Impact of Breast Milk-Acquired Cytomegalovirus Infections on Clinical Outcomes in Premature Infants

Erin Osterholm, M.D. and Mark Schleiss, M.D.

Infections with human cytomegalovirus (CMV) are common in children and babies. Most CMV infections that occur after birth do not cause illness or long-term issues, but CMV sometimes causes serious illness. Infants commonly acquire CMV infection by breastfeeding and normal term infants usually have no symptoms. In premature infants however, the spectrum of CMV disease is unknown. The purpose of this study is to determine the rate of transmission of CMV via breast milk and the range of illness caused by CMV in very low birth weight infants in the University of Minnesota Children's Hospital NICU. This study is funded by the University of Minnesota Department of Pediatrics Cross Divisional Research Grant.
Because our smallest patients deserve our biggest brains.

**Intestinal Tract**

**SCAMP** Catherine Bendel, MD

The purpose of this study is to evaluate the safety and effectiveness of 4 different antibiotic treatment regimens (i.e. 4 different combinations of multiple antibiotics) for infants with complex infections involving the abdomen and intestines. The antibiotics evaluated are ampicillin, gentamicin, metronidazole, clindamycin and piperacillin-tazobactam. Each individual antibiotic is FDA-approved and commonly prescribed for infants. Currently there is not enough information about how the body of neonates use these antibiotics when given together, rather than individually. The study involves collecting small amounts of blood and urine to measure the pharmacokinetics of each medicine, especially in relation to what other medications are being given; as well as obtaining cultures to determine how effective the various combinations are at treating these complex infections. Ultimately, this study will also help us to understand the proper dose and combination of these antibiotics in treating our NICU patients. Infants less than or equal to 32 weeks gestational age, or greater than or equal to 34 weeks gestational age at birth, who have a complicated intra-abdominal infection may be eligible to participate in this study which is funded by a contract with the National Institutes of Child Health and Human Development and Duke University through its Duke Clinical Research Institute. Multiple NICUs across the country are participating in this study.

**The Role of the Intestinal Microbiome in Neonatal Health and Disease** Cheryl Gale, MD

The microorganisms that colonize the human intestinal tract have important roles in the development of immunity and metabolism and, when out of balance, can contribute to the development of disease. In addition, in premature infants, some intestinal microbes invade the immature and fragile intestinal mucosa, going on to cause serious life-threatening infections. In this project, the kinds and amounts of microorganisms in the premature infant intestinal tract (from fecal samples in diapers) will be characterized over time and compared to clinical features of infants. In this way, microbiomes associated with healthy outcomes, and the clinical treatments associated with the establishment of these healthy microbiomes, will be discovered. Infants of any gestational age admitted to the NICU soon after birth may be eligible for this study. This research is funded by the Minnesota Vikings Children’s Fund and the Division of Neonatology.

**Yeast (Candida) Interactions with Neonatal Mucosa and Skin** Catherine Bendel, MD

As mentioned above, the yeast *Candida* can be a major cause of infection in the preterm infant. The source of these infections is the unique yeast that is a part of the normal flora on the baby’s skin or in their intestines. Our laboratory is interested in better understanding how the yeast interacts with the mucosa/skin to adhere and colonize normally; as well as the risk factors leading to abnormal invasion, inflammation and wide-spread infection. We have both animal and tissue culture models to evaluate these interactions, with the ultimate goal of developing therapies to prevent infection from ever happening. This work is funded by the Division of Neonatology.

**Neonatal Iron Deficiency** Michael Georgieff, MD

Iron deficiency is one of the most common nutrient deficiencies worldwide, affecting two billion people and up to 30% of all pregnant women and their babies. We study the effect of iron deficiency in new born babies and its effects on the developing brain, especially those areas of the brain involved in learning and memory. We are studying the mechanisms by which iron is necessary for normal growth, development and interconnection of the nerves in the brain, why iron deficiency early in life leads to long term learning and memory problems, and whether other dietary supplements to either the mother during pregnancy or the baby after delivery can lessen the effects of early iron deficiency. These studies are funded by the National Institutes of Health, the Minnesota Medical Foundation, and Alfred and Ingrid Lenz Harrison.

**Nutrition and Brain Development** Raghavendra Rao, MD

Nutrients such as iron and glucose are important for normal brain growth and function. Deficiency of these nutrients is common in babies who are born premature or after certain pregnancy complications. Our research focuses on the effects of such deficiencies on the brain. Using powerful magnets (approximately 6 times more powerful than those used in clinical practice) and molecular methods, we study how nutritional deficiencies affect brain development. With this knowledge, we hope to develop strategies for optimizing brain development in babies. This work is funded by the National Institutes of Health.

**Inflammation and Brain Development** Tate Gisslen, MD

Infection and inflammation during pregnancy are the cause of nearly half of premature births. After birth, inflammation continues to affect these babies. Inflammation during this important time in their brain development might lead to long-term learning and memory problems. Our research focuses on discovering the mechanisms by which inflammation interferes with normal brain development so that we may find methods to improve long-term learning outcomes in these babies. This work is funded by the Minnesota Vikings Children’s Fund and the Division of Neonatology.

**Fetal and Neonatal (Developmental) Origin of Adult Diseases** Phu V. Tran, Ph.D.

Early-life environment (i.e., micronutrient deficiency, hypoglycemia, intrauterine growth restriction, hypoxic-ischemic encephalopathy) can have a long-term impact on adult health by increasing the risks of obesity, diabetes, hypertension, cardiovascular disease, and neurocognitive decline. Utilizing preclinical models, we investigate how early-life environment causes permanent change in expression of molecules (e.g., proteins, hormones) that maintain physiological homeostasis, including stress responses, fear and anxiety, and learning and memory. In particular, we focus on growth factors that play critical roles in the neuroendocrine system, a major regulatory system that can be influenced by early-life environment. With this knowledge we hope to uncover molecules that can be targeted for therapeutic development and provide insights into how fetal/neonatal conditions contribute to the risk of adult diseases. These will be essential in developing strategies for treatment and prevention of adulthood pathophysiologies. This work is supported by the Minnesota Medical Foundation, the Minnesota Vikings Children’s Fund, a Center for NeuroBehavioral Development at the University of Minnesota Seed Grant, and the National Institute of Child Health and Human Development.