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NATIONWIDE
Advancing the Conversation on Child Health

THE IMPACT OF OPIOIDS ON CHILDREN

| SPECIAL EXPANDED SECTION |

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THE IMPACT OF **OPIOIDS** ON CHILDREN

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A NOTE FROM THE EDITOR

The faces on the cover of this issue represent the young lives affected by the opioid crisis. Children who are losing their parents to addiction and overdoses. Children who live in instability and uncertainty. Children who spend their earliest weeks in withdrawal. And children who are at risk of developing their own addictions.

Here in Columbus, Ohio, we've had a front row seat to the opioid crisis. In the book *Dreamland*, Sam Quinones describes the day one physician from Nationwide Children's, after 20 years of treating young people with addiction, treated his first case of teenage heroin addiction. He became one of the first to sound the alarm and develop treatment plans tailored to teens and young adults with opioid addiction.

At a time when the opioid crisis was just beginning to get attention in the media, our neonatologists were developing protocols and collaborative quality improvement projects to treat the babies with neonatal abstinence syndrome who were flooding the neonatal intensive care units.

In this special section of *Pediatrics Nationwide*, we have collected stories, ideas and opinions from leading physicians and researchers at one of the largest pediatric health systems in the United States. They represent many others who are shifting research priorities, getting creative with clinical care and collaborating in new ways to bring hope and help to the children directly impacted by the opioid crisis.

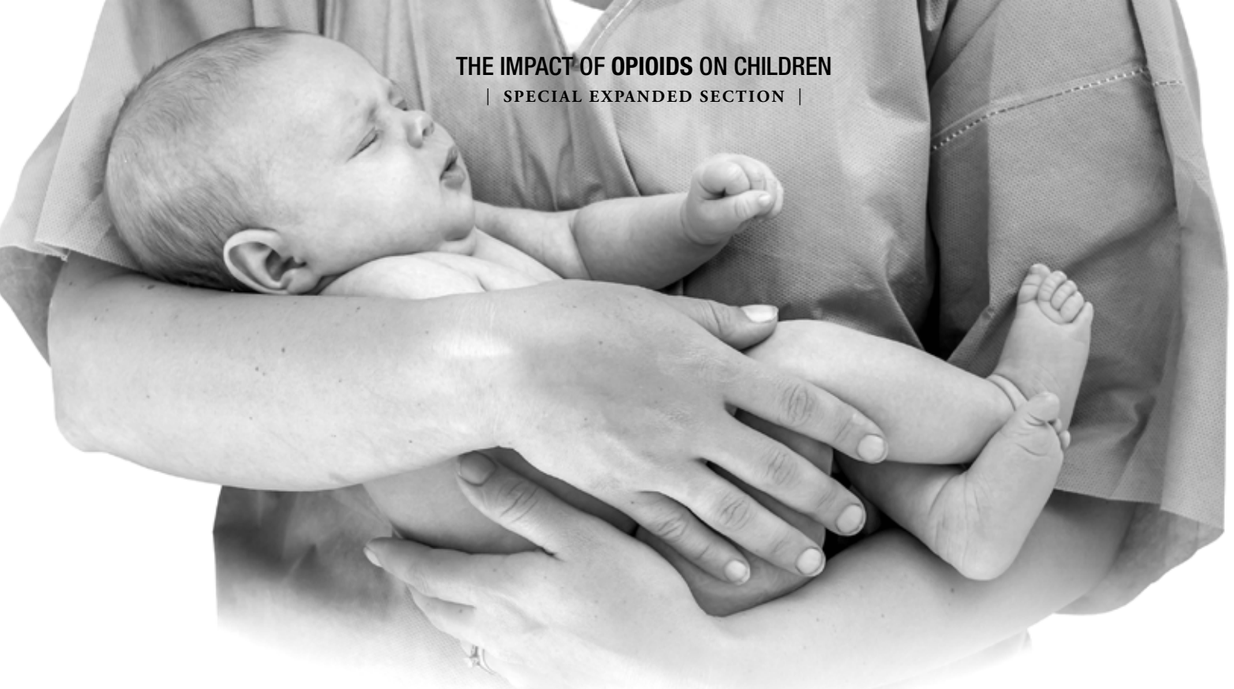
Thanks for reading. I hope you will join the conversation on Twitter @NCHforDocs.

"All kids need a transition process. It's really just developmental and learning how to navigate the health system when they become young adults. But not every person, chronic disease or not, needs the same level of intense support."

– Stacy Ardoin, MD, section chief of Rheumatology at Nationwide Children's Hospital

"Many of these kids started into opioid difficulties as early as age 12 or 13 and are now in the place where they need medication-assisted treatment to allow them to get free of this. It's a tough challenge and very few places have a facility that can handle that kind of circumstance."

– Francis Collins, MD, PhD, director of the National Institutes of Health



NEONATAL ABSTINENCE SYNDROME: Transforming Care for Newborns and Their Families

— by Abbie Roth —

If there's a success story to be told at this point in the history of the opioid crisis, it's in the newborn intensive care unit. From changing attitudes to standardizing treatment, clinical care for infants with neonatal abstinence syndrome (NAS) and their families is markedly different than it was 10 years ago.

CHANGING ATTITUDES AND CONFRONTING BIAS

"The way we view addiction in pregnancy has changed rather dramatically over time. We, as a society and in health care, tried to punish away drug-addicted pregnancy. We called it child abuse and punished the mothers severely," says Edward Shepherd, MD, section chief of Neonatology at Nationwide Children's Hospital. "This is a recipe for noncompliance with the medical system. It results in parents having no interest in being part of the medical system."

If moms feel judged by the medical system, they may delay coming to hospitals for care for themselves or their children. This results in more emergency care for big problems that regular care from a medical provider can prevent. That can be costly, both financially and in patient quality of life.

Dr. Shepherd and his team now offer care on the principle of partnership, not punishment. "One of our first goals was to figure out how to partner with parents to achieve what we want: healthy children and healthy families. At the end of the day, that's what everyone wants. We have the same goal," he says. "As long as it is safe to do so, we want to keep families intact."

Part of reaching that goal is to build a relationship of trust with parents and families. The NICU team builds trust with families by using nonjudgmental terminology, involving parents in the care of the infant as much as possible and offering social work consultations and follow-up care. Many mothers with addiction have a background of abuse and trauma. As part of the culture shift, trauma-informed training for nurses supported a better understanding of how to interact with families.

As the opioid epidemic has spread, nearly everyone has witnessed the effects of addiction. It's critical that everyone – especially care providers – recognize personal biases when dealing with families with addiction, says Kris Reber, MD, associate division chief of Neonatology at Nationwide Children's.

"If you just sit with these moms, it's really eye-opening," says Dr. Reber. "Opioid addiction affects people from all walks of life, but some of these mothers have lived through horrible things. They can't beat the cycle without a lot of help and support."

Not every baby with NAS is born to a mother in the throes of active addiction. A baby born to a mother who is using an opiate under the supervision of a physician, perhaps for an illness or injury or as part of a medication-assisted treatment regimen, can have NAS.

There is a notion that a parent is a bad parent if their child has this disease. Dr. Shepherd and his team are trying to get away from this idea by reducing the stigma of the NAS diagnosis.

"If there's one thing you learn in the NICU, it's that you can't always predict who the good parents are. There's no way to know if a person who is abusing drugs is going to be a good parent. Unfortunately, we all know that there are perfectly healthy people who are not good parents," says Dr. Shepherd. "There's a lot more to substance abuse than a character flaw."

STREAMLINING CARE TO REDUCE LENGTH OF STAY

In 2009, Erin Keels, DNP, APRN, NNP-BC, director of Advanced Practice in Neonatology at Nationwide Children's, was rounding with teams at each of the hospital's seven NICU sites when it became clear that everyone was struggling with the volume and complexity of babies who were withdrawing.

"In hindsight, we can see it was creeping up on us, but it really felt like that year we reached a tipping point," she says. "In one of our off-site NICUs, 50 percent of patients had NAS. We were running out of space for preemies because of all of the babies with NAS and their long lengths of stay."

Around the same time, Richard McClead, Jr. MD, MHA, associate chief medical officer at Nationwide Children's, began investigating why some of the NICUs in the network were experiencing long average lengths of stay. What he found was a dramatic increase in the number of babies with NAS and a lack of consistency in how they were treated.

"The staff in the NICUs knew this was a problem, but the rest of us didn't until we did the deep dive in the data. These infants were having long, expensive hospital stays because of NAS," says Dr. McClead.

"When we started looking closely at the problem, we found that we were not as good at assessing and managing the care for these infants as we thought. There was a lot of practice variability from location to location and even doctor to doctor. We also found that we had not adequately prepared and supported our staff for the challenges associated with caring for babies with NAS and their families," adds Dr. Keels.

Together – Dr. Keels from the nursing and staffing side and Dr. McClead from the administrative and quality improvement side – they created an NAS Taskforce with key stakeholders in the NAS care path. They knew they had a big problem to solve, and according to Dr. Keels, they took the first year to learn as much as they could about NAS.

"One of the best things we ever did was come up with a protocol and stick with it."

– Erin Keels, DNP, APRN, NNP-BC, director of Advanced Practice in Neonatology at Nationwide Children's

SCORING SYMPTOMS TO MANAGE MEDICATION

The Finnegan scale was developed in the 1960s to assess babies who were exposed to methadone *in utero* who were born otherwise healthy and at term.

"In our NICUs, an opioid-exposed baby may also be preterm, late-preterm or have another problem that needs addressed. And frankly, the combinations, quantities and types of drug exposures these babies are experiencing *in utero* are quite a bit different from methadone and heroin of the 1970s. The Finnegan scale doesn't account for that," says Dr. Keels. "Also, the Finnegan scale was designed to look at the first 28 days after birth. We're often assessing babies much longer than that."

These considerations have led the team at Nationwide Children's to modify the Finnegan to develop a chronic assessment scale for older babies. However, it is still cumbersome and time consuming, requiring regular training, retraining and dual scoring to ensure competency.

This is an added burden for the nurses, who are essential to the care of babies with NAS. The nurses' assessments drive the provider's orders for medication in the weaning protocols.

According to Dr. Keels and Barry Halpern, MD, a neonatologist affiliated with many central Ohio hospitals, including Nationwide Children's, the field may be moving further away from the Finnegan scale in favor of an "Eat, Sleep, Console" assessment. The idea behind it is this: Is the baby eating? Is the baby sleeping? Can the baby be consoled within a period of time? Drs. Keels and Halpern also add that ensuring that the baby is maintaining or gaining weight is another helpful measure in conjunction with Eat, Sleep, Console. If yes to all four, then maybe you don't need medication, or need less medication.

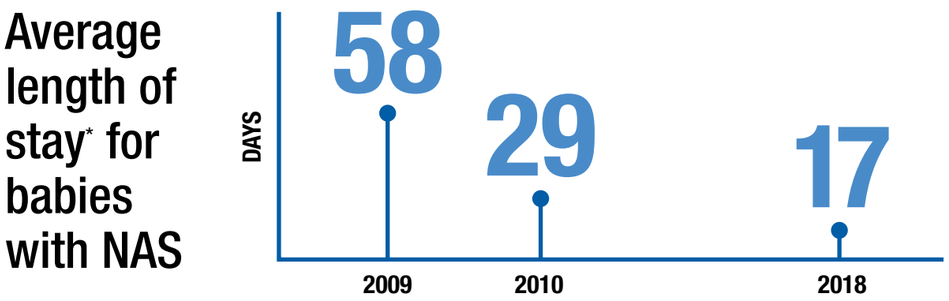
In Dr. Halpern's experience, the Finnegan scoring process can be alienating and adversarial for new moms of babies with NAS, who may already be feeling stigmatized.

"This is a critical period of involvement and bonding for the mom and baby. By assessing them with the Eat, Sleep, Console, Weight method, we can do the assessment in partnership with the mom, on the baby's schedule. Not on the Finnegan schedule or the nurses' schedules," he says.

This approach also ties closely to the philosophy that perhaps it is okay if a baby with NAS is a little upset or jittery for a period of time, as long as they are eating, sleeping, consolable and gaining weight. This philosophy results in further reducing drug exposures by significantly limiting the amount of medication used in the weaning process.

In addition to limiting the amounts of morphine and methadone used in weaning protocols, experts in the field are considering another medication – buprenorphine. The drug, also known by the brand name Suboxone®, is widely used in medication-assisted treatment for adolescents and adults with addiction. Could it be better for babies with NAS?

"There's certainly a need for more research in this area," says Dr. Keels. "We don't know exactly how these options impact the baby long term. And it's something we hope to figure out over time."



*Nationwide Children's data

Through a series of speakers and training sessions, the neonatology team began to learn about every aspect of NAS. They heard from obstetricians on the prenatal side. They learned how to interact with families in a nonjudgmental way. And they learned how to assess the baby using the Finnegan score – the widely accepted standard for monitoring withdrawal symptoms in infants.

EARLY IMPROVEMENTS AND A GROWING COLLABORATIVE

"We saw that as soon as we started paying attention to the problem, it started to improve. The speakers and trainings were having an effect as we started to put into practice what we were learning. By the end of the first year, we had reduced the average length of stay from 58 to 29 days," Dr. Keels says.

