National Ambulatory Antibiotic Prescribing Patterns for Pediatric Urinary Tract Infection, 1998–2007

AUTHORS: Hillary L. Copp, MD, MS,[a] Daniel J. Shapiro, BA,[b] and Adam L. Hersh, MD, PhD[c]

[a]Department of Urology and [b]Philip R. Lee Institute for Health Policy Studies, University of California, San Francisco, California; and [c]Division of Pediatric Infectious Diseases, University of Utah, Salt Lake City, Utah

KEY WORDS
urinary tract infection, antibiotic use, pediatric

ABBREVIATIONS

UTI—urinary tract infection
NAMCS—National Ambulatory Medical Care Survey
NHAMCS—National Hospital Ambulatory Medical Care Survey
CI—confidence interval

www.pediatrics.org/cgi/doi/10.1542/peds.2010-3465

doi:10.1542/peds.2010-3465

Accepted for publication Feb 1, 2011

Address correspondence to Hillary L. Copp, MD, MS, University of California, San Francisco, Department of Urology, 400 Parnassus, A610, San Francisco, CA 94130. E-mail: copphl@urology.ucsf.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: *The authors have indicated they have no financial relationships relevant to this article to disclose.*

Funded by the National Institutes of Health (NIH).

WHAT'S KNOWN ON THIS SUBJECT: Urinary tract infections represent a significant source of exposure to antibiotics in the pediatric population and often physicians must select the antibiotic treatment empirically. No examination of ambulatory antibiotic prescribing patterns in the United States for children with urinary tract infections has been performed.

WHAT THIS STUDY ADDS: Ambulatory care physicians commonly prescribe broad-spectrum antibiotics, especially third-generation cephalosporins, for the treatment of pediatric urinary tract infections. Given that narrower-spectrum alternatives are frequently appropriate options for the treatment of these infections, efforts are necessary to promote more judicious antibiotic prescribing for pediatric urinary tract infections.

abstract

NIH

OBJECTIVE: The goal of this study was to investigate patterns of ambulatory antibiotic use and to identify factors associated with broad-spectrum antibiotic prescribing for pediatric urinary tract infections (UTIs).

METHODS: We examined antibiotics prescribed for UTIs for children aged younger than 18 years from 1998 to 2007 using the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey. Amoxicillin-clavulanate, quinolones, macrolides, and second- and third-generation cephalosporins were classified as broad-spectrum antibiotics. We evaluated trends in broad-spectrum antibiotic prescribing patterns and performed multivariable logistic regression to identify factors associated with broad-spectrum antibiotic use.

RESULTS: Antibiotics were prescribed for 70% of pediatric UTI visits. Trimethoprim-sulfamethoxazole was the most commonly prescribed antibiotic (49% of visits). Broad-spectrum antibiotics were prescribed one third of the time. There was no increase in overall use of broad-spectrum antibiotics ($P = .67$); however, third-generation cephalosporin use doubled from 12% to 25% ($P = .02$). Children younger than 2 years old (odds ratio: 6.4 [95% confidence interval: 2.2–18.7, compared with children 13–17 years old]), females (odds ratio: 3.6 [95% confidence interval: 1.6–8.5]), and temperature ≥100.4°F (odds ratio: 2.9 [95% confidence interval: 1.0–8.6]) were independent predictors of broad-spectrum antibiotic prescribing. Race, physician specialty, region, and insurance status were not associated with antibiotic selection.

