

Five-year survival and outcome of treatment for postinfectious hydrocephalus in Ugandan infants

Clinical article

BENJAMIN C. WARF, M.D.,^{1,2} ARIELLA R. DAGI, B.A.,³ BRIAN NSUBUGA KAAAYA, B.S.,⁴ AND STEVEN J. SCHIFF, M.D., PH.D.⁵

¹Department of Neurosurgery, Children's Hospital Boston, Harvard Medical School; ²Program for Global Surgery and Social Change, Department of Global Health and Social Medicine, Harvard Medical School, Boston; ³Harvard College, Cambridge, Massachusetts; ⁴CURE Children's Hospital of Uganda, Mbale, Uganda; and ⁵Center for Neural Engineering, Departments of Neurosurgery, Engineering Science and Mechanics, and Physics, The Pennsylvania State University, University Park, Pennsylvania

Object. Neonatal infection is the most common cause of infant hydrocephalus in Uganda. Postinfectious hydrocephalus (PIH) is often accompanied by primary brain injury from the original infection. Since 2001, ETV (with or without choroid plexus cauterization) has been our primary treatment for PIH. The long-term outcome in these children is unknown.

Methods. We studied the 5-year outcome in a cohort of 149 infants treated for PIH from 2001 to 2005 and who lived in 4 districts close to the hospital. Survival analysis was performed using the Kaplan-Meier method. Statistical significance was determined using the Fisher, Breslow, and log-rank tests.

Results. The patients' mean age at presentation was 9.5 months (median 3.0 months). Eighty-four patients (56.4%) were successfully treated without a shunt. Operative mortality was 1.2% for ETV and 4.4% for shunt placement ($p = 0.3$). Five-year survival was 72.8% in the non-shunt-treated group and 67.6% in the shunt-treated group, with no difference in survival (log rank $p = 0.43$, Breslow $p = 0.46$). Of 43 survivors assessed at 5–11 years, those with shunts had significantly worse functional outcomes ($p = 0.003$ – 0.035), probably reflecting treatment selection bias since those with the worst sequelae of ventriculitis were more likely to be treated with shunt placement.

Conclusions. Nearly one-third of treated infants died within 5 years, and at least one-third of the survivors were severely disabled. There was no survival advantage for non-shunt-treated patients at 5 years. A randomized trial of endoscopic third ventriculostomy versus shunt placement for treating PIH may be indicated. Public health measures that prevent these infections are urgently needed. (DOI: 10.3171/2011.8.PEDS11221)

KEY WORDS • postinfectious hydrocephalus • endoscopic third ventriculostomy • choroid plexus cauterization • ventriculoperitoneal shunt • outcome • survival • Uganda • Africa

WE previously reported that PIH is the most common cause of infant hydrocephalus in Uganda, accounting for 60% of cases.^{4,5} Anecdotal evidence suggests a similar prevalence of PIH in other countries of sub-Saharan Africa. The majority of these cases are secondary to neonatal infection resulting in ventriculitis, which often results in primary brain injury in addition to the hydrocephalus. The pathogens and routes of infection are not known, but recent evidence implicates the role of gram-negative organisms, especially *Acineto-*

bacter species, and a possible seasonal pattern of occurrence.¹ The long-term survival of these infants after management of their hydrocephalus has not previously been studied. Such information is necessary to adequately assess the costs and benefits of treating PIH in this context. Understanding the fate of these children over time is also important for improving treatment and follow-up strategies as well as for strengthening the mandate for research that can ultimately lead to prevention. This study explores survival and outcome in a cohort of Ugandan infants treated aggressively for PIH at the CCHU.

Abbreviations used in this paper: CCHU = CURE Children's Hospital of Uganda; CPC = choroid plexus cauterization; ETV = endoscopic third ventriculostomy; PIH = postinfectious hydrocephalus; VP = ventriculoperitoneal.

This article contains some figures that are displayed in color online but in black and white in the print edition.

Postinfectious hydrocephalus outcome

Methods

Beginning in 2001, ETV was attempted as the initial treatment in all children with hydrocephalus presenting to CCHU.⁵ Later, in 2003, choroid plexus cauterization (CPC) was added to ETV, with the combined ETV/CPC procedure proving more effective overall than ETV alone in infants and children less than 1 year of age.³ In the study cohort presented here, 43 infants had the combined ETV/CPC procedure and 66 had ETV alone. The majority of the latter (45 infants) underwent surgery prior to our institution of the combined procedure. In the remaining 21 cases, CPC was omitted for a variety of reasons: 7 patients had an obstructed aqueduct (Fig. 1), a group for which we subsequently demonstrated no advantage to CPC;³ 3 had been in a trial cohort randomized to no CPC earlier in the study; 8 had choroid plexus that was either encased in scar (4), encased in purulence (1), severely atrophic (1), or very friable with easy bleeding (2); and in 3 infants the reason for omitting the CPC was not clearly documented.