At the end of the first year, the taskforce came up with as many evidence-based guidelines as they could to develop a NAS protocol. The essential part of that plan was the weaning protocol.

"One of the best things we ever did was come up with a protocol and stick with it," Dr. Keels says.

In fact, they would eventually find that what drug you use to wean these babies doesn't matter so much as following a plan. In a study conducted as part of the Ohio Perinatal Quality Collaborative (OPQC), the taskforce found that hospitals without a weaning protocol had a much longer length of stay compared to hospitals using either methadone or morphine protocols. Once they added a set practice, using methadone or morphine, the lengths of stay went down.

"Close collaboration with the clinical pharmacist was essential to our success in implementing the protocol," adds Dr. McClead.

In addition to guidelines for pharmacologic care, the taskforce, and later the OPQC, developed a toolbox of nonpharmacologic methods for treating babies with NAS and their families. Nonpharmacologic treatments include breastfeeding, skin-to-skin contact, quiet environments, dim lighting and nonbiased treatment.

"We know that breastfeeding is safe when the mother is on maintenance medication, and it's helpful for the baby. However, only about 25 percent of mothers of babies with NAS breastfeed, according to 2017 OPQC data," says Dr. Keels. "We'd like to see these rates improve, but in the absence of breastfeeding, feeding babies with NAS a high caloric density formula improves withdrawal symptoms compared to feeding regular formula."

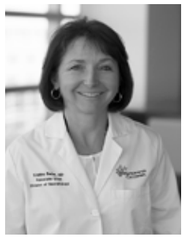
These nonpharmacologic treatments may seem like small changes, but together they make a big difference in the outcomes of the babies. In fact, some babies may not need pharmacologic treatment at all.

"It's ultimately a balancing act. We need to make sure that the baby gets enough hospital care but not so much that it increases hardship for the family," says Dr. Keels. "Right now, our average length of stay is about 17 days throughout the service line. And we think that's as low as we can go with the current care models and medications we use. For future improvements, we're really going to have to think outside the box."

GOING FROM "GOOD" TO "BEST"

So, what's next? While lengths of stay and treatment methods have improved, the problem of NAS isn't going away.

"While we've reduced the length of stay, and hospital, insurance and government policies have been put into place to reduce the number of prescription opioids



> "We know that babies born to mothers on maintenance medication – such as methadone or buprenorphine – have much better outcomes and fewer symptoms than those on multiple illicit substances or drugs that are not regulated by a physician."
>
> *– Kris Reber, MD, associate division chief of Neonatology at Nationwide Children's Hospital*

'out there,' we aren't seeing a reduction in patients with NAS," says Dr. Keels. "As a society, we have a lot more work to do."

Dr. Reber says that the role of a children's hospital begins before the mother is even in the delivery room. Pregnancy is often a trigger for a woman with addiction to seek treatment.

"We know that babies born to mothers on maintenance medication – such as methadone or buprenorphine – have much better outcomes and fewer symptoms than those on multiple illicit substances or drugs that are not regulated by a physician," says Dr. Reber. "A multidisciplinary team of health care providers, social workers and community partners is needed to engage with these mothers as soon as they become pregnant so that they can get into treatment."

This is the idea behind the Substance Abuse, Treatment, Education and Prevention Program (STEPP) clinic at The Ohio State University Wexner Medical Center. The clinic provides medication-assisted treatment, counseling, prenatal care and an opportunity for women to meet with neonatal nurses, social workers, lactation specialists, pediatricians and neonatologists such as Dr. Reber who can prepare moms for what caring for an opioid-exposed baby might require.

ON THE HORIZON: A REVOLUTION IN NAS CARE?

Experts suggest the next step is to move NAS care out of the NICU entirely.

The NICU isn't a quiet and restful place. Babies with NAS are already overstimulated. While efforts are underway to change the feel of the intensity of the NICU and make it more comfortable, it's not the ideal setting for infants with NAS. But the well-baby nursery isn't equipped to handle the special needs and extra care these babies and families require.

What Dr. McClead has in mind is something else entirely – but it will require creativity, collaboration and flexibility among insurance companies, birthing hospitals and pediatric institutions.

What if a baby with NAS could room-in with her mother? What if the mother and baby's hospital stays were both extended so that they could stay together, receiving medical support and counseling in a low intensity setting? What if this could be done in community hospitals as well as in major metropolitan health systems? Or even in an outpatient setting?

Proofs of those concepts are popping up in a few places around the country. A team at Dartmouth published a study in 2017 outlining the medical, financial and perhaps social benefits of keeping moms and their babies with NAS together in the postpartum period.

Here in central Ohio, Dr. Halpern led a successful pilot program funded by a grant from the State of Ohio that incorporated prenatal counseling and care with postnatal rooming-in and support from a highly trained nursing staff. The Mother-Infant Recovery Clinic included a weekly, half-day clinic in the Outpatient Care Center at Nationwide Children's. There, moms-to-be received medication-assisted treatment for their addiction, prenatal care, counseling and education about parenting and caring for babies with NAS all in one appointment. In the third trimester, Dr. Halpern would meet with each mom and talk to her about what to expect during the postnatal period.

Grant Hospital was the delivery hospital for the program. Hospital administrators agreed to let the moms and babies room-in together for up to 5 days – even if Medicaid didn't fully cover it. For vaginal deliveries, the insurance coverage is typically only 48 hours after delivery.

Labor and delivery nurses, as well as postpartum nurses,

Keeping moms and babies together can reduce NICU admissions and preserves the critical mother-child bond.

were trained about how to support the new moms in a positive, non-adversarial way.

"We can't stress enough that many of these women face challenges that many of us cannot fully understand. Many of them have experienced trauma that contributed to their substance abuse disorder. Many also have a behavioral health diagnosis, and few have strong social and socioeconomic support systems," says Dr. Halpern. "Treating moms well in the health care setting so that they can learn skills they need to parent helps them build the confidence they need to be good moms. That in turn gives them the confidence they need to continue treating their own disease."

By the time the pilot ended, 90 percent of babies born to mothers in the program never saw the inside of the NICU. They were treated with nonpharmacologic methods only and were discharged to home within 3 to 5 days.

"These are huge gains," says Dr. Halpern. "We went from a 50 percent admission rate to the NICU for this population to 10 percent. That's an outstanding savings in cost and unnecessary exposures to the drugs required for weaning, and it's an outstanding benefit to families. Preserving that mother-child bond is critical for reducing the risk of future child abuse or neglect."

According to Dr. Halpern, the findings of the pilot could be translated to maternity hospitals large and small, but it requires collaboration and funding. He and his team are currently working to fund the program in a sustainable way, so that it is not dependent on state grants, which have run out.

Dr. Reber suggests that this rooming-in could also be done if the baby is on pharmacologic treatment. And she points to the possible role of supportive living facilities where moms and babies could continue to get multidisciplinary support during the transition period after discharge from the hospital.

"We do a great job taking care of the moms and babies when they are in the hospital. But then we send them out into the unknown – usually without the resources they need to be successful in sobriety," she says.

In his "free time," Dr. Halpern meets with pregnant women at a local medication-assisted treatment clinic.

"All moms, including women with addiction, deserve the best chance for themselves and their babies," he says. "We can and we must continue to do better for them."

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What Happens When Opioid-Exposed Babies Go Home?

FOLLOW-UP FOR BABIES WITH NAS OR PRENATAL OPIOID EXPOSURE IS ESSENTIAL FOR UNDERSTANDING RISKS AND OUTCOMES.

— by Abbie Roth —

Despite the growing number of babies who are exposed to opioids *in utero*, researchers and clinicians still don't have a strong sense of what the long-term developmental risks are. Part of the reason for this murky view is that a large percentage of infants with neonatal abstinence syndrome (NAS) and others who are exposed but not treated are lost to follow-up.

"We know a lot more about the long-term effects of marijuana, smoking, alcohol and even cocaine than we do about the long-term implications of opioid use during pregnancy," says Mark Klebanoff, MD, director of the Ohio Perinatal Research Network and principal investigator in the Center for Perinatal Research at The Research Institute at Nationwide Children's Hospital. "Following these babies as they age is a difficult task. They are often lost to care, and they don't often participate in research studies."

Even when follow-up is part of a standardized care path, as it is for all babies who are discharged from the neonatal intensive care unit (NICU) at Nationwide Children's, opioid-exposed babies are more often lost to care.

Last year, 240 babies were referred to the Nationwide Children's NAS Follow-Up Clinic. Only 67 percent completed new patient visits despite phone calls and the availability of social work support, says Nathalie Maitre, MD, PhD, director of the NICU Follow-Up Program at Nationwide Children's. These numbers are comparable to or even a little better than those of most such clinics in the United States.

The high number of patients who have been lost to follow-up care has several implications. First, it means that many children are not receiving the additional neurodevelopmental surveillance and support they need. It also means that what clinicians and researchers are learning about the long-term neurodevelopmental effects of prenatal opioid exposure is based on a biased sample.

"Babies who are lost to follow-up may be the ones with the highest risk profiles, potentially leading current data regarding outcomes to underestimate the risks associated with prenatal exposure," says Dr. Maitre.

She and her team in the NAS Follow-Up Clinic, led by Jennifer Haase, MD, have recently received a grant to increase the number of babies who receive specialized comprehensive follow-up care.

For the 79 infants referred to the NAS Follow-Up Clinic last year who were lost to care, Ryan Nicoll, LISW-S, identifies several barriers to care that families may experience.

"Barriers to follow-up for this population can be both socioeconomic and psychosocial," she explains.

Socioeconomic barriers include lack of transportation, funds for gas, lack of childcare for siblings and lapses in insurance coverage. They also can include communication difficulties. "Many times, these families are relying on prepaid or government-subsidized phones, which can r esult in phone numbers changing frequently," says Nicoll.

Psychosocial barriers include changes in custody status, concerns about stigmatization or lack of a support system to help facilitate coming to appointments.

"Our goal through the grant project is to remove as many barriers as we can," says Dr. Maitre. "Sometimes, we need to schedule home visits with the physician and a therapist and actually go to the patient. Or, with the support of the clinic team and especially the social worker, we may offer an appointment at a research site that is less intimidating than the main hospital."

By meeting the patients and their caregivers where they are, the team hopes to build trust and reintegrate families into the medical system while gathering data that will help the team understand the risks associated with this patient population. Their goal is 80 percent follow up, which is when researchers can start to trust their outcomes.

However, some babies who were exposed to opioids *in utero* were not treated in a hospital for NAS. Currently, the team cannot estimate how large this population is. But they are answering calls from pediatricians who are asking for more information on risk factors, early signs of developmental problems specific to exposed infants, and referral pathways.

One of the most prevalent identified problems for these infants is neuroregulation – the ability to balance their sensory inputs and outputs. Babies exposed to opioids before birth can appear fussy. They have difficulty integrating stimuli from the outside with what they are feeling on the inside.

"We see this in babies with NAS, but it may also be present in babies who were not treated for NAS. In some cases, the pediatrician may be the first to identify prenatal opioid exposure during a well-baby checkup," says Dr. Maitre.

The grant will also support initial steps to develop an app for pediatricians that will enable them to assess babies with NAS or prenatal exposure for specific risks. And for physicians in Ohio and West Virginia, the app will ultimately help connect them to specialists and therapists who can help.

"For example, babies with NAS may be at higher risk for torticollis, as a study from our Cincinnati colleagues showed," says Dr. Maitre. "With the app, the provider would enter clinical data into specific fields, such as birth type, APGAR, drug exposures – although drug exposure is sometimes a guess. Then, the PCP could be prompted at 3 months to look for signs of torticollis. If the physician is in the target area, they can connect directly to trained therapists through the app."

In the meantime, Dr. Maitre and her team have begun a massive educational campaign to support early intervention by training more than 200 providers in Ohio and West Virginia in standardized neurological exams.

"As we get deeper into our research, we're going to get better at caring for these babies. We're going to know how to follow them. And we're going to be able to tell pediatricians where to refer them," she says.

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PRIMARY CARE PROVIDER GUIDE to NAS Follow Up

Pediatricians have a unique challenge when it comes to caring for the broad spectrum of needs associated with opioid-exposed infants. Some babies who were treated with pharmacological methods in a hospital will be discharged home still on neuro-active medications. Other babies did not receive a neonatal abstinence syndrome (NAS) diagnosis or specific treatment after birth but are at high risk and may show signs of developmental problems. Nathalie Maitre, MD, PhD, director of the NICU Follow-up Program at Nationwide Children's Hospital, and her team have developed two key algorithms to support the care of opiate-exposed infants.

Patients who are discharged on phenobarbital need to be weaned using a standardized protocol. The following protocol is an example of one that has been successfully utilized in the Nationwide Children's NAS Clinic, but there are no evidence-based protocols for phenobarbital weaning in the outpatient setting for patients diagnosed with NAS.

