

BIOGRAPHICAL SKETCH

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NAME: Warf, Benjamin

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Professor of Neurosurgery

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Harvard Medical School, Boston, MA	MD	05/1984	Medicine
Case Western Reserve University, Cleveland, OH	Resident	06/1991	Neurosurgery
Boston Children's Hospital, Boston, MA	Fellow	06/1992	Pediatric Neurosurgery
Harvard-Macy Institute	Scholar	04/1999	Medical Education

A. Personal Statement

1. I am a Professor of Neurosurgery at Harvard Medical School and hold the Chair in Hydrocephalus and Spina Bifida at Boston Children's Hospital. After serving as Chief of Pediatric Neurosurgery and Director of Graduate Medical Education for the Dept. of Surgery at University of Kentucky, I became the founding Medical Director of CURE Children's Hospital of Uganda from 2000 to 2006. During that time, I reported neonatal infection as the primary cause of infant hydrocephalus in the region, with a cyclical incidence that coincides with the seasonal rain patterns. Ongoing work is focused on defining the pathogenesis upon which to base prevention strategies. I also developed a novel procedure to treat infant hydrocephalus that avoids shunt dependence (ETV/CPC), refining its indications and predictors of outcome, and introducing the procedure to centers in North America. I am Principal Investigator of an NIH-funded RCT comparing developmental outcomes and brain growth between ETV/CPC and shunt placement for treatment of post-infectious hydrocephalus in Ugandan infants. I founded a program (CURE Neuro) to train and equip surgeons from developing countries in the ETV/CPC technique. I am founding Board Chairman of NeuroKids, a non-profit to promote pediatric neurosurgery in LMIC. By invitation, I have presented our work at the CDC, NIH, and USAID. I have testified before the US House Subcommittee on Africa, Global Health, and Human Rights, in support of the introduction of the International Hydrocephalus Treatment and Training Act (HR 3525) into the House of Representatives, and the subsequent introduction of HR 1468, the "Global Brain Health Act of 2015". In 2012 I was named a MacArthur Fellow.

1. Kulkarni AV, Schiff SJ, Mbabazi-Kabachelor E, Mugamba J, Ssenyonga P, Donnelly R, Levenbach J, Monga V, Peterson M, MacDonald M, Cherukuri V, **Warf BC**. Endoscopic Treatment versus Shunting for Infant Hydrocephalus in Uganda, *New England Journal of Medicine*, 377:2456-64, 2017.
2. Kahle KT, Kulkarni AV, Limbrick DD Jr, **Warf BC**. Hydrocephalus in children. *Lancet*. 2016 Feb 20;387(10020):788-99. PubMed PMID: [26256071](#).
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*. 2005 Dec;103(6 Suppl):475-81. PubMed PMID: [16383244](#).
4. **Warf BC**. Hydrocephalus in Uganda: the predominance of infectious origin and primary management with endoscopic third ventriculostomy. *J Neurosurg*. 2005 Jan;102(1 Suppl):1-15. PubMed PMID: [16206728](#).

B. Positions and Honors

Positions and Employment

1992 - 2000 Associate Professor of Surgery and Pediatrics, University of Kentucky School of Medicine, Lexington, KY

2000 - 2006 Medical Director and Chief of Surgery, CURE Children's Hospital of Uganda, Mbale
 2006 - 2009 Clinical Professor of Neurosurgery, Thomas Jefferson Medical School, Philadelphia, PA
 2009 – Professor of Neurosurgery, Harvard Medical School, Boston, MA
 2009 – Director of Neonatal and Congenital Anomaly Neurosurgery, Boston Children's Hospital
 2009 – Neurosurgical Consultant, NICU, Beth Israel Hospital, Boston, MA
 2009 - Neurosurgical Consultant, NICU, Brigham and Women's Hospital, Boston, MA