Among patients with PIH, scarring in the prepontine cistern is a strong independent predictor of ETV failure,¹⁰ and based upon this finding it became our practice in more recent years to place a shunt (typically a ventriculoperitoneal shunt) at the time of the ETV when significant scarring was discovered. Additionally, in some patients, severe anatomical distortion or poor visibility from prior ventriculitis necessitated abandonment of the ETV attempt and placement of a shunt or tapping reservoir. A shunt was also placed in patients for whom endoscopic treatment had failed. Thus, shunt-treated patients included those for whom ETV (with or without CPC) had failed, those with severe arachnoid scarring of the prepontine

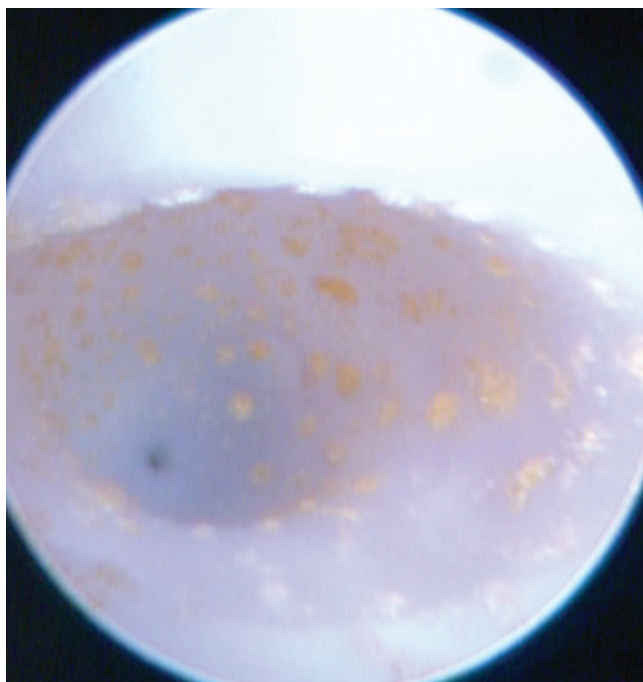


Fig. 1. Endoscopic view of the cerebral aqueduct in a child with PIH. The posterior commissure is seen in the upper third of the image. Note diffuse punctate inflammatory deposits and obstructing membrane over the aqueduct with only a pinhole-sized opening.

cistern discovered at the time of ETV, and those in whom the ETV attempt had been abandoned.

With appropriate institutional approval from both the Children's Hospital Boston and CCHU, the CCHU clinical database was reviewed to identify patients for study. Through the hospital outreach program, some patients lost to follow-up were contacted by telephone or home visit to determine their status. To optimize follow-up, and the likelihood that children with shunt malfunctions would have had urgent access to treatment, we chose to study a cohort of patients treated for PIH who came from the districts closest to the hospital (Mbale, Kumi, Sironko, and Tororo districts). All patients were within 80 kilometers of CCHU. From 2001 through 2005, 149 patients from these districts were treated for PIH. Standard clinical, radiological, and ventriculoscopic criteria were used to determine the diagnosis of PIH, as has been previously described.⁵

For each study patient, the following were determined: district of origin; age at treatment; whether the child had been treated with shunt placement and, if so, the number of subsequent shunt operations; whether the child was alive at 5 years after the definitive hydrocephalus operation (initial ETV or initial shunt placement if a shunt had ultimately been required), or, if not, the time to death after that procedure. In 3 patients known not to have survived 5 years, but for whom the date of death was unknown, length of survival was limited to the last known encounter with the patient (8, 15, and 39 months); thus, in these 3 patients, the length of survival has been underestimated. For patients who died while in the hospital, the cause of death was determined from the medical record. For those who died in another setting, the circumstances of death were ascertained, when possible, by interview. During the course of outreach efforts for patients lost to follow-up, selected gross historic parameters of function were determined by means of family interview. These included whether the child was continent, could walk or talk, could feed or dress independently, and was attending school.

