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Pediatric Urology (BA VanderBrink and RP Pramod, Section Editors)

Contemporary Management of Urinary Tract Infections in Children

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Abstract

Purpose of Review Urinary tract infection (UTI) in children is a major source of office visits and healthcare expenditure. Research into the diagnosis, treatment, and prophylaxis of UTI has evolved over the past 10 years. The development of new imaging techniques and UTI screening tools has improved our diagnostic accuracy tremendously. Identifying who to treat is imperative as the increase in multi-drug-resistant organisms has emphasized the need for antibiotic stewardship. This review covers the contemporary management of children with UTI and the data-driven paradigm shifts that have been implemented into clinical practice.

Recent Findings With recent data illustrating the self-limiting nature and low prevalence of clinically significant vesicoureteral reflux (VUR), investigational imaging in children has become increasingly less frequent. Contrast-enhanced voiding urosonogram (CEVUS) has emerged as a useful diagnostic tool, as it can provide accurate detection of VUR without the need of radiation. The urinary and intestinal microbiomes are being investigated as potential therapeutic drug targets, as children with recurrent UTIs have significant

alterations in bacterial proliferation. Use of adjunctive corticosteroids in children with pyelonephritis may decrease the risk of renal scarring and progressive renal insufficiency. The development of a vaccine against an antigen present on *Escherichia coli* may change the way we treat children with recurrent UTIs.

Summary The American Academy of Pediatrics defines a UTI as the presence of at least 50,000 CFU/mL of a single uropathogen obtained by bladder catheterization with a dipstick urinalysis positive for leukocyte esterase (LE) or WBC present on urine microscopy. UTIs are more common in females, with uncircumcised males having the highest risk in the first year of life. *E. coli* is the most frequently cultured organism in UTI diagnoses and multi-drug-resistant strains are becoming more common. Diagnosis should be confirmed with an uncontaminated urine specimen, obtained from mid-stream collection, bladder catheterization, or suprapubic aspiration. Patients meeting criteria for imaging should undergo a renal and bladder ultrasound, with further investigational imaging based on results of ultrasound or clinical history. Continuous antibiotic prophylaxis is controversial; however, evidence shows patients with high-grade VUR and bladder and bowel dysfunction retain the most benefit. Open surgical repair of reflux is the gold standard for patients who fail medical management with endoscopic approaches available for select populations.

Introduction

Urinary tract infection (UTI) is one of the most common diagnoses affecting children and infants, accounting for 0.7% of physician office visits and 5–14% of emergency room visits per year [65]. Over the last 10 years, there has been a shift in the management of UTI, particularly regarding diagnosis and antibiotic prophylaxis for recurrent infections. In this review article, we cover the diagnosis, workup, and treatment of children with suspected UTI. We also explore the role of antibiotic prophylaxis, investigational imaging, and approaches to unique populations. Our goal is to help familiarize clinicians with the current management of pediatric UTI as new data becomes implemented in clinical practice.

Risk factors for UTI

UTI in children is strongly associated with white race, age, bowel and bladder dysfunction (BBD), circumcision status, and congenital anomalies of the kidney and urogenital tract (CAKUT) [1, 2]. Other risks include systemic disease (diabetes, HIV, immunocompromise, sickle cell disease), spinal dysraphism, sexual activity, kidney stones, and urinary tract instrumentation [4].

Uncircumcised neonates have a particularly high incidence of UTI (2.15%) when compared to circumcised males (0.22%) and females of the same age (2.05%) [1, 2]. Furthermore, uncircumcised males have been found to have a higher resistance to narrow-spectrum antibiotics when compared to females in the same age group (2–71 months) [26]. Data has shown a higher prevalence of UTIs in white children when compared to African American cohorts; however, Latinx populations have also been found to have increased risk [1, 2]. It is possible that this is due to the higher uncircumcised population in the Latinx community [2].

