HYDROCEPHALUS ASSOCIATION

The mission of the Hydrocephalus Association is to promote a cure for hydrocephalus and improve the lives of those affected by the condition. We will accomplish this by collaborating with patients, caregivers, researchers and industry, raising awareness, and funding innovative, high-impact research to prevent, treat and ultimately cure hydrocephalus.

Hydrocephalus Association

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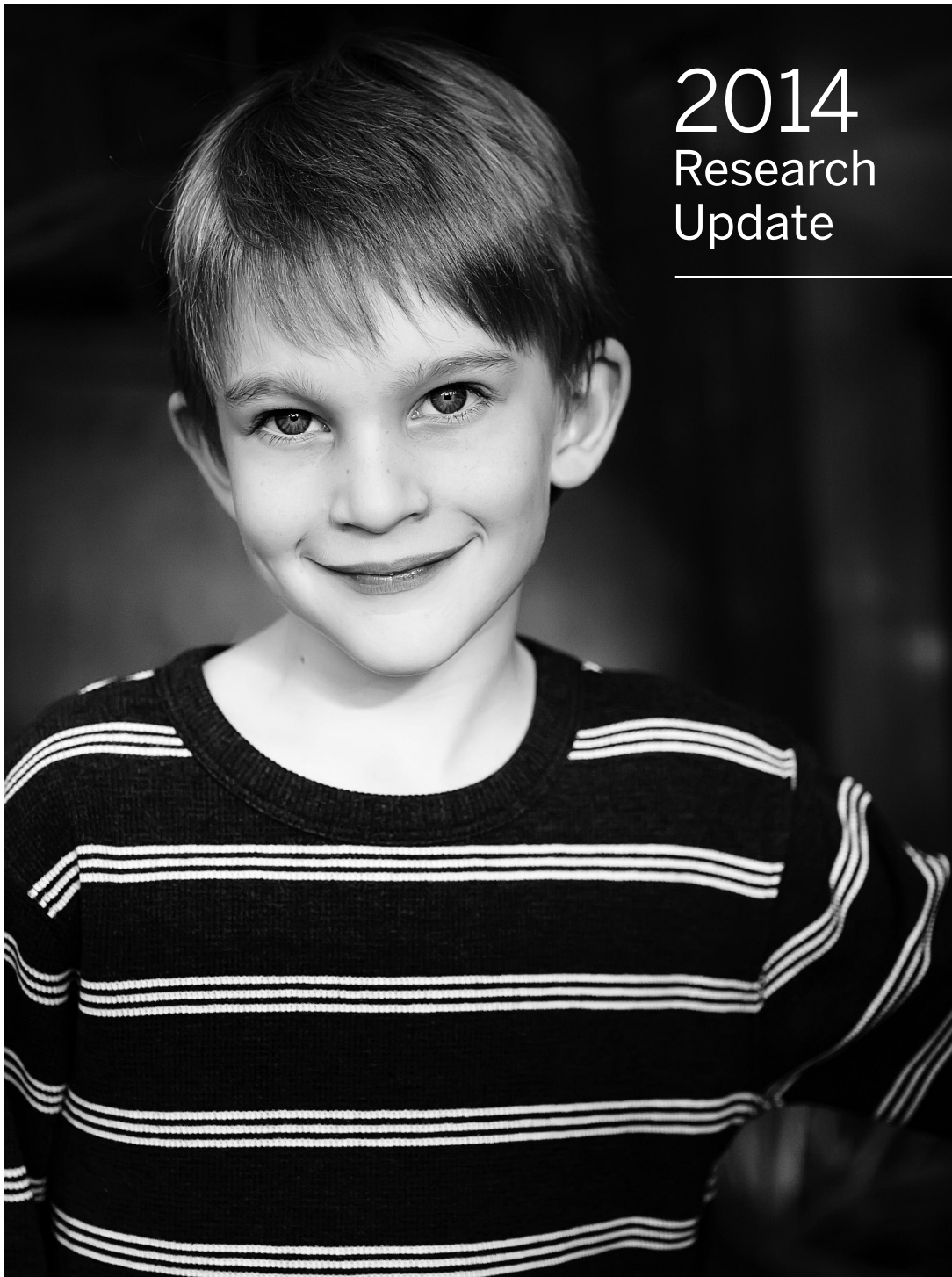
www.hydroassoc.org

