J Neurosurg Pediatrics 4:156–165, 2009

## Infection rates following initial cerebrospinal fluid shunt placement across pediatric hospitals in the United States

Clinical article

TAMARA D. SIMON, M.D., M.S.P.H.,<sup>1</sup> MATTHEW HALL, PH.D.,<sup>2</sup> JAY RIVA-CAMBRIN, M.D., M.Sc.,<sup>3</sup> J. ELAINE ALBERT, M.D.,<sup>4</sup> HOWARD E. JEFFRIES, M.D., M.B.A.,<sup>4</sup> BONNIE LAFLEUR, PH.D.,<sup>5</sup> J. MICHAEL DEAN, M.D., M.B.A.,<sup>6</sup> AND JOHN R. W. KESTLE, M.D., M.Sc.,<sup>3</sup> IN COLLABORATION WITH THE HYDROCEPHALUS CLINICAL RESEARCH NETWORK

Divisions of <sup>1</sup>Inpatient Medicine and <sup>6</sup>Critical Care, <sup>5</sup>Department of Pediatrics, University of Utah; <sup>3</sup>Division of Pediatric Neurosurgery, Department of Neurosurgery, University of Utah, Salt Lake City, Utah; <sup>2</sup>Child Health Corporation of America, Shawnee Mission, Kansas; and <sup>4</sup>Division of Critical Care, Department of Pediatrics, University of Washington, Seattle, Washington

*Object.* Reported rates of CSF shunt infection vary widely across studies. The study objective was to determine the CSF shunt infection rates after initial shunt placement at multiple US pediatric hospitals. The authors hypothesized that infection rates between hospitals would vary widely even after adjustment for patient, hospital, and surgeon factors.

*Methods*. This retrospective cohort study included children 0–18 years of age with uncomplicated initial CSF shunt placement performed between January 1, 2001, and December 31, 2005, and recorded in the Pediatric Health Information System (PHIS) longitudinal administrative database from 41 children's hospitals. For each child with 24 months of follow-up, subsequent CSF shunt infections and procedures were determined.

*Results*. The PHIS database included 7071 children with uncomplicated initial CSF shunt placement during this time period. During the 24 months of follow-up, these patients had a total of 825 shunt infections and 4434 subsequent shunt procedures. Overall unadjusted 24-month CSF shunt infection rates were 11.7% per patient and 7.2% per procedure. Unadjusted 24-month cumulative incidence rates for each hospital ranged from 4.1 to 20.5% per patient and 2.5–12.3% per procedure. Factors significantly associated with infection (p < 0.05) included young age, female sex, African-American race, public insurance, etiology of intraventricular hemorrhage, respiratory complex chronic condition, subsequent revision procedures, hospital volume, and surgeon case volume. Malignant lesions and trauma as etiologies were protective. Infection rates for each hospital adjusted for these factors decreased to 8.8–12.8% per patient and 1.4–5.3% per procedure.

*Conclusions.* Infections developed in > 11% of children who underwent uncomplicated initial CSF shunt placements within 24 months. Patient, hospital, and surgeon factors contributed somewhat to the wide variation in CSF shunt infection rates across hospitals. Additional factors may contribute to variation in CSF shunt infection rates between centers, but further study is needed. Benchmarking and future prospective multicenter studies of CSF shunt infection will need to incorporate these and other patient, hospital, and surgeon factors. (*DOI: 10.3171/2009.3.PEDS08215*)

# KEY WORDS•cerebrospinal fluid hydrocephalus•neurosurgeryinfection•epidemiology

EREBROSPINAL fluid shunt placement is the mainstay of hydrocephalus treatment.<sup>24</sup> While allowing children with hydrocephalus to avoid further brain injury, CSF shunts can also be associated with new and chronic surgical and medical problems.<sup>41</sup> Malfunction is frequent,<sup>4,6,7,23</sup> and with each revision the cumulative risk of CSF shunt infection rises for the patient.<sup>21,29</sup>

Infections are frequent complications of CSF shunt placement, and infection rates vary widely from study to study. Differences in reported rates are in part related to differences in study design including numerators and denominators,<sup>14,19,20</sup> shunt infection definition,<sup>5,33,42,45</sup> and duration of surveillance for infection.<sup>17,43</sup> Although differ-

J Neurosurg: Pediatrics / Volume 4 / August 2009

*Abbreviations used in this paper:* CCC = complex chronic condition; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification; IVH = intraventricular hemorrhage; PHIS = Pediatric Health Information System.

ences in study design account for some variation between studies, variation in infection rates may also be the result of patient, hospital, and/or surgeon factors. Patient factors considered in association with CSF shunt infection include chronological age,<sup>5,8,12,13,21,26,30,33,35–37,42</sup> gestational age,<sup>8,11,29,30</sup> postconceptional age,<sup>27</sup> sex,<sup>11,26,27,30,37</sup> birth weight,<sup>8,11</sup> weight at surgery,<sup>27</sup> indication for shunt placement including myelomeningocele and IVH,<sup>11,12,27,30,33,63,7,39,42</sup> comorbidities,<sup>12,27,37</sup> and length of hospital stay prior to shunt placement.<sup>27</sup> The results of the few multicenter studies of CSF shunt infection conducted suggest that hospital factors (hospital and its case volume<sup>9</sup>) and surgeon factors (including surgeon, experience, and his/her case volume,<sup>5,9,10,32,45</sup> and the time of year<sup>25</sup> as a reflection of resident surgeon experience) also contribute to CSF shunt infection.