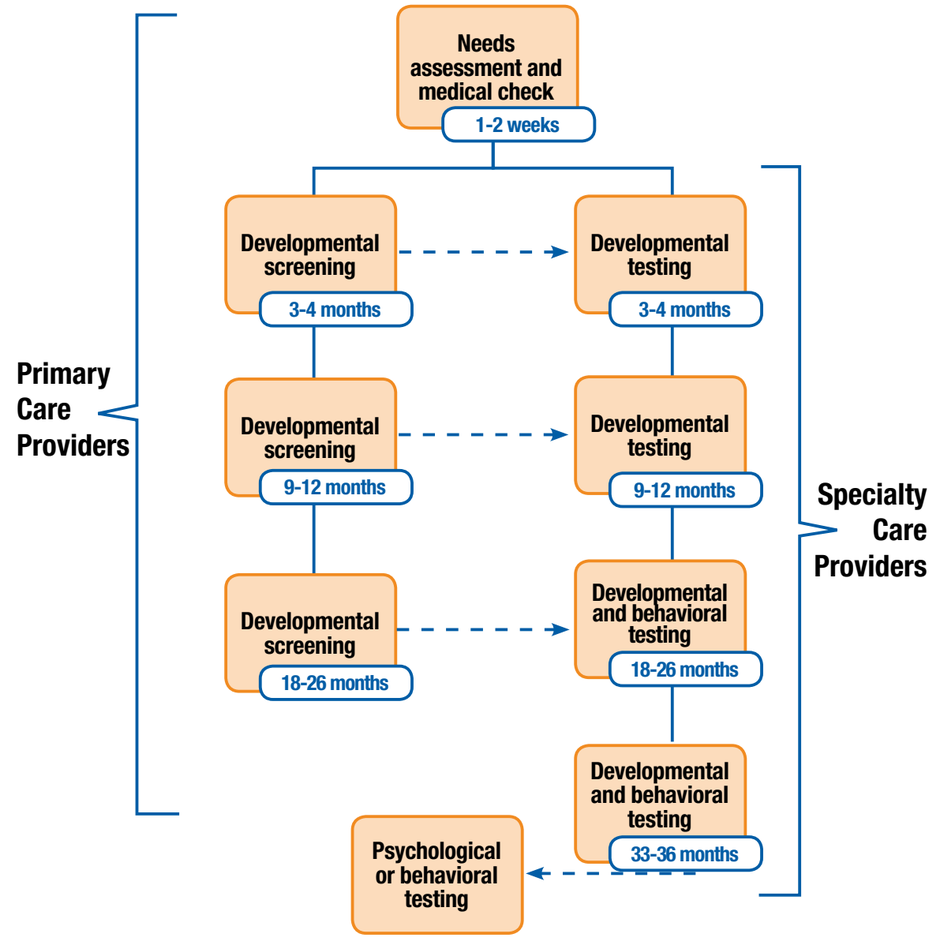
PHENOBARBITAL WEANING PROTOCOL FOR OUTPATIENT INFANTS WITH NAS

If > 5 mg/kg dosing twice per day then change to 5 mg/kg at night and have patients return in 2-4 weeks for remainder of wean. If ≤ 5 mg/kg once per day or at night, follow these steps:

1. If symptomatic with excessive neurologic symptoms (irritability, jitteriness/tremors, shrill cry and inability to calm interrupting sleep) then continue same dosing to outgrow without weight adjustment and return in 2-4 weeks. Sneezing, yawning and liquid stools are not reasons to stop wean.
2. If asymptomatic, start to wean with a reduction of 25-30% per week for 2-4 weeks with convenient home dosing. (i.e. 4 ml x 7 days, 3 ml x 7 days, 2 ml x 7 days, 1 ml x 7 days).
3. If increased symptoms occur during wean, have caregivers go back to the previous week's dose and call for further instruction. Have patient return for follow-up medication check and assessment.
4. After follow up, attempt again to decrease dose by 25-30% per week over 3-4 weeks.
5. Provider can use individual judgement and assessment to shorten or prolong wean. An infant no longer sleeping as well or no longer sleeping through the night are NOT reasons to stop the wean.

THE TIMING OF SCREENINGS AND TESTS FOR PATIENTS WITH NAS

For babies with NAS or prenatal opioid exposure, in addition to routine developmental screenings, primary care providers should use the ASQ-3, the so-called "Ages and Stages Questionnaire." Based on the results of the screens, primary care providers should refer to specialists who will follow up with additional testing, utilizing the Test of Infant Motor Performance and Bayley Scales of Infant and Toddler Development, among others.



What Can Bench Science Teach Us About Opioid Abuse?

IN VITRO MODELS CAN HELP ANSWER BIG QUESTIONS ABOUT NEONATAL ABSTINENCE SYNDROME AND FETAL DRUG EXPOSURE.

— by Abbie Roth —

Irina Buhimschi, MD, is an obstetrician and principal investigator best known for her work to prevent prematurity. As director of the Center for Perinatal Research in The Research Institute at Nationwide Children's Hospital, she says the opioid crisis has caused the center to adjust priorities.

"There are a lot of things that we don't know about how opiate exposure affects the fetus *in utero*, and how that exposure will affect the child long term," she says. "While we've made significant progress in the clinical care of these babies in terms of length of stay, we have an opportunity to further improve outcomes through basic research."

Among the questions that are unanswered:

- Is buprenorphine or methadone a better maintenance medication for pregnant women? Is there a genetic footprint that makes one better than another for a specific individual?
- Which medication – methadone, morphine or buprenorphine – is best for treating NAS?
- Why do some opioid-exposed babies develop NAS while others never withdraw? Is there a genetic susceptibility?
- How does the placenta metabolize illicit drugs, and how do those metabolites affect the fetal brain?

These questions are all difficult to study in the clinic.

"We have a group that has created different models to study some of these questions *in vitro*. Using these models, we're able to look at the genomics, proteomics and metabolomics involved," says Dr. Buhimschi, who is also a professor of Pediatrics and Obstetrics and Gynecology at The Ohio State University.

The models in question are organoids developed from induced pluripotent stem (iPS) cells, which are derived from skin or blood cells that have been reprogrammed back into an embryonic-like pluripotent state. Organoid placentas and brains hold incredible potential to answer questions about the role of all these "omics" in fetal drug exposure.

These models will enable the team to conduct several collaborative experiments aimed at better understanding the underlying mechanisms of NAS.

UNDERSTANDING EXPOSURES

"One of the major problems in studying the impact of prenatal exposure to drugs is that we usually don't know what exactly the baby was exposed to," says Mark Klebanoff, MD, director of the Ohio Perinatal Research Network. "In previous studies of marijuana use, we found that the accuracy of self-reporting was poor."

In those studies, mothers' responses compared to blood and urine toxicology often did not match up. Sometimes, mothers who said they had used marijuana during pregnancy had clean toxicology screens. Many times, mothers who said they did not use marijuana during pregnancy had positive toxicology screens.

When illicit substances are involved, knowing just what the baby was exposed to is even more difficult.

"Being illicit, those drugs could have anything in them," says Dr. Buhimschi. "We need ways to really understand what the exposures are. When we know that some exposure is present, umbilical cord blood toxicology and a urine screen from the mother can be helpful."

But it's nearly impossible to get good toxicology results for every opioid-exposed infant. Without that data, researchers can't accurately draw correlations between specific exposures and NAS symptoms.

Dr. Buhimschi's team hopes to be able to provide a controlled way to test different drugs and combinations of drugs on placental organoids. This may shed some light on which factors are the most important for predicting which babies will develop NAS.

"The placenta is likely a key factor in determining which babies develop NAS and which do not," says Dr. Buhimschi. "We don't know if the placenta is a high or low metabolizer of opioids. Other researchers do these experiments with viruses, we're trying to do it with drugs."

LONG-TERM EFFECTS

Another unknown is the long-term effects of opioid exposure on neurodevelopment. According to Dr. Klebanoff, who is also a principal investigator in the Center for Perinatal Research at Nationwide Children's and a professor of Pediatrics, Obstetrics and Gynecology, and Epidemiology at The Ohio State University, what little we know suggests that executive function is impacted later in childhood. But it is difficult to determine whether that is due more to the prenatal opioid exposure or to their environment.

"These mothers and children often end up back in the environment that contributed to the opiate abuse in the first place," he says. "At this point, we can't say whether some deficits in executive function at ages 5, 6 or 7 are the result of the prenatal exposure or the result of social determinants. It's probably some of both."

Again, Dr. Buhimschi's team believes that their models can help answer some of the neurodevelopmental questions.

"We've developed a brain organoid – in addition to a placental organoid – to create an *in vitro* model, a co-organoid system, to study the relationship between the placenta and brain," she says. "We hope to mimic the transmission of metabolites from the placenta to the fetal brain, then use an electroencephalogram (EEG) to measure the changes in electrical signals caused by exposure to those opioid metabolites."

MOVING FROM POSSIBLE TO PRACTICAL

As the researchers refine and validate the models and methodologies, they are also working to secure grant funding to do the experiments.

"By doing the experiments and collecting the data, we hope to learn valuable information that can be translated into practical solutions to further improve clinical care for these mothers and babies," says Dr. Buhimschi.

MANAGING PAIN IN AN ERA OF OPIOID ABUSE

— by Abbie Roth —

Managing pain is complicated. Not that long ago, perhaps 50 years or so, pain was understood to be a multidisciplinary issue requiring many different approaches. Doctors would recommend lifestyle changes, complementary therapies and medications to treat chronic pain.

Then something changed.

Opioids began being marketed as "nonaddictive." Pain became the "5th vital sign," and physicians were encouraged to treat it aggressively. Insurance companies stopped paying for nonpharmaceutical treatments, and pain management clinics became a hub for prescribing opioid medication.

Taken together, those factors ultimately contributed to the opioid crisis the nation now faces.

So how should pediatric providers manage patients with pain in an era where some families are drug-seeking, some are afraid of medications and reject them outright, and insurance companies still balk at covering nonpharmaceutical treatments?

"One of the first steps is to have honest conversations with patients and families about pain," says Tarun Bhalla, MD, MBA, vice chairman of Comprehensive Pain Services at Nationwide Children's Hospital. "The goal is to keep pain to a manageable and tolerable level. We're going to provide medications and other techniques to help to minimize pain, however it may not be completely at a 0 out of 10."

Improving pain to a tolerable level to allow the patient to function is the goal, and it may be a different pain score for each patient, adds Sharon Wrona, DNP, CPNP-PC, administrative director of the Comprehensive Pain and Palliative Care Service.

Honest conversations are part of the collaborative approach needed to manage pediatric pain successfully. In 2016, a team of physicians, nurses and administrators at Nationwide Children's formed the Opioid Safety Taskforce as a collaborative effort to address questions about prescribing practices and education. The result was a new spotlight on areas in need of attention and quality improvement plans to make the necessary changes.

"One of the first steps is to have honest conversations with patients and families about pain."

– Tarun Bhalla, MD, MBA, vice chairman of Comprehensive Pain Services at Nationwide Children's Hospital

QUALITY IMPROVEMENT TO DRIVE CHANGE

According to Dr. Wrona, who is also the leader of the taskforce, initial surveys and research indicated that clinicians were prescribing more pills than were needed for pain.

"Children who were prescribed opioids for acute pain after procedures generally use a fraction of what was prescribed for them," she says. "One of our first objectives was to lower the number of pills prescribed per home-going prescription."

Limiting the number of home-going prescriptions not only protects the child who gets the prescription, but it also reduces the number of leftovers available for misuse. According to a study in a 2007 issue of *Addiction*, 8 of 10 adolescents who report misusing prescription opioids stated that they accessed leftover drugs from family and friends.

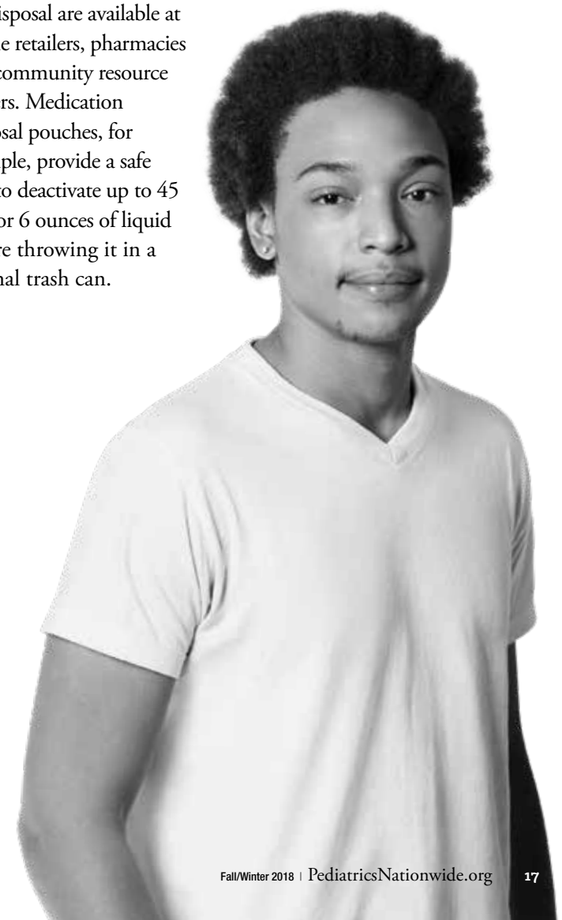
In addition to the Nationwide Children's quality improvement initiative, state legislators also began introducing new laws to limit prescribing. In August 2017, new prescribing rules in Ohio for acute pain limited the prescriptions of opioids to minors to 5 days.