Hope in Progress



2014 Research Update

About the Hydrocephalus Association Research Plan

The Hydrocephalus Association is dedicated to the advancement of promising research with the potential to advance the understanding, diagnosis, treatment and, ultimately, the prevention of hydrocephalus. Our organizational mission is bold: to promote a cure for hydrocephalus and improve the lives of those affected by the condition. Implementation of our Strategic Research Initiative is catalyzing a national effort to improve treatments and outcomes—and to find a cure for hydrocephalus. To that end, HA spends a significant portion of its organizational budget (46% in 2013 alone) to directly support research efforts. Our targeted initiative addresses the need for more research through three priority investment areas:

Priority Area 1: **Stimulate the research ecosystem**

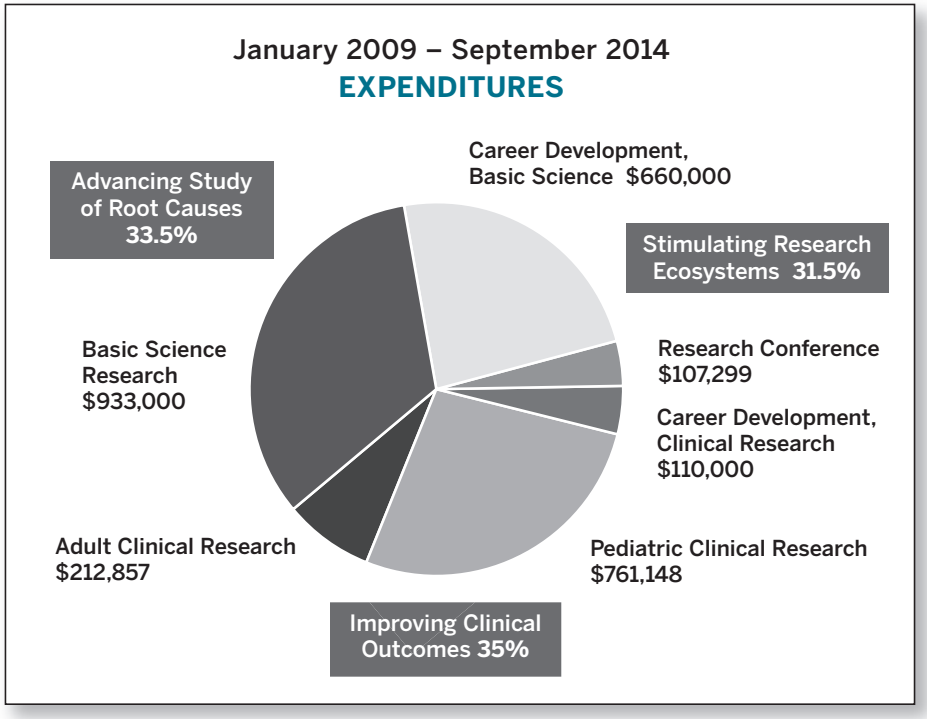
Hydrocephalus was perceived by some members of the medical community as "solved" by the introduction of the shunt, but so many issues remain. Conferences and workshops are needed to refocus and re-galvanize the research community to tackle this complicated condition. In addition, injecting young talent into the field of hydrocephalus research and creating a supportive career development path are essential to generating enough scientific activity to advance the field of research. Funding mentored young investigators and research conferences are critical components to creating a vibrant research environment to cure hydrocephalus.