The goal of this study was to better understand variations in CSF shunt infection rates between hospitals after applying a consistent definition of CSF shunt infection in a database containing administrative and clinical data from 41 children's hospitals. The specific objectives were to 1) determine CSF shunt infection rates after initial shunt placement at multiple pediatric hospitals; 2) determine patient, hospital, and surgeon factors associated with shunt infection; and 3) determine shunt infection rates after adjustments for significant patient, hospital, and surgeon factors. We hypothesized that infection rates between hospitals would vary widely, even after adjustment for patient, hospital, and surgeon factors, meaning that some, but not all, of the variation seen between hospitals is attributable to those factors.

#### Methods

#### Study Design and Data Source

We conducted a retrospective cohort study using the PHIS database. The PHIS database was developed by the Child Health Corporation of America and contains administrative and limited clinical data on all discharges from member hospitals (41 not-for-profit free-standing children's hospitals in the US). The data warehouse function for the database is managed by Thomson Reuters, and data are subjected to several reliability and validity checks before incorporation into the database. Patients can be identified using consistently encrypted medical record numbers, allowing cross-linking of encounters over time. The study was reviewed and exempted from annual review by the Institutional Review Boards at the University of Utah and Children's Hospital and Regional Medical Center.

#### Study Population

Children 0–18 years of ages who underwent initial CSF shunt placement with a discharge date between January 1, 2001, and December 31, 2005, were identified from all hospitals in PHIS. To identify children who underwent initial CSF shunt placement, we used an iterative query based on ICD-9-CM procedure and diagnosis codes (Fig. 1). This query uses primarily procedure codes so as to overcome the limitation of less specific diagnosis coding in administrative databases such as the PHIS. The query

is designed to obtain uncomplicated initial CSF shunt placements, eliminating children who may have been infected elsewhere from the comparison of infection rates between centers. After the initial analysis suggested that 88% of CSF shunt infections developed within 24 months of the initial CSF shunt placement, we limited the study population to children with 24 months of follow-up (7071 children).

#### Outcome Variables

The primary outcome variable was a subsequent admission with the ICD-9-CM discharge diagnosis code for shunt infection (996.63) through December 31, 2006. We conducted an independent chart review at a single institution, confirming that 92% (11 of 12) of that institution's CSF shunt infection admissions met National Nosocomial Infection Surveillance criteria for CSF shunt infection.<sup>1</sup> A secondary outcome variable was subsequent CSF shunt revision(s). Each patient's shunt revision procedures were identified by subsequent admissions with the ICD-9-CM discharge procedure codes for shunt removal (02.43) and shunt placement (02.3), or shunt replacement (02.42, 54.95), or the ICD-9-CM discharge diagnosis code for shunt malfunction (996.2).

#### Predictor Variable and Covariates

The main predictor variable of CSF shunt infection rate was hospital. Covariates available in the PHIS database include those patient, hospital, and surgeon factors shown in Table 1. Patient age was categorized a priori in groups relevant to the diagnosis and management of hydrocephalus. Race/ethnicity was categorized into 5 mutually exclusive designations (non-Latino white, non-Latino black, Latino, Asian, and Other). Payer was categorized by public (Medicare, Medicaid, Title V, other government payer), private (Blue Cross, other insurance company, HMO), or other (self pay, no charge). Indication for shunt placement was determined after review of the ICD-9-CM diagnosis codes that occurred at a frequency of  $\geq 1\%$  of the study population (the top 200 diagnosis codes). We assigned etiology at the time of initial shunt placement with the concurrent assignment of the following diagnosis codes: IVH (772.1x), myelomeningocele (653.7, 655.0, 741.x), CNS tumor (191-194, 198.3-198.4, 225.0-2 and 225.8-9, 237.0-1 and 237.5-7, 239.6), meningitis (320-322, 326), and trauma (767.4, 851.xx-854.xx, 995.55). The indications were neither mutually exclusive nor did they describe the entire population. Comorbidities were grouped into CCC, an ICD-9-CM diagnosis code-based system of classifying pediatric conditions associated with morbidity and mortality.15,16 We redefined the neuromuscular and malignancy categories to exclude indications for CSF shunts as previously described.<sup>41</sup> Distal shunt location was categorized by the assignment of any ICD-9-CM procedure code into ventriculoperitoneal (02.34) and other (any other 02.3x). Case mix severity, based on a patient's All-Patient Refined Diagnosis-Related Group (version 20, 3 M-Corp) and severity level, reflects both patient and hospitalization complexity. Categorization of hospital volume was done a priori, and surgeon volume was done after examination

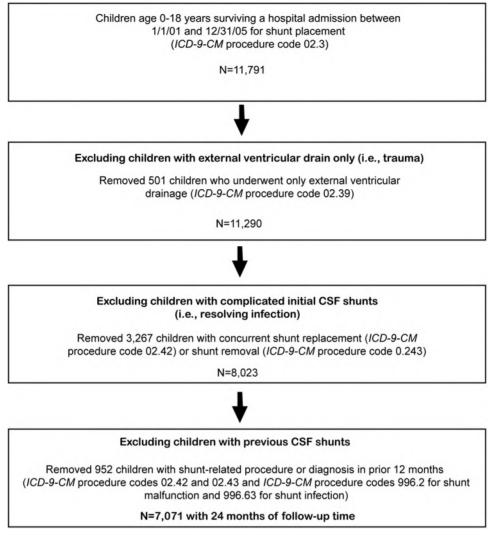


Fig. 1. Flow chart showing the PHIS database study cohort after excluding children with external ventricular drain placement only, complicated initial shunts, and previous CSF shunts.

of univariate distribution. We also considered the patient's CSF shunt revision procedures (categorized into none, 1, and  $\geq$  2) subsequent to initial placement but prior to first CSF shunt infection as a risk factor for infection.