Survival analysis was performed using the Kaplan-Meier method. The Fisher exact test with a 2-tailed *p* value was used to determine the significance of differences between groups. Log-rank (Mantel-Cox) and Breslow (generalized Wilcoxon) tests were used to assess statistical significance between survival curves, with SPSS (IBM) and R (<http://www.r-project.org/>) giving equivalent results. Confidence limits were calculated with Matlab (The Mathworks). All patients lost to follow-up and not known to have died were censored at the last known time of contact, and all patients who survived for the full 5 years of the study were censored at 60 months. For 3 patients known to have died, but for whom the date of death was not known, the time of last encounter was taken as the date of death.

Results

Figure 2 demonstrates the treatment pathway for the 149 children identified in the study cohort. The mean and median ages at time of initial presentation for treatment were 9.5 months and 3.0 months, respectively, with 88.6%

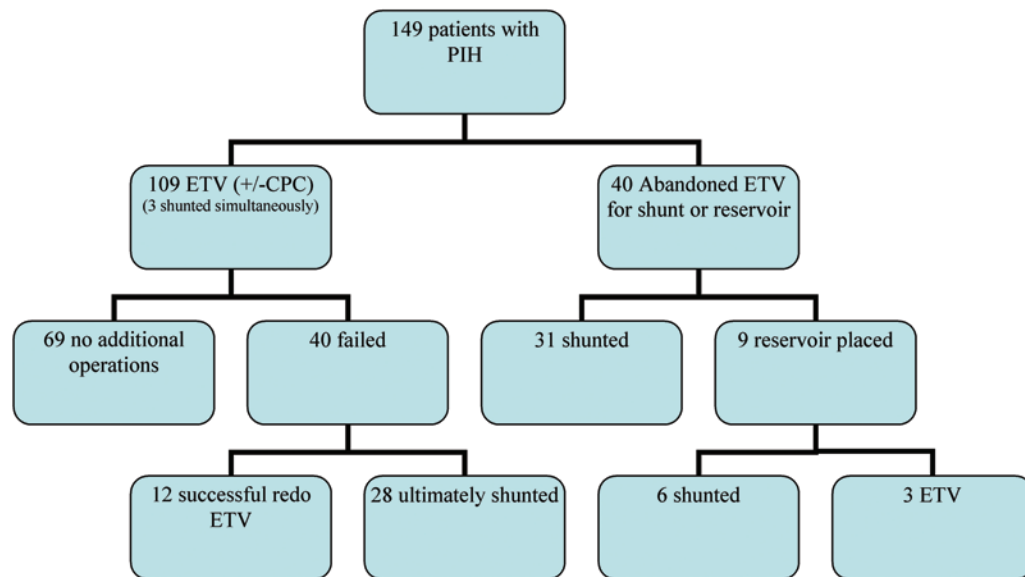


Fig. 2. Flowchart demonstrating the treatment path for 149 patients in the study cohort.

(132) being 1 year old or younger at initial treatment. At the time of the study, 84 (56.4%) children remained shunt-independent following ETV with or without CPC (including the 3 patients who underwent simultaneous shunt placement noted below), and a shunt had been placed in 65 (43.6%). Of the total of 68 shunts placed, 65 were ventriculoperitoneal, 2 were subdural–peritoneal, and 1 was a ventriculosagittal sinus shunt. The operative mortality (death from any cause within 30 days of the procedure) was 1.2% (1 death in 81 procedures) for ETV and 4.4% (3 in 68) for shunt placement, which does not represent a significant difference ($p = 0.3$). Twenty-eight patients (18.8%) were lost to follow up before 5 years at a mean of 20.2 months and a median of 20 months. The outcome for 121 (81.2%) patients was known for at least 50 months.

In 37 (54.4%) of 68 shunt-treated patients, a shunt was placed because the ETV attempt had been abandoned. This included 6 of 9 patients in whom the ETV attempt had been initially abandoned for reservoir placement due to poor visibility resulting from murky CSF. In 28 (41.2%) the shunt was placed after failure of the endoscopic procedure. In another 3 patients a VP shunt was placed at the time of successful ETV completion because of scarring noted in the prepontine cistern, based upon our finding of increased risk for ETV failure when cisternal scarring is encountered.¹⁰ These 3 patients were successfully treated with no additional operations at 25.5, 48, and 54 months of follow-up, respectively. Twelve of 40 patients with failed ETVs were successfully treated by repeat ventriculoscopy for reopening of the ETV. Three patients in whom ETV was initially abandoned for reservoir placement were able to have an ETV completed at a subsequent operation after the CSF had cleared. One of these had required no further treatment at 66 months follow-up, and the other 2 died at 2 and 4.3 months. Thus, of all 149 infants presenting for treatment of PIH, 84 (56.4%) were treated successfully without shunting and 65 (43.6%) required a shunt. Of 109 patients with a completed ETV (with or without CPC), 69 (63.3%) required no further surgery (Fig. 2).

