Why Premature Infants Bleed in the Brain and How Can This be Minimized?

Intraventricular hemorrhage (IVH) remains an important complication of prematurity worldwide. IVH takes an enormous toll on the family, society and the nation. Approximately half of preterm survivors with IVH develop cerebral palsy, mental retardation, and/or hydrocephalus.1 Approximately, a quarter of non-disabled survivors develop neurobehavioral disorders.2,3,4 Hence, IVH and its resultant neurologic and psychiatric sequelae continue to be a major public health concern.

Why preterm infants get brain bleed? IVH typically begins in the germinal matrix, which is located around the cavity of brain (cerebral ventricle).5 The germinal matrix consists of maturing neurons and glia and is rich in immature blood vessels. The causation of germinal matrix hemorrhage is attributed to a) the fragility of germinal matrix vasculature and b) fluctuation in the cerebral (forebrain) blood flow. A number of events including vaginal delivery, low Apgar score, severe premature lung problem, leaking of air in lung (pneumothorax), poor oxygenation, seizures, patent ductus arteriosus, infection, and others increase the fluctuations in the cerebral blood flow and contribute to the development of IVH.5 Fragility of germinal matrix vasculature has been evaluated by the author (P.B.) and his coworkers at the cellular and molecular levels; and these studies have unraveled a number of mysteries that explain why the microvasculature of this brain region is weak and vulnerable to hemorrhage. Briefly, we have shown that germinal matrix vasculature exhibits rapid angiogenesis, unlike other brain regions.5 The rapid angiogenesis results in formation of nascent vessels that lack the strengthening components of the vasculature, including pericytes (cells that wrap the capillaries) and fibronectin (matrix protein).5,6 In addition, glial fibrillary acidic protein (GFAP) is reduced in the astrocyte end feet (glial cells) of the germinal matrix vasculature, which further weakens the microvasculature of this brain region.6 Continued on page 3

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High Flow Nasal Cannula in the NICU: A Review of the Data

Heated, humidified high flow nasal cannula (HFNC) is a small, thin, tapered cannula used to deliver an adjustable mixture of heated and humidified oxygen and air at a variable flow rate. Over recent years, it has been utilized as a means of non-invasive respiratory support in infants and preterm neonates. High flow therapy (HFT) is popular amongst clinicians and nursing staff due to its ease of use and excellent tolerance by neonates. Purposed advantages include: easy apparatus setup, less nasal trauma when compared to nasal continuous positive airway pressure (NCPAP), excellent access to the patient, and the ability to nipple feed while on HFNC. For these reasons, many units (69% of US based fellowship training centers) have incorporated high flow therapy (HFT) into their standard of care.

Despite wide acceptance and rapid adoption of this new technique, optimal strategy for the delivery of HFT remains a subject of debate. Units vary in their indications for high flow with some units using HFT as a primary therapy and others employing HFT for weaning from mechanical ventilation. Furthermore, optimal flow rate and nasal cannula size remain hotly debated.

Few studies have compared the safety and efficacy of HFNC with other forms of non-invasive respiratory support in preterm infants. These studies differed in the interventions compared (CPAP; humidified low flow nasal cannula, non-humidified HFNC, intubation, etc.), the flow rates provided, the device used to deliver HFNC and the indications for support. Therefore, meta-analysis of these studies was not possible.

Compounding these practical issues, the mechanism of action of HFT continues to be elusive. The provision of positive end expiratory pressure (PEEP), tracheal gas washout and optimal gas conditioning have all been professed by the manufacturers. In addition, optimization of inspiratory flow and a reduction in the metabolic cost of gas conditioning have also been considered. To date, no theory has been proven correct; moreover, each theory is imbued with its own challenges and flaws.

Early studies have shown that it is possible to generate PEEP with HFNC. However, the amount of PEEP generated is unpredictable. Intrapharyngeal pressure measurements have recorded pressures ranging from zero to greater than ten centimeters of water. Even when infant size, cannula size and mouth position are considered, the amount of delivered PEEP is variable. In fact, in studies in which “high flow” liter flow is adjusted to deliver a specific PEEP, the infants treated with HFT suffered more respiratory complications due to both massive over and under inflation. This dangerous possibility has spawned numerous case reports and case series of air leak syndrome after the
Congratulations to the Lower Hudson Valley Perinatal Network (LHVPN) in receiving an award from the Maternal and Infant Community Health Collaborative (MICHC) initiative consisting of $508,594 annually to serve Westchester County & $310,00 annually to serve Rockland County. The total annual amount of $818,594 is for a five year contract period (which started October 1, 2013) and supports activities of this initiative with the overarching goal of improving health outcomes and reducing rates of prematurity, low birth weight, infant and maternal mortality in Westchester and Rockland counties. Toward achieving this goal, the Children’s Health and Research Foundation Inc.’s, Lower Hudson Valley Perinatal Network (LHVPN) will lay the groundwork to strengthen the capacity of the target population to be agents of change within their communities and at a county level. The Collective Impact (CI) model will be used to ensure that participants will work together to obtain healthier communities. CI is carried out by the collaborative efforts performed by a committed group of stakeholders to solve a specific social problem. It is based upon using a common agenda, aligning efforts, and using common measures of success.