#### Statistical Analyses

We first performed univariate analysis to describe our study population (Table 1). Next, we reported the proportion of patients in whom CSF shunt infections developed within 24 months after the initial CSF shunt placement at each PHIS hospital (that is, the cumulative incidence rates of CSF shunt infection aggregated by hospital). Because there was a > 60-fold difference between hospitals in the number of patients included, we report infection rates for the hospitals with adequate volume. In Fig. 2 we provide unadjusted 24-month infection rates for hospitals with at least 50 procedures performed during the study period (there were 37 hospitals with > 50 initial shunt placements and 39 hospitals with > 50 total shunt procedures).

Next we examined the association of patient, hospital, and surgeon factors with CSF shunt infection in bivariate

analysis using chi-square tests (Table 2). We then used generalized linear models to generate adjusted rates of CSF shunt infection per patient (rates per hospital adjusted for significant patient, surgeon, and hospital factors) and per procedure. Generalized linear modeling allows regression of Poisson distributed data, such as cumulative rates, after transformation by a link function (log link function for Poisson models). Again we report adjusted 24-month infection rates for hospitals with adequate volume (Fig. 3). Per patient rates were adjusted for hospital, sex, race/ethnicity, payer, and numbers of revisions; per procedure rates were adjusted for hospital, age, sex, race/ethnicity, IVH, CNS tumor, meningitis etiologies, the presence of cardiovascular, respiratory, and congenital CCCs, length of stay, shunt type, and case mix index.

Finally, we performed bivariate analysis of infection odds (Table 3). Significant predictors of CSF shunt infection (p < 0.10) were evaluated in a multivariable analysis. Generalized estimating equations were used for multivariable analysis to allow for a hierarchical structure (mixture of hospital-level and surgeon-level) covariates.<sup>44</sup>

## TABLE 1: Summary of characteristics of the 7071-patient study population $\ensuremath{^*}$

Characteristic	No. of Patients (%)
age	
≤30 days	2009 (28.4)
1–6 mos	1736 (24.6)
6–48 mos	1823 (25.8)
≥48 mos	1503 (21.3)
sex	
male	3982 (56.3)
female	3089 (43.7)
race/ethnicity*	
non-Latino white	3668 (54.8)
non-Latino black	1213 (18.0)
Latino	1067 (15.9)
Asian	99 (1.5)
other	657 (9.8)
payer‡	
public	3234 (45.7)
private	2313 (32.7)
other	1523 (21.5)
indication for shunt placement	
IVH	631 (8.9)
myelomeningocele	992 (14.0)
CNS tumor	933 (13.2)
meningitis	167 (2.4)
trauma	192 (2.7)
presence of CCC(s)	
neuromuscular	514 (7.3)
cardiovascular	739 (10.5)
respiratory	460 (6.5)
renal	157 (2.2)
gastrointestinal	37 (0.5)
hematological	36 (0.5)
metabolic	46 (0.7)
other congenital/genetic	505 (7.1)
malignancy	317 (4.5)
LOS prior to initial shunt placement	
0–2 days	2410 (34.1)
3–7 days	1849 (26.1)
8–14 days	1103 (15.6)
≥15 days	1709 (24.2)
distal shunt location	
ventriculoperitoneal	6942 (98.2)
other	129 (1.8)
case mix index at initial CSF shunt placement	· ·
low	4892 (69.2)
moderate	1153 (16.3)
high	1026 (14.5)
	(continued)

# TABLE 1: Summary of characteristics of the 7071-patient study population\* (continued)

Characteristic	No. of Patients (%)
revision admissions following initial CSF shu placement	nt
none	4517 (63.9)
1	1516 (21.4)
≥2	1038 (14.7)
hospital volume (initial CSF shunt placement yr)	rs/
1–20	360 (5.1)
21-40	1982 (28.0)
41–60	3156 (44.6)
≥61	1573 (22.2)
surgeon volume (initial CSF shunt placement yr)	ts/
<10	2042 (28.9)
11–20	2564 (36.3)
21–30	1379 (19.5)
>30	1086 (15.4)
season of initial CSF shunt placement	
spring	1928 (27.3)
summer	1882 (26.6)
fall	1570 (22.2)
winter	1691 (23.9)

\* LOS = length of stay.

† Race/ethnicity data are missing in 347 children (306 without infection, 41 with infection).

‡ Insurance data are missing in 1 child.

All statistical analyses were performed using commercially available software (SAS version 9.1, SAS Institute, Inc.), and probability values < 0.05 were considered statistically significant.

#### Results

For the time period we specified, the PHIS database contained information obtained in 7071 children with uncomplicated initial CSF shunt placements and 24 months of follow-up (Fig. 1). During the follow-up period, this group had 825 first CSF shunt infections and a total of 4434 subsequent CSF shunt revision procedures. The overall unadjusted 24-month CSF shunt infection rates were 11.7% per patient (825 of 7071 patients) and 7.2% per procedure (825 of 11,505 procedures). Description of the patient, hospital, and surgeon factors for the study population are shown in Table 1.

The unadjusted 24-month infection rates aggregated by hospital ranged from 4.1 to 20.5% per patient. (Fig. 2) The unadjusted 24-month infection rates aggregated by hospital ranged from 2.5 to 12.3% per procedure (data not shown).

Patient factors that were significantly associated with infection in bivariate analysis in this cohort included young age, African-American race/ethnicity, public insurance,

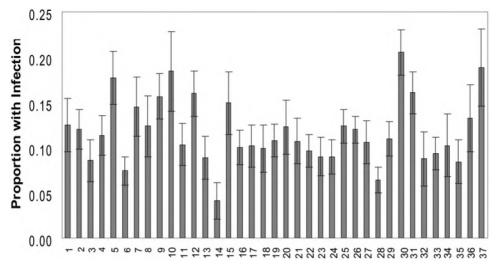


Fig. 2. Bar graph showing variation in unadjusted 24-month cumulative infection incidence rates per patient, aggregated by hospital in 6979 patients. *Error bars* indicate SE.

etiology of IVH, respiratory CCC, and subsequent revision procedures (Table 2). Female sex and Asian race/ethnicity were associated with infection, but not as strongly. Malignant lesions, including CNS tumor and malignancy CCC, and trauma etiology were protective. In addition, lower hospital and surgeon volumes were associated with CSF shunt infection.

