Variation in Definitions of Urinary Tract Infections in Spina Bifida Patients: A Systematic Review

abstract

OBJECTIVE: Urinary tract infections (UTIs) are a common source of morbidity among children with spina bifida (SB) and are a frequently reported outcome in studies of this patient population. However, the criteria for a diagnosis of UTI are often not stated. We evaluated the literature on SB patients for the criteria that authors use to define parameters in reporting UTI outcomes.

METHODS: Embase and Medline were queried with the medical subject heading terms “spinal dysraphism,” “myelomeningocele,” “infection,” and “urinary tract infection.” A second search with the exploded term “spina bifida” and “urinary tract infection” was performed. Original research studies reporting a UTI outcome in SB patients were included and evaluated by 2 independent reviewers for the presence of a UTI definition and diagnostic criteria.

RESULTS: We identified 872 publications, of which 124 met inclusion criteria. Forty-five of 124 (36.3%) studies reporting UTI as an outcome provided a definition of UTI. Of 124 studies, 28 (22.6%) were published in pediatric journals and 69 (55.6%) in urology journals. A definition of UTI was provided in 11 (39.3%) and 26 (37.7%) studies, respectively. “Fever, culture, and symptoms” defined a UTI in 17 of 45 studies. Journal category and presence of UTI definitions did not correlate (P = .71).

CONCLUSIONS: Explicit definitions for UTI are heterogeneous and infrequently applied in studies of SB patients, limiting study reliability and estimates of true UTI rates in this population. Future studies will benefit from the development and application of a standard definition for UTI in this population. Pediatrics 2013;132:132–139

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KEY WORDS
spinal dysraphism, urinary tract infection, neurogenic bladder, myelomeningocele

ABBREVIATIONS
CFU—colony-forming unit
CIC—clean intermittent catheterization
HPF—high-power field
SB—spina bifida
UTI—urinary tract infection
VUR—vesicoureteral reflux
WBC—white blood cell

Dr Madden-Fuentes conceptualized and designed the study, collected and analyzed the data, drafted the initial manuscript, and approved the final manuscript for submission. Dr McNamara assisted with study design, data collection, and data analysis; reviewed and revised early manuscript drafts; and approved the final manuscript for submission. Dr Lloyd assisted with designing the systematic review, reviewed and revised early manuscript drafts, and approved the final manuscript for submission. Dr Wiener assisted with study design, reviewed and revised early manuscripts, and approved the final manuscript for submission. Dr Routh assisted with designing the systematic review and data analysis, reviewed and revised early manuscript drafts, and approved the final manuscript for submission. Dr Seed contributed to the conception of this study, reviewed and revised early manuscripts, and approved the final manuscript for submission. Dr Ross conceptualized and designed the study, reviewed and revised early manuscripts, and approved the final manuscript for submission.

www.pediatrics.org/cgi/doi/10.1542/peds.2013-0557

doi:10.1542/peds.2013-0557

Accepted for publication Apr 18, 2013

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(Continued on last page)
In the United States, spina bifida (SB) afflicts 3.1 of 10,000 children aged 0 to 19. The vast majority of these children suffer from a neurogenic bladder. These patients are prone to renal deterioration secondary to recurrent urinary tract infections (UTIs) or deleterious bladder pressures. Although the introduction of clean intermittent catheterization (CIC) and antimuscarinic pharmacotherapy have resulted in improved renal protection and urinary continence in this patient population, UTIs continue to be a major source of morbidity. Fillier et al demonstrated that 50% of children with SB will experience their first UTI by 15 months of age and that 44% will have >5 UTI episodes by age 15 years. Indeed, other studies have demonstrated that the annual incidence of UTI in patients with neurogenic bladder is as high as 20%. Unpublished data from the National Spina Bifida Patient Registry demonstrate that >70% of SB patients perform CIC. In these patients, instrumentation of the urinary tract can promote bacteriuria in the absence of any associated symptoms, thus creating the diagnostic dilemma of urinary tract colonization versus infection. As a result, these children are frequently prescribed serial courses of antibiotics, often without symptomatic benefit. However, this practice is not without risks because it provides a selection force for more drug-resistant pathogens and potential side effects.