The LHVPN (www.lhvnp.net) is committed to mobilizing the community, eliminating disparities, and improving the health of women, children and families in the Lower Hudson Valley region, including Rockland and Westchester counties. The network has gained a reputation as a provider of quality educational materials and programs. Providers, organizations and consumers in the region are increasingly relying on LHVPN as a key perinatal resource.

In many ways therefore, MICHC is an extension of the work that the LHVPN has been performing over the past ten years of its existence. It has used a Social Ecological model approach which takes into account that a person’s community and the societal settings may all impact her health. For example, a person will find it hard to eat fruits and vegetables when there is no supermarket that she can easily access. Working with communities to make the healthy choice the easy choice, the MICHC project will establish targeted neighborhoods which will function as Healthy Lifestyle Zones. Each one will have a hub which is a community gathering place for residents where they can gather, learn and provide individual or group mentorship around healthy lifestyle topics, etc. This would bring the Collective Impact model to the local level – working within communities to improve health. The community would be engaged to identify and advocate for social, economic and physical environment changes which will address social determinants of health. These hubs will be used to hold meetings to discuss specific topics in healthy lifestyles and/or to live healthfully (through communal healthy cooking or exercise classes, etc.). Adult peer education will be a key component of strategies related to the hubs such as Walkers and Talkers, Community Café’s and Promoters. In Walkers and Talkers community members act as mentors to a few of their neighbors, Community Café’s will be held in people’s homes or within a community gathering place to discuss healthy topics in a private setting and will be led by a local parent and/or community leader and promoters will work to actively engage their fellow community members in a dialog about healthy lifestyles and to empower them through creative means (such as storytelling, role-plays, etc.).

Community Health Workers (CHWs) will be engaged to provide one-on-one support through home visiting, assistance to help clients obtain health and other supportive services and to link families to community resources. Mount Vernon Neighborhood Health Center, Planned Parenthood Hudson-Peconic and Hudson Health Plan will provide CHWs and promoters for this project.

To learn more about this project go to www.lhvnp.net or call 914-493-6435.

Congratulations are also in order for Maternal-Infant Services Network (MISN) who was also awarded a five-year Maternal-Infant Community Health Collaborative (MICHC) grant from the New York State Health Department in October 2013 to improve health across the life course for Medicaid eligible girls and women in Ulster and Sullivan Counties through systems change.

The MICHC initiative is driven by the New York State Prevention Agenda for 2013 – 2017, which has defined priorities to improve maternal and infant health outcomes including reducing preterm birth, reducing maternal mortality, and increasing rates of breastfeeding initiation and duration.

The project was shaped based upon in-depth review of comparative county health rankings for birth outcomes, chronic diseases, obesity, lifestyle habits like tobacco and substance use and abuse and focus group data collected from high needs populations in order to pinpoint and target pressing local challenges and barriers to accessing health care and making healthful decisions. Evidence-based and model strategies were reviewed that address maternal and infant health across the life course, including approaches that intervene at multiple levels: policy, community environments, organizational, family and individual.

Based on the comprehensive needs assessment for poor birth outcomes, the project focuses its activities in several zip code clusters around the City of Kingston, New Paltz and Ellenville in Ulster County and clusters around Monticello and Liberty in Sullivan County. In all of these zip codes birth outcomes are significantly worse for African Americans and Latinas, especially those without a high school diploma or for whom English is a second language. High rates of overweight and obesity from childhood and through adulthood exceed the state rates, as do smoking and mental health coupled with substance use.

Strategies aimed at moving the needle on these indicators include collaboration, coordination and on-going needs assessments through:

- Leveraging existing county-specific perinatal partnerships,
- Growing county-specific Advisory Coalitions with decision-makers across health, human services, government, faith, and other sectors who engage in the Collective Impact process from Stanford University;
- Mobilizing consumers from target populations as key informants and researchers to name and present the barriers to health across the lifespan they perceive and the solutions they propose;
- Changing organizational practices with public health detailing using Merry–K Moo’s “Every Woman, Every time” model and materials for preconception and interconception medical visits;
- Identifying and training employers of high risk, low wage earning women on the Business Case for Breastfeeding, and providing technical assistance to develop workplace policies;
- Social media marketing to infuse all levels of the community with key public health messages about the benefits and aspects of reproductive life planning before, during and between pregnancies within the context of life goals.
- Promoting access to health insurance and providing assistance to obtain in –person assistance from health insurance Navigators;
- Establishing uniform preconception, prenatal and interconception risk assessment tools to be adopted across health and human service providers;
- Implementing the Peer Place shared electronic referral system through the Lower Hudson Valley Perinatal Network’s Health Information Technology initiative, across health providers and facilities
As germinal matrix comprises dividing and maturing neurons and glia, the metabolic demand of this brain region is high. To meet the escalated metabolic need, nature makes highways in form of microvessels to transport oxygen and nutrients to this brain region. Unfortunately however, infants born very premature are taken away from the protected environment of mother’s womb and exposed to modern technology to make them survive including endotracheal intubation, endotracheal mechanical ventilation, placement of intravenous and intra-arterial lines and others. In addition, they suffer complications of prematurity including premature lung disease, patent ductus arteriosus, apneic episodes, seizures, poor oxygenation, and others. Hence, fluctuations in the cerebral blood flow can be minimized by reducing the stimulation to the infant and appropriately managing the common complications of prematurity. Delayed cord clamping in the delivery room and gentle ventilation, appropriate respiratory care, treatment of PDA in timely manner, and optimal fluid and electrolyte management are key measure that might prevent or minimize the development of IVH. Importantly, prenatal use of glucocorticoid (betamethasone or dexamethasone) to prevent respiratory distress syndrome in premature infants has emerged as the most effective intervention to prevent IVH. Our studies on human autopsy materials and rabbit model have shown that at the cellular level prenatal steroid prunes the immature vessels in the germinal matrix and thus reduces the risk of IVH. Comparison of prenatal betamethasone and dexamethasone has not conclusively shown superiority of one over the other and clinicians should choose whatever is available.