Other Experience and Professional Memberships

1992 - Member, Congress of Neurological Surgeons
 1992 - Fellow, American Association of Neurological Surgeons
 1993 - 2000 Chief of Pediatric Neurosurgery, University of Kentucky Medical Center
 1996 - Diplomate, American Board of Neurological Surgery
 1998 - Diplomate, American Board of Pediatric Neurological Surgery
 1998 - 1999 Harvard Macy Scholar in Medical Education, Harvard University
 1998 - 2000 Director of Surgical Education, University of Kentucky College of Medicine
 1999 - Member, American Association of Pediatric Neurosurgeons
 2005 - Medical Director, CURE Hydrocephalus
 2006 - Director of Research, CURE Children's Hospital of Uganda
 2007 - 2015 Board of Directors, International Federation for Neuroendoscopy
 2009 - Director of Neonatal and Congenital Anomalies Neurosurgery, Boston Children's Hospital
 2011 - Affiliate Faculty, Harvard Medical School Department of Global Health and Social Medicine
 2012 - 2020 Board of Trustees, CURE International
 2014 - Hydrocephalus and Spina Bifida Chair, Boston Children's Hospital
 2014 - Global Medicine Advisory Board, Boston Children's Hospital
 2015 - Global Expert Panel, International Federation for Spina Bifida and Hydrocephalus
 2016 - Director of Global Neurosurgery Fellowship, Harvard Medical School Program in Global Surgery and Social Change
 2018 - Board of Directors, Boston Children's Accountable Care Organization
 2019 - Board of Directors, Joni and Friends International
 2020 - Board of Directors (Chairman), NeuroKids

Honors

2005 Annual Award, International Federation for Spina Bifida and Hydrocephalus
 2005 Annual Award, International Federation for Neuroendoscopy
 2007 Humanitarian Award, American Association of Neurological Surgeons
 2011 Healthcare Achievement Award, Spina Bifida Association
 2012 MacArthur Fellow, John D. and Katherine T. MacArthur Foundation
 2019 Award for Global Education in Neuroendoscopy, International Federation for Neuroendoscopy

C. Contribution to Science

I was the first to report neonatal infection (ventriculitis) as the primary cause of infant hydrocephalus in East Africa (post-infectious hydrocephalus, PIH), and discovered a cyclical incidence of these infections that coincides with the seasonal rain patterns. I characterized the clinical, imaging, and endoscopic findings that define PIH, as well as optimal treatment strategies and long-term outcomes. Ongoing work is focused on defining the pathogenesis upon which to base prevention strategies, and developing methods to individualize and optimize treatment.

- a. Paulson JN, Williams BL, Hehnlly C, Sinnar S, Zhang L, Ssentongo P, Kabachelor E, Wijetunge DSS, von Bredow B, Mulondo R, Mishra N, Kiwanuka J, Bajunirwe F, Bazira J, Bebell, L, Burgoine K, Couto-Rodriguez M, Erickson JE, Erickson T, Ferrari M, Gladstone M, Guo C, Haran M, Hornig M, Isaacs AM, Kaaya BN, Kulkarni AV, Kumbakumba E, Li X, Limbrick DD, Magombe J, Morton SU, Mugamba J, Ng J, Olupot-Olupot P, Onen J, Roy F, Sheldon K, Townsend R, Weeks AD, S=Whalen AJ, Quackenbush J, Ssenyonga P, Galperin MY, Almeida M, Atkins H, **Warf BC**, Lipkin I, Broach J, Schiff SJ. The

Bacterial and Viral Complexity of Infant Postinfectious Hydrocephalus in Uganda. *Sci Transl Med.* 2020 Sep 30; 12(563) PubMed PMID: PMC7774825