When infection rates for each hospital were adjusted for significant factors, the range of 24-month infection rates decreased to 8.8-12.8% per patient (Fig. 3) and 1.4-5.3% per procedure (data not shown).

Factors that remained significantly associated with infection in multivariable analysis included young age, African-American race/ethnicity, Asian race/ethnicity, public insurance, subsequent revision procedure(s), and to a lesser degree female sex (Table 3). Hospital and surgeon factors tested did not remain significantly associated with infection. Interactions between age and other covariates and surgical volume and other covariates were tested,<sup>4</sup> and none were significant.

#### Discussion

In this large, multicenter longitudinal cohort of children undergoing uncomplicated initial CSF shunt placement, > 11% of children were readmitted within 24 months for subsequent CSF shunt infection. About 35% of these children were readmitted within 24 months for subsequent CSF shunt revisions, generating an overall infection rate per procedure of 7%. Infection rates aggregated by hospital ranged widely—from 4.1 to 17.4% per patient and 2.5–12.3% per procedure.

Patient factors that were significantly associated with infection in this cohort included young age, female sex, African-American race/ethnicity, Asian race/ethnicity, public insurance, and subsequent revision procedures. Lower hospital volumes and particularly lower surgeon volumes were associated with CSF shunt infections in bivariate but not multivariable analysis.

When infection rates for each hospital were adjusted

for significant factors, the range of 24-month infection rates decreased to 8.8-12.8% per patient and 1.4-5.3% per procedure. Some, but not all, of the variation in CSF shunt infection rates between hospitals was attributable to those factors.

#### Infection Rates

Published rates of CSF shunt infection vary widely from study to study, due in part to differences in study design including rate numerators and denominators,<sup>14,19,20</sup> definition of shunt infection, 5,33,42,45 and duration of surveillance.<sup>17,43</sup> In this study we were able to overcome 2 of these limitations, rate numerators and denominators and duration of surveillance, by applying a definition of CSF shunt infection (the discharge diagnosis code of CSF shunt infection confirmed by chart review at a single hospital) in a database containing administrative and clinical data from 41 children's hospitals. Although our study population is so uniquely constructed that there is no relevant prior literature to cite, our findings are not inconsistent with prior work given our relatively uncomplicated study patient population. This study demonstrated an overall CSF shunt infection rate per patient of 11.7% with a range of 4.1–20.5%. Although few studies report infection rates per patient, earlier reports of such infection rates range from 6.5 to 23.5%.<sup>3,5,10,13,18,23,42</sup> This study also demonstrated an overall CSF shunt infection rate per procedure of 7.2% with a range of 2.5-12.3%. The majority of studies report CSF shunt infection rates per procedure, and these rates are generally 8–10% in recent series but range from 0 to 35%.9,22,27,29,30,33,34,36,38-40,45 This cohort's 24-month shunt survival rate of 65% is higher than previously reported,<sup>4,23</sup> and likely reflects the fact that initial CSF shunts were uncomplicated and did not include children with surgical interventions such as reservoirs prior to shunt placement.

#### Factors Associated With CSF Shunt Infection

We were able to test the association of several patient factors with CSF shunt infection. As have authors of earlier studies, we found an association between CSF shunt

TABLE 2: Comparison of p	population with and without infection at 24 months
--------------------------	--

	No. of Pati	ents (%)
Characteristic	W/o Infection (6246 patients)	W/ Infection (825 patients
age (p < 0.001)		
≤30 days	1724 (27.6)	285 (34.5)
1–6 mos	1510 (24.2)	226 (27.4)
6–48 mos	1624 (26.0)	199 (24.1)
≥48 mos	1388 (22.2)	115 (13.9)
sex (p = 0.039)		
male	3545 (56.8)	437 (53.0)
female	2701 (43.2)	388 (47.0)
race/ethnicity (p < 0.001)*		
non-Latino white	3292 (55.4)	396 (50.5)
non-Latino black	1015 (17.1)	198 (25.3)
Latino	964 (16.2)	103 (13.1)
Asian	82 (1.4)	17 (2.2)
other	587 (9.9)	70 (8.9)
payer (p = 0.003)+		,
public	2811 (45.0)	423 (51.3)
private	2071 (33.2)	242 (29.3)
other	1363 (21.8)	160 (19.4)
indication for shunt placement	1000 (2110)	100 (10.1)
IVH (p = 0.03)	541 (8.7)	90 (10.9)
myelomeningocele (p = $0.12$ )	891 (14.3)	101 (12.1)
CNS tumor ( $p = 0.005$ )	850 (13.6)	83 (10.1)
meningitis ( $p = 0.000$ )	142 (2.3)	25 (3.0)
trauma (p = 0.03)	179 (2.9)	13 (1.6)
presence of CCC(s)	110 (2.0)	10 (1.0)
neuromuscular ( $p = 0.39$ )	460 (7.4)	54 (6.5)
cardiovascular ( $p = 0.65$ )	649 (10.4)	90 (10.9)
respiratory ( $p = 0.01$ )	390 (6.2)	70 (8.5)
renal ( $p = 0.36$ )	135 (2.2)	22 (2.7)
gastrointestinal ( $p = 0.87$ )	33 (0.5)	4 (0.5)
hematological ( $p = 0.92$ )	32 (0.5)	4 (0.5)
metabolic ( $p = 0.12$ )	44 (0.7)	2 (0.2)
other congenital/genetic ( $p = 0.77$ )	444 (7.1)	61 (7.4)
malignancy ( $p = 0.05$ )	291 (4.7)	26 (3.2)
LOS prior to initial shunt placement ( $p = 0.54$ )	201 (4.7)	20 (0.2)
0-2 days	2147 (34.4)	263 (31.9)
3–7 days	1622 (26.0)	203 (31.5) 227 (27.5)
8–14 days	972 (15.6)	131 (15.9)
o−14 days ≥15 days	1505 (24.1)	204 (24.7)
distal shunt location ( $p = 0.41$ )	1303 (24.1)	204 (24.1)
ventriculoperitoneal	6135 (98.2)	807 (97.8)
other	111 (1.8)	18 (2.2)
case mix index at initial CSF shunt placement (p = 0.26)	111 (1.0)	10 (2.2)
low	4301 (68.9)	591 (71.6)
moderate	1031 (16.5)	122 (14.8)
high	914 (14.6)	112 (13.6)

