

Towards the Establishment of Standards of Practice and the Initiation of Multi-Center, Multi-National Clinical Trials for Neonates and Children with Stroke'

Led by Dr. Gabrielle deVeber, Director, Children's Stroke Program, Senior Scientist

Initiated: January 2003, 11 Co-Investigators from Canada, US, UK; Original Co-Investigators: Dr. Gabrielle deVeber with Drs. Stephen Ashwal, Donna Ferriero, Rebecca Ichord, Fenella Kirkham, John K Lynch, Finbar O'Callaghan, Steve Pavlakis, Steve Roach, Guillaume Sébire and Andrew Willan

Mission: To perform international collaborative research aimed at understanding, preventing, and improving outcomes in pediatric stroke.

The ultimate mission of the IPSS is to expand knowledge on childhood stroke through publications.

Objective: overall objective of the network is to provide data and vehicle for clinical trials in paediatric stroke

Objective 1: To ascertain in a prospective, consecutive cohort study the numbers of newborns and children with ischemic stroke, their stroke sub-types and risk factors, their current treatments and outcomes within our centers. These data will provide the rationale and feasibility data for our group to design and implement the initial randomized controlled trials (RCTs) in paediatric stroke as well as other fundable grant proposals.

Objective 2: To develop standardized data collection forms and an appropriate database with web-based data entry from multiple study sites.

Objective 3: To develop standardized protocols for (1) diagnosis, (2) investigation of risk factors, (3) outcome assessment and 4) antithrombotic therapies of neonates and children with arterial ischemic stroke (AIS) and cerebral sinovenous thrombosis (CSVT)

Objective 4: Obtain grant funding to support and conduct additional multi-centre IPSS sub-studies

Methods: Multi-centre, multi-national consecutive cohort study
(<https://app3.ccb.sickkids.ca/cstrokestudy/>)

Pediatric AIS/CSVT 0 to <19 years; Diagnosed after Jan 2003

Planned development/implementation of consensus-based diagnostic, outcome and management protocols

Procedure: a) data collection process (data stored in a secure electronic database, REDCap*) and b) collaborative process (2 annual meetings, IPSS Sub-Groups – *see below for more details*)

*REDCap: The IPSS Investigators input patient data into the database (housed at SickKids), which serves as a clearing house and the submitting institution retains ownership and the right to publish their data

Study documentation: Acute and follow-up CRF's, Outcome Measures (The Pediatric Stroke Outcome Measure, PSOM; the Recovery and Recurrence Questionnaire, RRQ), de-identified CT and MRI's (sent through secure file transfer and stored in IPSS Imaging Repository)

Progress: N=5151 patients enrolled to date (Neonates, N= ~1800 and Children, N= ~3500)

18 IPSS Papers, 14 Abstracts, 12 Proposals *in progress**

Since 2003, 219 centers have participated in the IPSS from 54 countries,

Currently 60 active centers, over 200 active Investigators from 20 countries

41 Investigator Meetings

*12 proposals generated from the 2014 data close

4294 patients enrolled in the IPSS (Jan 1, 2003 – July 21, 2014)

Funding: Predominantly voluntary

Initial seed funding 2004-2006 Child Neurology Society/Foundation; Auxilium Foundation to 2010
The IPSS Network also successfully obtained National Institute of Neurological Disorders and Stroke (NINDS, 2007) and other source funding for targeted studies on clinical classification (Ped-NIHSS, CASCADE), etiology (the Vascular effects of Infection in Pediatric Stroke, VIPS), thrombolytic safety (Thrombosis In Pediatric Stroke, TIPS) and seizures (Paediatric Epilepsy Research Foundation for Seizures In Pediatric Stroke, SIPS)

The Auxilium Foundation supports IPSS Central Costs

Why Join the IPSS? The IPSS provides investigators with a free analysable database to store site patient data, while allowing sites to retain ownership of that data

Provides site investigators an opportunity to participate in IPSS publications as coauthors

IPSS gives contributing investigators the opportunity to be involved in several multicentre studies and make more statistically significant manuscripts by providing access to a larger dataset

Network Structure: Comprised of Collaborators from varying backgrounds: Neurologists (mainly pediatric but also adult), Radiologists (adult and pediatric), Hematologists, Emergency Medicine Physicians, Imaging Scientists, MR Physicists, Neuropsychologists, Registered Nurses/Nurse Practitioners, Biostatisticians, Research Staff (Project/Study Managers, Coordinators, Legal Counsel, Contracts Specialists etc.)

Research interests both clinical and lab-based

IPSS Executive Committee: Determines overall direction, membership policy and ideas of the IPSS and promotes and facilitates international collaboration among IPSS members.

Objective is to explore avenues for funding to support IPSS infrastructure and IPSS studies (Chair: Dr. Gabrielle deVeber)

IPSS Publications Committee: Supports Executive Committee in developing IPSS ideas. The group was established for the purpose of enabling timely publications of IPSS manuscripts whilst ensuring the maintenance of ethical standards, primacy of patient privacy and fair distribution of authorship for academic contributors. They are responsible for data use, ownership and analyses (Chair: Dr. Michael Rivkin, Boston Children's Hospital)

IPSS Sub-groups: Perinatal (Chairs: Drs. Adam Kirton, Jenn Armstrong Wells), CSVT (Chairs: Drs. Mahendra Moharir, Warren Lo), Cardiac (Chairs: Drs. Christine Fox and Kristin Guilliams), Arteriopathy (Chairs: Drs. Tim Bernard and Heather Fullerton), Standardization/Classification (Chair: Dr. Tim Bernard), Outcomes (Chairs: Dr. Warren Lo and Lori Jordan) and Neuroimaging (Chairs: Drs. Max Wintermark and Michael Rivkin)

Current studies: Vascular Effects of Infection in Pediatric Stroke Phase II (VIPS: NINDS funded, G deVeber dual Principal Investigator on VIPS I) enrolling 700 children with ischemic stroke; Seizures in Pediatric Stroke Phase II (SIPS: funded by Pediatric Epilepsy Research Foundation) enrolling 300 children with arterial ischemic stroke.

Headache in pediatric stroke, *in progress*

Neuroimaging Sub-group in collaboration with Pediatric Stroke Neuroimaging Consortium (PSNC, group of neuroradiologists/imaging scientists with specific interest in stroke) established consensus imaging protocols (hyper-acute, acute, and follow-up)

Outcomes sub-group developing an extension of the RRQ; specifically, a neurobehavioural component meant for children who have had a stroke.

Perinatal sub-group developing study to examine parental psychosocial outcome before and after informative video (video hypothesized to help relieve some of these emotional responses). Objective is to introduce on a large-scale to help people all over the world

Previous study: TIPS, The Thrombolysis in Pediatric Stroke (TIPS) study was phase I study which aimed to establish the safety, dosing and pharmacokinetics of intravenous (tissue plasminogen activator) tPA for childhood stroke. Study terminated.