A recurrent UTI is defined as an individual who is diagnosed with 2 or more UTIs in a 6-month period, or 3 within a 1-year period. The two risk factors shown to have the highest 2-year recurrence rate for UTI are vesicoureteral reflux (VUR) and bladder and bowel dysfunction (BBD), with the combination of both producing an even higher risk (56%) [1].

Risk factors for renal scarring after febrile UTI include children with high-grade reflux, delayed initiation of antibiotics past 72 h, recurrent UTIs, infectious organisms other than *E. coli*, and older age [5–8, 17]. Laboratory findings linked to renal scarring are fever (>39 °C), polymorphonuclear count>60%, CRP>40 mg/L, and an abnormal finding on renal and bladder ultrasound (RBUS) [9].

Diagnosis

Pre-verbal children present a diagnostic challenge, as they cannot communicate lower urinary tract signs. The most clinically proven symptom in this age group is fever, but other common symptoms that should raise suspicion include irritability, vomiting, diarrhea, prolonged jaundice, poor feeding, and failure to thrive [14]. Recent advent of UTI risk calculators for febrile infants has improved detection in this cohort. The University of Pittsburgh used their risk calculator to reduce rates of UTI testing (8.1%), increase accuracy of testing, and reduce treatment delays (10.6%) when compared to the AAP algorithm and dipstick urinalysis [63]. At our institution, we have employed a UTI clinical pathway to streamline and simplify diagnosis and treatment (Fig. 1). The goal of the Connecticut Children's Clinical Pathway program is to standardize best practice, improve patient outcomes, and reduce cost. This is accomplished by decreasing unnecessary variation while promoting safe, effective, and consistent patient care. The pathway for UTI was designed by physicians from the Department of Pediatrics with input from the urology and nephrology divisions. Quality metrics including appropriate use of antibiotics and imaging are tracked. Antibiotic recommendations are routinely reviewed to ensure that they are appropriate based on hospital antibiograms.

Since 5% of children between 2 and 24 months with a fever of unknown origin have a UTI [10], a urinalysis is an important diagnostic tool. In toilet-trained children, the collection method of choice is a mid-stream, clean-catch urine specimen after appropriate genital cleansing. Recent studies have shown a significant rate of urine culture contamination in children who did not perform perineal washings (23.9%) compared to those that did (7.8%) prior to mid-stream urine collection [11, 12].

In diapered children, three options exist: perineal bag collection, bladder catheterization, and suprapubic aspiration. Up to 85% of bag-collected specimens with a positive culture will be false positives [10]. Bag collection should be treated as an initial screening measure only: a negative result confirms the absence of a UTI [18]. Bladder catheterization is 95% sensitive and 99% specific, and is less technically difficult in comparison to suprapubic aspiration [10]. While some studies claim suprapubic aspiration is more painful and