(continued)

Characteristic	No. of Patients (%)	
	W/o Infection (6246 patients)	W/ Infection (825 patients)
revision admissions following initial CSF shunt placement (p < 0.001)		
none	4166 (66.7)	351 (42.5)
1	1318 (21.1)	198 (24.0)
≥2	762 (12.2)	276 (33.5)
hospital volume (initial CSF shunt placements/yr) (p = 0.005)		
1–20	314 (5.0)	46 (5.6)
21–40	1763 (28.2)	219 (26.5)
41–60	2747 (44.0)	409 (49.6)
≥61	1422 (22.8)	151 (18.3)
surgeon volume (initial CSF shunt placements/yr) (p = 0.03)		
<10	1786 (28.6)	256 (31.0)
11–20	2244 (35.9)	320 (38.8)
21–30	1236 (19.8)	143 (17.3)
>30	980 (15.7)	106 (12.8)
season of initial CSF shunt placement ( $p = 0.66$ )		
spring	1697 (27.2)	231 (28.0)
summer	1675 (26.8)	207 (25.1)
fall	1390 (22.3)	180 (21.8)
winter	1484 (23.8)	207 (25.1)

#### TABLE 2: Comparison of population with and without infection at 24 months (continued)

\* Race/ethnicity data are missing in 347 children (306 without infection, 41 with infection).

† Insurance data are missing in 1 child.

infection and younger chronological age.<sup>8,13,21,30,35,37,42</sup> as well as revision procedures.<sup>2,21,30,42</sup> Like previous work, our study found no association between CSF shunt infection and length of stay prior to shunt placement.<sup>27</sup>

In contrast to earlier studies,<sup>11,26,27,30,37</sup> ours found a small but statistically significant association between CSF shunt infection and female sex, both African-American and Asian race/ethnicity, and public insurance. These findings were seen in both bivariate and multivariable analyses. The effect sizes for female sex and public insurance were fairly small. The associations of African-American and Asian race/ethnicity with CSF shunt infection appear more significant and warrant further study. We may have had these findings because our population was substantially larger than that of most previous CSF shunt infection studies.

We were able to examine the association between CSF shunt infection and several different indications for shunt placement including IVH, myelomeningocele, CNS tumor, and meningitis. Because we limited our study population to uncomplicated initial CSF shunt placements, we had a very small proportion of children with IVH (8.9%) and few with trauma (2.7%). Of these indications, our study found

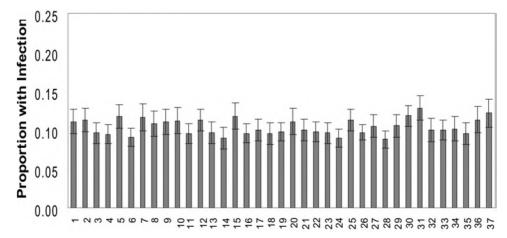


Fig. 3. Bar graph of the variation in adjusted 24-month cumulative infection incidence rates per patient, aggregated by hospital in 6979 patients. Rates were adjusted for hospital, sex, race/ethnicity, payer, and number of revisions. *Error bars* indicate SE.

#### TABLE 3: Odds of first infection\*

	OR (95% CI)	
Characteristic	Unadjusted	Adjusted
age		
≤30 days	2.0 (1.6-2.5)	1.6 (1.2–2.1)
1–6 mos	1.8 (1.4–2.3)	1.5 (1.1–2.0)
6–48 mos	1.5 (1.2–1.9)	1.5 (1.1–1.9)
≥48 mos	referent	referent
sex		
male	referent	referent
female	1.2 (1.0-1.3)	1.2 (1.0-1.4)
race/ethnicity	, , , , , , , , , , , , , , , , , , ,	, ,
non-Latino white	referent	referent
non-Latino black	1.6 (1.3-2.0)	1.5 (1.2–1.9)
Latino	0.9 (0.7-1.1)	0.9 (0.7–1.1)
Asian	1.7 (1.0-2.9)	1.7 (1.0-3.0)
other	1.0 (0.8–1.3)	0.9 (0.7–1.2)
payer	· · · ·	, ,
public	1.3 (1.1-1.5)	1.3 (1.1–1.6)
private	referent	referent
other	1.0 (0.8–1.2)	1.0 (0.8–1.3)
indication for shunt placement	· · · ·	, ,
IVH .	1.3 (1.0-1.6)	0.9 (0.7–1.2)
myelomeningocele	0.8 (0.7–1.0)	, ,
CNS tumor	0.7 (0.6-0.9)	1.1 (0.8–1.5)
meningitis	1.3 (0.9–2.1)	. ,
trauma	0.5 (0.3-1.0)	0.7 (0.4–1.3)
presence of complex chronic condi-	, ,	. ,
tion(s)		
neuromuscular	0.9 (0.7–1.2)	
cardiovascular	1.1 (0.8–1.3)	
respiratory	1.4 (1.1–1.8)	1.1 (0.8–1.5)
renal	1.2 (0.8–2.0)	
gastrointestinal	0.9 (0.3–2.6)	
hematological	0.9 (0.3–2.7)	
metabolic	0.3 (0.1–1.4)	
other congenital/genetic	1.0 (0.8–1.4)	
malignancy	0.7 (0.4–1.0)	0.8 (0.5–1.2)
LOS prior to initial shunt placement		
0–2 days	referent	
3–7 days	1.1 (0.9–1.4)	
8-14 days	1.1 (0.9–1.4)	
≥15 days	1.1 (0.9–1.3)	
distal shunt location		
ventriculoperitoneal	referent	
other	1.2 (0.7–2.0)	
case mix index at initial CSF shunt placement		
low	referent	
moderate	0.9 (0.7–1.1)	
high	0.9 (0.7–1.1)	

