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What Have We Learned About Hydrocephalus in Africa?

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The CURE Children's Hospital of Uganda was established in January 2001. Since then, over 750 children have been treated for hydrocephalus. This high volume of patients has allowed us to address questions about hydrocephalus in Africa that have previously been unanswered. The International Federation for Spina Bifida and Hydrocephalus has been a crucial partner in this project. This talk summarizes some of what we have learned over the past 3 ½ years.

How common is Hydrocephalus in Africa?

As will be discussed, the majority of hydrocephalus in Uganda is acquired in the first year of life, rather than being congenital. Therefore, a simple birth incidence would give an inadequate estimate of its prevalence among infants.

Although CURE Children's Hospital of Uganda (CCHU) serves all of Uganda as well as Western Kenya, access to our hospital is easier for families in the immediately surrounding districts that have community-based rehabilitation (CBR) programs. To estimate the minimum possible frequency for children developing hydrocephalus in the first year of life (either congenital or acquired) we looked at the number of children from those districts born during a given year who were treated for hydrocephalus at CCHU. The average for those born during the years 2001-2002 was 0.7/1000 live births (based upon the reported district populations and crude birth rates). Since this was based only upon the number of children we treated at our hospital, it excludes those who did not come to us for treatment for any reason (e.g. death and those either not treated or taken elsewhere for treatment). This therefore means that for every 3000 children born, **more** than 2 will develop hydrocephalus in infancy. Extrapolated to the entire country, more than 1200 infants develop hydrocephalus in Uganda per year. The real number could be twice that. There is no reason to think that Uganda should be unique in this respect among other countries in the region.

What causes hydrocephalus in Africa?

At CCHU, 60% of children presenting with hydrocephalus are determined to have acquired the condition as the result of infection (meningitis/ventriculitis). This is very different from the situation in developed countries. It appears, anecdotally, that infection is the most common cause of hydrocephalus in other countries of east and central Africa as well.

In our hospital, the designation of post-infectious hydrocephalus (PIHC) is determined according to several factors: age of onset of hydrocephalus; history of preceding febrile illness with or without seizures and its proximity in time to onset of clinically evident

hydrocephalus; ultrasonographic (or CT) findings of septations / loculations, anatomic distortion, or intraventricular deposits; and findings at ventriculoscopy which are consistent with prior ventriculitis. By convention, a designation of PIHC has been assigned only if there was: 1) no history consistent with hydrocephalus at birth; and either, 2) a history of febrile illness and/or seizures preceding the onset of clinically obvious hydrocephalus; or, 3) alternative convincing findings (i.e. imaging and endoscopic) indicative of prior ventriculitis.

In our experience to date, the most common clinical history was of a previously normal infant who had a febrile illness with convulsions and subsequently developed progressive hydrocephalus. In 80% of cases, this illness occurred prior to 1 month of age, i.e. during the neonatal period. The average time from illness to onset of noticeable hydrocephalus in the infant was 3 weeks. Among PIHC patients undergoing endoscopic examination of the ventricles (ventriculoscopy), almost 80% had unequivocal evidence of prior intraventricular inflammation (ventriculitis), and 2/3 of these had obstruction of the aqueduct of Sylvius (the narrow passage between the 3rd and 4th ventricles)[1].

Therefore, the single most common cause of hydrocephalus in Uganda is neonatal cerebrospinal fluid (CSF) infection (meningitis / ventriculitis). Thus, most hydrocephalus could have been potentially avoided. Why should this be such a common problem in Uganda, and how could it be prevented? Risk factors for neonatal sepsis and meningitis include protracted labor, premature rupture of membranes, and the perinatal environment. In Uganda, more than 60% of births occur without any sort of skilled assistant[2]. Furthermore, certain practices in our area, such as placing cow dung on the umbilical stump, may increase the risk of neonatal sepsis. Given that the mortality rate of neonatal meningitis is 50%[3], we must be seeing only a handful of survivors. In addition, many of the children we see have had partial or inappropriate treatment of their illness. Therefore, economic, cultural, and educational factors all play a role in the high incidence of PIHC. Again, these conditions are not unique to Uganda.

What is the best way to treat hydrocephalus in Africa?

A) Is the Chhabra shunt Safe and Effective?

The International Federation of Spina Bifida and Hydrocephalus (IF) supplies projects in developing countries with the Chhabra shunt, a device made by Surgiwear in India, and already widely used throughout East Africa. The advantage of this shunt is its cost – about $35 USD. This compares to other shunts manufactured in the West that cost from $500 to $1000. Concerns have arisen over the safety and cost-effectiveness of such an inexpensive alternative, and no trials had ever been conducted comparing the Chhabra shunt to one of the expensive, Western shunts.