Guidelines on diagnosis and management of UTI specific to the SB population are sparse. Clinicians often resort to general pediatric practice guidelines for insight on evaluation and treatment of UTI in this patient population. The American Academy of Pediatrics developed guidelines for diagnosis, evaluation, and treatment of UTIs in children based on available literature. These guidelines work well for children with normally functioning urinary tracts. However, the urologic complexity of the SB population makes universal application of these practices challenging. This challenge is not limited to clinicians who may infrequently care for SB patients but is also present among centers specializing in these patients. Elliott and colleagues demonstrated a lack of consensus among 59 specialty centers in the treatment and management of bacteriuria in patients with SB. In the setting of a positive urine culture and either signs or symptoms of a potential UTI, the study revealed significant variations in the decision to treat with antimicrobial agents.

As physicians, we rely on clinical evidence to support our practices, particularly in complex cases. In the SB population, significant heterogeneity in the diagnosis and treatment of UTI exists. In an effort to understand why such diversity exists, we performed a systematic review of the literature to assess how UTIs are defined in studies of SB patients. We predicted that the majority of peer-reviewed publications reporting UTI as an outcome would fail to define explicit parameters used to measure this outcome. Additionally, we hypothesized that when a definition was provided, a lack of consensus would be evident among publications.

METHODS

Search

Following Preferred Reporting Items for Systematic Reviews and Meta-Analyses and Assessment of Multiple Systematic Reviews guidelines, Embase and Medline were queried by using the medical subject heading terms “spinal dysraphism,” “myelomeningocele,” and “infection” was performed. All results were compiled and duplicates discounted. The records were accessed before October 1, 2012. The initial search was not limited by the language of origin or year of publication.

Inclusion and Exclusion

All abstracts were reviewed for a reported outcome of UTI. All selected publications were then evaluated for inclusion based on the presence of SB patients in the study (acceptable terms included myelomeningocele, lipomyelomeningocele, meningocele, SB, and myelodysplasia). A UTI outcome was defined as a reported rate of UTI in the study population. Editorial comments and systematic reviews were excluded because these do not directly assess UTIs in a study population. Case reports and case series were excluded because these reports do not measure UTI as an outcome but rather report all data available pertaining to 1 or a select few patient(s), without a priori intent to define UTI. Conference abstracts were excluded because of the abbreviated nature of methods, which may not adequately reflect whether an a priori definition was present or absent. Studies without an abstract were elected for full manuscript review. If a manuscript was not accessible, the publication was then excluded.

Data Abstraction

Two independent reviewers (RJM and ERM) evaluated the full manuscripts of the included studies. Disagreements were resolved by consensus. Non-English articles were evaluated with the aid of a fluent speaker of that language. The abstracted data included date of publication, journal of publication, study design, study population, number of SB patients in the study population, number of children (age
<18 years old), gender distribution if available, presence or absence of a UTI definition, and parameters used for such definition including urine culture, urinalysis, symptoms, or other methods. Studies were categorized as being published in pediatric journals if the target audience was deemed by both reviewers to be physicians caring for children. Similarly, studies were categorized as published in urological journals if the target audience of that journal was deemed to be primarily urologists. The primary outcome was the absence or presence of UTI definition in the publications identified. The secondary outcome was to determine the specific criteria used to define a UTI.

**Statistical Analysis**

Statistical analysis was performed by using Stata 11.2 (College Station, TX) and SAS version 9.2 (Cary, NC). A Fisher’s exact test or $\chi^2$ was used to evaluate correlation between categorical variables. The Cochran-Armitage trend test was used to evaluate association between definition of UTI and year of publication. Descriptive statistics were used for all other extracted data.

**RESULTS**

**Systematic Review of the Literature**

Eight hundred seventy-two publications were identified. Of these, 63.3% were original articles, 9.3% reviews, 18.4% case reports, 4.2% editorials, and 4.8% conference abstracts. Three hundred thirty-seven were excluded based on study type ($n = 320$) or absence of a full manuscript ($n = 17$). An additional 386 publications were excluded due to lack of a reported UTI outcome and 25 due to the absence of SB patients in the study (Fig 1). The remaining 124 publications from 58 different journals were included for analysis. These publications represented 6235 patients (43.7% boys, 95.2% children) and spanned a time frame from 1957 to 2012. Five articles were published in German, 4 in Japanese, 2 French, 2 Polish, and 1 in Korean. The distribution of publications by year is summarized in Table 1.

