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Dysfunctional Elimination Syndrome: Is It Related to Urinary Tract Infection or Vesicoureteral Reflux Diagnosed Early in Life?

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ABSTRACT. *Objective.* **It has been suggested that urinary tract infections (UTIs) early in life predispose to dysfunctional elimination syndrome (DES). This study evaluated the relationship between early UTI, vesicoureteral reflux (VUR), and DES by comparing two cohorts of school-aged children.**

Methods. **The UTI cohort ($n = 123$) included children previously enrolled in a prospective treatment trial conducted between 1992 and 1997. All were diagnosed with a febrile UTI before 2 years of age. The comparison cohort ($n = 125$) included children who were evaluated for fever in the emergency department between 1992 and 1997, whose urine culture was negative. Dysfunctional elimination symptoms were compared in the two cohorts by having families complete a revised version of the Dysfunctional Voiding Scoring System.**

Results. **Completed questionnaires were received from 248 children. There were no significant differences in selected demographic or clinical characteristics between the two cohorts. DES was present in 22% and 21% of children with and without a history of early UTI, respectively. Among children with UTIs, 18% of those with VUR and 25% of those without VUR had DES.**

Conclusions. **Dysfunctional elimination is common in a general pediatric population. Neither UTI nor VUR diagnosed before 2 years of age was associated with DES in school-aged children.** ***Pediatrics*** **2003;112:1134–1137;** ***dysfunctional elimination, voiding dysfunction, dysfunctional voiding, vesicoureteral reflux, urinary tract infection.***

ABBREVIATIONS. DES, dysfunctional elimination syndrome; UTI, urinary tract infection; VUR, vesicoureteral reflux; CI, confidence interval; OR, odds ratio.

Dysfunctional elimination syndrome (DES) refers to an abnormal pattern of elimination of unknown etiology characterized by bowel and bladder incontinence and withholding.[1] Symptoms of DES, also referred to as voiding dysfunction, usually present in toilet-trained children without underlying anatomic or neurologic abnormalities.

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In two previous retrospective studies, school-aged children with DES had a higher prevalence of previous urinary tract infections (UTIs) suggesting that UTIs early in life may predispose to DES.[2,3] Similarly, it has been suggested that congenital vesicoureteral reflux (VUR) and DES are associated.[4,5] However, most studies on DES have been conducted in children referred to specialists. Children with severe symptoms, VUR, and recurrent UTIs may be overrepresented in this referral population. To our knowledge, the associations between UTI, VUR, and DES have not been evaluated in a general pediatric population. This study was designed to describe the demographic and clinical characteristics of school-aged children with DES, and to determine 1) whether UTIs early in life are related to DES, and 2) whether VUR identified early in life and DES are associated.

METHODS

Subjects

Dysfunctional elimination symptoms were compared in two cohorts of school-aged children with use of a previously validated questionnaire. The first cohort (UTI cohort) consisted of children previously enrolled in a prospective, multicenter UTI treatment trial conducted between 1992 and 1997, the methods of which have been reported.[6] All received a prospective diagnosis of febrile UTI before 2 years of age. Children for the comparison cohort were identified retrospectively, by randomly selecting children younger than 2 years of age, who as part of their evaluation for fever, had a negative urinalysis and urine culture performed in the Emergency Department of the Children's Hospital of Pittsburgh during the same period (1992–1997). A negative urinalysis was defined as <10 white blood cells per cubic millimeter on a neubauer hemocytometer in an uncentrifuged specimen. A positive urine culture was defined as the presence of at least 5×10^4 colony forming units per milliliter of a single organism on a specimen obtained by catheter or at least 10^5 colony forming units per millileter of a single organism on a clean voided specimen. On chart review, 6 children identified in this manner were found to have had a documented febrile UTI at another visit before 2 years of age. These children were added to the UTI cohort. An attempt was made to balance the 2 cohorts in terms of race and gender by restricting selection of patients in the comparison cohort to females and whites in the later stages of recruitment. Six children with organic causes of dysfunctional voiding (eg, tethered cord, profound developmental delay) were excluded from the study.