We performed a randomised prospective trial comparing the one-year outcome for the Chhabra shunt to that for the Codman Hakim Micro precision Valve shunt system

(Codman, Johnson and Johnson, $650)[4]. The results of this study are presented in the tables below. Chhabra Group 1 comprised the patients in whom a Chhabra shunt was randomly selected for placement and the results compared to those for whom the Codman shunt had been randomly selected. This preceded our program of first attempting to treat all children with ETV (see below). Chhabra Group 2 comprised the second phase of the study in which the Chhabra shunt was placed after ETV failure or an abandoned ETV attempt. No Codman shunts were available during this phase. Statistical significance was determined by $P<0.05$ (Fischer's exact test).

Table 1: Group 1 Outcomes

	Chhabra - 1	**Codman**	**Total**	**P**
Total	47	43	90	-------
Lost < 1year	4	7	11	0.3402
Total followed	43 (91%)	36 (84%)	79 (88%)	-------
Dead < 1 mo	1 (2%)	0	1 (1.1%)	1.0000
No problem 1st year	22 (51%)	21 (58%)	43 (54%)	0.6508
Dead by 1 year	6 (14%)	6 (17%)	12 (15%)	0.7628
Infection	4 (9.3%)	4 (11%)	8 (10%)	1.0000
Wound complication	3 (7%)	2 (5.6%)	5 (6.3%)	1.0000
Valve malfunction	3 (7%)	0	3 (3.8%)	0.2463
Proximal obstruction	1 (2.3%)	1 (2.7%)	2 (2.5%)	1.0000
Distal obstruction	1 (2.3%)	0	1 (1.3%)	1.0000
Migration	3 (7%)	3 (8.3%)	6 (7.6%)	1.0000
Randomised by coin	5	13	18	------
Randomised by avail.	42	30	72	------

Table 2: Chhabra (Group 1) and Chhabra (Group 2) Outcomes

	Chhabra – 1	**Chhabra – 2**	**Total**	**P**
Total	47	105	152	------
Lost < 1year	4	8	12	1.0000
Total followed to endpoint	43 (91%)	97 (92%)	140 (92%)	------
Dead < 1 mo	1 (2%)	7 (6.7%)	8 (5.3%)	0.4348
No problem 1st year	22 (51%)	53 (55%)	75 (54%)	0.7173
Dead 1st year (total)	6 (14%)	16 (21%)	22 (15.7%)	0.8050
Infection	4 (9.3%)	9 (9.3%)	13 (9.3%)	1.0000
Wound complication	3 (7%)	5 (5.2%)	8 (5.7%)	0.7011
Valve malfunction	3 (7%)	3 (3.1%)	6 (4.2%)	0.3711
Proximal obstruction	1 (2.3%)	3 (3.1%)	4 (2.9%)	1.0000
Distal obstruction	1 (2.3%)	1 (1%)	2 (1.4%)	0.5215
Migration/disconnection	3 (7%)	5 (5.2%)	8 (5.7%)	0.7011

Table 3: Combined Results

1 year follow up	Chhabra 1&2	Codman	Total	P
Total	152	43	195	------
Lost < 1year	12	7	19	0.1410
Total followed	140 (92%)	36 (84%)	176 (90%)	------
Dead < 1 mo	8 (5.3%)	0	8 (4.1%)	0.3631
No problem 1st year	75 (54%)	21 (58%)	96 (54.5%)	0.7083
Dead by 1 year	22 (15.7%)	6 (17%)	28 (15.9%)	1.0000
Infection	13 (9.3%)	4 (11%)	17 (9.7%)	1.0000
Wound complication	8 (5.7%)	2 (5.6%)	10 (5.7%)	1.0000
Valve malfunction	6 (4.2%)	0	6 (3.4%)	0.3448
Proximal obstruction	4 (2.9%)	1 (2.7%)	5 (2.8%)	1.0000
Distal obstruction	2 (1.4%)	0	2 (1.1%)	1.0000
Migration	8 (5.7%)	3 (8.3%)	11 (6.3%)	0.6982

These results showed that there was no significant difference between the performances of these two shunt systems in any of the outcome parameters. Therefore, for the price of one Codman shunt, 20 patients could be shunted just as safely and effectively with the Chhabra shunt. Furthermore, this study demonstrated that outcomes for shunting in Uganda were comparable to those reported in North America. Therefore, the Chhabra shunt was able to be used in the context of an African country with results as good as those in developed nations.