CONCLUSIONS: Ambulatory care physicians commonly prescribe broad-spectrum antibiotics for the treatment of pediatric UTIs, especially for febrile infants in whom complicated infections are more likely. The doubling in use of third-generation cephalosporins suggests that opportunities exist to promote more judicious antibiotic prescribing because most pediatric UTIs are susceptible to narrower alternatives. *Pediatrics* 2011;127:1027–1033

Urinary tract infections (UTIs) affect up to 3.5% of children in the United States annually and represent a significant source of exposure to antibiotics in the pediatric population.[1,2] Frequently, a clinician must prescribe antibiotics empirically for UTIs because antibiotic administration is necessary before the return of urine culture results. Various factors are involved in antibiotic selection for outpatient treatment of UTIs, including patient age, allergies, cost, compliance and dosing frequency, and resistance patterns. The 1999 UTI practice parameter published by the American Academy of Pediatrics suggests a number of antibiotic options for the treatment of a suspected UTI.[3]

To our knowledge, no previous study has examined ambulatory antibiotic prescribing patterns in the United States for children with UTIs. Studies in the adult literature have demonstrated an increase in the use of broad-spectrum antibiotics for UTIs,[4–6] raising concerns that unnecessary broad-spectrum antibiotic use may lead to the development of antibiotic resistance through antibiotic selection pressures.[7] The goals of the present study were to determine trends in antibiotic prescribing for pediatric UTIs and to identify factors associated with broad-spectrum antibiotic prescription.

METHODS

Study Design

We performed a retrospective observational study examining antibiotics prescribed for pediatric outpatient visits for UTIs from 1998 to 2007 in the United States.

Data Sources

We analyzed data from the National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Ambulatory Medical Care Survey (NHAMCS) from 1998 to 2007. We grouped years into 5 study periods (1998–1999, 2000–2001, 2002–2003, 2004–2005, and 2006–2007) to add power to our analysis, as recommended by the National Center for Health Statistics.[8] The center administers these surveys annually to collect data on a nationally representative sample of outpatient visits to nonfederally funded, office-based physicians (NAMCS), emergency departments (NHAMCS-ED), and hospital outpatient departments (NHAMCS-OPD). By means of multistage, clustered probability sampling based on geographic location and provider specialty, various physicians throughout the United States are selected to participate in these surveys to generate national estimates. Different physicians and patients participate in each survey year. Each selected physician is randomly assigned a 1-week reporting period in which predetermined data from every patient visit during the period are recorded for the survey. National estimates are generated through a multistage estimation procedure and patient visit weights.[8] Monthly resident population data obtained from the US Census Bureau were used to generate population-based estimates.[9]

Visits for Urinary Tract Infections

NAMCS/NHAMCS collects data on up to 3 diagnoses related to the visit. The study population included all visits by patients younger than 18 years who had an International Classification of Diseases, Ninth Revision, code in any 1 of the 3 diagnosis fields consistent with UTIs (595.0, 595.9, 590.1x, 590.2, 590.8, 590.9, and 599). We included those codes representative of acute cystitis and pyelonephritis because there is frequently overlap between these diagnoses in children with fever and UTI. As described previously, we excluded a small number of visits in which patients were diagnosed with both a UTI and another infection for which antibiotics are commonly prescribed to ensure that UTI was the primary reason for the visit and any resulting antibiotic prescriptions.[6]

Urinary Tract Infection Antibiotic Visits

We defined "UTI antibiotic visits" as UTI visits during which an antibiotic was prescribed. The Multum Lexicon Plus system was used to identify drug classes and individual drugs.[8] The following antibiotic categories were included: penicillin, cephalosporin, macrolide, lincosamide, tetracycline, quinolone, urinary anti-infective agent, aminoglycoside, and trimethoprim-sulfamethoxazole. Antibiotics within the trimethoprim-sulfamethoxazole category included trimethoprims and sulfonamides prescribed alone and in combination. The urinary anti-infective group was composed of nitrofurantoins and methenamine mandelates. For the purposes of this study, broad-spectrum antibiotics were defined as amoxicillin-clavulanate, quinolones, macrolides, and second- and third-generation cephalosporins. Mode of antibiotic administration (oral versus parenteral) was not recorded. Therefore, the percentage of visits receiving parenteral therapy was determined based on identification of antibiotics for which only a parenteral formulation is available (eg, ceftriaxone).