Questionnaire

Dysfunctional elimination symptoms were assessed with the dysfunctional voiding scoring system, a previously validated scored questionnaire on dysfunctional elimination with a sensitivity of 93% and a specificity of 87% in girls and a sensitivity of 81% and a specificity of 91% in boys.[7] Minor changes were made to the wording of some questions to make them understandable to parents with low literacy levels. The dysfunctional voiding scoring

system quantifies abnormal stooling and voiding behaviors during the preceding month. It consists of 10 questions scored on a scale from 0 to 3 and includes one question on psychosocial stress. Parents were asked to have their children complete the questionnaire with them. DES was defined as a score of >6 in girls and >9 in boys, observing the validation study's recommendation.[7] To assess the chronicity of symptoms, we repeated each question on the dysfunctional voiding scoring system, asking instead whether the symptom had been consistently present for at least 6 months.

To assess for confounders, we collected data on type of insurance coverage, maternal education, age at the time of toilet training, enuresis (bed-wetting at least once a week), encopresis (soiling at least once a month or having frequent underwear streaking), number of UTIs, and treatment received for DES. Finally, a Child Vulnerability Scale was also included to permit adjustment for this potentially confounding variable; a score of at least 10 on this questionnaire is considered significant.[8] This validated scale measures both specific aspects of the vulnerable child syndrome and general concern about a child's health.

General Procedures

The Human Rights Committee at the Children's Hospital of Pittsburgh approved the study. The questionnaires and consent forms were mailed to all eligible families. Medical records of enrolled children were reviewed to confirm episodes of UTI, grade of VUR, and treatment for DES. If the questionnaire or medical records were inconsistent or incomplete, the child's parents and/or primary care providers were contacted for clarification. Parents and primary care providers of children with DES were notified by mail of the potential diagnosis and of the opportunity for further evaluation.

Statistical Analysis

A sample size of 242 children (121 per arm) was deemed necessary to detect a 15% difference in the proportion of children with DES between the two cohorts, assuming an α of 0.05, a 2-sided test, a power of 0.80 and a 0.15 prevalence of DES in the comparison group. Data entry was verified. All reported significance levels are 2-sided and all reported confidence intervals (CIs) are the 95% CIs. χ^2 tests were used to evaluate differences in proportions and Student's t tests were used to test for differences in mean values. Univariate and multivariate unconditional logistic regression analyses were used to identify variables associated with DES and recurrent UTIs.

RESULTS

In total, 574 questionnaires were mailed to eligible subjects (168 in the UTI cohort and 406 in the comparison cohort), and 248 completed questionnaires were returned. Questionnaire return rates in the UTI and comparison cohorts were 73% and 31%, respectively. Medical records of 97% of enrolled children were reviewed. The number of UTIs reported by parents could not be confirmed by chart review in 10 children. These children were excluded from analyses related to UTIs. All children included in the comparison cohort were confirmed to have had no UTI diagnosed before 2 years of age. In the UTI cohort, the mean age of infants at the time of the index infection was 8.8 months. Of the 8 boys in the UTI cohort, 3 were circumcised.

Comparison of the Cohorts

The two cohorts did not differ significantly with regard to selected demographic and clinical characteristics (Table). Both cohorts were predominantly female and white. The ages of children ranged from 4.3 to 10.6 years; all were toilet trained.

The prevalence of DES did not differ in children with and without a history of UTIs in infancy. Symptoms of DES were present in 22% and 21% of children in the UTI and comparison cohorts, respectively ($P = .82$; Fig 1). Among children with UTIs, the prevalence of DES did not differ in children with and without VUR identified early in life; 18% of those with VUR and 25% of those without VUR had symptoms of DES ($P = .52$; Fig 1). Further analyses using different questionnaire cutoffs or various combinations of dysfunctional symptoms, and adjusting for child vulnerability score and other potential confounding factors, did not yield different conclusions.

TABLE 1. Demographic and Clinical Characteristics of Children With and Without a History of Urinary Tract Infection(s) Before 2 Years of Age

Characteristic	UTI Cohort (n = 123)	Comparison Cohort (n = 125)	P
	N (% of cohort)		
Gender			
Female	115 (94)	120 (96)	.55
Male	8 (6)	5 (4)	
Ethnicity			
White	105 (85)	100 (80)	.34
Black/other	18 (15)	25 (20)	
Age (mean, y)	7.3	7	.07
Health insurance*			
Private	95 (77)	99 (80)	.64
Public/none	28 (23)	24 (20)	
Maternal education*			
≤High school	30 (24)	26 (21)	.65
>High school	93 (76)	97 (79)	
Enuresis	17 (14)	22 (18)	.52
Encopresis	30 (24)	34 (27)	.69
Age trained for urine/stool (mo)	29/30	28/29	.27
Child vulnerability score >9	10 (8)	19 (15)	.11

* Missing data not shown.

