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Global surgery for pediatric hydrocephalus in the developing world: a review of the history, challenges, and future directions

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OBJECTIVE Pediatric hydrocephalus is one of the most common neurosurgical conditions and is a major contributor to the global burden of surgically treatable diseases. Significant health disparities exist for the treatment of hydrocephalus in developing nations due to a combination of medical, environmental, and socioeconomic factors. This review aims to provide the international neurosurgery community with an overview of the current challenges and future directions of neurosurgical care for children with hydrocephalus in low-income countries.

METHODS The authors conducted a literature review around the topic of pediatric hydrocephalus in the context of global surgery, the unique challenges to creating access to care in low-income countries, and current international efforts to address the problem.

RESULTS Developing countries face the greatest burden of pediatric hydrocephalus due to high birth rates and greater risk of neonatal infections. This burden is related to more general global health challenges, including malnutrition, infectious diseases, maternal and perinatal risk factors, and education gaps. Unique challenges pertaining to the treatment of hydrocephalus in the developing world include a preponderance of postinfectious hydrocephalus, limited resources, and restricted access to neurosurgical care. In the 21st century, several organizations have established programs that provide hydrocephalus treatment and neurosurgical training in Africa, Central and South America, Haiti, and Southeast Asia. These international efforts have employed various models to achieve the goals of providing safe, sustainable, and cost-effective treatment.

CONCLUSIONS Broader commitment from the pediatric neurosurgery community, increased funding, public education, surgeon training, and ongoing surgical innovation will be needed to meaningfully address the global burden of untreated hydrocephalus.

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Hydrocephalus is the most common neurosurgical condition in children.[30] In developed countries, the incidence of congenital hydrocephalus is 0.5–1/1000 live births, while neonatal acquired hydrocephalus is 3–5/1000 live births[14,39,55,77] Although no reliable incidence estimate exists for hydrocephalus in most developing countries, it is likely higher due to nutritional deficiencies, low infant birth weight, greater incidence of perinatal and neonatal infections, and delayed antenatal diagnosis.[40,51] In addition to a higher disease incidence, developing countries also face a greater burden of care for hydrocephalus, likely attributed to a combination of medical and socioeconomic factors, including higher birth rates, poverty, cultural notions of health, poor infrastructure, unstable politics, and limited access to neurosurgical treatment.[10,51,67]

ABBREVIATIONS CPC = choroid plexus cauterization; DALY = disability-adjusted life-year; ETV = endoscopic third ventriculostomy; VP = ventriculoperitoneal.

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Thus, children with hydrocephalus in low- and middle-income countries face significant and unique barriers to treatment.[6,62,68,76] The past decade has witnessed increased awareness of the burden of hydrocephalus in developing countries, greater understanding of its etiology and characteristics, and the initiation of programs by a number of groups and organizations to increase access to treatment for these children. This narrative literature review attempts to summarize what is known, highlight what is being done, and encourage broader engagement from the pediatric neurosurgery community.

Methods

A literature search was performed using MEDLINE and Embase from database inception to the present, using terms pertaining to global surgery, developing countries and pediatric hydrocephalus, limited to English-language literature. This search strategy yielded 137 articles from MEDLINE and 241 articles from Embase, which were reviewed.

Global Burden of Disease

Global surgery for pediatric hydrocephalus is faced with a great burden of disease resulting from scarce resources, cultural and geographic barriers to treatment, differences in etiology, and inadequate neurosurgical manpower.

Increased Health Demand in Minimally Resourced Settings

Compared with children admitted to other hospital services, those with hydrocephalus require a disproportionately greater share of health resources for acute and longitudinal management.[50] Children with ventriculoperitoneal (VP) shunts, for instance, often undergo multiple admissions and surgeries over the course of their shunt-dependent life. In under-resourced settings where timely revision is often compromised by the cost to low- to middle-income families and great distances to neurosurgical centers, shunt failure may be associated with greater mortality than in high-income countries.[24,44,54,59]

