Preface

Susan J. Vannucci Robert C. Vannucci Steven W. Levison

Departments of Pediatrics/Neuroscience and Anatomy, Pennsylvania State University College of Medicine,
Hershey, Pa., USA

This special issue of *Developmental Neuroscience* represents the proceedings of the Second Hershey Conference on Developmental Cerebral Blood Flow and Metabolism, which was held at the Hershey Hotel, Hershey, Pa., June 8–11, 2000. Drs. Susan and Robert Vannucci organized this conference following the very successful initial conference in Hershey in June of 1997. The meeting was a relatively small international meeting (with approximately 70 participants), that was highly interactive, with its focus on the immature brain. Thirty-one participants from 10 countries, including the USA, presented plenary talks, with seven additional poster presentations. The conference brought together clinicians, basic scientists, fellows and graduate students in a relaxed setting to share their discoveries and thoughts with the goal of understanding the mechanisms that lead to perinatal brain injury. The conference was funded largely by the National Institute of Neurological Disorders and Stroke (1R13 NS 39832) with an additional contribution from the Department of Pediatrics at Hershey.

Scientific sessions began with a keynote address by Dr. Phillippe Evrard, Professor and Chief of the Service of Pediatric Neurology and Metabolic Disorders, INSERM E9935, Paris, France. Dr. Evrard discussed the pathophysiology of perinatal brain damage and neuroprotection. His talk set the stage for the remainder of the meeting by discussing basic mechanisms of normal and abnormal

development in human infants as well as experimental animal models. Other speakers who discussed the normal development of the brain included Susan Vannucci, PhD, Penn State University College of Medicine, Hershey, who discussed the expression and functions of nutrient transporters, Jean Lauder, PhD, University of North Carolina School of Medicine, Chapel Hill, who discussed the role of neurotransmitters as morphogens and growth factors, William J. Pearce, PhD, Loma Linda University, who discussed the changes in cerebral arterial sensitivity to cGMP during maturation, and Raymond Koehler, PhD, Johns Hopkins University, who discussed changes in pial arteriolar vasodilation in response to potassium influx.

A major focus of the meeting was on the mechanisms of hypoxic-ischemic brain damage. The neonatal rat model of unilateral hypoxia-ischemia developed in the Vannucci laboratory in 1981 is currently used throughout the world. Several of the studies presented at this meeting were based upon this model which provided a common basis for interpretation. Donna Ferriero, MD, University of California, San Francisco, provided a comprehensive analysis of oxidant mechanisms in neonatal hypoxia/ischemia and how oxidative stress leads to cell death. Frances Northington, MD, Johns Hopkins University, discussed her recent data implicating Fas as a pro-apoptotic signal after perinatal hypoxia/ischemia. This talk was comple-

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mented by presentations by Henrik Hagberg, MD, PhD, Sahlgrenska University, Sweden, who discussed the role of mitochondrial dysfunction and caspase activation in the immature CNS after hypoxia ischemia, and by Katherine Wood, PhD, Trevigen, Gaithersburg, Md., who discussed mechanisms of apoptosis in neurons. Martha Miller, MD, Children's Hospital, Cleveland, discussed her data showing that repeated hypoxia results in apoptotic death of neurons in the respiratory control neurons in the brainstem. Alistair Gunn, MD, University of Auckland, New Zealand, discussed the notion that the premature infant is especially vulnerable to hypoxic/ischemic brain damage.

A number of sessions focussed on positron emission tomography (PET) and magnetic resonance imaging (MRI) studies. Diane Chugani, PhD, Children's Hospital of Michigan, discussed developmental changes in cerebral glucose metabolism in human infants and children as studied with PET and compared these changes with those that occur in GABA-A receptor binding and serotonin synthesis. John Wyatt, MD, University of London, described MR studies in the neonatal piglet to examine cerebral oxygen and glucose consumption and cerebral lactate production during the development of secondary energy failure following hypoxia/ischemia. Kristina Thorngren-Jerneck, MD, Lund University Hospital, Sweden, presented PET scan data showing that the amplitude of the integrated EEG correlated with the rate of cerebral glucose utilization. Gorm Griesen, MD, Rigshospitalet, Copenhagen, Denmark, presented data using single photon emission computed tomography to show that cerebral blood flow in the premature human infant white matter is 17% of the flow to gray matter. Edward Novotny, MD, Yale University, used MR techniques in both immature rats and brain slices to correlate development of oxidative glucose metabolism with the functional development of the neocortex. Michael Smith, PhD, Penn State University College of Medicine, described the ability to predict brain damage using multi-slice T_1 , T_2 , and diffusion weighted imaging. Cacha Peeters, MD, Wilhelmina Children's Hospital, The Netherlands, presented data using MR spectroscopy and MRI to show that the compounds 2-Iminobiotin, and to a lesser degree allopurinol and deferoximine preserve cerebral energy status and prevent vasogenic edema.

Other presentations focused on the role of inflammation in perinatal brain damage. Audrey Foster-Barber, MD, University of California, San Francisco, presented data showing that levels of pro-inflammatory cytokines in the neonatal blood of infants correlated with a later diag-

nosis of cerebral palsy. The concept that antenatal infections sensitize the brain to injury was further developed by Carina Mallard, PhD, University of Göteborg, Sweden, who showed that a low dose of bacterial endotoxin increased the extent of brain damage as a result of mild hypoxia/ischemia.

Seizures are frequent in newborn infants and might reflect prior or concurrent brain injury, so they were a topic of several presentations. Ronnie Abi Raad, University of Auckland, New Zealand, discussed a new method for monitoring the electrocorticogram and seizures using newly available instrumentation from Mini-Mitter. Kjen Liem, MD, University Medical Center Nijmegen, The Netherlands, presented data demonstrating that when hypoxia is severe enough to cause a fall in mean arterial blood pressure below the limit of cerebral autoregulation, electrocortical brain activity will decrease. Jerry Yager, MD, University of Saskatchewan, Canada, presented data showing that controlled normothermia will protect the brain from further damage caused by seizures triggered by perinatal hypoxia/ischemia. Similar data were presented by Yukito Takei, MD, Tokyo Medical University, Japan, who showed that hypothermia protects the neonatal brain from seizure-induced damage by improving cerebral blood oxygenation as a consequence of inhibiting nitric oxide production. Astrid Nehlig, PhD, INSERM, France, presented data demonstrating that the immature brain is more resistant to seizure-induced damage than the juvenile or adult brain. Data presented by Mary McKenna, PhD which were obtained in collaboration with Dr. R. Schwarze's laboratory at the University of Maryland School of Medicine, provided one clue as to the resistance of the immature brain to damage in that the immature brain has high levels of the NMDA antagonist kynurenic acid.

Finally, a number of presentations discussed interventions that could be employed to enhance recovery from hypoxia/ischemia. John MacDonald, PhD, Washington University School of Medicine, presented results to suggest that embryonic stem cells have the capacity to regenerate cells lost to hypoxia/ischemia. Another approach discussed is the use of growth factors, such as IGF-1, which Jian Guan, MD, PhD, University of Auckland, New Zealand demonstrated, could protect cerebral white matter from damage after perinatal hypoxia/ischemia.

At the end of the conference there was complete agreement that this had been an extremely exciting and enlightening meeting, and it was unanimously decided to schedule the Third Hershey Conference on Developmental Cerebral Blood Flow and Metabolism for June 2002.