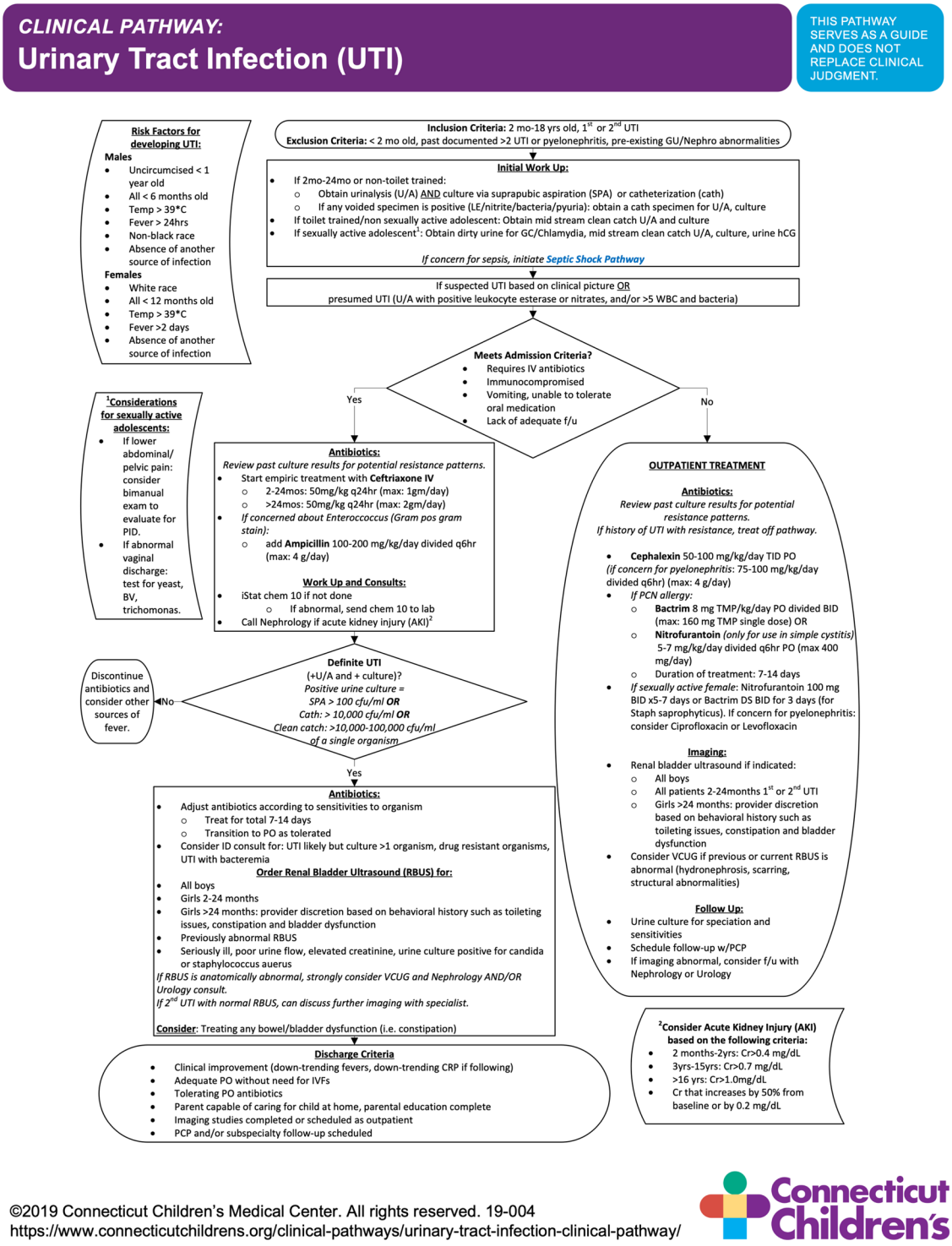

Fig. 1 UTI clinical pathway

has a higher rate of collection failure, it has also been shown to have a lower rate of false positives [13–15]. In our experience, with proper technique and selective use of bedside ultrasound, suprapubic aspiration can be quick and well-tolerated when bladder catheterization is not a good option.

Urinalysis, urine culture, common organisms

The American Academy of Pediatrics defines a UTI as the presence of at least 50,000 CFU/mL of a single uropathogen obtained by bladder catheterization with a dipstick urinalysis positive for leukocyte esterase (LE) or WBC present on urine microscopy [16]. Due to the high sensitivity of LE, it is commonly used to rule out UTI in its absence. Nitrites have a higher specificity, and are thus used to rule in disease [88]. The presence of bacteria, WBC, and RBC on urine microscopy can add confirmation to the diagnosis. Table 1 shows the sensitivity and specificity of these clinical indicators alone and in combination for diagnosis of UTI.

Culture diagnosis is dependent on collection method, with > 100,000 CFU/mL required for mid-stream specimen, > 50,000 CFU/mL for catheterization, and > 1000 CFU/mL for suprapubic aspiration [16]. Emerging data has suggested that in infants with fever and pyuria, lowering the colony count for catheterized specimens to 10,000 CFU/mL will accurately diagnose UTI without sacrificing specificity [89]. The most common organism responsible for UTI in children is *Escherichia coli*, with *Klebsiella pneumoniae*, *Enterococcus faecalis*, and *Proteus mirabilis* also frequently cultured [16, 66, 82]. Table 2 shows a breakdown of common organisms in the community and nosocomial setting.