Limited access to neurosurgical care also worsens the burden of disease in developing countries. In Africa, there is an unequal distribution of neurosurgical resources across the continent, with 86% of practicing neurosurgeons located in South Africa and North Africa.[22] In sub-Saharan Africa, there is approximately 1 neurosurgeon per 5 million people and in East Africa 1 neurosurgeon per 10 million people,[5,20] compared with 1 neurosurgeon per 100,000 people in European countries.[22] Furthermore, in sub-Saharan Africa, it is estimated that more than 100,000 newborns annually develop hydrocephalus before 1 year of age.[46] In Nigeria, hydrocephalus accounts for 32% of congenital neurosurgical conditions;[4] in Kenya, hydrocephalus represents the highest surgical burden of disease in male children;[78] and in Uganda, hydrocephalus accounts for 59% of neurosurgical conditions.[67] With more than half of Africa's population younger than 18 years, it is remarkable that fewer than 10% of neurosurgeons have subspecialty training in pediatric neurosurgery.[5] In Haiti, with a population of 10 million, one-third of whom are younger than 14 years of age living in poverty, access to neurosurgical care is also sparse.[76] In many impoverished countries of Central and South America, CSF-diverting procedures account for nearly 40% of total neurosurgical procedures.[37]

This high burden of disease is coupled with the reality that most families do not have ready access to specialized neurosurgical care, and many cultural and economic factors lead to delayed presentation to medical care, often weeks to months after the symptomatic onset of hydrocephalus.[27,29] Some factors include shame for carrying a sick child, unawareness of treatment, poverty, initial attempt with traditional healing methods, poor understanding of early signs and symptoms, social taboos, or lack of physical access to health care.[34,37,53,57] Limited access to already limited health resources, greater burden of pediatric hydrocephalus, and complex social and geographical barriers pose significant challenges for international global surgery efforts.

Hydrocephalus Etiology

The pathogenesis of pediatric hydrocephalus is multifaceted,[30] and emerging evidence suggests that different etiologies exist in developing versus developed nations.[49,64] While pediatric hydrocephalus in developed countries commonly arises from intraventricular hemorrhage of prematurity and congenital causes, in developing countries postinfectious hydrocephalus predominates, likely due to the greater incidence of neonatal sepsis. A combination of inadequate maternal-fetal care and unsanitary living environments contribute to more prevalent and severe cases of neonatal sepsis leading to postinfectious hydrocephalus, which accounts for 60% of hydrocephalus cases in Uganda[64] and 40% of cases in South Africa.[25] Postinfectious hydrocephalus, however, is not the leading etiology reported from all developing countries, with hydrocephalus secondary to neural tube defects being especially common, along with aqueductal stenosis and hemorrhage, in Kenya, Nigeria, Cameroon, Zambia, Zimbabwe, Malawi, and Saudi Arabia.[2,3,19,23,28,63,65]

The spectrum of bacteria causing neonatal sepsis and postinfectious hydrocephalus also differs between developing and developed countries.[32,36] In developed countries, *Group B Streptococcus*, *Escherichia coli*, and *Listeria monocytogenes* most commonly cause neonatal sepsis. In the developing world, gram-negative organisms, but rarely *Group B Streptococcus*, predominate.[32,36] Furthermore, differences in bacterial speciation may depend on the season: cases of postinfectious hydrocephalus had a greater prevalence of *Acinetobacter* species in the ventricular CSF of Ugandan infants during the rainy season.[36] Another study in Uganda found that the peak incidence of postinfectious hydrocephalus was related to climate, with infection-onset peaks in the intermediate period between rainy and dry seasons.[49]

Bacteriological studies to date raise concerns as to whether current antimicrobial protocols in developing nations include adequate coverage of gram-negative bacteria. Recent evidence supports this concern, as most of the gram-negative bacilli isolated from VP shunt infec-

tions in Kenya were resistant to cefazolin, ciprofloxacin, and gentamycin.[43] These findings invite future efforts in global surgery to assess the adequacy of current antibiotic regimens in neonatal sepsis, with the hope of adequately treating and preventing cases that may otherwise progress to postinfectious hydrocephalus.

Surgical Management

VP shunt insertion is the mainstay of hydrocephalus treatment in the developing world.[18,23] This treatment is effective, but is not without complications of shunt extrusion, breakage, overdrainage, obstruction, or infection and the potential for many revisions over a lifetime.[18] There is an especially high upfront burden of disease, with nearly half of all shunts failing in the first 2 years.[18] In developing countries, risk factors for poor outcomes after VP shunt treatment include younger age, comorbidities like anemia and malnutrition, advanced presentation, and the absence of adequate diagnostic imaging.[23] Worldwide complication rates of VP shunts are reported to be between 1% and 40%, but developing countries face the greatest burden.[23,31]

While the incidence of VP shunt infections ranges from 2% to 9% in developed countries,[15] in developing countries it reportedly occurs in 8.6%–50%.[8,12,23,26,31,33,41,42,56] The microbiology of shunt infection also differs. In developed countries, *Staphylococcus aureus* and *Staphylococcus epidermidis* species predominate, while isolates from developing countries are mostly gram-negative organisms.[7,21,35,43] However, not all studies report this pattern. While *Escherichia coli, Acinetobacter, Klebsiella, Pseudomonas, Salmonella typhimurium,* and *Proteus* are isolated in greater proportions of shunt infections compared with the developed world, *S. aureus* and coagulase-negative staphylococci were still common isolates in Malaysia, Kenya, and Nigeria.[1,42,56]