**UTI Definition**

Forty-five of 124 manuscripts (36.3%) reporting UTI as an outcome explicitly described the parameters used to arrive at a UTI diagnosis (Table 1). “Fever, culture, and symptoms” defined a UTI in 17 (37.8%), “culture alone” in 15 (33.3%), “culture and urinalysis” in 4 (8.9%), “culture and symptoms” in 4 (8.9%), “fever and culture” in 4 (8.9%), and “any episode documented as a UTI plus initiation of antibiotics” in 1 (2.2%; Table 2). Fever was defined as $\geq 38.0^\circ C$ in 7 of 45 studies. The colony-forming unit (CFU) count was frequently reported when the definition of UTI included a positive urine culture (29/45, 64.4%). Criteria for urine culture positivity were $>10^4$ CFU/mL in 8 of 45 (17.8%) studies and $>10^5$ CFU/mL in 19 of 45 (42.2%) studies (Table 3). The most common symptoms ascribed to UTI were flank/abdominal pain, change in continence pattern, change in urine odor, and dysuria (15/45). Urinalysis alone did not define a UTI in any of the studies but was part of the definition in 11/45 (24.4%). Leukocyturia $>50$ white blood cell (WBC)/high-power field (HPF) was a defining criteria in 3 of 45 (6.7%), $>10$ WBC/HPF in 3/45 (6.7%), and $>5$ WBC/HPF in 2/45 (4.4%) of studies. Positive leukocyte esterase was included in 2/45 (4.4%) and bacteriuria in 1/45 (2.2%) of the studies.

![Flow diagram](image-url)
The rate of UTI definition in manuscripts published in pediatric journals and urology journals were not statistically different than the rate of definitions published in nonpediatric or nonurology journals (pediatric journals versus nonpediatric journals, \( P = .71 \); urology journals versus nonurology journals, \( P = .72 \); pediatric and urology journals versus all other journal categories, \( P = .27 \)). Among the publications in pediatric and urology journals, the most common definition remained “fever, positive culture, and symptoms” in 5 of 11 (45.5%) and 11 of 26 (42.3%), respectively (Table 2).

**Category of Publication Journal and Study Type**

When analyzing by journal category, 28 of 124 (22.8%) articles were published in journals targeting physicians who treat children, and 69 of 124 (55.6%) articles were published in journals with urologists as the target audience. Of these studies, only 11 (39.3%) articles published in pediatric journals and 26 (37.7%) published in urology journals provided a definition of UTI (Table 1).

The rate of UTI definition in manuscripts published in pediatric journals and urology journals were not statistically different than the rate of definitions published in nonpediatric or nonurology journals (pediatric journals versus nonpediatric journals, \( P = .71 \); urology journals versus nonurology journals, \( P = .72 \); pediatric and urology journals versus all other journal categories, \( P = .27 \)). Among the publications in pediatric and urology journals, the most common definition remained “fever, positive culture, and symptoms” in 5 of 11 (45.5%) and 11 of 26 (42.3%), respectively (Table 2).

**Definition as a Factor of Time**

Over time, the likelihood of explicitly defined parameters to diagnose a UTI among all publications did not improve (Cochran-Armitage Trend test, \( P = .64 \); Table 1). On subset analysis of articles published in pediatric journals, urology journals, and all other journals separately, the likelihood of an explicit UTI definition did not improve over time (pediatric journals, \( P = .54 \); urology journals, \( P = .99 \); all other journals, \( P = .70 \)).