Priority Area 2: **Improve clinical outcomes and quality of life for those with the condition**

As with many conditions, variations in medical practice abound, with no evidence behind treatment options or scientific evaluation of outcomes. A focused and collaborative clinical research effort such as the pediatric focused Hydrocephalus Clinical Research Network (HCRN) can rapidly improve treatments and outcomes by reducing shunt infection rates, shunt failures and variations in clinical practice. Expanding off of the success of the HCRN, the newly created Adult Hydrocephalus Research Network (AHCRN) will bring the same high quality, high impact clinical research to the adult hydrocephalus population.

Priority Area 3: **Advance the study of root causes**

The basic mechanisms of brain injury and recovery as well as the function of cerebrospinal fluid (CSF) are poorly understood. Based on the work from three NIH workshops on hydrocephalus since 2005, research priorities in basic research were identified that our expert advisors believe could lead to important advances. Studies in biomarkers, CSF physiology and genetics are the most promising.



Research Update

MILES JOHNSTON, PH.D.
HOPE: RELIEVE PRESSURE IN THE BRAIN WITHOUT SURGERY

Miles Johnston, Ph.D., is Professor Emeritus at the Department of Laboratory Medicine and Pathobiology, University of Toronto, and a former Senior Scientist of the Brain Science Program at Sunnybrook Health Science Centre. Dr. Johnston received an Established Investigator grant awarded for his research investigating the role that the lymphatic vessels of the brain play in relation to cerebrospinal fluid (CSF) clearance. He was specifically testing how these lymphatic vessels respond to pharmaceutical interventions. The preliminary results have shown that certain drugs can change lymphatic vessel contractility, which affects CSF outflow.

TIMOTHY VOGEL, M.D.
HOPE: DISCOVER ROOT CAUSE OF HYDROCEPHALUS

Tim Vogel, M.D., is an Assistant Professor of Pediatric Neurosurgery at Cincinnati Children's Hospital Medical Center. In December 2012, a study published in *Nature Medicine* gave new insight into the role of cell signaling defects in the development of neonatal hydrocephalus. In 2013, Dr. Vogel received the Hydrocephalus Association Award in CSF Production, Regulation and Flow, Therapeutics and Diagnostics. His study, "Role of Neural Progenitor Cells in the Development of Neonatal Hydrocephalus," will focus on the cilia, hair-like structures, on the surface of neural progenitor cells in the brain. He will explore whether or not abnormal signaling through the cilia contributes to the development of neonatal hydrocephalus. Identification of these key signaling pathways could lead to preventative therapies.

SONIA PODVIN, PH.D.
HOPE: DEVELOP PHARMACOLOGICAL AGENT TO TREAT HYDROCEPHALUS

Sonia Podvin, Ph.D., is a post-doctoral fellow at the University of California, San Diego. Dr. Podvin was a recipient of one of HA's Mentored Young Investigator (MYI) Awards. Her MYI grant funded her research as a molecular pharmacologist aiming to develop safe, specific drugs to treat hydrocephalus. Her study investigates an anti-inflammatory hormone called augurin that circulates in CSF. Augurin may be able to control brain hydrodynamics and ultimately may be pharmacologically manipulated to treat hydrocephalus non-invasively.

JOHN KESTLE, M.D., FRCSC, FACS
HOPE: REDUCE SHUNT INFECTIONS

John Kestle, M.D., FRCSC, FACS, is a Professor and Vice Chair of Clinical Research in the Department of Neurosurgery at the University of Utah, Salt Lake City, Utah. His clinical practice specializes exclusively in pediatric neurosurgery, with a specific interest in pediatric epilepsy surgery. Dr. Kestle has developed a clinical protocol for treating hydrocephalus that has helped reduce post-operative infection rates for shunt surgery by more than 35%. He co-founded and chairs the Hydrocephalus Clinical Research Network, which is supported with funds from the Hydrocephalus Association. He is also a director of the American Board of Pediatric Neurological Surgery and a member of the HA Board of Directors.