The preponderance of gram-negative and enteric bacteria in shunt infections may be related to poor hygiene, malnutrition, and the hospital environments in developing countries. Hospital-acquired sources include operating rooms without sterile drapes or operating tables, suites shared with general surgery,[21] overcrowding, and poor isolation of those with gram-negative infections.[43] Overall, these data suggest that not only should public health measures improve surgical sterility, hygiene, and more efficacious isolation of those with known infection, but they must also ensure adequate antibiotic coverage for both gram-negative and gram-positive bacteria. Most gram-negative isolates in these settings are multidrug resistant—a factor that also contributes to the greater morbidity and mortality of shunt infections in the developing world.[43]

Endoscopic third ventriculostomy (ETV) offers freedom from hardware-related complications, and it seems especially appropriate in limited resource settings, where it offers a morbidity-reducing and cost-effective solution.[17,69] The addition of choroid plexus cauterization (CPC), with the goal of decreasing CSF production and changing CSF dynamics, was refined over the past decade through pioneering work in sub-Saharan Africa.[52,61,71,72,75] The success of ETV/CPC across all hydrocephalus etiologies ranges from 66% to 81.9%[9,60,61,63,70,71,74,75] and has been shown to be more efficacious than stand-alone ETV in children younger than 2 years. Limitations to ETV/CPC in global surgery include the absence of preoperative high-quality MRI[72] and a limited number of neurosurgeons skilled in endoscopic techniques.[21]

Economic Considerations

With the advent of the Millennium Development Goals, there has been a great emphasis on improving maternal health and reducing child mortality, malnutrition, and communicable diseases. Surgically managed conditions are commonly not perceived as cost-effective, while cost-effective health measures, such as vaccination, often take precedence in global health campaigns.[13]

Although the economic burden of hydrocephalus management is great, emerging evidence suggests that the neurosurgical management of hydrocephalus is cost-effective in the developing world. In a Ugandan study, the cost-effectiveness ratio for hydrocephalus surgery was $108.74 US dollars per disability-adjusted life-year (DALY)—comparable to WHO vaccination campaigns ($51.86–$220.39 per DALY).[13] Furthermore, although the up-front cost of treating all incident cases of hydrocephalus in sub-Saharan Africa in 1 year would approach $190 million, it would confer an estimated lifetime economic benefit of $1.4 billion.[69] Similar results have been demonstrated in cost-effectiveness analyses in Haiti[76] and Guatemala.[16] Furthermore, ETV averted nearly twice as many DALYs compared with VP shunting.[16] However, in centers unable to offer ETV or in patients with ETV failure, VP shunting continues to be the mainstay treatment, and successful use of cheaper shunt systems has minimized VP shunting cost without compromising outcome.[59] Other important considerations when evaluating the economic impact of hydrocephalus are the costs to the family, which include the costs of travel, opportunity, and investigations.[16] In a Nigerian study, 41% of patients presenting with suspected hydrocephalus could not afford transcranial ultrasound or CT.[2]

Overall, this work suggests that current neurosurgical interventions for hydrocephalus are cost-effective and that there is room for innovation to make surgery more affordable for families and health systems, without compromising safety.

Current International Efforts

A number of international efforts have helped provide global neurosurgical care and facilitate sustainable neurosurgical training.[62] Various organizations, including the Foundation for International Education in Neurological Surgery, the World Federation of Neurosurgical Societies, and the International Society for Pediatric Neurosurgery have contributed greatly to the development of global neurosurgical care, creation of medical infrastructure, and advancement of neurosurgical education. The extent of international efforts for neurosurgery is expanding and promising. International programs specifically providing treatment or neurosurgical education in the field of pediatric hydrocephalus are considered in this review and are highlighted in Table 1. These efforts span across Africa, Haiti, and Central and South America.