**DISCUSSION**

We performed a systematic review of the SB literature to assess the frequency with which authors provided a definition of UTI when this was reported as an outcome. Our analysis confirmed our hypothesis that the majority of publications reporting UTI as an outcome do not provide an explicit definition of UTI or the parameters used to arrive at the measured outcome. Only 36% of studies outlined the criteria to diagnose a UTI in their study population. Prospective and clinical trials were more likely to provide a definition (\( P \leq .01 \)); however, a definition was still not provided in 40% (12/30) of these studies. The rate of providing UTI definitions in peer-reviewed publications has not improved over the past 5 decades as might be expected to accompany more rigorous publication criteria (\( P = .64 \), Table 1). Interestingly, despite our expectation that publications in urology journals would outline a definition of UTI more frequently than nonurology journals, when we compared these 2 groups, there was no statistical difference (\( P = .72 \)). Our study highlights the lack of consistency and clarity that

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**TABLE 1 Rate of Explicit UTI Definition Stratified by Decade and by Study Category**

<table>
<thead>
<tr>
<th>Category of Publication</th>
<th>All Publications (n = 45)</th>
<th>Pediatric Journals (n = 11)</th>
<th>Urology Journals (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Publications, n</td>
<td>UTI Defined, n (%)</td>
<td>( P )</td>
</tr>
<tr>
<td>2010–present</td>
<td>21</td>
<td>7 (33.3)</td>
<td>.64</td>
</tr>
<tr>
<td>2000–2009</td>
<td>24</td>
<td>9 (37.5)</td>
<td>.72</td>
</tr>
<tr>
<td>1990–1999</td>
<td>18</td>
<td>12 (66.7)</td>
<td>.54</td>
</tr>
<tr>
<td>1980–1989</td>
<td>15</td>
<td>5 (33.3)</td>
<td>.72</td>
</tr>
<tr>
<td>1970–1979</td>
<td>11</td>
<td>10 (90.9)</td>
<td>.71</td>
</tr>
<tr>
<td>1960–1969</td>
<td>10</td>
<td>2 (20.0)</td>
<td>.71</td>
</tr>
<tr>
<td>1950–1959</td>
<td>1</td>
<td>0</td>
<td>.71</td>
</tr>
<tr>
<td>Journal category</td>
<td>Pediatrics</td>
<td>28</td>
<td>11 (39.3)</td>
</tr>
<tr>
<td></td>
<td>Urology</td>
<td>69</td>
<td>34 (50.7)</td>
</tr>
<tr>
<td></td>
<td>Nonurology</td>
<td>55</td>
<td>19 (34.5)</td>
</tr>
</tbody>
</table>

**TABLE 2 Definition Criteria Stratified by Publication Category**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>All Publications (n = 45)</th>
<th>Pediatric Journals (n = 11)</th>
<th>Urology Journals (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever, culture, symptoms</td>
<td>17</td>
<td>37.8</td>
<td>.54</td>
</tr>
<tr>
<td>Fever, culture</td>
<td>4</td>
<td>8.9</td>
<td>.54</td>
</tr>
<tr>
<td>Culture, symptoms</td>
<td>4</td>
<td>8.9</td>
<td>.54</td>
</tr>
<tr>
<td>Culture only</td>
<td>15</td>
<td>33.3</td>
<td>.54</td>
</tr>
<tr>
<td>Culture, urinalysis</td>
<td>4</td>
<td>8.9</td>
<td>.54</td>
</tr>
<tr>
<td>Other*</td>
<td>1</td>
<td>2.2</td>
<td>.54</td>
</tr>
</tbody>
</table>