- b. Schiff SJ, Ranjeva SL, Sauer TD, **Warf BC**. Rainfall drives hydrocephalus in East Africa. *J Neurosurg Pediatr.* 2012 Sep;10(3):161-7. PubMed PMID: [22768966](#).
- c. **Warf BC**, Dagi AR, Kaaya BN, Schiff SJ. Five-year survival and outcome of treatment for postinfectious hydrocephalus in Ugandan infants. *J Neurosurg Pediatr.* 2011 Nov;8(5):502-8. PubMed PMID: [22044377](#).
- d. Li L, Padhi A, Ranjeva SL, Donaldson SC, **Warf BC**, Mugamba J, Johnson D, Opio Z, Jayarao B, Kapur V, Poss M, Schiff SJ. Association of bacteria with hydrocephalus in Ugandan infants. *J Neurosurg Pediatr.* 2011 Jan;7(1):73-87. PubMed PMID: [21194290](#).

Because shunt-dependence is more dangerous in rural Africa, I developed and validated a novel treatment for hydrocephalus in infants by combining endoscopic third ventriculostomy and choroid plexus cauterization (ETV/CPC). I subsequently reported its efficacy in distinct etiologies of hydrocephalus and developed a scoring system that predicts outcome. To date, through CURE Hydrocephalus, surgeons in more than 20 countries have been trained and equipped in this technique, resulting in more than 20,000 hydrocephalus operations. Since joining Boston Children's Hospital in 2009, I have shown the efficacy of ETV/CPC for infant hydrocephalus in North America. My work has led to a North American multi-institutional prospective trial by the Hydrocephalus Clinical Research Network, in which I was responsible for training the participating neurosurgeons, having now trained 10 of them at our hospital in Uganda. The second edition of my monograph on the ETV/CPC technique was published in 2015. Ongoing work seeks to further optimize patient selection and clinical outcomes. Our current randomized controlled trial has established no difference in brain growth or cognitive development at one year between shunt and ETV/CPC (*NEJM* 377:2456-64, 2017).

- a. Lepard JR, Dewan MC, Chen SH, Bankole OB, Mugamba J, Ssenyonga P, Kulkarni AV, **Warf BC**. [The CURE Protocol: evaluation and external validation of a new public health strategy for treating paediatric hydrocephalus in low-resource settings](#). *BMJ Glob Health.* 2020; 5(2): e002100.
- b. Kulkarni AV, Schiff SJ, Mbabazi-Kabachelor E, Mugamba J, Ssenyonga P, Donnelly R, Levenbach J, Monga V, Peterson M, MacDonald M, Cherukuri V, **Warf BC**. Endoscopic Treatment versus Shunting for Infant Hydrocephalus in Uganda, *New England Journal of Medicine*, 377:2456-64, 2017.
- c. **Warf B**, Ondoma S, Kulkarni A, Donnelly R, Ampeire M, Akona J, Kabachelor CR, Mulondo R, Nsubuga BK. Neurocognitive outcome and ventricular volume in children with myelomeningocele treated for hydrocephalus in Uganda. *J Neurosurg Pediatr.* 2009 Dec;4(6):564-70. PubMed PMID: [19951045](#).
- d. **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. *J Neurosurg Pediatr.* 2008 Nov;2(5):310-6. PubMed PMID: [18976099](#).

Clinical outcomes in global neurosurgery have been an important part of my research. I documented the 5-year survival rates and functional outcomes for Ugandan infants treated for myelomeningocele and for post-infectious-hydrocephalus, and we have just published our results for 10-year survival in the myelomeningocele cohort. Our work was the first to demonstrate a survival benefit for WHO-endorsed community-based rehabilitation (CBR) programs, the first to demonstrate equivalence in early childhood development between ETV/CPC and conventional shunt treatment, and the first to document the affect of previous ETV or CPC on subsequent shunt function. I was the first to directly compare clinical outcomes using an inexpensive Indian-made shunt system commonly used in the developing world with North American shunt systems costing 10 to 20X more, demonstrating no difference in efficacy and carried out a RCT showing no difference in infection rate between antibiotic-coated and standard shunt catheters. We provided the original assessment of the burden of disease and economic impact for infant hydrocephalus in sub-Saharan Africa and a detailed cost-benefit analysis of its treatment, which was among the first studies to demonstrate cost-effectiveness for any surgical procedure in a limited resource setting.

