continue to be excited about the future of research at March of Dimes, the foundation of our mission to improve the health of every mom and baby. We remain committed to our four priority areas to advance our understanding of maternal and infant health: diagnostic biological markers, maternal microbiome and immune factors, maternal comorbidities and social and environmental drivers of health. In this newsletter, you’ll read about our work in a few of these key areas. Stories include:

- **COVID-19 antibodies and pregnancy:** We begin at Harvard and Massachusetts General Hospital to explore how COVID-19 confers antibodies to fight the virus, and if a pregnant mom can pass those antibodies along to her baby.

- **Social influences, biological impacts:** One of our researchers at Northwestern University at the Ann and Robert H. Lurie Children’s Hospital of Chicago is evaluating generational factors and the impact of a father’s education on birth outcomes.

- **A new drug strategy to combat preterm birth:** At the Vanderbilt School of Medicine researchers are testing older, previously approved drugs to combat preterm birth.

- **Why we give:** We introduce an inspiring donor who has supported March of Dimes for the past 20 years in the NICU with staff and families of preterm babies and at our annual fundraising event in Milwaukee, WI.

We know this work wouldn’t be possible without the dedication of our researchers and the generosity of people like you to improve the health of every family. For this, we thank you and wish you a wonderful and safe holiday season.
Proteins called antibodies are part of the body’s immune system. They’re mobilized when they sense the body has been infected by a foreign entity, such as a bacterium, or in the case of SARS-COV-2, a virus, and they neutralize it. It’s one of the ways our immune systems have adapted to protect us in a world full of endlessly mutating diseases.

There’s not much difference between pregnant and non-pregnant people when it comes to generating this healthy immune response, but while they both develop the necessary antibodies to fight off disease, a pregnant mom will also pass those antibodies along to the baby. SARS-COV-2 was able to cause a global pandemic is because it’s a novel coronavirus, and as such, we’re just learning how it behaves and how our bodies behave in response. One of the most important things we don’t know is whether a pregnant mom who’s had COVID-19, or a COVID vaccine, will pass antibodies through the placenta, the umbilical cord and breast milk, to the baby. A study funded in part by March of Dimes is looking to provide the answer.

“March of Dimes is always at the forefront of advocating for moms and babies and especially this traditionally understudied group—pregnant women—and we’re grateful to them for funding this vital work,” said Andrea Edlow, M.D., MSc. “This study examines the question of whether, how well and when, as a result of natural infection with SARS-COV-2, maternal antibodies cross the placenta, get into the umbilical cord, and even into breast milk, to give the neonate some protection against the virus. This is critical information because some of the respiratory infections that merely make adults sick, like flu, whooping cough or COVID-19, can be fatal to a six-month old.”

SARS-COV-2 rarely infects children, but when it does, some of the most vulnerable groups are neonates and infants. We need to understand how those most vulnerable can get the antibodies to fight COVID-19 because children can’t be vaccinated in general until they’re at least a year old. A major public health strategy to protect new babies from other infections has been to immunize their moms and get the mom’s body to make antibodies that give the baby some protection for the first year of life. SARS-COV-2 poses a whole new set of questions about whether this same strategy will work and for how long.

“We’ve found that COVID antibodies don’t cross over to the baby as well as others. And here again, we don’t know exactly why, but suspect it has something to do with the sugar receptors on the antibodies and in which trimester the infection occurs because better transference happens earlier in the pregnancy,” said Dr. Edlow. “Even so, the good news is that in the last trimester, the placenta will step in and upregulate its receptors to get more antibodies over to the baby. It’s an amazing feat we’re just beginning to learn about. It’s a significant part of our effort to provide clinically relevant data to help advance vaccine and breastfeeding strategies.”

Dr. Edlow’s research is staffed with a multidisciplinary team that includes other fetal medicine specialists, high-risk obstetricians, immunologists, neonatologists and lactation experts. Together, they’re able to review the challenge from all angles to bring the best knowledge to bear a potential solution. The results may be able to guide women and their families in making decisions about when to be vaccinated and when to get pregnant to maximize the mom’s safety and baby’s protection.
ANDREA EDLOW, M.D., MSc
Obstetrics and Gynecology Faculty, Harvard Medical School
Maternal-Fetal Medical Specialist, Massachusetts General Hospital
How healthy a baby is, how successful they become and whether their children will experience the same disparities they suffered may depend more on their ZIP code than genetic code. That’s what Dr. James Collins is learning from more than a decade of studies examining the relationships among racial and birth disparities and adverse birth outcomes. More specifically, Dr. Collins’ research has focused on two key areas: generational factors affecting birth outcomes, like systemic neighborhood poverty, and the impact of a father’s education (made possible by recent funding from March of Dimes).