MARK HAMILTON, M.D., FRCSC
HOPE: IMPROVE TREATMENT AND DIAGNOSTIC METHODS FOR NPH

Mark Hamilton, M.D. is a neurosurgeon and director of the Adult Hydrocephalus Program at the University of Calgary. Dr. Hamilton is currently the chair of the Adult Hydrocephalus Clinical Research Network (AHCRN). AHCRN is focused on addressing the needs of both transitional patients and adults that acquire hydrocephalus and is being funded by HA. Now launched, AHCRN will conduct multisite research while developing an electronic image database and cerebrospinal fluid (CSF) biobank. These research efforts are focused on finding better treatments for hydrocephalus and identifying new diagnostic methods for normal pressure hydrocephalus (NPH). Dr. Hamilton is a member of the HA Board of Directors.

HEATHER KATZEN, PH.D.
HOPE: IMPROVE THE PSYCHOLOGICAL HEALTH OF ADULT HYDROCEPHALUS PATIENTS

Heather Katzen, Ph.D., is a neuropsychologist and principal investigator for the AHCRN. Dr. Katzen has been instrumental in the development of the AHCRN Neuropsychological Core Battery. The neuropsychological core will track cognition and psychological health. The neuropsychological battery includes the Montreal Cognitive Assessment (MOCA), the Symbol Digit Modalities Test (SDMT), the Lawton Instrument of Daily Living Scale (ADL/IADL), and the Beck Depression Inventory-II (BDI-II). These tests are designed to assess various forms of cognitive impairment and the psychological health of adults with hydrocephalus. This data will be used to assess how interventions such as a lumbar puncture or external lumbar drainage affect neuropsychological outcomes.

MARK LUCIANO, M.D., PH.D.

HOPE: IDENTIFY CSF BIOMARKERS TO IMPROVE TREATMENT OF HYDROCEPHALUS

Mark Luciano, M.D., Ph.D., is a neurosurgeon and AHCRN principal investigator at the Cleveland Clinic. Dr. Luciano recently co-authored a paper published in *Clinical Neurology and Neurosurgery* which looked at vascular endothelial growth factor (VEGF) levels in the cerebrospinal fluid (CSF) of patients with enlarged ventricles and is spearheading the development of the AHCRN CSF biobank. The CSF collected from patients will be stored in a central biobank and will be available to clinical, translational, and basic researchers. The CSF biobank may be used to study a variety of research questions such as: Can a biomarker distinguish Normal Pressure Hydrocephalus (NPH) from Alzheimer's disease? and Does CSF composition affect shunt survival rates?

NORMAN RELKIN, M.D., PH.D.

HOPE: DEVELOP PHARMACOLOGICAL AGENT TO TREAT NPH

Norman Relkin, M.D., Ph.D., is a neurologist, director of the Weill Cornell Memory Disorders Program, and AHCRN principal investigator at Weill Cornell Medical Center. Dr. Relkin is an expert in neuroimaging and is directing the development of the AHCRN Imaging Database. The image database will collect and maintain MRI and other scans which will be used to follow structural changes in the brain, but will also be used in future clinical studies. These studies may assess the success of different treatment options, determine the best option for shunt placement, or be used to develop noninvasive diagnostic techniques for NPH. By centralizing and standardizing images in the database, the AHCRN will be able to conduct high quality research more quickly.

The AHCRN will also help to further important research on pharmacological agents to treat NPH. In April 2014, Dr. Relkin co-authored a paper published in *Neurology*. This study, Low-dose acetazolamide reverses perventricular white matter hyperintensities in iNPH, tested the effects of daily low-dose acetazolamide on a small number of probable idiopathic normal pressure hydrocephalus (iNPH) patients. In the majority of patients, acetazolamide treatment resulted in improved gait and a decrease in periventricular white matter hyperintensities. There are currently no approved pharmacological treatments for iNPH, but this study is a promising first step.

Hydrocephalus Clinical Research Network

The mission of the HCRN is to dramatically improve the lives of kids suffering from hydrocephalus by conducting important and field-changing, multi-center clinical research.

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Adult Hydrocephalus Clinical Research Network

The mission of the AHCRN is to increase awareness and understanding, accelerate research, and improve treatments for adults living with hydrocephalus.

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