However, *shunts still present a problem under the best of circumstances*. A multicenter prospective study in North American children's hospitals recently demonstrated a 43.6% incidence of shunt failure (which included an 8.1% infection rate) within the first two years of placement[5]. These problems are magnified in Africa by barriers to the access of neurosurgical care (geography, infrastructure, economics, security, manpower), as well as malnutrition, poor hygiene, and severe macrocephaly. Thus, shunt-dependency is simply more dangerous in the context of emerging countries where obtaining prompt competent treatment for a shunt malfunction or infection may be virtually impossible.

B) Is endoscopic third ventriculostomy (ETV) a viable alternative to shunting in Africa?

ETV is a surgical procedure in which an endoscope is used to make an opening in the floor of the third ventricle of the brain in order to allow CSF to escape and be absorbed normally. At CCHU, 300 children with hydrocephalus underwent endoscopy for attempted ETV between June 2001 and March 2003[6]. (The equipment for performing this procedure was donated by IF.) The usefulness of ETV in older children with congenital aqueductal stenosis had been previously established, but its efficacy in a population like ours (80% < 1 year of age and 60% with post-infectious hydrocephalus) had been questioned. The results of this study are summarized in the tables below.

Severity of Macrocephaly

Head circumference	Number of patients (%)
< 50th %ile	22 (8%)
50-95th %ile	15 (5%)
95th %ile to 2cm > 95%ile	65 (24%)
2-4 cm > 95th %ile	61 (22%)
4-6 cm > 95th %ile	33 (12%)
>6 cm > 95th %ile	80 (29%)

Procedure at First Endoscopy

Procedure	Number of patients (%)
ETV	219 (73%)
VPS	55 (18%)
Reservoir	21 (7%)
CPX	3 (1%)
None	2 (1%)
Total	300 (100%)

Reasons for Abandoning ETV

Reason	Number of patients
Distorted anatomy (PIHC)	30
Turbid CSF (PIHC)	26
Congenital anomaly	11
Thick floor	6
Basilar artery	5
Scarred cistern	2
Basilar artery aneurysm	1

Completed ETV by Age

Age (months)	Number of patients (%)
0-3	78 (34%)
>3-6	61 (26.6%)
>6-12	42 (18%)
>12-24	17 (7.4%)
>24	31 (13.5%)
Total	229 (100%)

Results of First ETV

Result	Number of patients
Success	115 (115/224 = 51%)
Failure	105
Lost to f/u	5
Expired	4 (4/224 = 1.8%)
Total	229

Management of ETV Failure

Procedure	Number of patients
Repeat endoscopy	65
Shunting	39
None (lost to f/u)	1
Total	105

Procedure at Repeat Endoscopy for ETV Failure

Procedure	Number of patients
Repeat ETV	40 (62%)
VPS	19
CPX	4
Reservoir	2
Total	65

Of the 220 patients with sufficient follow up who received an ETV, 129 (59%) were treated successfully without the need for a shunt. Of all 300 children who had undergone endoscopy 151 (including those in whom an ETV was unable to be performed and those in whom ETV failed) ultimately received a shunt. Thus, ½ of all children presenting for treatment of hydrocephalus were spared shunt-dependency. The operative mortality (including repeat ETV operations) was 2.7%, the infection rate was 1.1%, and the morbidity was 1.5%.

The results of ETV differed according to patient age, cause of hydrocephalus (PIHC = post-infectious hydrocephalus, NPIHC = non-post-infectious hydrocephalus, MM = hydrocephalus associated with myelomeningocele), and whether the aqueduct of Sylvius was open or closed. It was found that the latter characteristic could be reliably predicted by the size of the 4th ventricle on the preoperative cranial ultrasound. The results of ETV among various patient groups are summarized below. The 4 patient types are as follows: A < 1 year/aqueduct open; B > 1 year/aqueduct open; C < 1 year/aqueduct closed; D > 1 year/aqueduct closed.

Results of ETV by Age and Etiology

Etiology	Age (yrs)	Number successful/total (%)
PIHC	<1	60/101 (59%)
	≥1	22/27 (81%)
		p=0.0421
NPIHC	<1	21/52 (40%)
	≥1	18/20 (90%)
		p=0.0001
MM	<1	8/20 (40%)

Results of ETV by Patient Type and Etiology

Etiology	Type	Number successful/total (%)
PIHC	A	14/31 (45%)
	B	7/9
	C	44/63 (70%)
	D	8/10
		p=0.0254
NPIHC	A	8/26 (31%)
	B	4/6
	C	11/23 (48%)
	D	10/10
		p=0.2536
MM	A	4/11
	C	2/3

The important results of this study can be summarized as follows:

ETV can be performed with acceptable results in an emerging country.
ETV was successful among children older than 1 year (NPIHC=90%, PIHC=81%) and in infants under a year with post-infectious aqueductal obstruction (PIHC type C=70%). Other infants under 1 year had <50% success (PIHC/A=45%, NPIHC/A=31%, NPIHC/C=48%, MM=40%).