The 5-year survival rate was 70.5% for the entire cohort with a mean survival of 46.2 months (95% CI 42.6–49.9 months). The 5-year survival rate in the non-shunt-treated group was 72.8%, with mean survival of 47.4 months (95% CI 42.7–52.2 months). For the shunt-treated patients, 5-year survival was 67.6% with a mean survival of 44.8 months (95% CI 39.2–50.4 months) (Fig. 3). There was no significant difference in survival between the groups as assessed by log rank ($p = 0.43$) and Breslow (generalized Wilcoxon $p = 0.46$) methods. Twenty-one (48.8%) of 43 known deaths occurred in the 1st year after the initial ETV or shunt placement. The causes of death, as ascertained from the medical records or family interviews, are presented in Tables 1 and 2. Among patients with shunts, 5 (45%) of 11 known deaths in the 1st year were related to a shunt complication, while 1 death after that time was suspicious for a shunt malfunction. Among patients without a shunt, 2 deaths in the 1st year were secondary to ventriculitis (one of which was identified as a gram-negative infection). These deaths occurred at 1.2 months after the initial ETV and 1.0 month after a repeat ETV.

Shunt-treated patients had an average of 1.06 revision operations per patient (median 0). At least 1 shunt revision was performed in 25 (37%) of the shunt-treated patients, and 14 (21%) required 2–10 revisions during the follow up period (Table 3). Excluding those lost to follow-up, the average for 5-year survivors was 0.97 revisions per patient, and for nonsurvivors the average was 1.61. There was no statistically significant difference ($p = 0.4$) between the number needing at least 1 revision among survivors (11 of 32) and that among nonsurvivors (11 of 23). Flexible ventriculoscopy was invaluable in many cases for the fenestration of intraventricular septations that had caused multiloculated hydrocephalus.

Table 4 presents a gross assessment of overall functional outcome in 42 children between the ages of 5 and 11 years (mean age 7.3 years, median 7.2 years) in whom the information could be obtained. Although most were continent of urine, slightly less than 2 of 3 could walk,

Postinfectious hydrocephalus outcome

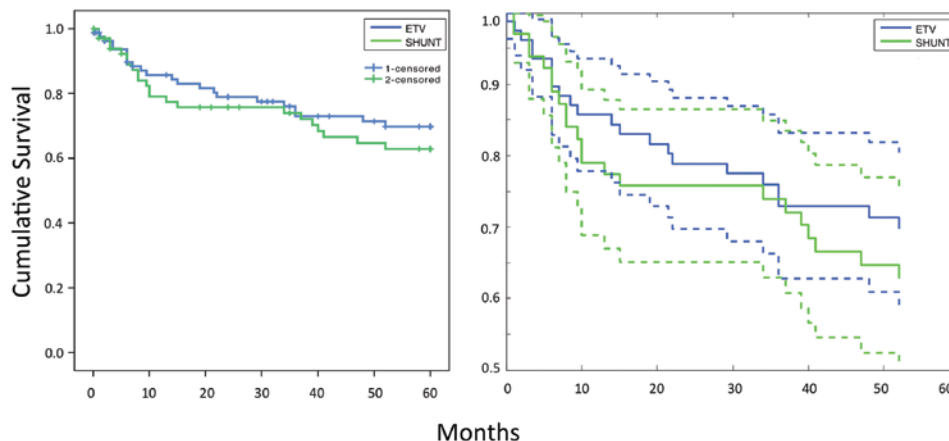


Fig. 3. Kaplan-Meier survival curves. **Left:** Graph showing survival curves for ETV with or without CPC and shunt treatment. The time points at which patients were lost to follow-up (without known subsequent death) are shown as censored (short vertical marks). For those patients known to have died but for whom the date of death was not known, the time of last encounter was considered the length of survival. Patients who reached 60 months' survival and who might have subsequently died were also censored for statistical calculations (but not marked). Note that there is a trend toward early and late shunt failures, but global statistical comparisons of the curves show that there is no overall statistical difference between the survival groups ($p > 0.4$ for both log-rank and Breslow generalized Wilcoxon tests). **Right:** Graph showing 95% CIs (broken lines, blue for ETV and green for shunt treatment) for the cumulative survival functions using Greenwood's formula (Mathworks implementation), demonstrating that the survival curves at all survival times remain within each others' CIs with the solitary exception of the shunt curve at 12 months.

talk, or feed and dress themselves independently. Only 38% of those for whom the information was available attended school. There was a statistically significant difference in functional outcomes between shunt-treated and non-shunt-treated patients. The majority of those without shunts could walk, talk, and feed and dress themselves; whereas, the majority of those with shunts could not.