- a. Mbabazi-Kabachelor E, et al, **Warf BC**. Infection risk for Bactiseal Universal Shunts versus Chhabra Shunts in Ugandan infants: a randomized controlled trial. *J Neurosurg Pediatr* 23(3):397-406, 2019
- b. Sims-Williams HJ, Sims-Williams HP, Kabachelor EM, Fotheringham J, **Warf BC**. Ten-year survival of Ugandan infants after myelomeningocele closure. *J Neurosurg Pediatr*. 2016 Oct 21;PubMed PMID: [27767901](#).
- c. **Warf BC**, Alkire BC, Bhai S, Hughes C, Schiff SJ, Vincent JR, Meara JG. Costs and benefits of neurosurgical intervention for infant hydrocephalus in sub-Saharan Africa. *J Neurosurg Pediatr*. 2011 Nov;8(5):509-21. PubMed PMID: [22044378](#).
- d. **Warf BC**, Wright EJ, Kulkarni AV. Factors affecting survival of infants with myelomeningocele in southeastern Uganda. *J Neurosurg Pediatr*. 2011 Feb;7(2):127-33. PubMed PMID: [21284456](#).

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

Title: Improving infant hydrocephalus outcomes in Uganda: Predicting developmental outcomes and identifying patients at risk for early treatment failure after ETV/CPC

Role: Co-PI with Ivy Lin, PhD

Sponsor: NIH (R01HD096693)

Date: 09/13/18-06/30/23

Summary: The objective of this project is to investigate the potential of early post-operative near-infrared spectroscopy to predict developmental outcome and identify patients at risk for early treatment failure in Ugandan infants treated for hydrocephalus with ETV/CPC.

Completed Research Support

Title: Control of Neonatal Sepsis and Hydrocephalus in sub-Saharan African

Role: Co-Investigator; PI: Steven Schiff, MD, PhD (Penn State University)

Sponsor: NIH (DP1HD086071)

Date: 02/01/17 – 01/31/19

Summary: The objective of this project is to identify the organisms causing neonatal sepsis and post-infectious hydrocephalus in Africa and to utilize engineering control principles to optimize treatment and prevention.

Title: Does arsenic increase risk of neural tube defects in a highly exposed population?

Role: Co-Investigator; PI Maitreyi Mazumdar, MD, PhD

Sponsor: NIH (R01ES026317)

Date: 01/01/16-12/31/20

Summary: The objective of this project is to investigate arsenic's known effects on maternal glucose regulation and folate status as possible mechanisms of arsenic's toxicity in neural tube defects.

Title: Prevention of Cerebrospinal Fluid (CSF) Shunt Infections

Role: Co-I; PI: Tamara Simon, MD, MSPH (Children's Hospital Los Angeles)

Sponsor: NIH (R01NS101029)

Date: 04/15/2018 – 03/31/2021

Summary: The objective of this project is to determine the comparative effectiveness of intrathecal antibiotics and antibiotic impregnated shunt tubing, two novel and controversial techniques, in the prevention of CSF shunt infection. The research team will collect a wide array of clinical information from patients who underwent their initial shunt placement at Boston Children's Hospital between 2007 and 2012.

Title: Neurocognitive outcomes and changes in brain and CSF volume after treatment of post-infectious hydrocephalus in Ugandan infants by shunting or ETV/CPC: a randomized prospective trial

Role: Co-PI with Steven Schiff, MD, PhD (Penn State University), Abhaya Kulkarni, MD, PhD (Hospital for Sick Children)

Sponsor: NIH (R01HD085853)

Date: 09/01/17 – 05/31/21

Summary: The objective of this randomized controlled trial is to evaluate the neurocognitive effects and volume changes in the brain from ventricular shunting versus endoscopic surgery in a population of post infectious hydrocephalic patients.