Children With Symptoms of Dysfunctional Elimination

Overall, among all children in the study, 19% of children reported urgency with at least half of their voids, 19% performed a "pee dance" with at least half of their voids, 10% had daytime urinary incontinence at least once a week, and 13% had to push or had pain with defecation at least half the time. A total of 53 children in the study (21%) met criteria for DES. Among children with DES, 28 (54%) had encopresis and 11 (21%) had recurrent UTIs.

On univariate analysis, variables related to DES included enuresis ($P < .001$; odds ratio [OR] = 3.8; 95% CI: 1.8–7.9), encopresis ($P < .001$; OR: 5.2; 95% CI: 2.7–9.9), recurrent UTIs ($P = .05$; OR: 2.2; 95% CI: 0.99–5), and a score of at least 10 on the child vulnerability scale ($P < .001$; OR: 5.4; 95% CI: 2.4–12.1). When these 4 variables were included in a multivariate model, only encopresis ($P < .001$) and a score of at least 10 on the child vulnerability scale ($P = .008$) remained significantly associated with DES. Gender, ethnicity, maternal education, insurance, age, age at toilet training, and VUR were not associated with DES. Only 2 children had undergone specific treatment for DES.

Overall, 20% of children reported symptoms of DES in the past (symptoms consistently present for at least 6 months). In these children, the mean age at onset of DES was 37 months and the mean duration of symptoms was 34 months. The prevalence of DES

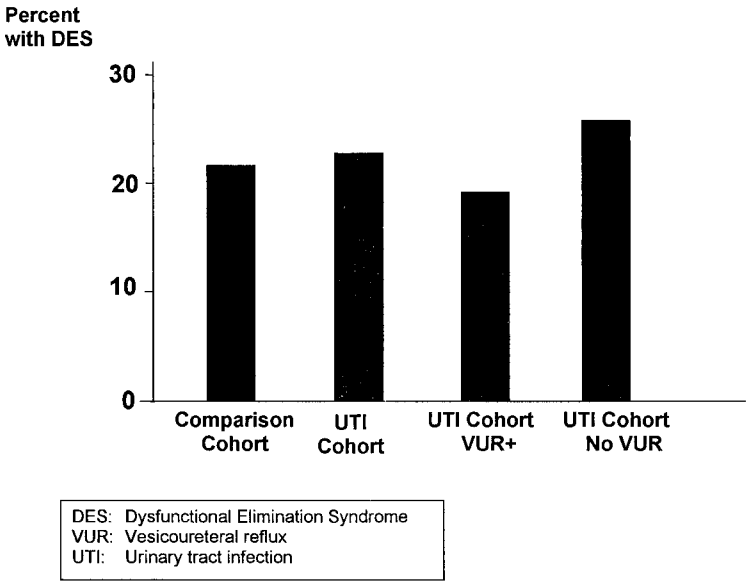

Fig 1. Percentage of children with symptoms of dysfunctional elimination according to history of UTIs and VUR.

in the past, age of onset of DES, and duration of DES did not differ between the UTI and comparison cohorts.

Children With Recurrent UTIs

A total of 31 children had recurrent (>1) confirmed UTIs. Of these, 13 (43%) had encopresis, 11 (36%) had DES, and 17 (55%) had VUR. On univariate analysis, variables associated with recurrent UTIs included: encopresis ($P = .03$; OR: 2.5; 95% CI: 1.1–5.4), DES ($P = .05$; OR: 2.2; 95% CI: 0.99–5), and VUR ($P = .07$; OR: 2.2; 95% CI: 0.9–5). On multivariate analysis, only encopresis remained significantly associated with recurrent UTIs ($P = .03$) when these 3 variables were included in the model.

Children With Vulnerable Child Syndrome

Given the statistically significant association between high child vulnerability scores (≥10) and DES, further analyses on this variable were conducted. A high child vulnerability score was not associated with history of UTI ($P = .11$), recurrent UTIs ($P = .37$), or VUR ($P = .52$). The association between dysfunction elimination symptoms and high scores on the child vulnerability scale remained significant after removal of the question related to stress from the DES questionnaire. The attacks of September 11 occurred in the middle of enrollment (48% of children had already entered). There was no change in the prevalence of DES after September 11, 2001 ($P = .46$).