In a number of clinical trials, indomethacin treatment has shown short-term benefit of reducing the incidence of IVH. As indomethacin reduces the occurrence of IVH, it was anticipated that this treatment will improve the neurodevelopment outcome of the infants. However, indomethacin treatment failed to reduce the rate of cerebral palsy, deafness and blindness on long term follow up. Hence, indomethacin is not recommended for routine prophylaxis against IVH. Maternal treatment of vitamin K or magnesium sulfate to prevent IVH did not demonstrate any benefit either.

In conclusion, pathogenesis of IVH is ascribed to accelerated angiogenesis and fluctuation in the blood flow. Use of prenatal glucocorticoids in pregnant women in preterm labor, delayed cord clamping at birth and appropriate resuscitation in the delivery room, and finally minimizing handling, gentle ventilation and appropriate neonatal care are key measures to prevent IVH in premature infants. However, there is a need for better therapies to further minimize the development of IVH. Strategies focused on enhancing the stability of the germinal matrix vasculature and reducing fluctuation of cerebral blood flow might lead to more effective strategies in preventing brain hemorrhage in premature infants.

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In the results, the authors reported a 34% failure rate in the HFT group and a 25% failure rate in the CPAP group. These numbers did not achieve statistical significance leading authors to conclude that HFNC was noninferior to CPAP. Analysis for secondary outcomes demonstrated no difference in rate of BPD, length of stay, weight at discharge, or air leak syndrome. The HFT group suffered less nasal trauma.

In this article we attempted to describe the features of the HFNC device and discuss current knowledge about the mechanisms of action and results of clinical studies in preterm neonates and infants with respiratory distress. In summation, HFNC seems to be effective in some patients. The precise mechanism of action remains subject to ongoing debate. Notwithstanding the uncertainty, clinical trials have shown that high flow therapy is a safe and effective means of support after extubation. However when compared to CPAP, HFNC has never been shown to improve outcomes. Moreover, in many clinical studies, there is a nonsignificant trend towards more extubation failure in the HFT group. Therefore, at this time, we would recommend against adopting HFNC as a standard of care.

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References available upon request.

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and human services providers to ensure that high risk, high needs women are afforded access to wide range of services as appropriate to their need.

The project will rely on contractual agreements with two Federally Qualified Community Health Centers; Hudson River Healthcare in Sullivan County and the Institute for Family Health in Ulster County. Both Centers will provide on-going outreach efforts to the most high needs women through Community Health Workers who will engage, refer and track high needs women across the life stages in health care and support services.

Peer Coaches, Health Insurance Navigators, and other grassroots helpers are recruited, trained, and provided with resources at multiple levels of engagement. A Program Coordinator will oversee the integration of strategies designed to reach individuals and families, and those that mobilize systems changes in the communities and environments in which people live, work, and play.

In addition to contractual agreements with the Institute for Family Health and Hudson River Health Care, key collaborators include the Ulster County and Sullivan County Health Departments, Planned Parenthood of the Mid-Hudson Valley, Ulster and Sullivan Community Action organizations, Agri-Business Child Development, Sullivan County Child Care Council, PRASAD Children’s Dental Health, Sullivan County Department of Community Services, Sullivan County Department of Family Services, Community Heart Health Coalition of Ulster County, Sullivan County BOCES Adult and Continuing Education, Ulster BOCES Adult Career Education Center, The Rose Women’s Care Service, Fallsburg Pediatrics, Sudden Infant Child Death and Resource Center, Ulster County Medicaid, Ulster Prevention Council, Health Alliance of the Hudson Valley, Catskill Regional Medical Center, and the Wawarsing Council of Agencies.

The MICHC initiatives benefits from integration with other MISN programs including Health Insurance enrollment and retention; Community Health Advocacy; Parenting Education, Teen Pregnancy Prevention, Youth Development; and referrals to essential community services.

For further information go to www.misn-ny.org
Or call: (845) 561-3575

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