As a result, we could now predict whether a patient was likely to benefit from ETV based upon very simple parameters that could be determined in virtually any setting in Africa: 1) age; 2) clinical history; and, 3) cranial ultrasound. And, one of the surprising outcomes in this study was the success of ETV among infants < 1 year with post-infectious aqueductal obstruction (the single most common type of patient encountered).

We have now had an opportunity to compare the 1-year outcomes for patients undergoing shunt placement (VPS) to those for patients treated by ETV. As demonstrated below, children treated by ETV had lower mortality rates and fewer repeat operations in the first

year after surgery. (NB: The general infant mortality rate in Uganda is 7.9%[7].) The total cost of the two procedures in our hospital (including all expenses such as cost of the Chhabra shunt and depreciation on the endoscopic equipment) are equivalent.

	VPS	ETV
Infection	**9.7%**	**1.1%**
Op mortality	**4.1%**	**2.7%**
1 year mortality	**15.9%**	**8.9%**
Re-ops 1st year	**0.67/pt**	**0.17/pt**
Re-ops 1st year	**120/333 (36%)**	**23/171 (16%)**
Cost/procedure	**$375 USD**	**$ 375 USD**

These results strongly suggest that ETV is a safer and more cost-effective method for the management of hydrocephalus in Africa than shunt placement.

C) Can the addition of choroid plexus cauterisation improve the results of ETV in infants < 1 year of age?

A likely reason for the reduced effectiveness of ETV in infants is their limited ability to absorb CSF, once an obstruction to CSF outflow has been bypassed by the ETV. In particular, infants with congenital hydrocephalus (NPIHC and MM) in which there is an obstructive component have not had an opportunity to develop normal CSF absorption. Our hypothesis has been that reducing the rate of CSF production by cauterisation of choroid plexus (the tissue that produces CSF in the ventricles) would improve the outcome of ETV in these patient groups. Although choroid plexus cauterization (CPC) has been used in the past with marginal success as an isolated technique, it has not been used in combination with ETV.
At CCHU we have added CPC to the ETV procedure in 200 consecutive patients, and now have preliminary data with 1-12 month follow up on 168. Interestingly, the addition of CPC had no benefit for patients older than 1 year or for infants under a year with post-infectious adqueductal obstruction (PIHC-C). However, ETV+CPC appears to be superior to ETV alone in infants with NPIHC (ETV=40% vs. ETV+CPC=62%), although the numbers have not yet reached statistical significance (P = 0.1). The results were almost identical for PIHC-A. Most notably, however, ETV+CPC is clearly superior to ETV alone in Spina Bifida infants (MM), almost doubling the success rate (ETV=37% vs. ETV+CPC=74%). This difference is statistically significant (P=0.01).

From the above, we can thus conclude the following:
ETV+CPC is significantly superior to ETV alone in MM children, with a success rate of about 75%.
ETV+CPC appears superior to ETV alone in infants with NPIHC and PIHC (except for PIHC-C), but the numbers have not yet reached statistical significance.

A randomised controlled trial of ETV+CPC vs. ETV alone is in order for PIHC and NPIHC infants < 1 year of age.
PIHC/C patients do not appear to benefit from the addition of CPC.
All MM infants should undergo ETV+CPC as the initial treatment for their hydrocephalus.

What have we learned about hydrocephalus in Africa?

Hydrocephalus is more common than in the West, and is mostly caused by neonatal infection. Efforts should be focused upon prevention.
ETV is the procedure of choice for all children >1 year of age (80-90% success).
ETV+CPC appears to be the procedure of choice for all infants with MM (75% success).
ETV+CPC is most likely the procedure of choice for all other infants under 1 year (>60% success), with the probable exception of PIHC-C (70% for ETV alone).
In the event that ETV is not possible or in those patients in whom it is not successful, the Chhabra shunt performs as well as an expensive Western shunt.

What relevance does this have for the West?

Many children (perhaps the majority) are un-necessarily shunt-dependent, although the African data does not include premature infants with post-hemorrhagic hydrocephalus.
75% of infants with Spina Bifida should be able to be spared shunt dependency and its attendant complications from the very beginning.
Shunts should be available worldwide at a fraction of their current cost.
We are very grateful to the International Federation of Spina Bifida and Hydrocephalus and to CURE International for their support of this on-going project.

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