(continued)

#### TABLE 3: Odds of first infection\* (continued)

	OR (95% CI)	
Characteristic	Unadjusted	Adjusted
revision admissions after initial CSF shunt placement		
none	referent	referent
1	1.8 (1.5–2.1)	1.7 (1.4–2.1)
≥2	4.3 (3.6–5.1)	4.2 (3.5–5.1)
hospital volume (initial CSF shunt place- ments/yr)		
1–20	1.4 (1.0-2.0)	1.3 (0.9–1.9)
21–40	1.2 (0.9–1.5)	1.0 (0.8–1.3)
41–60	1.4 (1.2–1.7)	1.2 (1.0–1.5)
≥61	referent	referent
surgeon volume (initial CSF shunt place- ments/yr)		
<10	1.3 (1.0–1.7)	1.2 (0.9–1.5)
11–20	1.3 (1.0–1.7)	1.1 (0.8–1.4)
21–30	1.1 (0.8–1.4)	0.9 (0.7–1.2)
>30	referent	referent
season of initial CSF shunt placement		
spring	1.0 (0.8–1.2)	
summer	0.9 (0.7–1.1)	
fall	0.9 (0.8–1.1)	
winter	referent	

\* Values shaded in gray are statistically significant (p < 0.05). Only covariates with p < 0.10 were included in the multivariate model.

an association of IVH with infection,<sup>11,36,42</sup> and negative associations with CNS tumor and trauma. These associations did not remain significant in multivariable analysis.

By using CCCs, we were able to examine comorbidities more extensively than has been done in earlier studies.<sup>12,27,37</sup> We found an association between respiratory CCC and an intriguing protective effect of malignancy CCC in the bivariate analysis. Neither association remained significant in the multivariable analysis.

We were also able to test several hospital and surgeon factors. As in earlier work,<sup>9</sup> we did find an association between CSF shunt infection and both hospital and surgeon volume. These associations did not persist in the multivariable analysis. We were unable to test either individual surgeon<sup>5,9,10,32,45</sup> or his/her experience level.<sup>9,10</sup> Unlike earlier work,<sup>25</sup> however, we did not find an association between CSF shunt infection and time of year.

#### Study Limitations

The major limitation of this study is that of the ecological fallacy:<sup>31</sup> that is, we cannot infer an individual patient's risk of infection based on the treating hospital's infection rate. In addition, data available from administrative datasets such as PHIS is limited. Although we can use some patient, hospital, and surgeon factors as covariates, many factors of clinical interest (such as gestational age, postconceptional age, birth weight, weight at surgery, individual surgeon, surgeon experience, and modifiable surgical decisions such as the use of prophylactic antibiotics) are not available. Some of the available covariates (such as indication for initial shunt and CCCs) are problematic given their dependence on ICD-9-CM diagnosis codes, which are less reliable than procedure codes.<sup>28</sup> For example, we cannot assess the association of aqueductal stenosis with CSF shunt infection. The restriction of our study population to only uncomplicated initial CSF shunt placements (due to ICD-9-CM coding) resulted in a relatively low-risk population, but allowed us to standardize comparisons across hospitals. Future prospective multicenter studies of CSF shunt infections will permit us to improve data collection for these and other risk factors. permitting us to overcome the limitations associated with the retrospective use of administrative data when comparing infection rates between centers. The study design assumes a patient is seen for follow-up at the same hospital where his shunt was placed, which may not be true; we assumed equal rates of drop-out across hospitals.

#### Infection Rates Following Adjustment

The new and most striking finding of this study was the demonstration of the degree to which patient, hospital, and surgeon factors contributed to the wide variation in CSF shunt infection rates across hospitals. Although unadjusted infection rates per patient for each hospital ranged from 4.1 to 20.5%, adjustment decreased the range of infection rates to 8.8–12.8%. Unadjusted infection rates per procedure for each hospital ranged from 2.5 to 12.3%, and adjusted rates ranged from 1.4 to 5.3% per procedure. Some, but not all, of the variation in CSF shunt infection rates between hospitals was attributable to differences in these patient, hospital, and surgeon factors between hospitals.

Although we were able to use some patient, hospital, and surgeon factors as covariates when comparing between centers, there are many factors of clinical interest that we were either not able to assess or not able to assess completely. These included factors previously considered in association with infection (such as gestational age, postconceptional age, birth weight, weight at surgery, indication for initial CSF shunt placement, comorbidities, individual hospital, individual surgeon, and surgeon experience); modifiable surgical decisions such as double gloving and the use of prophylactic antibiotics; and theoretical risk factors such as patient immune function and/ or bacterial load at the time of initial shunt placement. To allow for accurate comparisons between centers, future studies (such as benchmarking and/or future prospective multicenter studies of CSF shunt infection) must improve data collection to allow for consideration of these and other potential risk factors.

