ISSUE 18 • AUGUST 2024

Q: *Advances and Answers in Pediatric Health*

Pain Points

Endometriosis is a common, chronic pain condition that is both underdiagnosed and misunderstood in pediatric populations. A new multi-institutional study seeks to approve the first treatment just for adolescents. **P. 10**

Children's Hospital Colorado

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It starts with a Q:

A letter from a fellow questioner at Children's Hospital Colorado

Dear colleagues,

With this issue of Q: magazine, I have the honor of not only sharing a glimpse of the exceptional research underway at Children's Hospital Colorado, but also the launch of a new entity designed to facilitate a continued and expanded body of child health research.

The Colorado Child Health Research Institute was recently formalized as a committed partnership between Children's Colorado and the University of Colorado Anschutz Medical Campus. The two organizations, which share a home on the Anschutz Medical Campus, have birthed many collaborations over the years, but this new institute cements a model of shared governance, resources and minds in the service of children and families.

By putting this incredible partnership on paper, we will be able to work together in bigger and better ways. In addition to opening up new avenues for connecting researchers and ideas, we will establish accessible bidirectional communication channels, bring leaders to the table, ramp up research support, and develop a child health research seminar series that keeps every member of the team abreast of the latest in our field, among other endeavors.

This work is not just a quest for knowledge — it's a step toward offering families facing rare or serious diseases hope that few institutions around the country can. Children rely on us, and through our improved research capacity, we will continue designing and testing new therapies, bringing together the best and brightest, and invigorating the field of child health.

We know we can achieve incredible things together, and we must. Because the kids we treat today become tomorrow's adults. This institute isn't a magic wand, but it's just the thing we need to bring our research to a new level. By focusing on life-course research with a critical mass of investigators focused on pediatrics, we can treat and prevent a lifetime of illnesses and conditions to create a healthier world.

Sincerely,

RONALD SOKOL, MD, FAASLD

Chief Scientific Officer, Child Health, Children's Hospital Colorado

Bruce and Bev Wagner Family Endowed Chair in Child Health Research, Associate Dean for Child Health Research, Distinguished Professor, Pediatrics-Gastroenterology, Hepatology and Nutrition, University of Colorado School of Medicine

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Exploring New Angles

HEMATOLOGY/ONCOLOGY

Kids with hemophilia commonly experience musculoskeletal bleeding. While prophylactic medications can help prevent bleeding, they don't prevent the joint damage that comes along with it. While working to understand this type of bleeding and treatment options better, hematologist/oncologist Beth Warren, MD, recognized a gap in the research: movement.

"Logically if you have a musculoskeletal bleed, there should be a force involved in starting it," she says. "And for example, we saw that kids who play basketball actually don't seem to do worse than kids who don't play basketball. But is there something different about their movement patterns?"

With the encouragement of her pediatric hematology mentor, Marilyn Manco-Johnson, MD, Dr. Warren connected with research mentor James Carollo, PhD, and successfully applied for a National Institutes of Health K23 grant, which is designed to provide an intensive, supervised, patient-oriented research experience.

The pilot study compared movement patterns between children with severe joint damage from hemophilia and children without hemophilia. The team placed reflective markers on participant's bodies to track them as they went through a series of simulated sports movements that included squats, single-leg hops, treadmill running and more.

So far, the team has noticed significant differences in movement patterns between their two study populations. For example, kids with hemophilia tended to squat less deep and had lower knee flexion.

"We're seeing some differences in the forces that are being generated, and we're seeing some limitations imposed by the joint bleeding that's showing up in some of these differences," Dr. Carollo explains.

Whether those differences are adaptive and help stop bleeding or are creating more bleeding is still unknown. The team plans to conduct future research to understand this relationship better. Either way, gaining this new understanding will certainly help improve treatment options, and fast.