"Our efforts, combined with changes in legislation and insurance policies, led to a 30 percent reduction in doses prescribed per home-going opioid prescription overall across the institution," says Dr. Wrona. "Some department-specific efforts saw even greater reductions."

For example, an otolaryngology-specific initiative used non-opioid medications, such as acetaminophen and ibuprofen, on a schedule to help lower the need for opioids. Through the project, they decreased home-going doses of opioids prescribed per patient following a tonsillectomy and adenoidectomy from 45 doses to 20 doses – or in some cases, no doses of home-going opioids.

The taskforce has also created the Nationwide Children's opioid safety website to educate patients and families about safe use, storage and disposal. Resources are available in Spanish and Somali in addition to English.

Many times, leftover medications are accessed by those who intend to misuse or abuse them because caregivers don't know how to safely dispose. To aid in safe disposal, Nationwide Children's Outpatient Pharmacies will install medication drop boxes by the end of 2018. But other options are already available. Drug take-back days organized by local police and fire stations provide a safe place to drop off unused medications. And commercial products to neutralize medications for disposal are available at online retailers, pharmacies and community resource centers. Medication disposal pouches, for example, provide a safe way to deactivate up to 45 pills or 6 ounces of liquid before throwing it in a normal trash can.



Medication disposal pouches provide a safe way to deactivate up to 45 pills or 6 ounces of liquid before throwing it in a normal trash can.

A free medication lock box is supplied to all patients at Nationwide Children's who are prescribed an opioid.

OPIOIDS FOR CHRONIC PAIN

While opioids should never be the first line of defense against chronic pain, some patients still may have a need for longer-term opioid use. At Nationwide Children's, these patients are managed in the Chronic Pain Clinic and regularly screened for use and misuse. Algorithms for managing risk level and opioid misuse in this population ensure appropriate adjustments in care and referrals for addiction treatment as necessary.

As part of a taskforce initiative, the team is working to improve the quality and frequency of risk assessment. In addition to risk of abuse, prescription opioids carry a high risk of diversion – being sold or used by patients or caregivers.

"We need to screen patients and family members for risk of opioid abuse and diversion at each appointment," says Dr. Wrona. "Opioid abuse and addiction doesn't discriminate, and the current crisis increases the temptation to divert medications."

The hospital's Prescribing and Education QI Initiative aims to increase the percentage of patients who are engaged in a formal Opioid Risk Assessment for abuse and diversion from less than 5 percent to at least 75 percent. During assessment, key topics that nurses discuss with patients prescribed opioids long-term include:

1. Family and patient history of substance abuse
2. Family and patient history of mental health problems
3. Patient history of sexual or physical abuse

Opioid safety patient education compliance can now be tracked through the electronic medical record. And a free medication lock box is supplied to all of Nationwide Children's patients who are prescribed an opioid, says Dr. Wrona.

WHAT ARE NON-OPIOID OPTIONS FOR PAIN MANAGEMENT?

In addition to assessing and monitoring risk, experts in the Chronic Pain Clinic utilize non-opioid treatments for pain. Using a holistic approach, they incorporate behavioral health supports, healthy diet and exercise recommendations and complementary alternative medicine (CAM) to meet the needs of chronic pain patients.

"We like to approach pain multimodally," says Dr. Bhalla. "Whether we are talking about acute pain for a surgical procedure, chronic pain or even palliative care for someone with a terminal illness, we believe in using all the tools available to us to provide the best quality of life at the lowest risk to the patient."

"We need to screen patients and family members for risk of opioid abuse and diversion at each appointment. Opioid abuse and addiction doesn't discriminate, and the current crisis increases the temptation to divert medications."

– Sharon Wrona, DNP, CPNP-PC, administrative director of the Comprehensive Pain and Palliative Care Service at Nationwide Children's Hospital

Integrative medicine techniques such as acupuncture, physical therapy, aromatherapy, distraction techniques, mindfulness, biofeedback, hypnosis and others are used to manage pain and minimize opioid use.

One of the most powerful tools is regional anesthesia, which can be used to numb parts of the body by addressing central or peripheral nerves. This method enables surgeons to perform some procedures without general anesthesia, which in some cases may lead to a sooner discharge from the hospital. It is also helping patients in palliative care manage pain while preserving their quality of life. The anesthesiology team is studying how to expand the technique's use.

"Regional anesthesia is a great way to limit the amount of anesthesia and opioids we need to use," says Dr. Bhalla. "We perform about 200 regional anesthesia procedures a month, which is one of the busiest pediatric regional anesthesia services in the country. And we're continually learning how to improve and expand the benefit that it can have in pediatrics."

Other tools don't require medication at all. CAM harnesses the mind-body connection to reduce stress, reduce pain and support medical care. And yes, these tools have a place in the recovery room and chronic pain clinics, says Dr. Bhalla.

Parents and caregivers of young children frequently observe that mind-body connection.

Have you ever watched a young child fall down, get up and keep running? He's completely fine until minutes later when he sees a drop of blood on his knee. Then, it's the worst injury he's ever experienced – until you give him a *Paw Patrol* Band-Aid®. After that bandage sticks, he's good to go again.

"It's important to recognize that children's pain manifests differently than adult pain, and differently across the spectrum of ages that we treat," says Dr. Bhalla. "Especially in kids, pain is both mental and physical. Mental can be even more influential for younger kids. They haven't dissociated the mental and physical as much as adults."

CAM includes the use of acupuncture, physical therapy, aromatherapy, distraction techniques, mindfulness, biofeedback, hypnosis and other integrative medicine techniques. Success of CAM for pain management support depends on the patient and family, says Dr. Bhalla, who recently published an article in the *Journal of Pain Research* about caregivers' knowledge and acceptance of CAM.

"If it is done right and the patient and family are willing, it can be really effective," he says. "With the opioid crisis, more people are open to trying something that will keep their children away from the medications. We're happy to be able to do that in an appropriate way."

For more information about specialty-specific efforts to reduce opioid prescribing, visit PediatricsNationwide.org/Reducing-Opioid-Prescriptions.

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Breaking the Cycle: PREVENTING AND TREATING ADDICTION IN YOUTH

— by Abbie Roth —

Virtually all addictions begin during adolescence. And nearly 4 million 12-25 year olds in the United States have a substance abuse problem, according to the U.S. Department of Health & Human Services. Substance abuse in adolescents is not restricted to opioids, but in the midst of this national crisis, too many young people are finding themselves in the grips of opioid addiction.

In 2016, 3.6 percent of adolescents aged 12-17 reported misusing opioids over the past year. Among 18-25 year olds, that number was even higher: 7.3 percent. Between 1999 and 2016, 56,428 adolescents and young adults (ages 15-24 years) died from a drug overdose.

These staggering statistics underscore the need for effective treatment programs. At Nationwide Children's Hospital, members of the Adolescent Medicine Substance Abuse Program and Medication-Assisted Treatment for Addiction (MATA) Program have found that medication-assisted treatment (MAT), combined with behavioral health interventions and a focus on patient retention, results in more patients who enter and stay in recovery.

TREATING ADDICTION WITH MEDICATION

Despite the growing body of evidence showing the effectiveness of MAT in the treatment of opioid use disorders, providers – and even patients and parents – have been hesitant to embrace it. For some, treating opioid addiction with an opioid seems counterintuitive. They see the goal of recovery as being substance-free. For those for whom MAT has been life-saving, however, the understanding that medication can be part of a recovery process that enables them to live healthy, productive lives has made all the difference.

Relapse without MAT is high. According to the National Institute of Drug Abuse, MAT decreases the incidence of opioid use, opioid-related overdose deaths, criminal activity and infectious disease transmission. It also increases social functioning and retention in treatment.

Unfortunately, the adolescents and young adults are among those most likely not to receive MAT. According to a study recently published in *JAMA Pediatrics*, a majority of adolescents and young adults diagnosed with opioid use disorder are not receiving the recommended MAT. In fact, only 24 percent of youths aged 13-22 years receive one of the three FDA-approved medications – methadone, buprenorphine and naltrexone – within 3 months of diagnosis. For those under age 18, only 1 in 21 receive medication.

"There are far too few pediatric providers who prescribe medications for addiction, and stigma is still playing a role in deterring many patients and families from using these evidence-based medications," said Scott Hadland, MD, MPH, MS, pediatrician and researcher at the Grayken Center for Addiction at Boston Medical Center in a press release.

In the MATA Program at Nationwide Children's, the team uses buprenorphine/naloxone (brand names Suboxone® and Zubsolv®) as part of the comprehensive program. But that's not the case everywhere. Among all treatment programs for youth listed by the Substance Abuse and Mental Health Services Administration, only 37 percent offer MAT. In some cases, programs may deny admission to young people who are already on a maintenance medication.

"We use buprenorphine for three main purposes: first, to suppress withdrawal; second, to block or decrease the euphoric effect of illicit opiates; third, to titrate doses to minimize or even eliminate the craving for opioids. In combination with talk therapy and meeting other health needs, this approach gives our young patients the best chance at recovery," says Steve Matson, MD, medical director of the Adolescent Substance Abuse Program at Nationwide Children's.

BEYOND MAT

Patients in the MATA Program face a wide variety of challenges in addition to addiction, including pregnancy, sexually transmitted infections, hepatitis C, depression and anxiety. Integration into a primary care clinic supports coordinated care and reduces intake times. "We treat the whole patient, not just the withdrawal issues," Dr. Matson says.

The key components of the MATA Program at Nationwide Children's include:

- Point-of-care urine testing
- Narcan® overdose kits provided to every patient
- Weekly visit to the Adolescent Medicine Clinic
- Mental health assessments at 3 and 6 weeks

And now, the team can add integrated behavioral health support to the list. In the summer of 2018, Ashley Garrett, LISW-S, LICDC, became the MATA outpatient clinician. The position is partially funded by a grant from the Nationwide Children's Foundation.

"One of the things that we work on in addiction recovery therapy is answering these questions: What does a life in recovery look like for you? What does a recovered life look like? Once we know where we're going, we can talk about strategies to support and sustain that recovered life."

– ASHLEY GARRETT, LISW-S, LICDC, MATA OUTPATIENT CLINICIAN

Combining MAT with counseling in a comprehensive program offers adolescents and young adults the best chance at recovery.

"Therapy for patients with addiction is incredibly important," she says. "Many have a trauma history that has impacted their self-efficacy, and an appropriate therapeutic relationship is instrumental in demonstrating healthy relationships, improving one's self-concept and developing skills needed for life."

Some people are reluctant to participate in therapy, she adds. They don't want to "talk feelings." But getting a feel of the emotional landscape that contributed to addiction is essential for recovery.

Even so, therapy as part of treatment for addiction isn't all talk about feelings.

"One of the things that we work on in addiction recovery therapy is answering these questions: What does a life in recovery look like for you? What does a recovered life look like? Once we know where we're going, we can talk about strategies to support and sustain that recovered life," Garrett says.

Treatment and prevention have a lot in common from the behavioral health perspective. Preventing a teenager from abusing drugs starts long before they hit adolescence. And it requires more than scare tactics, "just say no" campaigns, and a parent's watchful eye. So does treatment.

Building resilience and making sure behavioral health needs are met is crucial to helping people at risk for addiction disorders. In fact, the U.S. Department of Health & Human Services lists "building strong relationships with adolescents" as the first step to connecting with youth on drug prevention. It's also the first step to connecting with them on treatment.

"Historically, I thought one of the biggest challenges to treatment for patients with addiction from the behavioral health side was managing the externalizing behaviors – the opposition and aggression," says Garrett. "After being in the field for several years, I see that it really comes down to love and belonging. The behaviors are a defense mechanism and a means of self-preservation."

"We can teach skills and techniques to manage substance use triggers and support recovery," she continues. "But it's more difficult to help find loving and supportive people to help them feel worthy to pursue recovery."

Those relationships can come from support groups and by destigmatizing addiction disorders.

In his visit to Nationwide Children's in March 2018, National Institutes of Health Director Francis Collins, MD, PhD toured the MATA Program. He acknowledged

"These kids, who virtually all come from difficult circumstances, feel it is safe to come and have a warm embrace from a care team that really wants to get to know them and isn't going to stigmatize them."

– FRANCIS COLLINS, MD, PHD, DIRECTOR OF NATIONAL INSTITUTES OF HEALTH

"People in recovery are brave. There's an incredible potential for success. They are resourceful, determined and creative. And with support, they can channel all of their skills and potential, and lead a recovered life."

– ASHLEY GARRETT, LISW-S, LICDC, MATA OUTPATIENT CLINICIAN AT NATIONWIDE CHILDREN'S

the difficulties that youth with addiction face and how the program can help.