#### Conclusions

In the present study, we examined infection rates in a large longitudinal cohort across several US hospitals using a standard CSF shunt infection rate numerator and denominator, definition, and duration of surveillance. An infection develops within 24 months in > 11% of children (4.1–20.5%) who undergo an uncomplicated initial CSF

shunt placement. Patient, hospital, and surgeon factors such as patient age, race/ethnicity, insurance, and number of shunt revisions, hospital volume, and surgeon volume contribute somewhat to the wide variation in CSF shunt infection rates across hospitals. Additional factors may contribute to variation in CSF shunt infection rates between centers, but further study is needed. Future work comparing CSF shunt infection between centers, such as benchmarking and future prospective multicenter studies, must take into account these factors.

#### Disclosure

Tamara D. Simon is a Primary Children's Medical Center Foundation Scholar, and her work is supported by a Primary Children's Medical Center Innovative Research Grant and in part by the Children's Health Research Center, University of Utah. None of the authors have financial agreements and/or other involvements, nor conflict(s) of interest, to disclose.

#### Acknowledgments

Tamara D. Simon is responsible for study conception and design, analysis and interpretation of data, and drafting of the manuscript; Matthew Hall had full access to the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis; all other authors (J.R.C., J.E.A., H.E.J., B.L., J.M.D., and J.R.W.K.) contributed to the study conception and design, analysis and interpretation of data, and critical revision of the manuscript.

The authors appreciate the efforts of their colleagues Jay Berry and Susan Bratton in facilitating this multiinstitutional effort, as well as Charles A. Cowan and Anthony M. Avellino for facilitating their access to PHIS. The authors thank the Division of Inpatient Medicine for its support and feedback; Mike Malowney for critical logistical support; and Stephan J. Nemeth for his valuable feedback.

The Hydrocephalus Clinical Research Network consists of: John Kestle, Jay Riva-Cambrin, Tamara Simon, Marion Walker, Tracey Bach, Marcie Langley, Jeff Yearley, Richard Holubkov of the Primary Children's Medical Center/University of Utah, Salt Lake City, Utah; Abhaya Kulkarni, James M. Drake, Lindsay O'Connor of the Hospital for Sick Children/University of Toronto, Canada; Jerry Oakes, John Wellons, Courtney Shannon of the Children's Hospital of Alabama/University of Alabama at Birmingham, Alabama; and William Whitehead, Thomas Luerssen, Sheila Nguyen of the Texas Children's Hospital/Baylor College of Medicine, Houston, Texas.

#### References

- Albert JE, Simon TD, Hall M, Kestle J, Jeffries HE: Improved identification of pediatric neurosurgical procedure infections. E-PAS2008 62:3792.6, 2008 (Abstract)
- 2. Albright AL, Pollack IF, Adelson PD, Solat JJ: Outcome data and analysis in pediatric neurosurgery. **Neurosurgery 45**: 101–106, 1999
- 3. Amacher AL, Wellington J: Infantile hydrocephalus: long-term results of surgical therapy. **Childs Brain 11:2**17–229, 1984
- Berry JG, Hall MA, Sharma V, Goumnerova L, Slonim AD, Shah SS: A multi-institutional, 5-year analysis of initial and multiple ventricular shunt revisions in children. Neurosurgery 62:445–454, 2008
- Borgbjerg BM, Gjerris F, Albeck MJ, Borgesen SE: Risk of infection after cerebrospinal fluid shunt: an analysis of 884 first-time shunts. Acta Neurochir (Wien) 136:1-7, 1995
- Browd SR, Gottfried ON, Ragel BT, Kestle JR: Failure of cerebrospinal fluid shunts: part II: overdrainage, loculation, and abdominal complications. Pediatr Neurol 34:171–176, 2006
- Browd SR, Ragel BT, Gottfried ON, Kestle JR: Failure of cerebrospinal fluid shunts: part I: obstruction and mechanical failure. Pediatr Neurol 34:83–92, 2006

- Bruinsma N, Stobberingh EE, Herpers MJ, Vles JS, Weber BJ, Gavilanes DA: Subcutaneous ventricular catheter reservoir and ventriculoperitoneal drain-related infections in preterm infants and young children. Clin Microbiol Infect 6:202–206, 2000
- 9. Cochrane DD, Kestle J: Ventricular shunting for hydrocephalus in children: patients, procedures, surgeons and institutions in English Canada, 1989–2001. Eur J Pediatr Surg 12 (1 Suppl): S6–S11, 2002
- Cochrane DD, Kestle JR: The influence of surgical operative experience on the duration of first ventriculoperitoneal shunt function and infection. Pediatr Neurosurg 38:295–301, 2003
- Dallacasa P, Dappozzo A, Galassi E, Sandri F, Cocchi G, Masi M: Cerebrospinal fluid shunt infections in infants. Childs Nerv Syst 11:643–649, 1995
- Davis SE, Levy ML, McComb JG, Masri-Lavine L: Does age or other factors influence the incidence of ventriculoperitoneal shunt infections? Pediatr Neurosurg 30:253–257, 1999
- 13. Di Rocco C, Marchese E, Velardi F: A survey of the first complication of newly implanted CSF shunt devices for the treatment of nontumoral hydrocephalus. Cooperative survey of the 1991–1992 Education Committee of the ISPN. Childs Nerv Syst 10:321–327, 1994
- Fan-Havard P, Nahata MC: Treatment and prevention of infections of cerebrospinal fluid shunts. Clin Pharm 6:866–880, 1987
- Feudtner C, Christakis DA, Connell FA: Pediatric deaths attributable to complex chronic conditions: a population-based study of Washington State, 1980–1997. Pediatrics 106:205– 209, 2000
- Feudtner C, Hays RM, Haynes G, Geyer JR, Neff JM, Koepsell TD: Deaths attributed to pediatric complex chronic conditions: national trends and implications for supportive care services. Pediatrics 107:E99, 2001
- Filka J, Huttova M, Tuharsky J, Sagat T, Kralinsky K, Krcmery V Jr: Nosocomial meningitis in children after ventriculoperitoneal shunt insertion. Acta Paediatr 88:576–578, 1999
- Frykberg T, Olden L: Infection as a cause of peritoneal catheter dysfunction in ventriculo-peritoneal shunting in children. Z Kinderchir 38 (2 Suppl):84–86, 1983
- 19. Gardner P, Leipzig T, Phillips P: Infections of central nervous system shunts. Med Clin North Am 69:297–314, 1985
- Gardner P, Leipzig TJ, Sadigh M: Infections of mechanical cerebrospinal fluid shunts. Curr Clin Top Infect Dis 9:185– 214, 1988
- George R, Leibrock L, Epstein M: Long-term analysis of cerebrospinal fluid shunt infections. A 25-year experience. J Neurosurg 51:804–811, 1979
- Griebel R, Khan M, Tan L: CSF shunt complications: an analysis of contributory factors. Childs Nerv Syst 1:77–80, 1985
- Kestle J, Drake J, Milner R, Sainte-Rose C, Cinalli G, Boop F, et al: Long-term follow-up data from the Shunt Design Trial. Pediatr Neurosurg 33:230–236, 2000
- Kestle JR: Pediatric hydrocephalus: current management. Neurol Clin 21:883–895, vii, 2003
- 25. Kestle JR, Cochrane DD, Drake JM: Shunt insertion in the summer: is it safe? J Neurosurg 105:165–168, 2006
- Kontny U, Hofling B, Gutjahr P, Voth D, Schwarz M, Schmitt HJ: CSF shunt infections in children. Infection 21:89–92, 1993
- Kulkarni AV, Drake JM, Lamberti-Pasculli M: Cerebrospinal fluid shunt infection: a prospective study of risk factors. J Neurosurg 94:195–201, 2001
- McCarthy EP, Iezzoni LI, Davis RB, Palmer RH, Cahalane M, Hamel MB, et al: Does clinical evidence support ICD-9-CM diagnosis coding of complications? Med Care 38:868–876, 2000