"No one in the hemophilia world has really taken a motion-analysis approach to being able to understand what causes these bleeds, what is dangerous for the bleeds and what is the long-term outcome if you keep bleeding," Dr. Warren says. "Treatments for hemophilia are getting better and better, and that is causing kids to want to do more and more. I think what we learn from this is going to help us figure out how to prevent injury." ●

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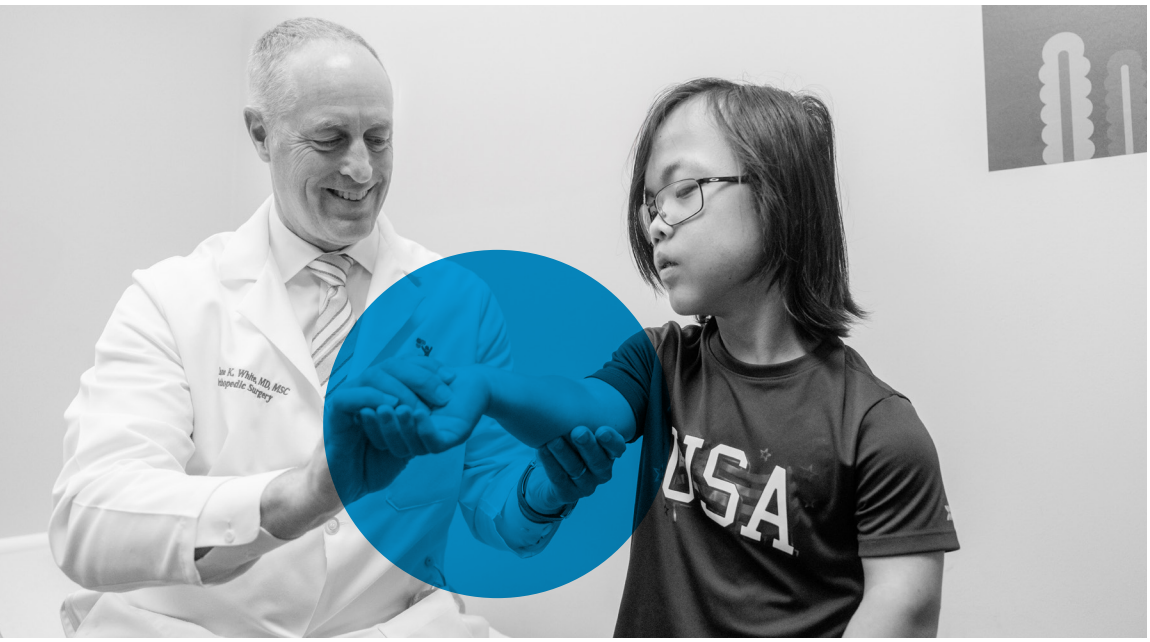

PRECISION MEDICINE

Widening the Aperture

Q: How can an orthopedic center provide next-level care for kids with a range of rare bone diseases?

Children's Hospital Colorado is home to one of the largest pediatric orthopedic centers in the country offering comprehensive support for skeletal dysplasia and other genetic bone diseases. Through clinical trials, precision medicine and a multidisciplinary clinic, this full-service program tailors treatment to each child's condition to provide a level of care unlike ever before.

CLINICAL TRIALS

As Chair of Pediatric Orthopedics, Klane K. White, MD, researches osteogenesis imperfecta, a genetic disease in which a child's bones are brittle and break easily. Traditionally, treatment for osteogenesis imperfecta has relied on generic bone-building drugs designed for adults with osteoporosis, in combination with physiotherapy, pain treatment and acute fracture treatment. Though effective, these treatments are not tailored to this condition or its genetic origins.

To improve the treatment protocol, Dr. White became involved in two clinical trials exploring the use of the drug setrusumab, which aims to increase bone mineral density. The first trial is part of the Orbit study and is aimed at treating patients aged 5 to 25. Now in phase 3 trials, it has shown a 14% average increase in bone mineral density and a 67% reduction in annual fracture rates.