Measurements

Age was evaluated as a categorical variable with categories of younger than 2 years, 2 to 5 years, 6 to 12 years, and 13 to 17 years because the prevalence of UTI varies by age in a nonlinear fashion.[10–12] Race was dichotomized into white versus nonwhite and insurance status was categorized into private versus nonprivate because of sample size limitations. Private insurance included those with health maintenance organization and preferred provider organization coverage. Nonprivate insurance included government forms of coverage (Medicare, Medicaid, and other governmental programs) plus self-pay, charity care, and no charge. Geographic region was recorded in the survey as Northeast, Midwest, South, and West. Physician specialty was divided into 3 categories: pediatrics, family practice, and emergency department/other. Major reason for visit was classified as acute problem, chronic problem, or other (pre- or postsurgery, injury follow-up, or nonillness care).

The clinical characteristics recorded for each visit included: presence of fever (temperature ≥100.4°F) from 2003 to 2007 when such data were available, whether a urinalysis was collected, and whether hospital admission was required.

Statistical Analysis

To account for the multistage probability sampling frame, all analyses were performed using survey design variables and appropriate survey commands in Stata 11 statistical software (Stata Corp, College Station, TX). Descriptive statistics were completed on the general characteristics of UTI visits and the type of antibiotic used at each UTI antibiotic visit. To assess trends in the population-adjusted rate of UTI diagnoses, we used a linear test for trend across 2-year periods. Across the same 2-year intervals, we examined trends in the prescription of antibiotics and of broad-spectrum antibiotics using logistic regression. Because of sample size limitations, use of individual antibiotic classes was compared between the first and last 3-year periods (1998–2000 vs 2005–2007).

Unadjusted associations were tested between predictor variables and the outcome variable (broad-spectrum antibiotic prescription) using the χ^2 test. Multivariable logistic regression was performed to identify factors associated with broad-spectrum antibiotic prescription. Covariates with $P < .2$ on univariate analysis were included in the final model. All analyses were 2-sided, and $P < .05$ was considered statistically significant. All estimates were notated that had relative SEs >30% or that were based on <30 observations. This research was approved by the Committee on Human Research of the University of California, San Francisco.

RESULTS

Visit Characteristics

There were an estimated 16 million (95% confidence interval [CI]: 14–18 million) visits for UTIs in children aged younger than 18 years in the United States from 1998 to 2007 based on 1828 visits captured by NAMCS/NHAMCS. The number of UTI visits averaged ~1.5 to 1.75 million annually, with no change over time ($P = .71$). The majority of visits were by female patients with an acute problem (Table 1). Less than 1% of the total visits for pediatric UTIs required hospital admission. Temperature ≥100.4°F was recorded in 11% of patients. Urinalysis was obtained in 72% of UTI visits.

Antibiotic Prescription Trends

Antibiotics were prescribed for 70% of pediatric UTI visits (ie, UTI antibiotic visits) during the observation period, with no change in the percentage of UTI antibiotic visits over time ($P = .88$) (Table 2). Parenteral therapy was used in 10.6% of UTI antibiotic visits, with no time trend observed. Third-generation cephalosporins constituted the majority of parenterally administered antibiotics (77%) and, among these, ceftriaxone was selected in 95% of the visits. Trimethoprin-sulfamethoxazole was prescribed in 49% of UTI antibiotic visits and was the single most commonly prescribed antibiotic throughout the study period. First-generation cephalosporins and urinary anti-infective agents comprised <5% and 8% of antibiotics prescribed for UTIs, respectively. In 32% of UTI antibiotic visits, a broad-spectrum antibiotic was prescribed, and there was no change in the percentage of broad-spectrum antibiotics prescribed ($P = .67$) over time. Amoxicillin-clavulanate use ranged between 4% and 9% of UTI visits, with no significant change in trend over time. However, third-generation cephalosporin use doubled from 12% in 1998–2000 to 25% in 2005–2007 ($P = .02$).