TABLE 1. Current organizations providing global neurosurgery medical and training services in developing countries, with a focus on pediatric hydrocephalus

Location	Organization & Website	Year Established	Volume	Services	Impact
Uganda	CCHU & CH cure.org/hydrocephalus	2001	1200 pediatric neurosurgical operations per year at CCHU, more than half for hydrocephalus. The CH program has provided more than 18,000 hydrocephalus operations since 2001.	CCHU provides general pediatric neurosurgery, including hydrocephalus, congenital anomalies, CNS tumors, & epilepsy. CH trains neurosurgeons in other LMIC to perform ETV/CPC, provides their home institutions w/ the necessary equipment, & funds local support for patient follow-up & data collection.	ETV/CPC was pioneered & rigorously studied at CCHU & has demonstrated benefit & cost-effectiveness. CH has trained 27 surgeons, established partner hydrocephalus treatment sites in 18 countries, & performed 18,000 hydrocephalus operations since 2001.
Kenya	BethanyKids at Kijabe Hospital (BKKH) www.bethanykids.org	2004	In 2011, 410 shunt operations & 131 ETVs were performed.	More than half of all neurosurgical cases are pediatric, mostly spina bifida or hydrocephalus.	A pediatric neurosurgery fellowship program was established in 2011. A network of outreach clinics across Kenya has been established. BKKH is the single largest provider of treatment for children w/ hydrocephalus & spina bifida in Kenya.
	Neurological Society of Kenya & Neurosurgery Education & Development Foundation nedfoundation.wordpress.com	2006	As of 2013, 376 children w/ hydrocephalus had undergone ETV across 21 hospitals in 7 different countries.	Unique service of mobile outreach neuroendoscopy.	As of 2013, 72 local surgeons have been trained. This program has provided a solution to address the inadequate numbers of neurosurgeons in rural areas of East Africa, & has stimulated the interest of many local neurosurgeons to adapt neuroendoscopic techniques into their own practice.
Haiti	HHK haitihealthykids.org	2003	Since 2003, more than 500 patients w/ hydrocephalus have been treated.	Offers 10 surgical trips each year that are focused on hydrocephalus. HHK takes on American & European neurosurgeons who ultimately mentor Haitian medical providers. HHK has offered the first ETV surgeries in Haiti.	Over the years HHK reports a decrease in the number of children presenting w/ late clinical features of hydrocephalus, perhaps due to greater public education efforts.
South & Central America	IHC ih4c.wordpress.com	2001	In all, 414 children have undergone 463 operations, w/ nearly 40% of these surgeries including initial shunt placement &/or shunt revision.	From 1996 to 2008, 19 surgical trips to Guatemala, St. Vincent & the Grenadines, Honduras & Guyana have been coordinated. Moreover, more than 40 senior neurosurgical residents from North America have participated in IHC trips.	The IHC model of care sets an important precedent internationally by emphasizing & upholding a commitment to long-term follow-up. By maintaining close relationships w/ local physicians & hiring full-time local staff in St. Vincent, Belize, & Guatemala, who are familiar w/ the local infrastructure, IHC continues to monitor the postoperative progress of the patients it has served.
	Project Shunt: University of Michigan, Healing the Children, & the Pediatric Foundation of Guatemala medicine.umich.edu/dept/neurosurgery/projectshunt	1997	During the latest medical mission, 16 operations were performed for pediatric neurological congenital disorders.	Neurosurgical missions to Guatemala for the treatment of congenital disorders including myelomeningocele, untethering of spinal cord, & CSF diversion for hydrocephalus.	In addition to surgery, the group provides teaching to surgeons, nurses, & parents, & fosters sustainable neurosurgery.

BKKH = BethanyKids at Kijabe Hospital; CCHU = CURE Children's Hospital of Uganda; CH = Cure Hydrocephalus; HHK = Haiti Healthy Kids; IHC = International Hospital for Children; LMIC = low- to middle-income countries.

Major Challenges

Limitations in Health Care Infrastructure

Providing neurosurgery in a developing country is a fine balance between operating under suboptimal conditions and upholding an obligation to nonmaleficence. Managing hydrocephalus peri- and postoperatively is challenged by limits in neurosurgical manpower, supportive consultations, ICU capabilities, imaging technology, operative tools, and medications.[20,38,47,58,76]

Government remuneration models also contribute unique challenges to conducting pediatric neurosurgery in the developing world. In Kenya for instance, the government's health care budget is $15/year per person, resulting in a large discrepancy between the capacity to treat and the ability to afford treatment.[47] With many families making a daily income of $2, it makes affording a CT scan ($75) impossible for most.[47] The provision of care at the Kijabe Hospital in Kenya is further complicated by the government's remuneration of $29 per day for hospital operating costs.[47] Similarly, in Guatemala, a mere $256 per capita is spent on health care, whereas the United States spends $6096 per capita.[37] Therefore, the majority of hydrocephalus care is financially supported by funding agencies and donations of surgical materials by manufacturers in developed nations and the surgeon's personal expense.[37,76]