Discussion

Postinfectious Hydrocephalus

In sub-Saharan Africa, probably between 80,000 and 375,000 infants develop hydrocephalus each year, and the most conservative estimates suggest a potential economic burden to the region, in US dollars, ranging from \$1 billion (using a human capital approach) to as much as

\$56 billion (using the value of a statistical life approach) per year.⁶ In 2005, we provided the first report of neonatal infection as the major cause of infant hydrocephalus in an African country.⁵ In addition to the hydrocephalus (PIH), which can be treated, some of these children have devastating brain injuries from the initial ventriculitis (Fig. 4). Thus, the treated population includes survivors with varying degrees of neurocognitive and motor disabilities.

Although the major pathogens for infections that lead to neonatal ventriculitis in Uganda are not known, we recently reported that, of the 94% of PIH patients who had bacterial DNA recovered from their CSF at the time of surgery for hydrocephalus treatment, the most commonly detected DNA was that of gram-negative bacteria in the phylum Proteobacteria.¹ Furthermore, within this phylum, Gammaproteobacteria predominated in patients who had developed their initial illness during the rainy season, with *Acinetobacter* species identified in the majority. By contrast, Betaproteobacteria predominated in

TABLE 1: Causes of death in 23 patients with shunts

Death w/in 1 yr	Death After 1 yr
shunt infection	"hydrocephalus" (?shunt malfunction)
shunt infection	malaria
shunt infection	malaria
shunt infection/malfunction	measles
exposed shunt/aspiration	vomiting
malaria, anemia	vomiting & diarrhea
malaria, anemia	respiratory infection
febrile illness, cardiac arrest	malnutrition
cardiac arrest, unknown illness	neglect, "rejected by clan"
unknown	unknown
unknown	unknown
unknown	unknown

TABLE 2: Causes of death in 20 patients without shunts

Death w/in 1 yr	Death After 1 yr
ventriculitis	malaria
ventriculitis	malaria, anemia, malnutrition (marasmus)
malaria, diarrhea	severe malnutrition
malaria, anemia	severe malnutrition
malaria, pneumonia	diarrhea, vomiting
malaria, cardiac arrest	sudden death in sleep
gastroenteritis, hematuria	unknown
tachycardia, cardiac arrest	unknown
unknown	unknown
unknown	unknown

TABLE 3: Shunt revisions in 68 shunt-treated patients

No. of Shunt Revisions	No. of Patients (%)
0	43 (63)
1	11 (16)
2	4 (5.9)
3	4 (5.9)
5	1 (1.5)
6	2 (2.9)
7	2 (2.9)
10	1 (1.5)

the CSF of children who had become ill during the dry season. Work is in progress to better characterize the seasonal patterns, modes, and specific pathogens of these infections to develop public health strategies for effective prevention and treatment.

Treatment Paradigm and Success

Given the lack of urgent access to treatment for shunt failure in rural Uganda, we have emphasized the benefit of avoiding shunt-dependence whenever possible. Treatment with ETV/CPC has proven very effective for congenital infant hydrocephalus of several etiologies including that associated with myelomeningocele,^{3,7} encephalocele,¹² the Dandy-Walker complex,⁹ and congenital aqueductal stenosis.³ In the case of PIH, the outcome is very dependent upon whether there is obstruction from subarachnoid scar within the prepontine cistern. During the time of treatment for the patient cohort presented here, most infants with cisternal scarring were given an opportunity for shunt independence. Subsequently, we demonstrated that cisternal scar was an independent risk factor that more than doubled the likelihood of ETV failure.¹⁰ Therefore, at CCHU, most patients with PIH and significant cisternal scar now receive shunts at the time of the ETV. Unfortunately MR imaging with fast imaging employing steady-state acquisition (FIESTA), which can demonstrate cisternal scarring prior to surgery, is not available in Uganda and most other developing countries.⁸