Cultures are susceptible to contamination from feces and skin flora. Signs of contamination include > 10 squamous epithelial cells/HPF, presence of > 2 bacteria, low bacterial colony count, and growth of non-uropathogens (*Lactobacillus*, *Corynebacterium*, *Viridans streptococci*) [18]. When asymptomatic bacteriuria (AB) is encountered on culture analysis, treatment should be avoided as it can promote symptomatic infections, antibiotic-resistant organisms, and

Table 1 The sensitivity and specificity of these clinical indicators alone and in combination for diagnosis of UTI

Diagnostic variable	Sensitivity	Specificity	AUC
Leukocyte esterase*	48–86%	17–93%	0.814
Nitrite**	45–60%	85–98%	0.635
Pyuria (10 leukocytes/hpf)	92%	71%	0.817
Nitrite + pyuria	82%	99%	
LE OR nitrite with pyuria	94%	84%	0.845

All values include influence from study population demographics

*Accuracy found to be highest in patients in urology clinics

**Accuracy found to be highest in pregnant women and the elderly

AUC, area under the curve—for prediction of positive urine culture for infection

Data generated from references [89, 90]

Table 2 A breakdown of common organisms in the community and nosocomial setting

Bacteria	Culture-positive infection (%)	Nosocomial infection rate (%)	Associations	Antibiotics with highest resistance patterns
Escherichia coli	80–90%	26%	More common in females (83%), than males (50%) ESBL species with growing prevalence	Bactrim (24%), ampicillin (45%)
Enterococcus	17%	13%	More common in males More common with underlying renal abnormality	1st–3rd gen cephalosporin (24%), fluoroquinolones (20%)
Proteus mirabilis	11%		More common in males	Nitrofurantoin (94%)
Klebsiella	10%	6%	More common in males ESBL species with growing prevalence	Ampicillin (81%)
Pseudomonas	7%	10%	More common in males	Bactrim (94%)
Enterobacter	5%	6%	More common in males	Augmentin (91%), Ampicillin (78%), cephalothin (96%), cefazolin (91%)
Candida	5.5%	19%	Primarily found in nosocomial infections	

Data generated from references [85–88]

side effects. While contamination is common, true AB is an extremely rare event, with prevalence in infant boys and girls found to be < 0.5%, and in boys after infancy, < 0.1% [91]. Higher rates exist in children requiring use of foreign body instrumentation in the GU tract, such as those requiring daily CIC [90].

Treatment

Once the clinician has reached a suspected diagnosis of UTI, the child should be treated with antibiotics within the first 48 h to prevent likelihood of renal scarring [6, 7, 25]. There is likely a linear relationship between the prevalence of renal scar formation and delayed time to treatment [7].

Antimicrobial stewardship is more important than ever with the rise of multi-drug-resistant pathogens. This includes extended spectrum beta-lactamase (ESBL) producing organisms, which have been found increasingly in community acquired UTIs [27–29]. One study found ESBL-producing *E. coli* composed nearly half of the bacterial strains in their culture-proven cohort [66]. The AAP recommends Bactrim, Augmentin, or cephalosporins (cefixime, cefpodoxime, cephalexin) as first-line agents for uncomplicated pediatric UTI; our institution's clinical pathway recommends Ceftriaxone IV or Cephalexin PO. Unfortunately, there is data suggesting the most common empiric antibiotics (Bactrim, Augmentin, ampicillin, and first-generation cephalosporins) have the highest growth of antibiotic resistance among UTI-producing bacteria [27–29]. Regardless of the first-line agent typically chosen, clinicians must also review patient-specific culture results and follow local antibiograms and antimicrobial sensitivity patterns available at their institution.

