Born with brain injuries. Why – and when – some neonates suffer strokes has become just the first part of one physician’s “30-year project” to cure them.

First-of-its-kind study seeks to link mothers’ health on stroke, cerebral palsy

Looking to Mom to Understand Neonatal Brain Injury

By Todd Neff

The young physician held Elsie Drobnick on her lap. She bounced the baby’s hands as she talked with Elsie’s parents, Jillian and Jim, who had driven down from Fort Collins to Children’s Hospital Colorado on the Anschutz Medical Campus for these 15 minutes. Elsie, two months old, was exceptionally cute; she was, however, a not uncommon patient for stroke neurologist Jennifer Armstrong-Wells, MD, MPH.

Elsie had suffered a perinatal stroke – whether before, during or just after birth is not quite clear. Armstrong-Wells focuses on children like Elsie at University of Colorado Hospital and, through a new, pioneering study, seeks to tease out how inflammation and blood clotting in high-risk mothers-to-be might lead to brain injury in humanity’s newest arrivals.

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Armstrong-Wells has long been drawn to the challenge of caring for babies with brain injuries. Somehow preventing those injuries would be better yet, she figured.

Preventing disability. Some of the pioneering work in linking maternal health with the brains of babies was done at the University of California, San Francisco while Armstrong-Wells was working through dual residencies in pediatrics and child neurology. She is now an assistant professor of Neurology in the CU School of Medicine’s Department of Pediatrics, and is affiliated with the Center for Women’s Health Research and the Hemophilia and Thrombosis Center. She is director of the Perinatal and Hemorrhagic Stroke programs at UCH and Children’s Hospital Colorado.

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Shortly after arriving at CU three years ago, Armstrong-Wells applied for a Building Interdisciplinary Research Careers in
Women’s Health grant from the National Institutes of Health. The grant involves young investigators working with mentors on multidisciplinary problems. She met with Virginia Winn, MD, PhD, a professor in Maternal Fetal Medicine and Basic Reproductive Sciences at the School of Medicine. Winn is a perinatologist and researcher in placental biology and preeclampsia, or high blood pressure during pregnancy. They decided to pursue the link between preterm premature rupture of membranes (PPROM) and the risk of cerebral palsy and other brain injury in infants.

The population of mothers whose water breaks too early accounts for a third of premature deliveries, Winn said. PPROM, which happens prior to 37 weeks gestation and often well before that, increases the risk of chorioamnionitis, an infection of the fetal membranes. Chorioamnionitis is a risk factor for perinatal stroke and brain injury.

Armstrong-Wells was awarded the grant with Marilyn Manco-Johnson, MD, as a co-investigator and study mentor. Manco-Johnson, a pediatric hematologist and director of the Hemophilia and Thrombosis Center, is an expert in blood clotting.

**Multilayered problem.** They launched the study a year ago. Women arriving at UCH for PPROM-related bed rest and antibiotics, and who join the study, are screened for biomarkers of clotting disorders as well as for inflammation.

When the baby is born, Armstrong-Wells’ team also samples the baby’s cord blood as well as the placenta – the baby’s connection with its mother – which placental pathologist Miriam Post, MD, then assesses for evidence of inflammation and clotting problems.

Next, Armstrong-Wells uses ultrasound and exams to check the baby for possible brain injury.

Clotting alone isn’t the problem, Armstrong-Wells believes.

“We know that women have increased clotting when pregnant, but it’s a safety thing, because the risk of hemorrhage is so great,” she explained. “The same goes for babies. It’s a natural process.”

Nor does inflammation alone seem to bring about newborn brain injury, she says.

“Most likely, it’s a combination of clotting and inflammatory disorders that causes brain injuries in the child,” she said.

The study is now enrolling three to four women a month, Armstrong-Wells said, with about 40 mothers having joined so far. Data are already coming in, she added, and there have been some surprises. The team wants to be certain of its findings before it starts publishing.

“The dream is that we’re going to cure perinatal brain injury – find out what causes it and develop an intervention,” Armstrong-Wells said.

Continued
It might take awhile.

“I call this my 30-year project,” she quipped.

But Armstrong-Wells and Winn believe that the study has the potential to trigger changes in the standard of care in the near future, too. For example, it could be that it’s safer for babies in ruptured membranes to be born prematurely than remain in what Armstrong-Wells described as “a hostile pregnancy environment.”

“I think the work she’s doing is going to provide some insights that can really direct obstetric management,” Winn said.

For more on Jennifer Armstrong Wells and her work, check out Denver 7NEWS’s feature here.