In the present study, 56.4% of the children had remained shunt-independent over the course of follow-up (including the 3 who underwent simultaneous ETV and shunt placement because of cisternal scarring). Some in-

fants presenting with PIH were simply unable to undergo ETV because of severe anatomical distortion from ependymal and parenchymal destruction and intraventricular scarring, and a shunt was placed. In this study cohort, 54.5% of shunt placements were performed for that reason. Among 109 patients with a completed ETV with or without CPC, 69 had no additional operations, including 55 with good outcomes, 3 with good outcomes who had simultaneous shunt placement when a scarred prepontine cistern was encountered, 1 who died, and 10 who were lost to follow-up. Ninety-five of the 109 patients with a completed ETV were neither lost to follow-up nor treated with shunt placement at the time of the initial ETV or ETV/CPC procedure; in 55 (57.9%) of these 95, the procedure was successful and no further surgery was required. There was no significant difference in success between those with ETV alone (32 [59.3%] of 54) and those with ETV/CPC (23 [56.1%] of 41, $p = 0.835$). This corresponds to the lack of significant difference in outcome between ETV and ETV/CPC we reported previously for a larger cohort of infants with PIH.³ Of the 40 patients in whom endoscopic treatment failed, 12 were treated successfully by repeat ETV, and 28 required shunt placement (Fig. 2).

The shunt-treated group had an average of 1.06 revision operations per patient. At least 1 shunt revision was performed in 37% of these patients, and 21% required 2–10 revisions during the follow-up period (Table 3). This does not include those patients, known and unknown, who died of a shunt malfunction or infection without the benefit of operative treatment. Excluding those lost to follow-up, 5-year survivors had an average of 0.97 shunt reoperations per patient, whereas the average for nonsurvivors was 1.61. However, we found no statistically significant difference between survivors and nonsurvivors in the proportion undergoing at least 1 shunt revision ($p = 0.4$). In this study group the operative mortalities (4.4% for shunt placement and 1.2% for ETV) were very similar to those previously reported from CCHU.^{2,3,5}

Survival

The 5-year survival rate was 67.6% for shunt-treated patients and 72.8% for those without a shunt; however, this difference was not statistically significant. For comparison, the 5-year survival rate of Ugandan infants in the general population is estimated at 84%.¹³ As with the functional outcomes discussed below, a trend toward better survival in the non-shunt-treated group might be

TABLE 4: Functional outcomes in 42 patients 5–11 years of age with and without a shunt*

Measure	No Shunt		Shunt		p Value	Total "Yes"
	No	Yes	No	Yes		
continent?	3	25 (89.3)	1	13 (92.9)	1.000	38 (90.5)
walks?	6	19 (76.0)	8	5 (38.5)	0.035	24 (63.2)
talks?	6	21 (77.8)	9	6 (40.0)	0.021	27 (64.3)
feeds self?	5	22 (92.6)	10	5 (33.3)	0.003	27 (64.3)
dresses self?	8	19 (70.4)	10	5 (33.3)	0.027	24 (57.1)
in school?	13	9 (40.9)	9	3 (25.0)	0.465	13 (38.2)

* Mean age 7.3 yrs, median 7.2 yrs. Values represent numbers of patients (%) unless otherwise indicated.