Multiple studies show a 2- to 4-day course of oral antibiotics is just as effective as a 7- to 14-day course in children with cystitis [18, 30, 31]. Those with acute pyelonephritis can also be treated with oral antibiotics for 10–14 days or IV antibiotics for 2–4 days followed by oral therapy [18, 32].

Imaging

The purpose of imaging is to identify genitourinary anomalies that increase the risk of recurrent UTI and injury from repeat infections (renal scarring, renal insufficiency). A renal and bladder ultrasound (RBUS) should be obtained in all infants aged 2–24 months after first febrile UTI [18]. Children who are older than 2–24 months who experience recurrent febrile UTIs should also be evaluated, though RBUS has a poor sensitivity for detecting mild-moderate VUR [18].

Voiding cystourethrogram (VCUG) is indicated if an abnormality is found on RBUS or for recurrent febrile UTI [18]. VCUG is used to identify children with high-grade (IV–V) reflux who are at risk for renal deterioration but should be used selectively given the need for catheterization and the radiation exposure [18]. Multiple studies have found that low-grade VUR does not

increase risk of renal damage and is frequently self-limiting; therefore, the use of VCUG has become increasingly selective. Data has shown less than 40% of children are found to have VUR after their first febrile UTI and among this group, less than 10% have high-grade VUR (IV, V) [16, 61, 62]

Contrast-enhanced voiding urosonogram (CEVUS) has emerged as a radiation-free method of evaluating children for VUR. The method works by using contrast-containing echogenic microbubbles that are easily detected using low-mechanical index ultrasound. The diagnostic accuracy of CEVUS for VUR is excellent, with recent studies quoting a sensitivity of 90.4–92% and a specificity of 92.8–98% [20, 21•]. Concordance with VCUG for detection and grading of VUR is 84.3% and 81.8%, respectfully [21•], with a multitude of data confirming non-inferiority of CEVUS when compared to VCUG [20, 21•, 22–24].

Dimercaptosuccinate (DMSA) scans can be used to identify patients with renal scarring, however are also sensitive for detecting renal anomalies such as small or absent kidneys, ectopic kidneys, and duplex systems. The AUA recommends DMSA scans when initial RBUS is abnormal or when there is a concern for renal scarring (breakthrough UTIs) [19]. A DMSA scan has a higher sensitivity for detecting renal parenchymal injury when compared to RBUS; however, inflammatory changes to the kidney can cause false-positive scans if performed in the first 4–6 months following an infection [16, 19]. Similar to VCUG, the pitfall of DMSA is radiation exposure, with one study proving the average exposure per scan is 2.84 mSv, equal to 28 chest X-rays per year [60]. DMSA can also be difficult for radiologists to obtain.

Antibiotic prophylaxis

Continuous antibiotic prophylaxis (CAP) can be prescribed to prevent renal injury in children who experience recurrent febrile UTIs. Recommendations on prophylaxis can be controversial. Proponents for CAP reference the RIVUR trial, a randomized study that investigated use of CAP in preventing recurrent febrile UTIs in patients with dilated and non-dilated VUR. Bactrim decreased the rate of recurrent UTIs by 50% in all patients with VUR; dilated VUR found the most benefit [33•]. However, the study found no difference in the rate of renal scarring between treatment groups, the outcome of interest to most physicians. This was confirmed by the CUTIE trial, which showed no difference in renal scarring between children with or without VUR who did not receive CAP after febrile UTI [3]. To date, there is no level I data to show CAP has any effect on renal scarring [3, 33•, 44].

A meta-analysis sought to validate the benefit of CAP in children with VUR and found that with the addition of the RIVUR trial data, statistical significance was achieved [34•]. However, a recent publication using advanced analysis has doubted the statistical power of these results [34•, 35]. Adding to the skepticism is the multitude of publications noting CAP has no significant effect on preventing recurrent UTI in kids with VUR [39–42, 45, 46], not to mention that there is a three-fold higher risk of antibiotic-resistant organisms present in infected patients with low-grade VUR on CAP therapy [48].