"These kids, who virtually all come from difficult circumstances, feel it is safe to come and have a warm embrace from a care team that really wants to get to know them and isn't going to stigmatize them," he said.

MANAGING DUAL DIAGNOSES

More than half of people with an addiction to opioids also have a behavioral health diagnosis. If left untreated, that behavioral health problem can further drive the addiction. "Dual diagnosis" is the term used when someone has both a mood disorder and a substance abuse disorder.

"Historically, substance use treatment and behavioral health were siloed," says Garrett. "Nationwide Children's has an incredible amount of collaboration, which I believe is still rare. It's getting better, however, as dual diagnosis is more widely accepted."

In many cases of dual diagnosis, substance abuse begins as an attempt to self-medicate for depression, anxiety or other behavioral health problems. It may have led to the addiction, and it may persist after the patient begins treatment for the substance abuse disorder.

"Self-medication with marijuana and alcohol may complicate recovery when the patient is participating in the MAT program," says Dr. Matson. "We work with them on this. It's better for them to get the behavioral health support they need and to get on appropriate prescription medication for those issues if it is needed."

Dr. Matson says that he and his team have learned from experience that developing relationships with these patients is vital to helping them move forward in the recovery process.

"Getting them off opioids and onto buprenorphine is the first step. Then, you work with them on the other stuff," he says. "If you push too hard too fast, they don't always come back. The best thing you can do is meet them where they are. Then you can move forward together."

SEEKING A RECOVERED LIFESTYLE

Recovery is hard. In addition to the physical symptoms of withdrawal, patients in recovery face an entire upheaval of their world. The people, places and things that are most familiar to them may be triggers of addiction and barriers to their sobriety. A person seeking recovery is asked to let go of all of it. And many do so without the backing of supportive family and friends.

"People in recovery are brave. There's an incredible potential for success," says Garrett. "They are resourceful, determined and creative. And with support, they can channel all of their skills and potential, and lead a recovered life."

But getting there is a long road. Perhaps especially so for young people who may resent the restrictions their sobriety may impose and who don't have a strong support system.

"It's a hard thing for a 20 year old in a recovery program to consider that they are going to turn 21 and not be able to go have a drink. And maybe not ever. The jury is still out on whether a person in recovery can consume any addictive or commonly abused substance," says Dr. Matson. "We teach our patients strategies for maintaining lifelong sobriety – no opioids, no alcohol, no marijuana."

The life changes required for recovery also include restricting or eliminating contact with the people and places who were part of the addicted life. For a person in recovery, maintaining relationships with friends and connections who participated in or supported the addiction is difficult. For some youth, that means distancing themselves from their family.

"Some of these young people don't have any support

"The incentives make a big difference. A little reward – such as drawing a gift card out of a bowl – for achieving a milestone in their recovery gives our patients recognition of their hard work. And that $25 gift certificate to Walmart might help provide the gas money they need to get to their next appointment."

– STEVE MATSON, MD, MEDICAL DIRECTOR OF THE ADOLESCENT SUBSTANCE ABUSE PROGRAM AT NATIONWIDE CHILDREN'S

for their recovery at home," Dr. Matson says. "That makes it very hard for them to continue treatment – in our program or any other."

KEEP THEM COMING BACK

From 2009 to 2012 at Nationwide Children's, only 9 percent of patients stayed in the program at 12 months. This low retention rate mirrored those of others programs around the country.

To improve retention in the program, Dr. Matson and his team embarked on a quality improvement project. Among the actions taken, they began an incentive program funded by grant support.

"The incentives make a big difference," says Dr. Matson. "A little reward – such as drawing a gift card out of a bowl – for achieving a milestone in their recovery gives our patients recognition of their hard work. And that $25 gift certificate to Walmart might help provide the gas money they need to get to their next appointment."

Other interventions included additional social work support and follow-up calls to remind patients to come to their appointments. Through a QI project, retention increased to 40 percent at 12 months and 60 percent at 6 months.

WHAT'S NEXT?

"I was inspired by the clinic," said Dr. Collins after his visit. "Many of these kids started into opioid difficulties as early as age 12 or 13 and are now in the place where they need medication-assisted treatment to allow them to get free of this. It's a tough challenge and very few places have a facility that can handle that kind of circumstance. I wish we had lots of those clinics all over the country. There are only a few, maybe because people aren't quite sure that they would work – it looks like it's working."

As the need for treatment centers that can care for youth with addiction increases, the staff at Nationwide Children's are training the next generation of clinicians who are joining the front lines.

"Some of our fellows are actually moving on to start similar clinics in other institutions in the region," says Dr. Matson. "We're really proud of that. The more opportunities for treatment that these kids have, the better. Patients in our clinic travel from several counties to get care – some of them driving more than an hour each way."

The biggest challenge for the future of addiction treatment in youth is much the same as that for adults. It's expensive. And things like incentive programs, continued therapy, a broader focus on detox and follow-up care aren't always covered by insurance.

"We depend on a lot of grants to do the things that make our program as effective as it can be," says Dr. Matson. "Looking at how we fund and support comprehensive treatment programs across the country is essential to continued improvement and success in treating this epidemic. These kids are trying to do better, but it's not easy for them. We're working hard to provide the support they need to succeed."

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U.S. Department of Health and Human Services. HHS.gov/opioids

Do You Know How to Use Narcan?

Naloxone, the medication in Narcan® nasal spray, rapidly reverses opioid overdoses. It works by binding to the opioid receptors and reversing or blocking the effects of other opioids. Naloxone does not reverse overdoses caused by non-opioid drugs. However, if you are unsure what drugs caused the overdose, give naloxone anyway.

IF SOMEONE IS UNRESPONSIVE AND YOU SUSPECT AN OVERDOSE:

1. Call 9-1-1.
2. Perform rescue breathing.
3. Give Narcan nasal spray.

HOW TO USE NARCAN:

1. Remove Narcan from the package.
2. Hold it with your thumb on the bottom of the plunger and your first and middle fingers on either side of the nozzle.
3. Insert the tip of the nozzle into a nostril while tilting the person's head back and supporting the neck with your hand.
4. Press the plunger firmly.
5. If there is no response in 3-5 minutes, repeat the dose.

Narcan is often prescribed to people in treatment programs, because overdoses are common during a relapse due to the lowered tolerance of the person with addiction. Police officers, civil servants and other community members may also carry it as potential first responders.

How to Reduce Cast Complications in Orthopedics

A quality improvement project resulted in almost total elimination of cast complications in a busy pediatric department.

In early 2015, the Department of Orthopaedics at Nationwide Children's Hospital saw 5.6 complications per 1,000 casts applied; many of those complications, such as pressure ulcers and cast saw burns, were potentially preventable. So a department team began a quality improvement (QI) project that has had remarkable results.

A new report of that project, published in the *Journal of Pediatric Orthopedics*, shows the cast complication rate declined by 97 percent to 0.15 per 1,000 in less than a year, and that low rate has been sustained.

"We implemented a number of interventions, but the introduction of a formalized monthly resident casting education program with a competency checklist made the quickest, most notable difference," says Julie Balch Samora, MD, PhD, orthopedic surgeon at Nationwide Children's, director of Quality Improvement for the hospital's Department of Orthopaedics and lead author of the study.

Over the course of a two-year period documented in the research, a total of 40 people were involved in cast application, bivalving or cast removal. More than half were rotating residents. While efforts were made to train them in casting before the project began, there was no formal program, says Dr. Samora.

So the QI team created one. Education sessions were held at the beginning of every rotation, and residents were required to participate even if they had completed a prior rotation. A "lead cast technician" was designated to teach each resident. Residents had to demonstrate competency in applying and removing casts using a key component checklist, including attention to water temperature, cast padding and cast saw technique.

Other QI interventions in the project included:

- Creation of a robust complication reporting system, after it became clear that not all incidents were documented
- Education for cast technicians, allied health professionals and physicians
- Requirement that AquaCast® Saw Stop Protective Strips be applied as an extra barrier between cast saws and skin
- A daily audit of casting inventory and a daily status check of casting saws

The complication rate dropped by almost half after just the first month of interventions and continued to decline as the interventions were refined.

"Nationwide Children's has a focus on QI, and these projects are the right things to do," says Dr. Samora. "We can have better outcomes, improve patient care, save stress and expense for families and save money. In this case, we could do all of those simultaneously."

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— Jeb Phillips

How Sweet It Is: Honey Attenuates Button Battery-Induced Esophageal Damage

Discovery of honey's protective effects results in new National Capital Poison Center guidelines.

After years of searching for a palatable household liquid to help counteract esophageal tissue damage in children who had swallowed a button battery, physician-scientists have struck liquid gold. Honey – tasty enough for kids to happily sip and readily available in most homes – has natural acidity that effectively lowers tissue pH around highly alkaline button batteries lodged in the esophagus, and its viscous composition helps coat the battery to slow additional damage until it can be extracted.

Kris Jatana, MD, a pediatric otolaryngologist and director of Pediatric Otolaryngology Quality Improvement at Nationwide Children's Hospital who is also part of the leadership of the American Academy of Pediatrics' National Button Battery Task Force, tested everything from vinegar to apple juice before landing on honey as a potential first-aid solution for button battery ingestions. More than 3,000 cases occur per year, mostly among children younger than age 6, and severe cases are on the rise. Lodged button batteries can cause rapid injury, including permanent bilateral vocal cord paralysis and even death.

Dr. Jatana, co-principal investigator of the study published in *The Laryngoscope*, first studied the various liquids alone, then initiated tests with tissue samples. Both honey and sucralfate (Carafate®) were able to effectively neutralize the tissue pH and reduce visible injury compared to saline and other household liquids. He then confirmed these preliminary findings with live animal studies, in collaboration with co-principal investigator Ian Jacobs, MD, medical director of the Center for Pediatric Airway Disorders in the Division of Otolaryngology (ENT) at Children's Hospital of Philadelphia and other researchers.

The team's work won the distinguished 2018 Broyles-Maloney Award from the American Broncho-Esophagological Association. The investigators previously collaborated on a study published last year that found a weak acetic acid rinse (sterile vinegar) can help neutralize tissue pH and protect the esophagus from continued tissue breakdown after battery removal. This irrigation concept has now been successfully used in children around the world with good clinical outcomes.

"When we're up against a severe hazard like this, we're looking to do anything we can to reduce the severity of injury. We know that some pre-removal interventions like this are better than none. Now we will continue to study outcomes as we implement these protective measures in children," says Dr. Jatana, who has been advocating for improved safety requirements for electronics and battery packaging, as well as consumer awareness, since seeing his first complicated case of battery ingestion more than 10 years ago.

"It's crucial for parents and caregivers to be aware of these batteries as hazards that can be life-changing and life-threatening," Dr. Jatana stresses. "Advise them to keep all batteries stored in secure containers, out of reach or sight of children, and to check that all battery-powered electronics contain the batteries in a secured compartment that requires a tool to gain access."

As a result of the recent study, the National Capital Poison Center has released new guidelines for the management of lodged button batteries in children ages 1 and older.

For a summary of the guidelines and a downloadable handout to educate parents and caregivers, visit PediatricsNationwide.org/Button-Battery-Guidelines.

Anfang RR, Jatana KR, Linn RL, Rhoades K, Fry J, Jacobs IN. pH-neutralizing esophageal irrigations as a novel mitigation strategy for button battery injury. *The Laryngoscope*. 2018 Jun 11. [Epub ahead of print]

Jatana KR, Rhoades K, Milkovich S, Jacobs IN. Basic mechanism of button battery ingestion injuries and novel mitigation strategies after diagnosis and removal. *The Laryngoscope*. 2017 Jun;127(6):1276-1282.

— Katie Brind'Amour, PhD

Lymphocyte Response After a Burn Predicts Infection

Abnormal lymphocyte percentage three days after a burn injury is associated with adverse outcomes, including increased risk of infection.

Burns are a major cause of injury in children. At the American Burn Association-certified pediatric burn center at Nationwide Children's Hospital, clinicians see about 200 admissions a year.

Burns put patients at risk for many complications, especially infections. But diagnosing infection after a moderate-to-large burn injury is challenging, given the massive inflammatory response that follows. Burns cause profound changes in the immune system, including an elevation of the white blood cells and neutrophils and a reduction of the lymphocyte count.

"When we see patients admitted after a major burn, it's difficult to tell if it is just the normal response to the burn or if there is an infection," says Rajan Thakkar, MD, a pediatric surgeon and associate medical director of the Burn Program at Nationwide Children's. "Due to this hyper-inflammatory response, these patients have the same clinical symptoms as infections."

In a new study published in the *Journal of Surgical Research*, Dr. Thakkar and colleagues looked at whether recovery of immune response predicted outcomes in pediatric burn patients. Specifically, they evaluated white blood cell, neutrophil and lymphocyte counts, clinical parameters that are obtained routinely upon admission. Typically, these cell counts start to return to normal about 72 hours after a burn injury.

The researchers looked at those three markers of immune response 72 hours post-burn injury in 84 pediatric patients. They found that abnormal lymphocyte numbers were the most predictive of adverse outcomes.