Postinfectious hydrocephalus outcome

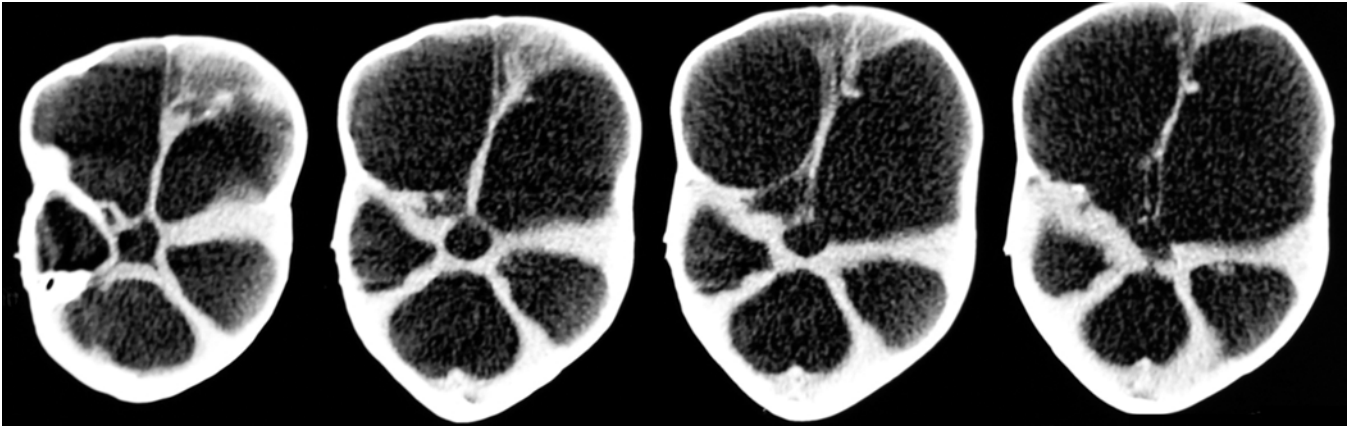


Fig. 4. Noncontrast axial CT scan of the brain obtained in a 5-month-old girl with a history of fever and seizures at 1 month of age and rapid development of macrocephaly. Note the severe, diffuse parenchymal destruction. A tapping reservoir was placed to externally drain CSF for 2 weeks until it was sufficiently clear. Ventriculocopy revealed severe, diffuse ependymal scar, yellow intraventricular inflammatory deposits, and an occluded aqueduct. Endoscopic third ventriculostomy revealed arachnoid scarring within the prepontine cistern. Treatment with ETV/CPC failed and a VP shunt was placed 1 month later.

expected due to treatment selection bias, given that shunt-treated patients most likely had more severe primary brain injuries and thus were more debilitated from the outset. Our work has previously suggested that in Uganda young children with disabilities may have higher mortality from treatable conditions, such as infectious diseases and malnutrition, than their unaffected peers by virtue of their disability,^{12,13} and that survival can be significantly enhanced by the “observer effect” of a community-based program that entails home visits.^{4,13} The 70.5% overall 5-year survival for PIH is similar to that for infants from the same region of Uganda treated for myelomeningocele (63%)¹³ and encephalocele (61%).¹² This study did not demonstrate a significant difference in survival between shunt-treated and non-shunt-treated patients. We had similarly demonstrated no significant difference in 5-year survival among infants with myelomeningocele treated at CCHU in regard to whether or how hydrocephalus had been treated.¹³

These findings suggest that sufficient equipoise exists to evaluate the clinical outcomes and assess the relative costs and benefits of primary CSF shunting for PIH compared with the primary endoscopic approach in a prospective randomized trial. It is worth noting, however, that nearly half of all known deaths occurred within the 1st year, and that in shunt-treated patients nearly half of the deaths were related to a shunt complication (mostly infection). Also, the patients in this study were, by design, relatively close to the treating facility, with better access to treatment of shunt complications than the majority of children treated at CCHU. Furthermore, in a recent assessment of hydrocephalus treatment in Uganda, we concluded that avoiding shunt dependence decreased the total cost of care over time.⁶

Functional Outcome

There was a statistically significant difference in functional outcome between the shunt-treated and non-shunt-treated patients who were surveyed (Table 4). This is not surprising, given the fact that shunt-treated patients

would have had the most severe ventricular and cisternal scar and anatomical deformity, which would likely be consistent with a more severe primary brain insult. Thus, this most likely reflects a treatment selection bias, and does not suggest that patients who undergo shunt placement have a worse functional outcome by virtue of the fact that they are treated by means of CSF shunting. In a previous study we did not find an overall statistically significant difference in early neurocognitive outcome measures between infants with myelomeningocele whose hydrocephalus had been treated by ETV/CPC and those treated by VP shunt placement.¹¹ Infants with PIH who were able to be treated endoscopically were likely, on the whole, to have had a less severe inflammatory brain insult. In this group, the majority were able to walk, talk, and feed and dress themselves, in contrast to the majority of those with shunts, who could not. The number attending school could be confounded by economic, social, and environmental factors, and there was no difference between groups in that regard.

It is notable here that of patients successfully treated for PIH and surviving more than 5 years, more than 1 in 3 appear to be severely permanently disabled from the initial infection as determined by their inability to independently perform basic activities of daily living. The only way to avoid this is by prevention, or at least timely effective treatment, of neonatal sepsis in the region. This can only be accomplished after the pathogens and routes of infection have been identified. We emphasize that infants with PIH represent a subset of children affected by neonatal sepsis, many of whom did not survive to develop hydrocephalus.