Nonetheless, children with *high-grade* VUR and BBD have consistently been shown to derive benefit from CAP [33•, 34•, 36–38, 43]. The work comparing time to febrile UTI after discontinuing CAP has identified BBD and high-grade VUR as independent risk factors for early recurrence [37, 38].

Given this evidence, the American Urologic Association and our own practice are to recommend continued antibiotic prophylaxis (CAP) for a child < 1 year of age with VUR and a history of febrile urinary tract infection [19]. Prophylaxis should be considered for all patients with high-grade VUR (III–V). CAP is also recommended for children > 1 year of age if they have BBD and VUR [19]. For children with VUR or renal cortical anomalies without BBD, CAP is optional and should be discussed as part of a shared decision-making process.

Treatment of bladder and bowel dysfunction

Bladder and bowel dysfunction is defined by a constellation of lower urinary tract symptoms (LUTS) in conjunction with bowel dysfunction, most notably constipation or encopresis [82, 96, 97]. LUTS include, but are not limited to, dysuria, frequency, incomplete emptying, incontinence, nocturia, and retention. It is thought that the retention of stool in the rectal vault mechanically compresses the bladder, leading to decreased compliance and frequent urination. In addition, there seems to be a neurologic component, with chronic retention of urine and stool leading to a decreased afferent response from the bladder and pelvic floor. This results in an attenuated sensation to urinate and poor relaxation of the pelvic floor during voiding [82, 96, 97]. Children with BBD have increased rates of reflux, UTI, and renal sequelae [96, 97]. Compounding the issue, those with BBD treated medically or surgically for VUR have increased rates of recurrence and poorer outcomes [64, 82].

About 50% of children with BBD will improve with behavioral intervention alone [98]. Treatment starts with adequate hydration to improve bladder cycling, timed voiding every 2–3 h, appropriate voiding posture, and pelvic floor muscle training (PFMT) with or without biofeedback therapy [82, 96]. In biofeedback, monitors placed on the skin electronically record pelvic floor musculature in real time allowing for improved voluntary control during voiding. Studies have shown a UTI prevention rate of 68–86% in children treated with behavioral therapy and PFMT alone [96, 99–103]. Medications such as alpha agonists and muscarinic antagonists are pursued if symptoms persist in spite of behavioral treatment and adequate management of constipation for 6 months. If these treatments fail, OnabotulinumtoxinA and sacral neuromodulation are among last resort options [96].

The initial treatment for constipation in children includes increased fiber intake, proper hydration, and stool softeners. Polyethylene glycol is the most commonly prescribed stool softener in children [96, 98]. Children are often encouraged to sit on the toilet for 10 min after meals to take advantage of the gastrocolic reflex. If these treatments fail to resolve constipation, retrograde enemas, dis-impaction, and anterograde continence enema (ACE) procedures can be employed [96, 98]. There is some data showing the use of

neuromodulation can simultaneously improve overactive bladder and constipation in children with BBD; however, this should be selectively utilized given the invasive nature of the treatment [104, 105].

Surgical treatment

The index patient who may benefit from surgery is one who has proven VUR and experiences breakthrough UTIs while receiving CAP therapy [19]. Other reasons include non-compliance with antibiotics or new renal cortical lesions found on surveillance screening [16, 19].

The most common approaches for ureteral reimplantation are the Politano-Leadbetter, Lich-Gregoir, modified Lich-Gregoir, and Cohen cross-trigonal reimplant. Historically, open surgery remained the gold standard; in recent years, robotic-assisted laparoscopic approaches have good data supporting their efficacy, with lower rates of post-operative pain, less opioid use, shorter hospital stay, and improved cosmesis [50, 51, 53–55]. Furthermore, there is data proving non-inferiority in VUR downgrading and radiographic resolution when compared to open techniques [50, 52, 54]. In non-experienced centers, robotic-assisted approaches have seen a higher 90-day complication rate and a significantly higher cost to the patient's family [56].