Predictors of Broad-Spectrum Antibiotic Use

In bivariate analysis, children aged younger than 2 years were more likely

TABLE 1 Demographic Characteristics of Visits for Pediatric UTIs

Characteristic	Percentage of UTI Visits
Overall ($N = 1828$[a])	
Age, y	
<2	15
2–5	27
6–12	33
13–17	25
Gender	
Female	82
Male	18
Race	
White	79
Nonwhite	21
Physician specialty	
Pediatrics	43
Family practice	21
Emergency department/other	36
Region	
Northeast	18
Midwest	23
South	42
West	17
Insurance type ($n = 1748$)	
Private	58
Medicare/Medicaid/SCHIP	33
Self-pay/other	9
Major reason for visit ($n = 745$)	
Acute/new problem	78
Chronic problem	16
Other	6

SCHIP indicates State Children's Health Insurance Program.

[a] A total of 1828 sample visits correspond to an estimated 16 million visits in the United States.

TABLE 2 Antibiotics Prescribed for Pediatric UTI Visits[a]

Antibiotic Prescribed	Percentage of Pediatric UTI Visits Receiving Antibiotic		
	All Years	1998–2000	2005–2007
Trimethoprin-sulfamethoxazole	49	52	47
Amoxicillin/ampicillin	9	11	5
Urinary anti-infective agents[b]	8	7	10
Nitrofurantoin[b]	8	7	9
Amoxicillin-clavulanate	6	9	4
First-generation cephalosporins[b]	5	2	7
Second-generation cephalosporins[c]	3	6	1
Third-generation cephalosporins[d]	17	12	25
Oral[b]	9	4	15
Parenteral	8	8	10
Quinolones[c]	5	5	4
Other[c]	3	1	7
Broad-spectrum antibiotics[e]	32	32	35

[a] Because >1 antibiotic was prescribed in a few cases, classes will sum to >100%.
[b] The estimate for one 3-year period (the smaller percentage) relies on <30 observations, and the relative SE is >30%.
[c] The estimate for each 3-year period relies on <30 observations, and the relative SE is >30%.
[d] Third-generation cephalosporin use increased from 12% to 25% ($P < .02$).
[e] Broad-spectrum antibiotics include amoxicillin-clavulanate, quinolones, macrolides, and second- and third-generation cephalosporins.

to receive broad-spectrum antibiotics (52% of the time) than children aged 13 to 17 years (23%) ($P = .01$) (Table 3). Children with fever and children admitted to the hospital were also more likely to receive broad-spectrum antibiotics compared with those without fever and those not admitted to the hospital, respectively ($P = .01$). In multivariable analysis for all years of the study period, children aged younger than 2 years (odds ratio: 3.7 [95% CI: 1.7–7.7] compared with children aged 13–17 years) had increased odds of being prescribed broad-spectrum antibiotics. On subanalysis of the years for which data on temperature were available (2003–2007), children younger than 2 years (odds ratio: 6.4 [95% CI: 2.2–18.7] compared with children aged 13–17 years), females (odds ratio: 3.6 [95% CI: 1.6−8.5]), and having a temperature ≥100.4°F recorded during the visit (odds ratio: 2.9 [95% CI: 1.0−8.6]) were independent predictors of broad-spectrum antibiotic prescribing. Race, physician specialty, region, and insurance status were not associated with broad-spectrum antibiotic selection. Similar trends were observed with third-generation cephalosporin prescription; however, there were insufficient data to perform multivariate analysis.

TABLE 3 Factors Associated with Prescribing Broad-Spectrum Antibiotics for Pediatric UTIs

