTI, observed no such distinction of new renal scarring between the prophylaxis-treated group and placebo-treated group (Greenfield et al., 2016; Meena & Hari, 2019). These findings were confirmed in later meta-analyses, and there has been a modest absolute risk reduction in recurrence with a high number needed to treat, along with risks of antibiotic side effects, disruption of the microbiome, and promotion of bacterial resistance (Williams & Craig, 2019). Prophylaxis use is therefore highly selective. The present indications now only

apply to choosing high-risk circumstances, including high-grade VUR (Grade IV-V), multiple febrile UTIs, the detection of significant renal anomalies on ultrasound, or cases of breakthrough febrile UTIs despite already being on prophylaxis. Ongoing antibiotic prophylaxis is unnecessary in the vast majority of infants with a first febrile UTI and minimal risk factors.

The Significance of Pediatric Nephrology Follow-up

Providing a planned follow-up regimen is a simple but often overlooked component of care that bridges the gap between acute treatment and continued renal health. The emergency department clinician plays a crucial role in initiating this process by referring patients appropriately. Referral to a pediatric urologist or nephrologist is recommended for infants with recurrent UTIs, high-grade VUR, abnormal renal ultrasound findings (e.g., suspected dysplasia, hydronephrosis), evidence of renal scarring on DMSA

scan, or elevated serum creatinine (Kosmeri et al., 2019; Nadkarni et al., 2020). The basis for long-term follow-up is the awareness of the fact that renal scarring is a significant risk factor for chronic kidney disease and hypertension. Therefore, all individuals with a history of febrile UTI, particularly those with signs of scarring or high-grade VUR, should be followed annually for blood pressure. Periodic assessment of renal function (serum creatinine) and screening for proteinuria, a key marker of progressive renal damage, is also suggested (Wong et al., 2006; Thapa et al., 2023). And last but not least, education and empowering parents represent a significant preventative measure. This entails teaching them to recognize the signs of potential UTIs, with the importance of completing courses of antibiotics, and, in older babies, the promotion of regular voiding and bowel habits to reverse functional bladder pathologies that lead to recurrent infection (Table 2 & Figure 2).

Table 2: Post-Diagnosis Management: Imaging, Prophylaxis, and Follow-up to Prevent Scarring

Intervention	Traditional Paradigm	Current Paradigm (2015-2024)	Key Rationale for Change
Renal Bladder Ultrasound (RBUS)	Routinely recommended.	Routinely recommended.	Identifies anatomical abnormalities; a normal US does not rule out VUR.
Voiding Cystourethrogram (VCUG)	Routine after the first febrile UTI.	Selective: Only if RBUS shows hydronephrosis, scarring, or other abnormality; or with atypical/ recurrent UTIs.	Most VUR is low-grade and self-resolving; prophylaxis offers limited benefit. Avoids over-testing.
DMSA Scan	Sometimes used routinely.	Not routine. Reserved for complex cases (recurrent UTIs, high-grade VUR, severe illness).	High sensitivity for pyelonephritis/scarring but does not change management for most first-time UTIs.
Antibiotic Prophylaxis	Common for any VUR.	Highly Selective: For high-grade VUR (IV-V), recurrent febrile UTIs, or significant renal anomalies.	RIVUR trial & meta-analyses show modest benefit for preventing recurrence but no significant reduction in new scarring.
Long-Term Follow-up	Variable.	Structured: BP monitoring annually for those with scarring/VUR. Renal function checks. Pediatric nephrology referral for high-risk cases.	Renal scarring is a risk factor for hypertension and chronic kidney disease; proactive monitoring is key.

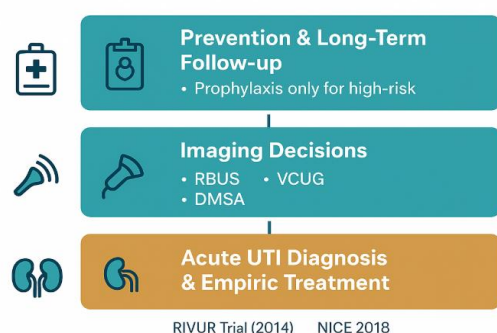


Figure 2: Risk-Stratified Management and Renal Scarring Prevention Framework

Conclusion and Future Directions

The management of the febrile infant with UTI has evolved from the indiscriminate, aggressive imaging and prophylaxis strategy to a subtle, evidence-based, risk-stratified approach. The ED plays a pivotal role in this cascade, with the onus of proper and timely diagnosis through appropriate urine collection and urinalysis interpretation and the institution of appropriate empiric antimicrobial therapy. The decision to perform invasive imaging with VCUG is no longer necessary on a routine basis but is reserved for those infants with identifiable risk factors on ultrasound or clinical course. Routine use of

continuous antibiotic prophylaxis has appropriately been reduced, now only necessary in a minority of high-risk patients and thereby avoiding unnecessary antibiotic exposure and risk of resistance.

The basis for the prevention of long-term sequelae, including renal scarring, hypertension, and CKD, is no longer solely based on the identification of VUR and the suppression of bacteria by prophylaxis. Instead, it lies in a multidimensional strategy: aggressive therapy of acute infection, selective identification of high-grade anatomical defects, and close long-term follow-up with monitoring of blood pressure and renal function assessment. Parent education remains a powerful tool. Subsequent research should focus on enhanced biomarkers for the risk of scarring in an individual, enhancement of risk stratification techniques for imaging selection, and antibiotic-free prevention measures against UTI. In the meantime, the composite strategy of pediatric nephrologists, emergency physicians, and primary care practitioners, guided by the aggregate evidence considered here, remains the best path toward safeguarding renal function in this at-risk group.

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