Endoscopic treatment (ET) involves an injection of a subureteral or intraureteral bulking agent. Dextranomer and hyaluronic acid (Deflux) is the most common anti-reflux agent. There is data showing no difference in prevention of UTI recurrence or renal scarring in patients with VUR undergoing ET when compared to CAP alone [47, 49]. However, endoscopic therapy is still used commonly in clinical practice with the index patient being one with low-grade VUR or an older patient in which reimplantation would be more technically difficult.

It is important to note that children with lower urinary tract dysfunction have an increased surgical failure rate for reflux resolution in both open and endoscopic series. Thus, treating the underlying urinary symptoms should preclude any attempt at surgical intervention for VUR [64].

Unique populations

The majority of children born with spina bifida (SB) suffer chronically from increased bladder storage pressures, difficulty emptying, and dependency on catheter drainage, which put them at risk for recurrent UTI and renal deterioration [67]. One paper demonstrated 50% of children with spina bifida will experience a UTI by 15 months and 44% will have > 5 UTIs by 15 years old [68]. Based on the National Spina Bifida Patient Registry, > 70% of spina bifida patients perform CIC. This population presents a diagnostic challenge to discern asymptomatic colonization versus symptomatic infection. There is no uniform consensus on symptomatic UTIs in SB patients; however, in a systematic review, fever, positive culture, and

symptoms were the most reported criteria [70]. Symptoms included flank pain, abdominal pain, change in continence patterns, increased urine odor, and dysuria [70, 71]. The primary goal in identifying SB patients with symptomatic UTIs is to prevent renal damage; however, multiple studies have shown that renal function is largely preserved in patients with asymptomatic bacteriuria in the absence of VUR and hostile bladder parameters on urodynamics [69]. Therefore, complete evaluation including urodynamics and ultrasound is key to identify patients at risk for infectious sequelae. Preventing high detrusor pressures, urinary stasis, and constipation will also attenuate risk for infection. While the research does not provide uniform guidelines, patients with fever, culture-positive urine, and new-onset symptoms should be prioritized for antibiotic treatment.

Bladder exstrophy (BE) is a rare condition with an exposed bladder plate, epispadias, and pelvic diastasis [82]. After initial bladder closure, ureteral insertion is commonly at a 90° angle with a very limited intramural tunnel. Thus, a significant number of patients will have VUR and may be at risk of recurrent febrile UTI if ureteral reimplantation is not performed during the operation [81]. Ureteral reimplantation during bladder exstrophy repair has been shown to decrease rates of infection and renal scarring [72, 73, 81]. If reimplantation is not performed primarily, emphasis should be placed in identifying those with VUR and use of prophylactic antibiotics should be considered. Continence remains a challenging issue in this population, with a high rate of CIC dependence or augmentation cystoplasty, both of which are associated with UTI [107]. In addition, those found to have continence after repair tend to have higher rates of VUR and recurrent febrile UTI [81, 108]. One unique option for UTI in patients with urologic reconstructions who already perform CIC is intravesical antibiotic instillation, either as prophylaxis or treatment. In one study that evaluated intravesical gentamycin, serum levels were indetectable and development of antibiotic resistance low (4.16%) [109]. Since patients with BE report high rates of recurrent UTI and renal scarring in adulthood, this population requires close urologic care in childhood and beyond [107].

Future directions

Emerging research has identified a relationship between vaginal, intestinal, and urinary bacteria and the development of recurrent UTI. Intestinal bacteria have historically been a focus of research as introital and periurethral colonization with these organisms remains a common etiology for adult female UTIs [74]. In a recent publication, children with recurrent UTIs were found to have higher proportions of fecal bacteria from the *Enterobacter* family as compared to the *Peptostreptococcaceae* family found in those without UTI [77]. It is an important distinction, as a 1% relative abundance of *Escherichia* or *Enterococcus* species acts as independent risk factor for UTI [75]. In another study, patients with recurrent UTI and *Clostridium difficile* colitis underwent a fecal transplant, leading to a significant reduction in their UTI