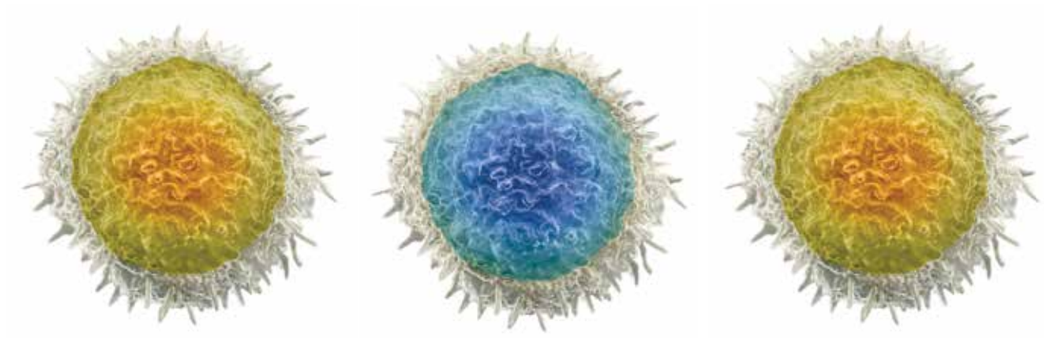
"On the third day after injury, if the lymphocytes were still low, those patients were more likely to have a longer length of stay in the hospital, more days in the ICU and more days on the ventilator," says Dr. Thakkar. "When we controlled for everything else, patients with an abnormal lymphocyte count after 72 hours were seven times more likely to get an infection."

This study suggests lymphocyte count may be helpful in identifying patients with increased likelihood of developing complications. These patients could benefit from more aggressive treatment or surveillance strategies.

"We have more studies to do, but the trend suggests we could use lymphocyte count as an early warning sign of patients who might have some type of infection," says Dr. Thakkar, who is also a principal investigator in the Center for Clinical and Translational Research in The Research Institute at Nationwide Children's. "It might help alert the practitioner to suspect infection and possibly send cultures earlier or begin antibiotics with these patients."

Thakkar RK, Diltz Z, Drews JD, Wheeler KK, Shi J, Devine R, Fabia R, Hall M. Abnormal lymphocyte response after pediatric thermal injury is associated with adverse outcomes. *The Journal of Surgical Research*. 2018;228: 221-227. Doi: 10.1016/j.jss.2018.03.039.

— Mary Bates, PhD



Treating Pilonidal Disease with Laser Hair Depilation

In a pilot study, laser hair depilation was shown to prevent recurrence of pilonidal disease in adolescents and young adults.

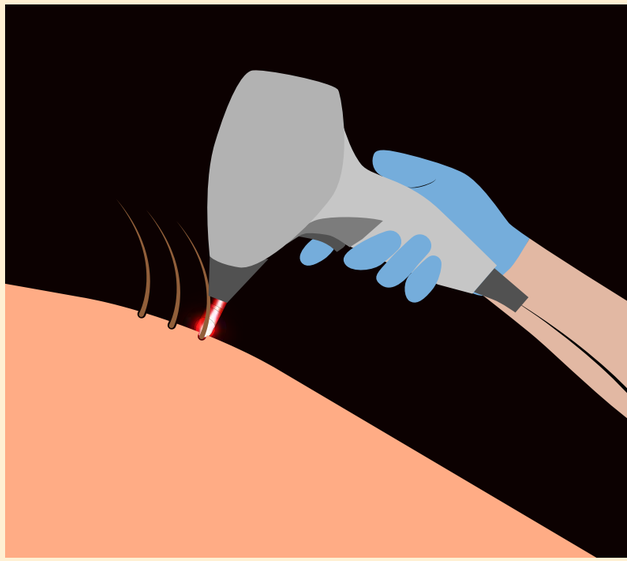
Pilonidal disease poses a challenge for patients and clinicians. The painful disorder, characterized by skin infections in the gluteal cleft near the tailbone, has a recurrence rate of as high as 30 to 40 percent. Recurrent disease is often treated with surgical incision and drainage or excision of the infected area. However, surgical treatment can lead to wound complications and can still have greater than 10 percent recurrence, so treatments that aim to minimize recurrence and prevent the need for surgery are needed.

Hair removal by shaving or depilatory cream is recommended as an adjunct to standard treatment, as hair is thought to play a critical role in pilonidal disease development. Recently, laser hair depilation has emerged as another option for hair removal. It is a durable and effective depilation technique and is used commonly for cosmetic purposes, but data on its tolerability and effectiveness in pilonidal disease is limited.

A new pilot study published in *Surgical Infections* assessed the safety, tolerability and efficacy of laser hair depilation in adolescents with pilonidal disease. Led by Katherine Deans, MD, and Peter Minneci, MD, co-directors of the Center for Surgical Outcomes Research at Nationwide Children's Hospital, the researchers set out to see if this hair removal method could decrease recurrence rate and prevent chronic pilonidal disease in adolescents.

"The results were very encouraging," says Dr. Minneci, who is also an associate professor of surgery and pediatrics at The Ohio State University College of Medicine. "Based on our historical data, we expected about 20 percent of the patients to have a recurrence within one year of being seen at the hospital. We found that none of the 13 patients in our study had a recurrence within a year of laser hair depilation treatments."

In addition, treatments were well tolerated and safe, with no patients unable to complete a treatment session due to discomfort and no incidents of second-degree burns.



Although the results suggest that laser hair removal is a safe and effective way to decrease pilonidal disease recurrence in adolescents, Drs. Minneci and Deans are actively recruiting patients for a larger, prospective, randomized, controlled trial of the technique. Dr. Minneci says this type of study is necessary to compare laser hair depilation with chemical and mechanical depilation methods and to determine with more certainty if laser hair removal decreases recurrence rate.

"We do know that hair removal in the area is beneficial and laser hair removal appears to be a promising and convenient way to remove hair long-term," says Dr. Minneci. "We are currently running a study to try to answer this question definitively."

Lopez JJ, Cooper JN, Fischer BA, Gonzalez DO, Deans KJ, Minneci PC. Tolerability of laser hair depilation in pilonidal disease: A pilot study. *Surgical Infections*. 2017;18(8):890-893.

— Mary Bates, PhD

Enzyme Treatment Slows Decline in Common Form of Batten Disease

Study also indicates early treatment may provide best outcomes.

With every diagnosis of CLN2 Batten disease, Emily de los Reyes, MD, a neurologist and director of the Nationwide Children's Batten Disease Center of Excellence, had a difficult conversation with parents.

"I always told parents this is a brain disorder that will result in the early death of your child and that you may see your child melt before your eyes," says Dr. de los Reyes. "Now, I can tell them that we have a treatment. Or maybe even a cure if children get the treatment before they lose function."

Dr. de Los Reyes and Lenora Lehwald, MD, an attending neurologist at Nationwide Children's and co-investigator of the CLN2 trials, led the U.S. portion of an international study that shows an enzyme treatment delivered directly to the brains of children with CLN2 significantly slows motor and language declines. The study is published in *The New England Journal of Medicine*.

CLN2, also called neuronal ceroid lipofuscinosis type 2, is a rare lysosomal storage disorder caused by the lack of the enzyme tripeptidyl peptidase 1 (TPP1).

Most children with the disease function normally until they're 2 to 4 years old. Then, they typically begin with language delay followed by difficult-to-control seizures.

A rapid decline in motor, language, cognitive and visual function follows. Most die by early adolescence.

In this study, 23 children, aged 3 to 16, received an infusion of cerliponase alfa, a recombinant proenzyme form of human TPP1, every two weeks for at least 96 weeks. The researchers infused the enzyme directly into the right lateral ventricle of each child's brain, through an implanted Rickham reservoir.

During the 96 weeks, no treated children suffered an unreversed 2-point decline on a CLN2 clinical rating scale of their language and motor skills. Historical controls reached a mean 2-point decline at just under a year.

The decline rate among treated children was a mean of 0.27 points per 48-week period versus 2.12 points for the historical controls per 48-week period.

The difference in measurements of motor, language, cognitive and visual function between the treated and untreated children grew over time, indicating the treatment benefit persisted, Dr. de los Reyes says.

Adverse events included convulsions, vomiting, hypersensitivity reactions, failures of the intraventricular device and infection. They resolved themselves or were treated medically, but none required children to stop receiving treatment.

All 23 children continue to receive the infusions, more than four years after the study began.

The youngest two participants had no signs of impairment due to CLN2 at the beginning of the study and continue to have none, suggesting that early treatment may provide the greatest benefit, Dr. de los Reyes says. To test that hypothesis, the researchers are now studying the treatment in children younger than 3 years.

Schulz A, Ajayi T, Specchio N, de Los Reyes E, Gissen P, Ballon D, Dyke JP, Cahan H, Slasor P, Jacoby D, Kohlschutter A; for the CLN2 Study Group. Study of intraventricular cerliponase alfa for CLN2 disease. *The New England Journal of Medicine*. 2018;378:1898-1907.

— Kevin Mayhood

The Changing Medical and Legal Landscape for Cannabidiol

With FDA approval of Epidiolex®, the pace of research on CBD medication is likely to increase.

The first federal approval of a non-synthetic, plant-based cannabis drug for two epilepsy syndromes may help change the legal landscape for medical professionals who wish to study similar formulations – and lead to further treatments for pediatric patients.

In June, the U.S. Food and Drug Administration approved cannabidiol (CBD) under the brand name Epidiolex, for the treatment of seizures associated with Lennox-Gastaut and Dravet syndromes. Both are considered severe, treatment-resistant forms of epilepsy, and children with the conditions can have dozens of brief seizures per day.

That approval set in motion the rescheduling of cannabidiol by the FDA.. Marijuana (like heroin and LSD) has been considered a Schedule I drug, meaning it has no accepted medical use and has a high potential for abuse. Because of its Schedule I status, the trials that ultimately established cannabidiol's efficacy and safety were conducted under especially difficult regulatory conditions, says Anup Patel, MD, section chief of Neurology at Nationwide Children's Hospital.

Dr. Patel was co-lead author of a May 2018 study in the *The New England Journal of Medicine*, which showed cannabidiol could lead to a significant reduction in the number of drop seizures for patients with Lennox- Gastaut syndrome. He and Nationwide Children's also participated in a 2017 *NEJM* study showing cannabidiol could reduce seizures for patients with Dravet.

"First, the FDA approval of cannabidiol will change the lives of many families who deal with Lennox-Gastaut and Dravet, and that's very important," Dr. Patel says. "Second, the rescheduling by the DEA will ultimately make cannabidiol easier to study in the future."

Dr. Patel began studying cannabidiol at Nationwide Children's in 2014 and had to obtain a special license from the Drug Enforcement Agency under the Controlled Substances Act to dispense the drug. The FDA approval means that any physician could potentially write a prescription for the medication; the DEA rescheduling means that a special license and DEA oversight will no longer be needed for trials.

Dr. Patel and other academic medical researchers continue to emphasize that the medication approved by the FDA is greater than 98 percent CBD, and it has no psychoactive properties. Care providers and consumers should not confuse it with other products labeled "cannabidiol" that make a variety of health claims and can be obtained over the internet and from other outlets.

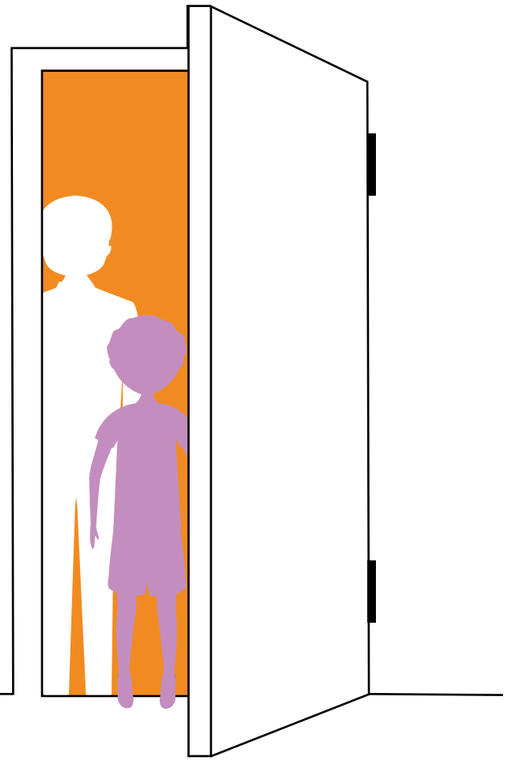
"What we wanted to do, and have done, is put this specific medication through the same rigorous research process as any other medication on the market," says Dr. Patel. "That's why the FDA approved it, that's why the DEA is rescheduling it, and that's why we now have the potential for other research and treatments."

Devinsky O, Cross JH, Laux L, Marsh E, Miller I, Nabbout R, Scheffer IE, Thiele EA, Wright S; Cannabidiol in Dravet Syndrome Study Group. Trial of cannabidiol for drug-resistant seizures in Dravet syndrome. *The New England Journal of Medicine*. 2017 May 25; 376(21):2011-2020.