* Other: “any episode documented as a UTI plus initiation of antibiotics.”
Symptoms physicians 38% of the time if a urine culture was ordered by treating centers highlighted the differences in caring for SB patients at specialty centers. A recent survey of physicians queried, respondents valued patient symptoms; however, the remaining 35 centers required a confirmatory culture before progressing to treatment. When queried, respondents valued patient complaints, fevers, or foul-smelling urine more than positivity of nitrite and/or leukocyte esterase on urinalysis or leukocytes on microscopy. Lastly, a Saudi Arabian survey by Al Taweel et al reported that 40% of urologists would treat bacteriuria in the presence or absence of symptoms. Our systematic review supports the observations within these studies demonstrating that UTI definitions are variable across centers treating SB patients. Frequently, a diverse group of specialists are involved in the care of SB patients, including adult and pediatric urologists, nephrologists, pediatricians, internists, and emergency department physicians, each of whom may interpret urinary tract signs and symptoms differently. Differentiating asymptomatic bacteriuria (colonization) from true infection in these patients is perplexing largely because of the frequent high bacterial counts, presence of multidrug-resistant organisms, and the diverse species isolated, particularly in patients performing CIC. Further complicating accurate diagnosis is the altered and varied abdominal innervation in SB patients.26 A recent report evaluating preoperative urine cultures in asymptomatic patients with neurogenic bladder demonstrated growth of >100,000 CFU/mL in 53.2% of bacterial cultures and multidrug-resistant organism isolates in 46.3% of specimens. This highlights the potential for over-reporting of UTI outcomes in studies that include SB patients. Explicitly stating how the outcome is measured affords the reader a better appraisal of the true UTI rate. In the SB patient population, this an important distinction given that these patients may require long hospitalization and intravenous antimicrobial agents, both of which are taxing to the patient, families, and the health care system. For example, Armour et al demonstrated that admissions for UTI in SB patients occurred at a rate of 22.8 per 1000 patients, whereas admission for UTI occurred at a rate of 0.44 per 1000 patients without SB.27 Furthermore, on analysis of the Nationwide Inpatient Sample, Dicianno et al found that UTI was the most common cause of hospital admission in SB patients. In this cohort, hospital stay was 6.9 days (95% confidence interval 6.6–7.2), and cost was $28,918 (95% confidence interval $27,367–$30,469) per admission.20 Limiting recurrent antibiotic courses may affect the development of resistant organisms; whether this translates into a change in the rate of hospitalization or selection for multidrug-resistant organisms remains to be evaluated.

TABLE 3 Parameters Defined for UTI Diagnosis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Publications (n = 45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td></td>
</tr>
<tr>
<td>38°C</td>
<td>4</td>
</tr>
<tr>
<td>38.5°C</td>
<td>3</td>
</tr>
<tr>
<td>Included but not specified</td>
<td>14</td>
</tr>
<tr>
<td>Not included</td>
<td>24</td>
</tr>
<tr>
<td>Culture (CFU/mL)</td>
<td></td>
</tr>
<tr>
<td>&gt;10⁴</td>
<td>8</td>
</tr>
<tr>
<td>&gt;10⁵</td>
<td>19</td>
</tr>
<tr>
<td>&gt;10⁶ or &gt;10⁵a</td>
<td>2</td>
</tr>
<tr>
<td>Included but not specified</td>
<td>15</td>
</tr>
<tr>
<td>Not Included</td>
<td>1</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
</tr>
<tr>
<td>Specified</td>
<td>15</td>
</tr>
<tr>
<td>Included but not specified</td>
<td>5</td>
</tr>
<tr>
<td>Not Included</td>
<td>25</td>
</tr>
<tr>
<td>Urinalysis</td>
<td></td>
</tr>
<tr>
<td>Leukocyturia &gt;50 WBC/HPF</td>
<td>3</td>
</tr>
<tr>
<td>&gt;10 WBC/HPF</td>
<td>3</td>
</tr>
<tr>
<td>&gt;5 WBC/HPF</td>
<td>2</td>
</tr>
<tr>
<td>Leukocyte esterase</td>
<td>2</td>
</tr>
<tr>
<td>Bacteriuria</td>
<td>1</td>
</tr>
<tr>
<td>Not included</td>
<td>34</td>
</tr>
</tbody>
</table>

*10⁴ CFU/mL if specimen collected by suprapubic aspirate; 10⁵ CFU/mL if collected via catheterization.

TABLE 4 Presence of Definition Stratified by Study Type

<table>
<thead>
<tr>
<th>Study Type</th>
<th>UTI Defined, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective</td>
<td>89 (25)</td>
</tr>
<tr>
<td>Cross-sectional cohort</td>
<td>5   (2)</td>
</tr>
<tr>
<td>Prospective</td>
<td>23 (12)</td>
</tr>
<tr>
<td>Controlled trial</td>
<td>7 (6)</td>
</tr>
<tr>
<td>Total</td>
<td>124 (45)</td>
</tr>
</tbody>
</table>