The bad news is, the effects of these disparities are biologically persistent: Black women who were born poor, whose moms were poor, and who were of low birth weight, were more likely to give birth preterm to low-birth-weight babies because of the fetal programming they had experienced as babies. This occurred even if they were no longer living in poverty. In other words, racial and economic disparities have effects that echo down through generations. But the good news is, those effects are epigenetic, meaning that even though they may produce genetic changes, their causes aren’t genetic, so they can be reversed. And that’s a dynamic that can be materially and positively affected by the presence and education level of the baby’s father. Ironically, those very tangible effects begin with something decidedly intangible—acknowledgement.

In the past few years, Dr. Collins and others have shown that fathers make a difference. The father’s education and even acknowledgement on the birth certificate seemed to have a major impact, even more than the mom’s education. So what is it about acknowledgement?

“We thought that maybe socioeconomic position has a role to play, and it does, but we found that moms or kids who had dads who were acknowledged on the birth certificate, those moms were more likely to have received adequate prenatal care, more likely to have optimal weight gain, less likely to smoke cigarettes and so on,” said Dr. Collins. “So while dads have some direct financial impact for some families, their impact in terms of social support is powerfully and directly associated with improved birth outcomes. Hopefully, public policymakers can do something with that information. That would greatly impact the generations to come, to be born into a more just, more equitable world.”

Poverty is associated with poor birth outcomes and later on, life outcomes. If we can reduce poverty, we can chip away at the disproportional impact it has on Black birth outcomes. That said, poverty taken alone as a societal measure changes, albeit slowly, across generations because inflation and wealth tends to go up. So, the next big goal for Dr. Collins’ work is to study poverty’s impact on birth outcomes by looking at a third generation of women to see if the fetal imprinting he believes occurs, reverses itself or disappears. That work will show whether societal influences that have biological impact, can ultimately be reversed.

Poverty is bad for lots of reasons, but what we now know is that one of the most significant is that it leads to adverse birth and life outcomes. “I hope that policy makers and public health officials will start doing the math, because economically, this is killing us,” said Dr. Collins. “I’m a neonatologist and I know that while it’s very expensive to take care of one preterm infant, the same things that cause prematurity in the first place also lead to not doing well in school, who attends college and who doesn’t, and of course, crime rates. That’s why we have to look at this problem from a public health perspective, not just a medical one.” March of Dimes is very proud to support this important work because we believe, as does Dr. Collins, that it’ll help improve the lives of families.
DR. JAMES COLLINS, M.D., MPH
Medical Director of the Neonatal Intensive Care Unit and Professor of Pediatrics, Northwestern University, Feinberg School of Medicine
Associate Program Director of the Pediatric Residency Training Program, Ann and Robert H. Lurie Children’s Hospital of Chicago
A NOVEL DRUG DISCOVERY STRATEGY

Getting new drugs approved to combat preterm birth can take as long as 20 years. So, researchers are testing older, previously approved drugs that just might work.

The process that brought several COVID-19 vaccines to market in record time was an anomaly; typically drug discovery, development, research, clinical trials and approval takes 10 years, and sometimes twice that long. Given the current preterm birth crisis, researchers in the field are taking a novel approach to bring new treatments to market. Two Vanderbilt researchers are employing the latest technology to test thousands of already approved compounds and possibly repurpose those to impede various preterm birth triggers in order to bring effective and safe treatments to market faster.

Dr. Jeff Reese and Dr. Jennifer Herington have the kind of working relationship that clicked right from the beginning, but didn’t begin until 20 years after they’d first met.

“We finally reconvened at Vanderbilt when Dr. Herington was between projects in reproductive biology and I had some projects in mind that I couldn’t figure out how to get done,” said Dr. Reese. “She and I sat down in a one-day planning session and talked about how her areas of strength overlapped with some important ideas in the field that hadn’t been touched on yet, and the next day, she presented me with basically a mini grant proposal that I thought was brilliant. We took a chance on each other—her as the post-doc and me as the investigator. Her ideas were so good, she has made an amazing career out of them and we’re now doing some very exciting work.”