Factor	Broad-Spectrum Prescribing Rate	*P*	Adjusted Odds Ratio (95% CI), 1998–2007	Adjusted Odds Ratio[a] (95% CI), 2003–2007
Age, y		.01		
<2	0.52		3.7 (1.7–7.7)[b]	6.4 (2.2–18.7)[b]
2–5	0.36		1.7 (0.9–3.3)[b]	1.6 (0.5–4.5)[b]
6–12	0.27		1.2 (.6–2.6)[b]	1.4 (0.5–3.7)[b]
13–17	0.23		Reference	Reference
Gender		.19		
Female	0.33		2.0 (0.8–4.9)[b]	3.6 (1.6–8.5)[b]
Male	0.23		Reference	Reference
Race		.36		
White	0.33		—	—
Nonwhite	0.27		—	—
Physician specialty		.17		
Pediatrics	0.40		Reference	Reference
Family practice	0.26		0.6 (0.3–1.4)[b]	0.3 (0.1–1.1)[b]
Emergency department/other	0.30		0.7 (0.4–1.1)	0.5 (0.2–1.4)[b]
Region		.76		
Northeast	0.33		—	—
Midwest	0.27		—	—
South	0.35		—	—
West	0.29		—	—
Insurance		.41		
Private	0.30		—	—
Nonprivate	0.35		—	—
Major reason for visit		.40		
Acute/new problem	0.33		—	—
Chronic problem[b,c]	0.27		—	—
Other[b,c]	0.11		—	—
Temperature		.01		
<100.4°F	0.57		—	Reference
≥100.4°F	0.31		—	2.9 (1.0–8.6)[b]
Admission to hospital		.01		
No	0.32		—	—
Yes[c]	0.72		—	—

[a] Subanalysis from 2003 to 2007 when temperature was available as a data point.
[b] Relative SE >30%.
[c] Fewer than 30 observations and therefore not included in multivariable analysis.

DISCUSSION

Summary of Findings

To our knowledge, this is the first study to describe ambulatory prescribing patterns and factors associated with broad-spectrum antibiotic prescription for pediatric UTIs on a national level. Not only did we find that broad-spectrum antibiotics were prescribed in a significant percentage of children receiving antibiotics for UTI, we also identified a substantial increase in the use of third-generation cephalosporins.

When considered in the context of national patterns of antibiotic resistance, our findings suggest that there may be a mismatch between empiric prescribing and resistance patterns. The 1999 UTI practice parameter recommends numerous antibiotic options, including sulfonamide combinations, amoxicillin, ampicillin, gentamicin, tobramycin, ticarcillin, and first-, second-, and third-generation cephalosporins, for the empiric treatment of UTIs.[3] Ultimately, it is the treating physician who is charged with determining the appropriate antibiotic regimen. The specific clinical and microbiologic conditions that might favor the selection of 1 antibiotic class versus another vary based on factors that are simultaneously unique to the individual (eg, age, tolerance, compliance) and dependent on the external environment (eg, local resistance patterns, formulary availability). Empiric treatment is also based on what will typically be the cause of the UTI; ~80% to 90% of the time the causative organism is *Escherichia coli*, even in the setting of recurrent UTI.[13–16] A study of national uropathogen resistance rates among pediatric UTIs found that *E coli* isolates, on average, were resistant to first-generation cephalosporins <3.5% of the time in female patients and 6.5% of the time in male patients.[14] It is therefore surprising that we found that first-generation cephalosporins were only prescribed in 5% of visits. Conversely, we found that trimethoprim-sulfamethoxazole was prescribed consistently throughout the observation period for ~50% of UTI antibiotic visits, despite publication of numerous studies demonstrating that resistance rates to this antibiotic range from 20% to 40%.[14,17–19]

Broad-spectrum antibiotics were administered in approximately one third of UTI antibiotic visits. Whether this is an example of overprescribing of broad-spectrum antibiotics in the empiric treatment of UTI is difficult to establish. Specific clinical information that is invaluable in the decision-making process for determining appropriate empiric UTI treatment is not captured in NAMCS/NHAMCS. This information includes factors that have been shown to be associated with an increased risk of UTI by a resistant organism, such as the current use of prophylactic antibiotics, previous antibiotic therapy, hospitalization within the previous year, or genitourinary tract abnormality.[13,16,17,20,21] Our findings reveal that although broad-spectrum antibiotics were administered in a significant percentage of UTI antibiotic visits, this number did not increase over time. Furthermore, we observed no differences in antibiotic prescribing based on nonclinical factors such as physician specialty or insurance type. Rather, broad-spectrum antibiotic prescription was associated with younger age, female gender, and those with fever. Although broad-spectrum antibiotics may nonetheless be overprescribed for many of these patients, these groups do represent pediatric subpopulations at higher risk for UTIs and associated complications, which may justify more aggressive empiric antibiotic selection.[10,22]