exists in reporting outcomes in this patient population. The dearth of guidelines to study and report on UTIs among patients with SB introduces great variability in reporting, diagnosis, and management. The pervasiveness of this problem is not limited to research; clinical care of these patients is hindered by unclear definitions and inconsistent reporting as well. A recent survey of physicians caring for SB patients at specialty centers highlighted the differences in interpretation of data to diagnose and manage UTIs. For example, a urine culture was ordered by treating physicians 38% of the time if a urine microscopy showed 0 to 8 WBC/HPF, 63% if 8 to 50 WBC/HPF, 80% if >50 WBC/HPF, 63% if the urinalysis had positive leukocyte esterase, and 62% if the urinalysis had positive nitrites. When questioned if they would begin empirical antimicrobial therapy before urine culture results when the urinalysis showed 0 to 8 WBC/HPF, 8 to 50 WBC/HPF, >50 WBC/HPF, positive leukocyte esterase, or positive nitrites, antibiotics would be started by 11%, 31%, 43%, 27%, and 26% of physicians, respectively. Thus, despite having the same test results, the management of these patients varied significantly. A similar European survey of 41 centers that care for patients with SB reiterated the heterogeneity of approaches to diagnosing and treating UTIs. In that study, 2 centers relied on home test strip results alone to initiate treatment of a UTI, and 4 centers relied on home test strip results plus symptoms; however, the remaining 35 centers required a confirmatory culture before progressing to treatment. When queried, respondents valued patient complaints, fevers, or foul-smelling urine more than positivity of nitrite and/or leukocyte esterase on urinalysis or leukocytes on microscopy. Lastly, a Saudi Arabian survey by Al Taweel et al reported that 40% of urologists would treat bacteriuria in the presence or absence of symptoms. Our systematic review supports the observations within these studies demonstrating that UTI definitions are variable across centers treating SB patients. Frequently, a diverse group of specialists are involved in the care of SB patients, including adult and pediatric urologists, nephrologists, pediatricians, internists, and emergency department physicians, each of whom may interpret urinary tract signs and symptoms differently. Differentiating asymptomatic bacteriuria (colonization) from true infection in these patients is perplexing largely because of the frequent high bacterial counts, presence of multidrug-resistant organisms, and the diverse species isolated, particularly in patients performing CIC. Further complicating accurate diagnosis is the altered and varied abdominal innervation in SB patients. A recent report evaluating preoperative urine cultures in asymptomatic patients with neurogenic bladder demonstrated growth of >100,000 CFU/mL in 53.2% of bacterial cultures and multidrug-resistant organism isolates in 46.3% of specimens. This highlights the potential for over-reporting of UTI outcomes in studies that include SB patients. Explicitly stating how the outcome is measured affords the reader a better appraisal of the true UTI rate. In the SB patient population, this an important distinction given that these patients may require long hospitalization and intravenous antimicrobial agents, both of which are taxing to the patient, families, and the health care system. For example, Armour et al demonstrated that admissions for UTI in SB patients occurred at a rate of 22.8 per 1000 patients, whereas admission for UTI occurred at a rate of 0.44 per 1000 patients without SB. Furthermore, on analysis of the Nationwide Inpatient Sample, Dicianno et al found that UTI was the most common cause of hospital admission in SB patients. In this cohort, hospital stay was 6.9 days (95% confidence interval 6.6–7.2), and cost was $28,918 (95% confidence interval $27,367–$30,469) per admission. Limiting recurrent antibiotic courses may affect the development of resistant organisms; whether this translates into a change in the rate of hospitalization or selection for multidrug-resistant organisms remains to be evaluated.
The ultimate goal in the management of SB patients with neurogenic bladder is renal preservation. UTIs may contribute to renal deterioration when the infection involves the upper tract. Multiple reports have demonstrated preserved renal function in patients with asymptomatic bacteriuria and absence of vesicoureteral reflux (VUR). Ottolini et al demonstrated that 85% of 207 patients had asymptomatic bacteriuria. Univariable analysis failed to demonstrate an association between renal scarring and asymptomatic bacteriuria. However, scarring occurred in 20% of the study group and was associated with a febrile UTI and VUR. Leonardo et al retrospectively evaluated risk factors for renal scarring in patients with lower urinary tract dysfunction. On univariable and multivariable analysis, the strongest predictor of scarring was VUR. Bacteriuria was present in 47% of this study group and was not associated with renal scarring. Other studies have also demonstrated that asymptomatic bacteriuria alone does not lead to renal scarring. Ultimately, it is essential to be able to differentiate asymptomatic bacteriuria (colonization) and symptomatic bacteriuria (UTI) when reviewing SB literature as it pertains to interpreting study results and applying these to clinical practice.