“That’s the origin story for this work,” said Dr. Herington “When I transitioned to faculty as a perinatal researcher in the Division of Neonatology, I started by developing a drug discovery strategy that identifies novel small molecules to develop into therapeutics to arrest preterm uterine contractions. Then more recently, my research team began to explore drug repurposing of current FDA-approved drugs for novel use to inhibit preterm uterine contractions. This strategy lets us screen thousands of compounds to find drugs that might prevent it and bring them to market faster.”

Which is easier said than done. Dr. Herington’s work in identifying potentially helpful drugs is painstaking and complicated. Other investigators have examined small numbers of drugs for their uterine inhibitory potential, whereas Dr. Herington’s research uses high-throughput technologies to screen vast numbers of small-molecular compounds. She’s working with human uterine cells that she isolates from biopsies donated from women having caesarean births. She plates the cells with a high degree of reproducibility and then adds drugs onto the uterine muscle cells to determine which cells contract and how strongly they respond. Using a 384-well plate, she places a different compound in every well, looking for which drug can inhibit contractions. When she loads multiple plates, with the help of automated liquid-handling robots in the high-throughput screening core, she can scan thousands of drugs at a time and pick out the very small number that prevent uterine cells from contracting. Once she has that information, she can start testing their efficacy, potency and their toxicity, then take the drugs that look promising and see if they’ll stop the uterine muscle from contracting in an organ-bath assay. The next step is to use those drugs to stop preterm labor using animal models.

The ultimate goal of the project is to yield drugs with a better safety profile for both mom and infant compared to tocolytics—the class of drugs currently used to inhibit uterine contractions. That research has already started in Dr. Reese’s lab to examine whether drugs have an effect on the fetal ductus arteriosus—a vessel that detours oxygenated blood away from fetal lungs in utero and has unfortunately been an off-target of some drugs being used off-label for tocolytic use. And not a moment too soon, because currently, there are no FDA-approved drugs for stopping the uterine contractions that initiate preterm birth. What’s special about this work is that Dr. Herington is targeting her strategy to drugs already known to be approved for women. That could make all the difference.

“She’s doing things that haven’t been done before,” said Dr. Reese. “She’s not looking for a needle in a haystack. She’s screening a thousand needles at a time. And finding the best ones.”
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Vanderbilt University School of Medicine
(left)

JEFF REESE, M.D.
Mildred Thornton Stahlman Chair in Perinatal Research
Professor
Departments of Pediatrics, Cell and Developmental Biology, Biomedical Engineering
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(right)
WHY SANTA VISITS THE NICU

When Greg and Marlene Phelps’ son, Kyle, was born, he spent his first Christmas in the NICU. Now, he and Greg go back every Christmas for a very special visit.

Like so many parents we talk to, that first experience in the NICU can be daunting. Can you talk a little bit about your experience?

Greg Phelps: Kyle spent the first 98 days of his life in the neonatal intensive care unit (NICU) at Ascension St. Joseph’s hospital in Milwaukee. I’d never been in a NICU before. And as a parent, when you first walk in, it’s intimidating and scary. And all these questions just ran through my mind. What’s going to happen to my little boy? Is Kyle even going to live? And nobody can answer those questions for me. So, I was overcome with anxiety, with fear, and it was overwhelming and very emotionally draining. As we spent days there, we got to know the staff, nurses and doctors, and they explained all the equipment and apparatuses Kyle was attached to, so that helped put us at ease because we had a little more knowledge about what was going on.

Did you have any experience with March of Dimes at that time?

Greg Phelps: Not really. When I first walked into that NICU, I had no idea that March of Dimes had an affiliation with neonatal intensive care units. The only thing I knew about March of Dimes was back in the 1950s, they were a part of developing the polio vaccine. But I quickly learned how instrumental March of Dimes was in establishing NICUs and even some of the procedures used there. For instance, they funded the development of surfactant, the drug given to preterm babies to help clear out the mucus in their lungs to help them breathe better. Kyle got surfactant, twice. I know that without the treatment, without surfactant, he most likely would not be here today. So, the connection we have with March of Dimes goes way beyond fundraising.

Did your wife, Marlene, have a history of preterm birth in her family?