DISCUSSION

DES is a condition of unknown etiology with potentially significant health and behavioral consequences. Whether DES, UTIs, and VUR are etiologically related has important therapeutic implications. This study did not find an association between DES and either UTI or VUR diagnosed early in life.

Our results suggest that UTI before 2 years of age does not result in a higher likelihood of DES in school-aged children, a finding that differs from previous reports.[3] Methodological limitations of previous studies include retrospective identification of UTIs and a lack of a validated screening tool for DES. Given the similarity of UTI and dysfunctional elimination symptoms, a retrospective design may not be ideal. In contrast, we identified children with UTI prospectively and used a validated tool for identifying DES. However, because we only studied children with UTI diagnosed before 2 years of age, additional research is warranted to determine whether UTIs in older children are related to DES.

In our study, the presence or absence of DES was not associated with a history of VUR diagnosed early in life. The relationship between DES and VUR has been a subject of some interest. A first hypothesis is that VUR is almost always secondary to DES.[4,5] The evidence for the proposition that DES plays a primary role in the pathogenesis of VUR in both infants and older children comes from urodynamic studies that have shown high bladder voiding pressures in infants with VUR.[11,14] The clinical significance, natural history, and outcome of these high pressures, however, has not been established. A second hypothesis is that although in younger patients VUR is secondary to a congenitally short mucosal tunnel; in older children VUR is secondary to DES. The extent to which DES plays a role in initiating VUR in older children, however, has not been rigorously studied. A third hypothesis is that VUR and DES are causally independent conditions, which can coexist or exacerbate each other. The frequent coexistence of DES and VUR may result from selection bias, because children with both conditions are more likely to be detected and referred to specialists. Evidence suggesting that VUR is exacerbated by DES arises from studies that have found persistence of VUR in children with DES,[1,9] and the improvement of VUR by treating DES.[10] The exacerbation of one condition by the other, however, does not necessarily imply causality. In our study, conducted in a general pediatrics population, no association was apparent between DES and VUR diagnosed in the first 2 years of life,

suggesting that these two conditions may be etiologically unrelated.

This study adds to the literature on the epidemiology of DES in a general pediatric population. The relatively high prevalence (21%) of DES suggests that children frequently have abnormal voiding patterns, a finding consistent with previous reports.[2,3,12] A total of 20% of children in this study reported having had symptoms of DES in the past; the average duration of symptoms was 34 months, suggesting that abnormal voiding is persistent in many children. Only 2 children received specific treatment for DES, indicating that this condition is frequently underdiagnosed and undertreated by primary care providers.

The demographic and clinical factors associated with DES were investigated. Previous studies have suggested that early or late toilet training may be related to the development of DES.[13] In our study, there was no relationship between the age at the time of toilet training and DES. In the multivariate model, only two variables remained associated with DES: encopresis and high child vulnerability scores. Approximately 50% of children with DES had encopresis, underscoring the importance of addressing constipation in these children. Approximately 29% of children with DES had high child vulnerability scores. It seems possible that parents who consider their child to be vulnerable may be more likely to report symptoms of DES. Conversely, as with other chronic conditions, DES may lead parents to consider their child more vulnerable. The association between vulnerable child syndrome and DES, not previously reported, warrants further study. The events of September 11, 2001, provided us with an opportunity to assess the association of an acute stressful event with DES. No difference was apparent in the incidence of DES before and after the events of September 11.

Children with recurrent UTIs were likely to have DES, encopresis, or VUR, highlighting the importance of treating these conditions in the management of children with recurrent UTIs.

A limitation of our study, as of any nonrandomized study, is the possibility of selection bias. We attempted to minimize this by identifying a comparison cohort as similar as possible to the UTI cohort. We attempted to assess all factors potentially related to DES and adjusted for these in the analysis. The response rate in the comparison cohort is similar to published rates for mailed surveys. The high response rate in the UTI cohort was expected because we had previous long-term follow-up with those families. The prevalence of DES in both groups is similar to previously published survey data.[2,3] We are also limited in our ability to be certain whether children reporting voiding abnormalities truly represent children with DES given that we did not evaluate each child clinically. We used a validated questionnaire with excellent ability to discriminate between groups of children with and without DES when compared with clinical evaluation by an experienced urologist. Finally, the study conclusions remained unchanged when different questionnaire cutoffs and various combinations of questions were used.

CONCLUSIONS

DES is a common condition in a general pediatric population which is frequently underdiagnosed and undertreated. Neither UTI nor VUR diagnosed in early childhood were associated with an increased likelihood of DES later in life.

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