- 29. McGirt MJ, Leveque JC, Wellons JC III, Villavicencio AT, Hopkins JS, Fuchs HE, et al: Cerebrospinal fluid shunt survival and etiology of failures: a seven-year institutional experience. Pediatr Neurosurg 36:248–255, 2002
- McGirt MJ, Zaas A, Fuchs HE, George TM, Kaye K, Sexton DJ: Risk factors for pediatric ventriculoperitoneal shunt infection and predictors of infectious pathogens. Clin Infect Dis 36:858-862, 2003
- Morgenstern H: Uses of ecologic analysis in epidemiologic research. Am J Public Health 72:1336–1344, 1982
- Nelson JD: Cerebrospinal fluid shunt infections. Pediatr Infect Dis 3:S30–S32, 1984
- Odio C, McCracken GH Jr, Nelson JD: CSF shunt infections in pediatrics. A seven-year experience. Am J Dis Child 138: 1103–1108, 1984
- Piatt JH Jr, Carlson CV: A search for determinants of cerebrospinal fluid shunt survival: retrospective analysis of a 14-year institutional experience. Pediatr Neurosurg 19:233–242, 1993
- Pople IK, Bayston R, Hayward RD: Infection of cerebrospinal fluid shunts in infants: a study of etiological factors. J Neurosurg 77:29–36, 1992
- Quigley MR, Reigel DH, Kortyna R: Cerebrospinal fluid shunt infections. Report of 41 cases and a critical review of the literature. Pediatr Neurosci 15:111–120, 1989
- Renier D, Lacombe J, Pierre-Kahn A, Sainte-Rose C, Hirsch JF: Factors causing acute shunt infection. Computer analysis of 1174 operations. J Neurosurg 61:1072–1078, 1984
- Ronan A, Hogg GG, Klug GL: Cerebrospinal fluid shunt infections in children. Pediatr Infect Dis J 14:782–786, 1995
- Schoenbaum SC, Gardner P, Shillito J: Infections of cerebrospinal fluid shunts: epidemiology, clinical manifestations, and therapy. J Infect Dis 131:543–552, 1975
- Shurtleff DB, Stuntz JT, Hayden PW: Experience with 1201 cerebrospinal fluid shunt procedures. Pediatr Neurosci 12:49–57, 1985
- 41. Simon TD, Riva-Cambrin J, Srivastava R, Bratton SL, Dean JM, Kestle JR: Hospital care for children with hydrocephalus in the United States: utilization, charges, comorbidities, and deaths. J Neurosurg Pediatr 1:131–137, 2008
- 42. Vinchon M, Dhellemmes P: Cerebrospinal fluid shunt infection: risk factors and long-term follow-up. Childs Nerv Syst 22: 692–697, 2006
- Vinchon M, Lemaitre MP, Vallee L, Dhellemmes P: Late shunt infection: incidence, pathogenesis, and therapeutic implications. Neuropediatrics 33:169–173, 2002
- Wen SW, Demissie K, August D, Rhoads GG: Level of aggregation for optimal epidemiological analysis: the case of time to surgery and unnecessary removal of the normal appendix. J Epidemiol Community Health 55:198–203, 2001
- 45. Younger JJ, Simmons JC, Barrett FF: Operative related infection rates for ventriculoperitoneal shunt procedures in a children's hospital. **Infect Control 8**:67–70, 1987

Manuscript submitted July 30, 2008.

Portions of this work were presented in poster form at the Pediatric Academic Societies meeting, Honolulu, Hawaii, May 3, 2008, and as proceedings at the Pediatric Hospital Medicine meeting, Denver, Colorado, July 26, 2008.

Address correspondence to: Tamara Simon, M.D., M.S.P.H., Department of Pediatrics, Division of Inpatient Medicine, 100 North Mario Capecchi Drive, Salt Lake City, Utah 84113. email: Tamara. Simon@hsc.utah.edu.

Accepted March 26, 2009.