Devinsky O, Patel AD, Cross JH, Villanueva V, Wirrell EC, Privitera M, Greenwood SM, Roberts C, Checketts D, VanLandingham KE, Zuberi SM; GWPCARE3 Study Group. Effect of cannabidiol on drop seizures in the Lennox-Gastaut syndrome. *The New England Journal of Medicine*. 2018 May 17; 378(20):1888-1897.

— Jeb Phillips

Opening the Door to ADULT MEDICINE



Care transition plans aren't just for kids with congenital conditions anymore. Could your practice benefit from a proactive transition plan for all patients?

— by Katie Brind'Amour, PhD —

In the shift from pediatric to adult care, young patients have the responsibility to adjust to a new life of self-management. But health care providers also play an important role in this rite of passage.

Some physicians believe that care transition planning is both important and practical to implement for children of all health statuses. Others believe it is most reasonable to leave care transition planning to pediatric subspecialists – those in charge of the most complicated care for the most complex patients with chronic conditions.

Which approach is most feasible and appropriate? And how can physicians who are new to the practice begin to implement transition planning?

COMING TO TERMS WITH THE CONCEPT

The definition of care transition varies both by patient population and provider, but it typically encompasses the migration of young adults from the pediatric health care world into the realm of adult medicine, with personal health obligations shifting to the patient. And in all cases, care transition is more than a simple referral.

"The majority of patients seen by a generalist are going to be a 'referral plus' – kids who don't have a lot of health problems who are leaving high school, with limited health concerns in the background that need to be made known to an adult practitioner who will take them over," says Karen McCoy, MD, chief of the Section of Pulmonary Medicine at Nationwide Children's Hospital.

For generally healthy children, she says, transitioning mostly involves sending the medical records and doing a quick call or letter if needed to explain important health history or management needs, plus having a chat with the patient and family to discuss who they're being referred to and whether they have any questions.

"Preparing to transition a patient with a highly specialized condition and lots of comorbidities is obviously more of an ordeal," says Dr. McCoy, who has developed and implemented a detailed care transition program involving face-to-face education for patients who have cystic fibrosis and other pulmonary conditions. A paper detailing her team's highly protocolized efforts is pending publication.

"It's important to start prepping them no later than the mid-teens about the need to transition and to develop skills to manage their own care once they are an adult."

For patients with congenital issues requiring lifelong care, preparation may begin even earlier, with many groups at Nationwide Children's initiating the topic at age 12 or younger.

No matter the complexity of care needs, however, care transition involves the segue from being treated as a child to being treated as an adult – both in the parental sense and medical sense. Responsibility will eventually fall on the young patient to know when to fill prescriptions, how to take medications, what to put in an advanced health care directive, how to monitor symptoms and when to reach out to a pharmacist or physician. This self-sufficiency certainly isn't learned overnight.

"From day one, we raise the topic that eventually they will be transitioned to an adult care provider, just to set that expectation. We then periodically revisit that talk as patients get closer to adolescence, and around age 12, we start doing transition readiness surveys for patients and parents," says Alessandra Gasior, DO, director of Colorectal Transition of Care at the Center for Colorectal and Pelvic Reconstruction at Nationwide Children's. The program is the first to connect Nationwide Children's patients with irritable bowel disease, Hirschsprung disease and anorectal malformations to adult providers at The Ohio State University Wexner Medical Center. "For someone with a congenital or lifelong problem who has been coming to a pediatric center their entire life, it can take a lot of time and effort to create a smooth transition for the patient – you need everyone to be familiar with each other and the specific care required."

CHALLENGES TO EFFECTIVE TRANSITIONS

The concept of handing over care is fairly straightforward, but its historic implementation has been inconsistent and often ineffective at best. Research continues to uncover the loss to follow-up and poor health outcomes experienced by young adults with various health conditions who fail to transition effectively. Patients who discontinue needed care often present years later with severe or urgent health problems that could have been avoided with proper ongoing management. On the flipside, patients who experience planned and facilitated hand-offs to adult practitioners tend to fair better than those with no assistance.

The barrier to facilitating an effective transition is more nuanced than a simple lack of time or effort on behalf of patients or physicians, however. Especially among patients who have long received care from a pediatric practice, the importance of a supportive and welcoming environment in their next care experience may override the basic understanding that health services are critical for their wellbeing.

"If patients can establish a good relationship with the new provider, they will go back for care," says Dr. Gasior. "But the difference in adult and pediatric centers can be shocking for patients – they're alone and have to be independent and autonomous, and people treat them differently."

This problem may be particularly pertinent for the many freestanding children's hospitals with limited physical or referral ties to adult institutions. Although separation has allowed great growth in pediatric hospital size and expertise, it has also created the hurdle of changing locations and health systems.

The jarring difference is compounded by the problem of having few adult practitioners available who understand certain congenital or historically pediatric diseases. Some physicians struggle to locate an adult care provider who is willing and able to take on the long-term management of a patient with these conditions, such as congenital heart disease, myelomeningocele and cystic fibrosis. The disparity in knowledge is a two-way street, however.

"Most patients with lifelong pediatric conditions seem to prefer staying at their pediatric centers, and if we could provide that specialized care it would be ideal," says Daniel DaJusta, MD, medical director of the Center for Colorectal and Pelvic Reconstruction in the Section of Urology at Nationwide Children's. "But when they get to a certain age they start to have real adult problems that have nothing to do with what we do in pediatrics, and at that point they need adult providers like everyone else. Adult care is better provided in an adult hospital."

The Section of Urology currently continues to see patients with complex congenital problems into adulthood due to a lack of adult providers familiar with congenital urologic conditions, but a formal transition collaboration with urologists at The Ohio State University Wexner Medical Center is under development.

"The disconnect between what we take care of in pediatric subspecialties and adult medicine – not just in age but

life stages, and structural differences due to congenital versus acquired conditions – is at the crux of why care transition matters," says May Ling Mah, MD, director of ACHD In-Patient Services in The Heart Center at Nationside Children's and a practitioner in Nationwide Children's Adolescent and Adult Congenital Heart Disease Program.

Dr. Mah believes a global adult transition program – one in which adult providers housed within freestanding children's hospitals offer onsite care for adult-related problems as well as pediatric-specific health issues – may offer a creative way to address this growing challenge.

LOOKING AT LOGISTICS

The general consensus in care transition planning is that something is probably better than nothing. But the devil is always in the details.

"All kids need a transition process. It's really just developmental and learning how to navigate the health system when they become young adults," says Stacy Ardoin, MD, section chief of Rheumatology at Nationwide Children's, an active contributor to the development of condition-specific transition guidelines for the American College of Rheumatology, and a clinician-researcher engaged in numerous studies on the transition process. "But not every person, chronic disease or not, needs the same level of intense support. We need a way to identify those individuals at risk for not having a good transition and then tailor more intense support for them."

For this reason, readiness assessment is key. When resources are limited (and perhaps even when they're not), those who would suffer the most from a disconnect in care or who are least likely to be able to transition independently should be the focus of physicians' attention in the provision of active care transition planning.

In practice, care transition planning can be initiated with little effort. For example, physicians can simply begin asking patients between the ages of 12 and 16 about their understanding of their own care and future responsibilities. Physicians can then gradually work toward appointments wherein primarily the child answers the questions and discusses their care needs, rather than the parent.

"We do know that patients who have gone through an orderly transition process are more likely to show up at their adult provider and have other markers of compliance with medications," says John Mahan, MD, program director for the Pediatric Residency Program for Nationwide Children's and The Ohio State University. "It would be nice to see more outcomes data on care transitions so we can see which approaches are the best. Until we know that, however, it's important to simply recognize the importance of having a system – an intentional process for assessing transition readiness and teaching kids to take on their own management."

For those practices – subspecialty or otherwise – that want ready-made tools and guides to incorporate into a formal plan, options abound. A popular resource for existing toolkits and foundational materials is GotTransition.org, which offers a collection of practice resources for children with a wide range of chronic conditions as well as some general readiness assessment tools and customization strategies.

Other options exist as well, including the Transition Readiness Assessment Questionnaire (TRAQ) and the University of North Carolina STAR Transition Readiness Method, both highlighted in context with numerous other strategies for implementing care transition efforts in an article on the topic authored by Dr. Mahan last year in *Pediatrics in Review*. The academic literature is flooded with other tools for myriad conditions as well as advice for primary care.

Essentially, the distinction between a basic referral and effective care transition hinges on physician involvement, readiness assessment and proactive, organized preparation. Guiding all children – and their parents – toward more independent care and active adulthood participation in essential health-related self-care is a lofty goal, but it is a goal that may one day be expected as standard care for patients of all health care needs.

Mahan JD, Betz CL, Okumura MJ, Ferris ME. "Self-management and transition to adult health care in adolescents and young adults: A team process." *Pediatrics in Review* 2017 Jul;38(7):305-319.

Ten Steps Toward Starting Care Transition Planning in Your Practice

10 STEPS

A compilation of advice from the physicians contributing to the feature story

1. Read about it. Familiarize yourself with the literature to better understand the relevant theories, frameworks, and principles for your practice.

2. Form a group devoted to the topic. Having a dedicated physician or team of staff to examine the options and be accountable for progress keeps the effort organized.

3. Network with adult providers. The referral process is smoother when you personally know and respect the physician to whom your patient will transition. Build a list of competent and welcoming providers in multiple areas nearby and consider joint meetings to introduce them to your patients. Then follow up with both after their first visit.

4. Start small and start young. Even a single step toward transition assistance can get you started and may open the door to future protocolized changes and ideas. Begin those small changes, such as readiness assessment, in patients' early or mid-teen years.

5. Get feedback from families. Ask patients and parents what they want in terms of assistance on an ongoing basis. Remember that parents play an important role in both relinquishing control of their child's care and encouraging the child to be self-reliant.

6. Use a defined process. Once your practice is willing and ready to address care transition formally, develop a plan. It removes the guesswork during early implementation and provides a formal set of steps to refine over time.

7. Don't reinvent the wheel. Take advantage of existing transition resources. Consider adopting "Got Transition's" six areas of emphasis, or use existing readiness assessment tools, such as TRAQ or the STAR Transition Readiness Method, to prioritize patients for transition assistance.

8. But don't be afraid to customize. If existing resources don't work in their entirety, adapt them to your practice's needs. If your patient population doesn't typically require heavy transitioning efforts, consider simple options to meet your specific needs, such as form letters or checklists.

9. Communicate with the child's other care providers. Communication between primary care physicians and subspecialists can help identify gaps in the transition process or highlight opportunities for improved care planning. Children with complex needs may require separate transition processes for chronic and primary care pathways.

10. Think of it as quality assurance. Since formal budget and reimbursement are not often provided for this type of care activity, manage the process as you would one of quality improvement to ensure regular outcome measurement and incremental, steady improvement.

QI Project Increases Value of Asthma Care in a Large Primary Care Network

MULTIPLE STEPS LEAD TO BETTER CONTROL OF DISEASE, FEWER EMERGENCY DEPARTMENT VISITS AND $5 MILLION IN SAVINGS.

— by Kevin Mayhood —

A quality improvement project helped kids achieve better control of their asthma, reduced emergency room visits and cut costs in a primary care network serving 10,000 children with the disease.

Through multiple steps, including standardizing assessments and documentation, opening asthma specialty clinics within network offices and providing better education to patients and parents, the long-term project decreased emergency department (ED) visits by 4 percent annually from 2010 to 2016, or a total of 24 percent. Savings totaled more than $5 million while the quality of care improved.

Project leaders, at Nationwide Children's Hospital Primary Care Network (PCN), suggest that the project – in part or completely – can be implemented at other institutions.

More than 6 million children in the United States suffer from asthma, one of the most common long-term noncommunicable diseases, according to the Centers for Disease Control and Prevention. African-American children suffer at nearly twice the rate of white children and the poor at significantly higher rates than those above the poverty line.

The project, which won a Children's Hospital Association Pediatric Quality Award last year, took aim at the most vulnerable patients. The patient population is diverse, urban and 90 percent of families are Medicaid eligible. The PCN serves patients from 13 offices, located largely in pockets of poverty in central Ohio's Franklin County.

"As a primary care network, we changed how we think about and treat asthma," says Dane Snyder, MD, section chief of Ambulatory Pediatrics at Nationwide Children's and a project leader.

"A lot of things go into that; one is recognizing that what you're doing is not necessarily a best practice. There was room for improvement and standardization," says Judith Groner, MD, a primary care physician and another leader of the effort. Other core team members include Steve Hersey, MD, Elizabeth Allen, MD, and Jeanne Wickliffe, RN, CPN.

When the project team began, emergency department visits – an indication of poor asthma control – were increasing. Poor control is known to cause children to miss school days, suffer from poorer academic performance, and cause parents to miss work.

The first steps to address the issues were developing standardized questions to assess children with asthma, and a standardized and more efficient way to document the assessment in electronic medical records.

To improve asthma control, the PCN staff changed from talking with a patient and family about the disease only when family brought it up to bringing it up each time the child came in, no matter the reason. The PCN also set a goal of administering the Asthma Control Test or Childhood Asthma Control Test to at least 70 percent of children with the disease at each visit, no matter the reason. The network met the goal within six months and has exceeded it since.