An additional complexity of antibiotic treatment selection in pediatric UTI is its customary management in the outpatient setting. The 1999 UTI practice parameter supports outpatient management of febrile UTIs in children who are nontoxic, not dehydrated, and can tolerate oral intake.[3] By prescribing broad-spectrum antibiotics, there is an increased likelihood that the causative organism will be susceptible to the prescribed therapy and, therefore, less risk that inadequate treatment will be administered even when follow-up cannot be guaranteed. A randomized controlled trial published by Hoberman et al[23] in 1999 likely additionally popularized the use of a specific class of broad-spectrum antibiotics, third-generation cephalosporins, by reporting that oral cefixime was safe and effective for the outpatient treatment of pyelonephritis. However, a more recent meta-analysis evaluating different antibiotic regimens for acute pyelonephritis in children found that there was no difference in the effectiveness of oral therapy with third-generation cephalosporins compared with amoxicillin-clavulanate.[2] Moreover, third-generation cephalosporins may no longer offer the assured antimicrobial coverage for patients with complicated UTIs that they once did. Lutter et al[21] reported that children receiving antimicrobial prophylaxis with breakthrough UTIs were often infected with an organism resistant to third-generation cephalosporins, despite the fact that none of these children were taking cephalosporin prophylaxis.

Another potential reason for the observed increase in use of third-generation cephalosporins is due to the selection of a specific antibiotic, ceftriaxone, which is popular because of its availability as a parenteral formulation with once-daily dosing. A 1-time dose of parenteral antibiotic therapy in combination with oral treatment is a commonly used strategy for the outpatient management of pyelonephritis.[24] This regimen assures complete medication delivery in the clinic or emergency department, reducing concerns regarding compliance or tolerance in patients who can become very ill and potentially unable to retain oral medications as outpatients. It also ensures 24 hours of additional time to safely monitor the evolution of the illness in the outpatient setting with little risk that insufficient therapy has been administered. Unfortunately, due to sample size limitations, we were unable to determine if oral, parenteral, or a combination of both formulations was responsible for the overall increase in prescription of third-generation cephalosporins.

Limitations

Our results should be interpreted in the context of important limitations. As mentioned, the data sets do not contain certain clinical information that would enable assessment of the appropriateness of the antibiotic choice. For example, we were unable to take into account important factors such as the presence of genitourinary anomalies, history of UTI, bacterial etiologies of UTI, prior antibiotic exposure, recent hospitalizations, medication intolerance, or local antibiotic resistance patterns. All of these variables clearly influence a provider's prescribing decisions and would permit more reliable judgment as to how well suited the selected antibiotic was for the given clinical scenario. In addition, mode of drug administration was not recorded. However, we were mainly interested in determining the mode of delivery for third-generation cephalosporins, and each specific antibiotic within this class typically has a single formulation (eg, ceftriaxone is only available by parenteral administration). Finally, the inability to discern whether a visit was a follow-up or initial visit may explain why 30% of patients at UTI visits did not receive an antibiotic. Depending on the timing of a follow-up visit for UTI, additional therapy might not be necessary if adequate therapy had already been completed. The fact that urinalysis was also not obtained in 28% of visits supports the fact that some of these encounters may have been scheduled follow-up visits to assess how patients were faring clinically after initiation of antibiotic therapy. Similar percentages of UTI visits were without antibiotic prescription in previous NAMCS/NHAMCS studies performed in the adult population.[4–6]