Conclusions

Neonatal infection is the most common cause of hydrocephalus in Ugandan infants. This study provides the first assessment of an aggressive program of PIH treatment with an emphasis on preventing shunt dependence, which was ultimately avoided in more than half of the

patients. Around one third of treated infants died within 5 years, and at least one-third of the survivors were severely disabled. There was no significant difference in survival between those with and those without shunts. Although functional outcomes appeared worse for shunt-dependent children, this most likely reflected treatment selection bias because those with the worst sequelae of ventriculitis were more likely to have undergone shunt placement. Nonetheless, half of the deaths occurred within 1 year of the original ETV or shunt placement, and shunt complication was the single most common cause of death for shunt-treated patients during that period. Our results suggest that a randomized prospective trial to study survival, functional outcomes, and cost-benefit analysis for primary ETV compared with primary shunt placement in African infants with PIH would be useful. These findings also lend urgency to the call for public health measures that will lead to prevention and effective early treatment of the infections leading to PIH, which is a significant and under-recognized global health problem.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Warf. Acquisition of data: Warf, Dagi, Kaaya. Analysis and interpretation of data: Warf, Dagi, Schiff. Drafting the article: Warf. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Warf. Statistical analysis: Schiff. Administrative/technical/material support: Warf, Dagi. Study supervision: Warf.

References

1. Li L, Padhi A, Ranjeva SL, Donaldson SC, Warf BC, Mugamba J, et al: Association of bacteria with hydrocephalus in Ugandan infants. Clinical article. **J Neurosurg Pediatr** 7:73–87, 2011
2. Warf BC: Comparison of 1-year outcomes for the Chaabra and Codman-Hakim Micro Precision shunt systems in Uganda: a prospective study in 195 children. **J Neurosurg** 102 (4 Suppl):358–362, 2005
3. Warf BC: Comparison of endoscopic third ventriculostomy alone and combined with choroid plexus cauterization in infants younger than 1 year of age: a prospective study in 550 African children. **J Neurosurg** 103 (6 Suppl):475–481, 2005
4. Warf BC: Hydrocephalus associated with neural tube defects: characteristics, management, and outcome in sub-Saharan Africa. **Childs Nerv Syst** (in press)
5. Warf BC: Hydrocephalus in Uganda: predominance of infectious origin and primary management with endoscopic third ventriculostomy. **J Neurosurg** 102 (1 Suppl):1–15, 2005
6. Warf BC, Alkire BC, Bhai S, Hughes C, Schiff S, Vincent JR, et al: Costs and benefits of neurosurgical intervention for infant hydrocephalus in sub-Saharan Africa. Clinical article. **J Neurosurg Pediatr** 8:509–521, 2011
7. Warf BC, Campbell JW: Combined endoscopic third ventriculostomy and choroid plexus cauterization as primary treatment of hydrocephalus for infants with myelomeningocele: long-term results of a prospective intent-to-treat study in 115 East African infants. Clinical article. **J Neurosurg Pediatr** 2:310–316, 2008
8. Warf BC, Campbell JW, Riddle E: Initial experience with combined endoscopic third ventriculostomy and choroid plexus cauterization for post-hemorrhagic hydrocephalus of prematurity: the importance of prepontine cistern status and the predictive value of FIESTA MRI imaging. **Childs Nerv Syst** 27:1063–1071, 2011
9. Warf BC, Dewan M, Mugamba J: Management of Dandy-Walker complex-associated infant hydrocephalus by combined endoscopic third ventriculostomy and choroid plexus cauterization. Clinical article. **J Neurosurg Pediatr** 8:377–383, 2011
10. Warf BC, Kulkarni AV: Intraoperative assessment of cerebral aqueduct patency and cisternal scarring: impact on success of endoscopic third ventriculostomy in 403 African children. Clinical article. **J Neurosurg Pediatr** 5:204–209, 2010
11. Warf BC, Ondoma S, Kulkarni A, Donnelly R, Ampeire M, Akona J, et al: Neurocognitive outcome and ventricular volume in children with myelomeningocele treated for hydrocephalus in Uganda. Clinical article. **J Neurosurg Pediatrics** 4:564–570, 2009
12. Warf BC, Stagno V, Mugamba J: Encephalocele in Uganda: ethnic distinctions in lesion location, endoscopic management of hydrocephalus, and survival in 110 consecutive children. Clinical article. **J Neurosurg Pediatr** 7:88–93, 2011
13. Warf BC, Wright EJ, Kulkarni AV: Factors affecting survival of infants with myelomeningocele in southeastern Uganda. Clinical article. **J Neurosurg Pediatr** 7:127–133, 2011

Manuscript submitted May 27, 2011.

Accepted August 10, 2011.

Address correspondence to: Benjamin C. Warf, M.D., Department of Neurosurgery, Children's Hospital Boston, 300 Longwood Avenue, Boston, Massachusetts 02115. email: benjamin.warf@childrens.harvard.edu.