Challenges in Neurosurgical Training

Training of local physicians and other health care providers is a necessary catalyst to generate future pediatric neurosurgeons. There is an immense need for pediatric neurosurgeons in the developing world, but also a significant gap in the capacity to train them. Many countries do not have neurosurgery residency programs, and in some places where residency programs do exist, additional challenges like inadequate operative resources, funding, research opportunities, and career mentorship are prevailing issues.[38] In contrast to residents in North America who learn primarily by operating with the attending physician, residents in Africa rely heavily on textbooks and observation.[5] Even after graduating, trainees are strongly encouraged to obtain training in Europe or North America.[5] The scarcity of neurosurgeon teachers, limited residency programs, and high attrition of residents and neurosurgeons to other countries with greater resources, makes training a difficult feat in developing countries.[68] However, some residency training programs have endeavored to train neurosurgeons for countries in sub-Saharan Africa, including those at University of Cape Town, Mohamed V University in Morocco, and through the College of Surgeons of East, Central, and Southern Africa.[22,62] Other residency programs in under-resourced countries have residents rotate through more rural areas such as the program at the University of Nairobi where residents complete 1–3 months of pediatric neurosurgical training in rural Kijabe.[5,38] Nonetheless, until adequate infrastructure, residency training programs, and initiatives to retain local neurosurgeons are in place, the training of local general surgeons has been proposed.[62,76] Of course such an endeavor, if adopted, would have to be selective in teaching reasonably acquirable skills relevant to common neurosurgical cases in areas without current neurosurgical care.[68]

Ethics of International Aid

Unique challenges exist for international surgical aid in developing countries. Criticisms exist for medical missions that periodically provide care, as they can promote increased dependency on foreign aid and the disenfranchisement of local health care providers.[16,58,76] Another important issue is that of surgical follow-up,[76] as many surgical missions perform needed surgery, but continuity of care is compromised when a medical team leaves a country. Many of the international surgical initiatives for hydrocephalus to date have attempted to address the aforementioned issues by improving the longevity and continuity of local initiatives, providing training for local health professionals and fellowship programs for the next generation of local neurosurgeons, following up with patients, and crafting innovative interventions, such as ETV/CPC, that are ultimately more suitable to a developing nation's scarce resources.[10,11,45,48,62,66,68]

Future Directions

Our review of the literature underscores that pediatric hydrocephalus is an important and inadequately addressed component of the global burden of disease. Existing approaches to this problem provide templates for future refinement and expansion of programs that seek to increase access to optimal treatment for children everywhere. In addition, there needs to be a fundamental reframing of the current global perspective that regards pediatric neurosurgery as being too specialized of a service for developing nations. Many have appropriately advocated for investments in primary care and disease prevention; however, we find evidence suggesting that the burden of pediatric hydrocephalus in many developing nations is sufficiently significant to warrant greater attention. Training and equipping neurosurgeons to establish an increasing number of sustainable centers for hydrocephalus treatment will be an ongoing and important challenge. In addition, the burden of pediatric hydrocephalus is intimately connected to more general public health concerns, such as malnutrition, communicable diseases, maternal risk factors, and education. As such, we suggest that future efforts, in addition to increasing access to neurosurgical treatment, should also focus on preventable causes of hydrocephalus including neonatal sepsis, neural tube defects, and infant prematurity. This may include education and policy promoting sanitary birthing practices, identification of the key pathogens responsible for postinfectious hydrocephalus (which may vary by region and season), modification of antibiotic regimens for neonatal infections, and continued research on the potential environmental sources of infection. Another crucial element to decrease the morbidity and mortality associated with delayed presentation is public education. We need to create community-based initiatives that provide information about hydrocephalus, as well as education initiatives for primary health care providers and health policy advisors and authorities. Organizations already engaged in such international educa-

tion and advocacy work include the International Federation for Spina Bifida and Hydrocephalus (www.ifglobal.org) and the PUSH! Global Alliance (www.pu-sh.org).

Conclusions

We have provided an overview of pediatric hydrocephalus in the context of global health. We have reviewed the health and economic burdens of hydrocephalus, revealed evidence that suggests regional variations in etiology, highlighted innovative surgical approaches and current international efforts to increase access to treatment, and suggested future directions, including the need to reduce the global burden of disease through prevention. It is a daunting task that begs the engagement of many partners.

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Author Contributions

Conception and design: all authors. Acquisition of data: all authors. Analysis and interpretation of data: all authors. Drafting the article: all authors. 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. Administrative/technical/material support: Warf. Study supervision: Warf.

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