Relation to Clinical Practice

Nationally, broad-spectrum antibiotics and, specifically, third-generation cephalosporins are prescribed in a significant percentage of UTI antibiotic visits. It is not possible to determine if this is appropriate using NAMCS/NHAMCS data; thus, further studies using data with more detailed clinical information will need to be performed to assess our prescribing decisions. What is clear is that once a broad-spectrum antibiotic is prescribed, an important aspect of responsible prescribing is tailoring of therapy.[25,26] The Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America recommend deescalation of therapy as 1 of the key steps in decreasing antimicrobial exposure, antibiotic selection pressures, and the subsequent emergence of resistance.[7] Therefore, if the clinician makes the decision to empirically prescribe broad-spectrum antibiotics, then he or she has an obligation to follow-up on urine culture results and to tailor antibiotic therapy when appropriate. This represents a significant challenge in the outpatient environment when many of those who seek care in an emergency setting do not necessarily follow-up within the same health care system.

CONCLUSIONS

Ambulatory visits for UTIs in children are common, accounting for at least 1.5 million visits annually in the United States. Among these visits, broad-spectrum antibiotic prescribing, especially of third-generation cephalosporins, was common and associated with clinical factors such as young age, female gender, and fever. Given that narrower-spectrum alternatives are frequently appropriate options for UTIs, these findings support the need for interventions that promote judicious antibiotic selection for the treatment of pediatric UTIs.

ACKNOWLEDGMENTS

Dr Copp is supported by the University of California, San Francisco KURe Career Development Program (National Institutes of Health grant 1-K12-DK-083021), which did not have any role in the design or conduct of the study, analysis of data, or drafting of the manuscript.

The authors thank Amy J. Markowitz, JD, for her critical review of the manuscript.

REFERENCES

1. Freedman AL, Urologic Diseases in America Project. Urologic diseases in North America Project: trends in resource utilization for urinary tract infections in children. *J Urol*. 2005;173(3):949–954
2. Hodson EM, Willis NS, Craig JC. Antibiotics for acute pyelonephritis in children. *Cochrane Database Syst Rev*. 2007(4):CD003772
3. Practice parameter: the diagnosis, treatment, and evaluation of the initial urinary tract infection in febrile infants and young children. American Academy of Pediatrics. Committee on Quality Improvement. Subcommittee on Urinary Tract Infection [published corrections appear in *Pediatrics*. 1999;103(5 pt 1):1052, 104(1 pt 1):118, and 2000;105(1 pt 1):141]. *Pediatrics*. 1999; 103(4 pt 1):843–852
4. Caterino JM, Weed SG, Espinola JA, Camargo CA Jr. National trends in emergency department antibiotic prescribing for elders with urinary tract infection, 1996–2005. *Acad Emerg Med*. 2009;16(6): 500–507
5. Huang ES, Stafford RS. National patterns in the treatment of urinary tract infections in women by ambulatory care physicians. *Arch Intern Med*. 2002;162(1):41–47
6. Kallen AJ, Welch HG, Sirovich BE. Current antibiotic therapy for isolated urinary tract infections in women. *Arch Intern Med*. 2006; 166(6):635–639
7. Dellit TH, Owens RC, McGowan JE Jr, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis*. 2007;44(2): 159–177