recurrence [76]. While intestinal bacteria can act as a nidus for genitourinary infections, the vaginal flora has a number of mechanisms to protect against bacterial invasion and proliferation. In Stapleton et al.'s randomized phase II trial of adult women, intravaginal instillation of *Lactobacillus crispatus* led to a significant reduction in recurrent UTIs [78]. Studies on vaginal microbiome transplant have shown preliminary evidence for remission of recurrent bacterial vaginosis, further validating this area as a potential therapeutic target [79]. While research on the pediatric urinary microbiome is still growing, there is data suggesting bacterial dysbiosis in children with recurrent UTI. Kinneman et al. found differences in both the alpha diversity (number of different species at a single site) and the beta diversity (differences in species at multiple sites) in children presenting with UTI when compared to those without UTI [80], highlighting an investigational difference in bacterial proliferation between these two cohorts.

Clinicians have long sought to prevent renal parenchymal scarring secondary to urinary infection which can lead to hypertension, proteinuria, and chronic renal failure. In recent years, it has been proposed that adjuvant use of corticosteroids in children with pyelonephritis can limit the development of inflammatory cytokines that lead to renal scarring. The data has been mixed, with the largest known clinical trial failing to reach accrual but claiming a non-statistically significant trend towards favorability of adjunctive use of steroids [58]. Smaller investigations have also boasted a significant decrease in DMSA-proven renal scarring [57, 59]. All three studies were underpowered, but two clinical trials are underway (NCT04654507, NCT02034851) which hope to shed more light on this controversial topic.

With the advent of the HPV vaccine in the mid-2000s and now the multitude of vaccines targeting the novel coronavirus, primary prevention has become an intense topic of research, and UTIs are no exception. Scientists from Sequoia Sciences Inc. have recently published a phase I, dose escalation trial of a vaccine targeted against a preserved antigen present in *E. coli* bacteria [110•]. The vaccine consists of a protein called FimCH adjuvanted with a TLR4 agonist. FimCH is a naturally occurring antigen present on type I pili in *E. coli*. Type I pili are bacterial appendages that help bacteria bind to oligomannose-containing glycoproteins in human bladders [110•]. The researchers theorize that patients inoculated with their vaccine will build a IgG-mediated antibody response to FimCH proteins that will penetrate the mucosal surface of the bladder and prevent recurrent infections from occurring. The results of the study proved the vaccine to be extremely well-tolerated, with adverse events limited to mild localized skin reactions, headaches, nausea, and fatigue. All subjects receiving the four-dose vaccination schedule were seropositive after 30 days. The cohort of women with recurrent UTI demonstrated a 150-fold increase in antibodies against FimH proteins [110•]. While this is the first study of a FimH vaccine in humans, prior research has proven its efficacy with a 99% reduction of in vivo *E. coli* colonization using murine models [111]. A randomized, phase II, placebo-controlled trial has been approved.

Conclusion

Pediatric UTI remains a significant source of morbidity in children, especially uncircumcised males in the first year and females throughout life. UTI risk calculators, algorithms, and optimized collection techniques will decrease the rate of false positives and unnecessary antibiotic treatment. Antibiotic-resistant organisms are increasing rapidly; therefore, antibiotic stewardship and use of local antibiograms are more important than ever. Young children with febrile UTI and older children recurrent UTI should undergo investigational imaging. VCUG is invasive and requires radiation; however, newer imaging techniques such as CEVUS provide excellent detection of upper tract disease without the use of radiation. CAP in the setting of VUR is controversial; children with BBD and high-grade VUR derive the most benefit. Patients with complex urologic conditions such as SB and BE require unique approaches to urinary infections. Research into corticosteroids, urinary microbiomes, and UTI vaccinations could change how we treat UTIs and prevent chronic renal insufficiency in high-risk patients.

Declarations

Conflict of interest
Philip Olson, Anne G. Dudley, and Courtney K. Rowe declare that they have no conflict of interest.

Human and animal rights and informed consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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