Greg Phelps: No, Marlene had what’s called placenta previa, where the baby’s placenta implants very low along the uterus. As the baby begins to grow and get bigger, it will push and cause bleeding, which is a very common cause of preterm birth. So, Marlene was hospitalized with Kyle very early, when she was 18 weeks pregnant, and was in the hospital for 10 weeks. Fortunately, when the placenta abrupted she was still in the hospital, and they immediately took her down the hall to the operating room to ultimately save Kyle’s life.

And how big was he when he was born?

Greg Phelps: He was 2 pounds, 9 ounces, 14 ½ inches long. This was around the time that the little dolls, the Cabbage Patch Kids, were popular. These dolls were the same size as the babies in the NICU, so they used the doll clothes to dress them because that was really the only thing that would fit. So, Kyle was literally the size of a Cabbage Patch doll.

Nationally, about 10 percent of births are preterm. In Milwaukee, where Kyle was born, it’s 14 percent. That’s why we’re aligned with the hospital where he was born. We know all too well that Kyle could have left this world before we even got a chance to see him with his eyes open or hear him speak. So, we want to give back and be involved in an organization that provides so many resources, to try to prevent or at least improve these terrible statistics.

Can you tell us about the role philanthropy plays in your family, and why it’s so important to you?

Greg Phelps: Well, even though everyone is older and has their own lives now, we never take what we’ve been given, our family and our health, for granted. That’s why Kyle and I visit the NICU every year and I’m Santa Claus in the NICU. We’ve been doing it for 20 years now and Kyle’s gone with me every single year since he was four years old. We do it because that’s the personal connection we have, not just to the hospital of the NICU, but to the people who are there scared out of their minds for their babies. And the parents love taking pictures with us, but also love talking to Kyle because he’s the success story, a graduate from that exact NICU. And the parents, they cry, they hug him, they want to know all about him. It’s just a great feeling for all of us.
Your story is so rich because you have so many touch points, not only with March of Dimes, but also with the physicians, the nurses and the babies and their parents in the NICU.

**Greg Phelps:** Again, this goes to the idea of philanthropy as service. People don’t remember what you said or what you did, but they remember how you made them feel. Contributing to March of Dimes, an organization that invests in clinical studies, services and resources, ultimately makes people who are in a terrible situation, feel better.

Greg and Kyle continued their visits to the NICU even when they lived in Portland for five years. Every December, they flew halfway across the country, spent 48 hours in Milwaukee to appear as Santa Claus and then flew back for Christmas in Portland. Back in Milwaukee during COVID-19, they still found a way to show those parents and kids how much they care. Kyle, who is now a digital media professional, had the idea to create a 7-foot cardboard cutout of Greg dressed as Santa Clause...wearing a mask. Parents and NICU staff had their pictures taken with the cutout, which was dubbed “COVID Claus.”
Congratulations to March of Dimes current grantees who include experts working on everything from development of antibodies to prevent necrotizing enterocolitis (NEC) and an aspirin regimen for preeclampsia to addressing racial and health disparities in birth outcomes and so much more.

- Ripla Arora, Ph.D., Michigan State University
- Phil Bennett, M.D., Ph.D., FMEDSci, Imperial College London
- Rupsa Boelig, M.D., Thomas Jefferson University
- Eliezer Calo, M.D., Massachusetts Institute of Technology
- Jennifer Condon, Ph.D., Wayne State
- Andrea Edlow, M.D., MSc, Massachusetts General Hospital
- Sarah England, Ph.D., Washington University
- Tim Hand, Ph.D., University of Pittsburgh
- Ethan Goldberg, M.D., Children’s Hospital of Philadelphia
- Russ Lehrman, Ph.D., BioSuperior
- Corina Lessuer, M.D., Icahn School of Medicine
- Brian Kalish, M.D., Hospital for Sick Children
- Deborah Karasek, Ph.D., UCSF
- Kok Lim Kua, M.D., Indiana University
- Louise Laurent, M.D., Ph.D., UCSD
- Jamie Lo, M.D., Oregon Health and Sciences University
- Marina Sirota, Ph.D., University of California, San Francisco
- Shruthi Mahalingaiah, M.D., Boston Medical Center
- Carole Ober, Ph.D., University of Chicago
- Samuel Parry, M.D., University of Pennsylvania
- David K. Stevenson, M.D., Stanford University
- Sing Sing Way, M.D., Ph.D., Cincinnati Children’s Hospital

DONATE TODAY

For more information on how you can be a part of this effort, please contact:

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