An alert added to the electronic medical record was a key to assessing and testing children more frequently.

One result of more consistent and frequent monitoring was that physicians increased their employment of medicines for poorly controlled asthma, instead of sending the child to a pulmonologist.

Another change was the addition of an "orange" level to the action plan the PCN provides each patient at each visit. The plan is color coded red, orange, yellow and green, corresponding with severity of symptoms from severe to absent.

Parents told PCN staff that they thought bringing their child to the ED when symptoms got bad was a normal part of the disease. Through the addition of "level orange," the team encouraged families to bring their children to the PCN before symptoms reach emergency levels.

"We can manage almost all kids in the primary care setting," Dr. Groner says. "Instead of sending a child to a specialist, people are comfortable maximizing what they can do in primary care."

A year after the project got off the ground, the network started a pilot asthma specialty clinic at one office and gradually spread clinics to all locations. The clinic enabled the staff to spend more time with patients, particularly high-risk and more complex patients they would have sent to a specialist in the past.

Staff created an asthma patient registry to contact patients regularly. They monitored patients by employing the standardized assessment and documentation and obtained spirometry when indicated. A multidisciplinary team provided the patient and family with education, including tutorials on a computer tablet.

Asthma emergency department visits by children in this group declined by more than 25 percent each year from 2013 to 2015, while patients receiving the usual care saw increases in ED visits ranging from 3.8 percent to 16.2 percent during those years.

The project added two asthma health coaches, registered nurses who proactively contacted high-risk patients. As that proved beneficial, the PCN expanded the health coach team to include four registration specialists who handle outreach and four RNs who work in the asthma specialty clinics held in each office.

"With a population this large, it takes resources, not only in personnel but in training," Dr. Snyder says. "We have several hundred people involved; it took all 100 providers and several hundred nurses and staff to commit."

The team believes still too many network kids are going to the emergency room. To reduce numbers further, the PCN has begun opening walk-in clinics.

The medical records team continues working on ways to make it easier for the clinicians to do their job. They've developed a sidebar in the electronic records that allows providers to quickly see key indicators of risk, such as a child's last hospital visit and number of times in the hospital. The hospital's Research Information Solutions and Innovation team is developing a risk scoring system to help predict which children are at greatest risk of an emergency room visit for asthma in the next year. This risk score will be displayed in the sidebar of the electronic medical record for the clinician to easily view.

For an example of the color coded action plan, visit PediatricsNationwide.org/Asthma-QI.

Sangvai S, Hersey SJ, Snyder DA, Allen ED, Hafer C, Wickliffe J, Groner JA. Implementation of the Asthma Control Test in a large primary care network. *Pediatric Quality and Safety*. 2017 Aug 21;2(5):e038.

Snyder DA, Thomas OW, Gleeson SP, Stukus DR, Jones LM, Regan C. Shamansky A, Allen ED. Reducing emergency department visits utilizing a primary care asthma specialty clinic in a high-risk patient population. *Journal of Asthma*, 2018 Jul;55(7):785-794.

HOUSING FOR HEALTH:

An Early Look at What Can Happen When a Pediatric Health System Begins to Treat a Neighborhood as a Patient

by Abbie Roth

Neighborhood effect syndrome, characterized by symptoms of extreme poverty including blight, housing insecurity, racial segregation, trauma, violence, poorly performing schools, low social cohesion and support and environmental toxins, has debilitating consequences on child health. Health care providers frequently encounter challenges in caring for children from affected neighborhoods, and these children often experience poorer outcomes compared to peers in unaffected neighborhoods. Historically, institutions have been largely ineffective in changing these outcomes with one-child-at-a-time tactics.

In a novel approach to improving outcomes for these children, Nationwide Children's leaders with community partners decided to address neighborhood effect syndrome as a target for pediatric health care – treating the neighborhood as a patient. In 2008, Nationwide Children's began collaborating with residents, government entities and social services agencies to develop the Healthy Neighborhoods Healthy Families (HNHF) initiative.

The hospital's first patient neighborhood was the Southern Orchards neighborhood of Columbus, Ohio, located adjacent to the Nationwide Children's main campus. Before the intervention, the neighborhood experienced high rates of poverty and violent crime.

"The Southern Orchards neighborhood, right by the hospital, was one with gun violence, high infant mortality rates and high asthma rates in children," says Kelly J. Kelleher, MD, director of the Center for Innovation in Pediatric Practice at Nationwide Children's and lead author of the *Pediatrics* publication. "Houses were boarded up and vacant. You didn't see kids playing outside much."

The target area includes all of Census Tract 56.10 and Census Tract 56.20. In 2009, the neighborhood was characterized by the following:

- Home to 4,300 persons, 23 percent of whom were children
- 50 percent of children in the neighborhood were living in poverty
- 50 percent of children in the neighborhood were African American
- 25 percent of children in Livingston Elementary School and 33 percent in South High School were regularly changing schools
- 1 in 3 residents over the age of 16 were employed full time

The chief concern uncovered through multiple sources of data and information was neighborhood safety associated with population loss and surge in vacant and abandoned property.

"Residents were deeply concerned about blight and gang/drug activity, including on vacant properties in proximity to the school," says Dr. Kelleher. "Our primary target for intervention became housing."

According to Dr. Kelleher, the publication describes $23 million invested in upgrading more than 300 homes through the HNHF Realty Collaborative, which was formed with the not-for-profit development corporation Community Development For All People (CD4AP). The entity is owned by CD4AP with a board of directors selected by the two groups. To date, the investment has grown to more than $40 million.

The partnership, with collaboration from the Columbus Mayor's Office, accessed Neighborhood Stabilization Program funds from the city, acquired properties from the city's Land Bank program and gathered support from contractors and realty agents.

The multifaceted intervention launched by the collaborative included a home repair program, rehabilitation and homeownership program, home construction program, workforce development program and rental housing development.

The community development efforts by the HNHF Realty Collaborative are still in early phases, considering Southern Orchards has experienced neighborhood effects syndrome for 80 years. Still, some measurable outcomes are observed:

- Investments have transformed housing stock in the area and reduced blight.
- The vacancy rate declined from more than 25 percent to 6 percent.
- Youth who have participated in area development programs have shown progress in emotional health and academic performance.
- The high school graduation rate has risen from 64 percent in 2013 to 79 percent in 2017.
- For owner-occupied homes, the market has seen a 50 percent increase in sales volumes and a 22 percent increase in sales prices.
- No homicides were reported in the immediate Southern Orchards neighborhood in the last year.

"By taking both short- and long-term views of community development, Nationwide Children's and our partners have ambitious goals across many domains," says Dr. Kelleher. "The community-level approach allows the integration of epidemiology approaches, business resources and neighborhood development to support a mixed-income community. Our next challenges will be to continue growth with new partners and to measure outcomes on children's health in the neighborhood."

HNHF community partners include CD4AP, United Way of Central Ohio and the City of Columbus.

Kelleher K, Reese J, Sandel M. The Healthy Nighborhood, Healthy Families Initiative. *Pediatrics*. 2018 Sep;142(3):e20180261.

The Southern Orchards neighborhood in Columbus, Ohio, has been the target of a housing initiative that includes programming focused on home repair, ownership, rehabilitation, rental properties and workforce development.

MOVING FROM CHILD HEALTH CARE TO CHILD HEALTH

by Kelly Kelleher, MD, director of the Center for Innovation in Pediatric Practice in The Research Institute at Nationwide Children's Hospital

As pediatricians, we want children to be healthier, even the ones who never come through our doors. At Nationwide Children's Hospital, the board and leadership have aimed to do just that by setting the highest bar yet for our organization – we want central Ohio children to be the healthiest in the United States.

But what does that mean? How do we measure it? And how can Nationwide Children's change health for so many children who are not patients? What are we, as a pediatric institution, accountable for beyond health care?

Traditionally, Nationwide Children's measured quality and clinical outcomes of specific health care services they way other hospitals do, by considering the volume of services delivered and the safety/quality of those services. Such measures are especially important for children and adolescents (and their families) with severe and persistent diseases where appropriate and timely services are the difference between life and death. As a result, our quality measures for particular diseases are, for the most part, outstanding.

Unfortunately, clinical services do not address many of the problems children, adolescents and their families currently face. A torrent of new research confirms what our clinicians and staff already know – medical care can do little for common conditions brought about by poverty and other social determinants of health in some of our neighborhoods. Every day in our practices, physicians are confronted with families battling violence, housing insecurity, food insecurity and challenged schools.

The consequences of these social determinants are devastating. While our safety and medical quality measures are outstanding, community rates of asthma, adolescent suicide, infant mortality and other diseases driven by social determinants are high and sometimes rising.

Nationwide Children's has already been a leader in innovative practices to address social determinants through the Healthy Neighborhoods Healthy Family initiative, the Ohio Better Birth Outcomes initiative and our School Care Connection programs, among others. However, that work has underscored the need to measure our progress in these community health initiatives and programs as we do in all areas of our work.

Beginning two years ago, Steve Allen, MD, chief executive officer at Nationwide Children's, and Richard Brilli, MD, chief medical officer at Nationwide Children's, led two small gatherings of national leaders in pediatrics to discuss what types of measures would better capture not just pediatric health care delivery but, more importantly, the health of the children in the community. It was clear that measures would have to address the health of patients and the health of all children in the community.

At the same time these leadership meetings were taking place, the National Academy of Medicine published their Vital Signs for Healthcare, a call for a dramatic simplifying of health care accountability measures and the inclusion of community health measures as part of health systems accountability. As part of the original document, the Vital Signs committee noted that children and adolescents would need special attention in designing accountability measures because of their rapid development, susceptibility to physical and social environmental influences, and regional health care systems. After a period of negotiations, pediatric leadership organizations nationally have embraced the Vital Signs framework and are preparing a child-focused response to the original Vital Signs document.

The convening of the National Academy of Medicine, the Children's Hospital Association, the American Academy of Pediatrics, and other major organizations will take time and patience. Meanwhile, Nationwide Children's is already planning to test some of the measures that have been proposed in early discussions, such as teen pregnancy rate, high school graduation rate and infant mortality rate. Nationwide Children's is a logical leader for this work because of size, dominance in the local pediatric market, access to Partners For Kids data and expertise with community health activities. Partners for Kids is one of the oldest and largest accountable care organizations in the country.

Dr. Brilli will be leading a multidisciplinary team to develop these potential measures of health for Franklin County children, baseline data and key driver diagrams with possible improvement activities. Early candidates for measures beyond those listed above include teen tobacco use, a preventive services composite, kindergarten readiness and an outpatient harm index. This plan will be the first of its kind for a childrens hospital, and more importantly, it offers a roadmap from being a provider of health care to a partner in producing health for central Ohio children.

Of course, we do not face improving these measures alone. The Mayor's Office, the United Way, Goodwill Industries, Community Development For All People – a faith-based non-profit community development organization – and many others are with us at each step knowing that this work will take years and resources. But the opportunity to shift the focus from health care to health is too good to pass up, and the staff at Nationwide Children's has delivered time and again on aspirational goals.

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Generating the Genome: How Scientists Changed the Face of Cancer Research

by Katie Brind'Amour, PhD

Team science. Ongoing innovation. Brilliant minds. Here's how The Cancer Genome Atlas spawned a revolution in cancer research and technology. The project's ambitious efforts are mostly complete, but its impact is just beginning. The Cancer Genome Atlas has made waves that will carry a wealth of discoveries to the world's future cancer patients.

PediatricsNationwide.org/Generating-the-Genome

Is Your Patient Really Allergic to Penicillin?

by Abbie Roth

Ten percent of people have been told that they are allergic to penicillin. Ninety percent of them do not have a true allergy and could safely take the medication. Instead, they have had an adverse reaction, an unrelated symptom that coincided with taking the medication, or a normal symptom of their illness that was mistaken for a medication reaction. So what's a physician to do when seeing a patient with a listed drug allergy?

PediatricsNationwide.org/Penicillin-Allergy

Feeding Difficulties in Opioid-Exposed Infants – Mechanics and Possible Causes

by Kevin Mayhood

Sudarshan Jadcherla, MD, led what appears to the be first study identifying possible mechanics underlying feeding difficulties commonly seen in premature infants with fetal exposure to opioids. His team compared the strength and coordination of the esophagus of six infants with fetal exposure to 12 infants without, while at rest and while swallowing. The group suggests the differences may be due to upregulation of central vagal effects with heightened excitatory and inadequate relaxation responses.

PediatricsNationwide.org/Feeding-Difficulties-Opioid-Exposure

> "Bad times have a scientific value. These are occasions a good learner would not miss."
>
> *– Ralph Waldo Emerson*

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The Opioid Education Toolkit: For Providers and Parents

Do you know all the options for safe medication disposal? How can you help your patients access medication lock boxes? What are evidence based methods for screening and assessing risk of opioid abuse? Find the answers to these questions and more in the Opioid Toolkit, your one-stop for resources, links and information to assist providers in keeping their patients safe.

For more information about opioid education, visit PediatricsNationwide.org/Opioid-Toolkit.

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