8. Centers for Disease Control and Prevention. National Center for Health Statistics. Ambulatory Health Care Data. Available at: www.cdc.gov/nchs/ahcd/ahcd_questionnaires.htm. Accessed September 20, 2010
9. US Census Bureau. Population estimates data. Available at: www.census.gov/popest/national/asrh/. Accessed April 2, 2010
10. Shaikh N, Morone NE, Bost JE, Farrell MH. Prevalence of urinary tract infection in childhood: a meta-analysis. *Pediatr Infect Dis J*. 2008;27(4):302–308
11. Winberg J, Andersen HJ, Bergström T, Jacobsson B, Larson H, Lincoln K. Epidemiology of symptomatic urinary tract infection in childhood. *Acta Paediatr Scand Suppl*. 1974;(252):1–20
12. Zorc JJ, Levine DA, Platt SL, et al. Clinical and demographic factors associated with urinary tract infection in young febrile infants. *Pediatrics*. 2005;116(3):644–648
13. Conway PH, Cnaan A, Zaoutis T, Henry BV, Grundmeier RW, Keren R. Recurrent urinary tract infections in children: risk factors and association with prophylactic antimicrobials. *JAMA*. 2007;298(2):179–186
14. Gaspari RJ, Dickson E, Karlowsky J, Doern G. Antibiotic resistance trends in paediatric uropathogens. *Int J Antimicrob Agents*. 2005;26(4):267–271
15. McLoughlin TG Jr, Joseph MM. Antibiotic resistance patterns of uropathogens in pediatric emergency department patients. *Acad Emerg Med*. 2003;10(4):347–351
16. Paschke AA, Zaoutis T, Conway PH, Xie D, Keren R. Previous Antimicrobial Exposure Is Associated With Drug-Resistant Urinary Tract Infections in Children. *Pediatrics*. 2010;125(4):664–672
17. Allen UD, MacDonald N, Fuite L, Chan F, Stephens D. Risk factors for resistance to "first-line" antimicrobials among urinary tract isolates of *Escherichia coli* in children. *CMAJ*. 1999;160(10):1436–1440
18. Gaspari RJ, Dickson E, Karlowsky J, Doern G. Multidrug resistance in pediatric urinary tract infections. *Microb Drug Resist*. 2006;12(2):126–129
19. Zhanel GG, Hisanaga TL, Laing NM, et al. Antibiotic resistance in outpatient urinary isolates: final results from the North American Urinary Tract Infection Collaborative Alliance (NAUTICA). *Int J Antimicrob Agents*. 2005;26(5):380–388
20. Cheng CH, Tsai MH, Huang YC, et al. Antibiotic resistance patterns of community-acquired urinary tract infections in children with vesicoureteral reflux receiving prophylactic antibiotic therapy. *Pediatrics*. 2008;122(6):1212–1217
21. Lutter SA, Currie ML, Mitz LB, Greenbaum LA. Antibiotic resistance patterns in children hospitalized for urinary tract infections. *Arch Pediatr Adolesc Med*. 2005;159(10):924–928
22. Shaw KN, Gorelick M, McGowan KL, Yakscoe NM, Schwartz JS. Prevalence of urinary tract infection in febrile young children in the emergency department. *Pediatrics*. 1998;102(2). Available at: www.pediatrics.org/cgi/content/full/102/2/e16
23. Hoberman A, Wald ER, Hickey RW, et al. Oral versus initial intravenous therapy for urinary tract infections in young febrile children. *Pediatrics*. 1999;104(1 pt 1):79–86
24. Nelson DS, Gurr MB, Schunk JE. Management of febrile children with urinary tract infections. *Am J Emerg Med*. 1998;16(7):643–647
25. Lieberman JM. Appropriate antibiotic use and why it is important: the challenges of bacterial resistance. *Pediatr Infect Dis J*. 2003;22(12):1143–1151
26. Paterson DL, Rice LB. Empirical antibiotic choice for the seriously ill patient: are minimization of selection of resistant organisms and maximization of individual outcome mutually exclusive? *Clin Infect Dis*. 2003;36(8):1006–1012

ADVANCES IN TISSUE-ENGINEERING: *Autologous tissue-engineering, the biomechanical science of growing tissues and organs from a patient's own cells, is viewed as having the potential to transform the field of transplant medicine and offer new treatment options for a variety of conditions. Researchers now report that the practice can successfully treat urethral injury in young boys (Raya-Rivera* et al. Lancet*. March 8, 2011). Five boys aged 10 to 14 with urethral damage secondary to trauma underwent urethroplasty with grafts made from autologous cells grown onto a tubular scaffold. Two of the patients required subsequent surgical treatment for complications (transurethral incision for stenosis and pubovesical sling for pelvic disruption), but all five eventually achieved complete urinary continence (follow-up lasted 36 to 71 months). Although further studies and procedural modifications are in order, this achievement will hopefully lay a critical foundation for future tissue grafting experiments. A future in which patients would no longer need immunosuppressive medications following transplantation would be a landmark success indeed.*

Noted by Patrick Huffer, MS-IV