A lack of clarity in defining parameters of research outcomes in the pediatric urology literature has also been highlighted in previous studies. Lloyd et al demonstrated that definitions of continence in the extrophy-epispadias complex population were variable among authors and frequently not reported. Other fields have encountered a similar problem and continue to encourage authors to establish standardization on how certain outcomes are defined.

Currently, recommendations for a standard definition of UTI in patients with SB are lacking. However, in our study, 55.6% of the definitions provided required a urine culture (most frequently >100,000 CFU/mL) and signs and symptoms suggestive of a UTI to arrive at a diagnosis. Urinalysis was infrequently a defining parameter. This is likely due to the paucity of data to guide interpretation of urinalysis in patients with neurogenic bladder. Clinically, leukocyturia denotes a degree of bladder inflammation that correlates with presence of bacteria, and thus we believe it is a relevant parameter to define a UTI in this population. Schlager et al demonstrated that 67% of urine specimens with bacterial growth >100,000 CFU/mL from children with neurogenic bladder had >5 WBC/HPF. Samples with <5 WBC/HPF did not have bacterial growth. Elliott et al reported that 31% of practitioners in specializing centers would treat with antimicrobial agents in the presence of >8 WBC/HPF and a positive urine culture. Conversely, only 15% would treat with urine microscopy demonstrating 0 to 8 WBC/HPF and a positive urine culture. Thus, current practice appears to value urine microscopy as an adjunct to culture to decide if antimicrobial therapy is warranted in SB patients.

In future prospective studies, we propose that investigators use the following definition based on our findings and review of the available literature: ≥2 signs/symptoms (fever >38°C, abdominal pain, new back pain, new or worse incontinence, pain with catheterization or urination, or malodorous/cloudy urine) and >10 WBC/HPF on urine microscopy. We suggest using this definition as a uniform starting point, and its application will allow for further validation and refinement. Its applicability to the clinical diagnosis of UTI in SB patients will depend on the outcomes of such studies.

Our study is not without limitations. The exclusion of conference abstracts curtails the number of studies evaluating UTI as an outcome in SB patients. However, it was deemed appropriate to exclude them due to the brevity of methodologic descriptions in abstracts and the lack of a detailed peer-reviewed process. More studies may have been potentially assigned to a “no UTI definition” category had these been included. In this review, we also did not account for studies reporting on patients with idiopathic neurogenic bladder, sacral agenesis, or postprocedural urinary dysfunction, all of whom may be afflicted by recurrent UTIs. Nevertheless, there are likely few studies that solely report on these patients. These patients are more commonly grouped with SB patients and therefore treated similarly. Lastly, although not described explicitly in the manuscripts, investigators may have adhered to stringent parameters to collect data on UTI outcomes. In this case, our study would underestimate the number of studies using a regimented definition of UTI.

The application of a standard definition for UTI will increase the value of clinical studies in the SB population by allowing validation of the study, facilitating comparison of UTI outcomes between studies, improving a study’s reliability, and providing applicable estimates of UTI rates in the SB population. Ultimately, this may provide insights into factors playing a role in UTI in this population, reduce overtreatment of asymptomatic patients, and facilitate additional work on novel measures of treatment and prevention.
CONCLUSIONS

Most published reports of SB patients with UTI as an outcome fail to define the methods used to diagnose a UTI. An accurate assessment of the risk of UTI based on these studies is problematic. A collective effort for a consensus definition for UTI in SB patients may improve the quality and value of research in this population and ultimately improve medical care.

ACKNOWLEDGMENTS

We thank Bethany Jun; Andreas Neisius, MD; Mari Shinohara, PhD; Malgorzata Poniewierska; and Marek Poniewierski, MD, MS, for their assistance with translation.

REFERENCES


(Continued from first page)
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*Pediatrics* 2013;132;132; originally published online June 24, 2013; DOI: 10.1542/peds.2013-0557

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