Meanwhile, the second trial, called the Cosmic study, is comparing setrusumab to intravenous bisphosphonate (IV-BP) therapy in patients ages 2 to 7. "These new therapies are more directed at the actual biology of bone growth information," Dr. White explains. "There may be hope for them that this will improve their long-term health and outcomes directly."

PRECISION MEDICINE

In addition to that work, Dr. White also researches achondroplasia, a genetic condition that slows bone growth and results in shorter limbs. While the mechanisms behind this type of skeletal dysplasia are understood, it has remained difficult to study the wide-ranging, and often lifelong, comorbidities associated with the condition, including arthritis, sleep apnea, back pain, hearing loss and obesity.

While achondroplasia treatments are intended to encourage bone growth, the goal of Dr. White's research isn't just to help children with this condition grow taller, but to understand how increasing a person's height might mitigate challenging and painful symptoms and improve quality of life.

Despite the many advancements made possible by clinical trials, they typically don't last long enough to measure meaningful results. "The problem is that there's no way to demonstrate improvement in health outcomes or health-related outcomes in six to 12 months, which is the timeline for these trials," Dr. White says.

To overcome the limitations of traditional trials, he's teaming up with a colleague at Johns Hopkins University to develop a first-of-its-kind biobank that will house the DNA of achondroplasia patients across the U.S. By merging with a national multicenter study group, which houses clinical data on more than 1,000 patients, the biobank will allow researchers to examine and better understand trends in DNA.

"We can look at the data and start finding patterns within certain presentations," Dr. White says. "If we take a group of patients who have significant spine problems, then we can say, 'OK, is there a commonality in their genome?'"

This will help the team at Children's Colorado build a stronger understanding of biochemical processes, improving its ability to address specific genetic differences. "Working with this robust clinical database and collecting DNA is going to give us the opportunity to provide precision medicine therapies in the future," Dr. White says.

Such work could hasten the delivery of new treatments, too. For example, infants born with achondroplasia have a 7% sudden death rate, but this statistic could be reduced by using this data to partner with the Colorado Fetal Care Center to diagnose the condition prenatally.

"Theoretically, if we can get that DNA, we can sequence it, do a risk profile on it, and then know whether a child is at risk," Dr. White says. "At some point, we could have very targeted therapies to help with their growth and help prevent these fatalities and complications."

MULTIDISCIPLINARY CLINIC

The Children's Colorado Special Care Clinic is the largest of its kind nationwide, serving more than 5,000 patients annually. Geneticist Ellen Roy Elias, MD, who serves as Clinic Director, cares for children with skeletal dysplasia and those with a range of other rare bone diseases. Working alongside orthopedic providers, physical therapists, sleep specialists, nurses, dieticians and more, Dr. Elias brings her understanding of genetics to patients in the clinic to help care for their inherited, underlying medical conditions.

"There are a lot of medically complicated things that can happen for these patients," Dr. Elias says. "It's really important to know all about that, so that when the patients come here, we can make sure we know what they need."

Another unique aspect of the Special Care Clinic at Children's Colorado is that it respects families who take pride in their genetic differences, some of whom don't want to focus on growth therapies solely for the sake of societal acceptance. In these instances, the team supports patients by helping improve their overall health and quality of life.

"I think to be a full-service skeletal dysplasia program, we need to be able to offer these treatments to families who are interested, and for those who aren't, to say that's an acceptable and respected choice," Dr. White says.

Dr. Elias adds that her team helps foster education among pediatricians and families regarding nutrition and growth development. For instance, many pediatricians don't know there is a special growth curve for children with skeletal dysplasia, but using this baseline is essential to ensuring these children are developing in a healthy way.

"In the multidisciplinary skeletal dysplasia clinic, we actually care for many different kinds of diagnoses," Dr. Elias says. "Knowing what the underlying genetic diagnosis is can totally change how we care for these kids."

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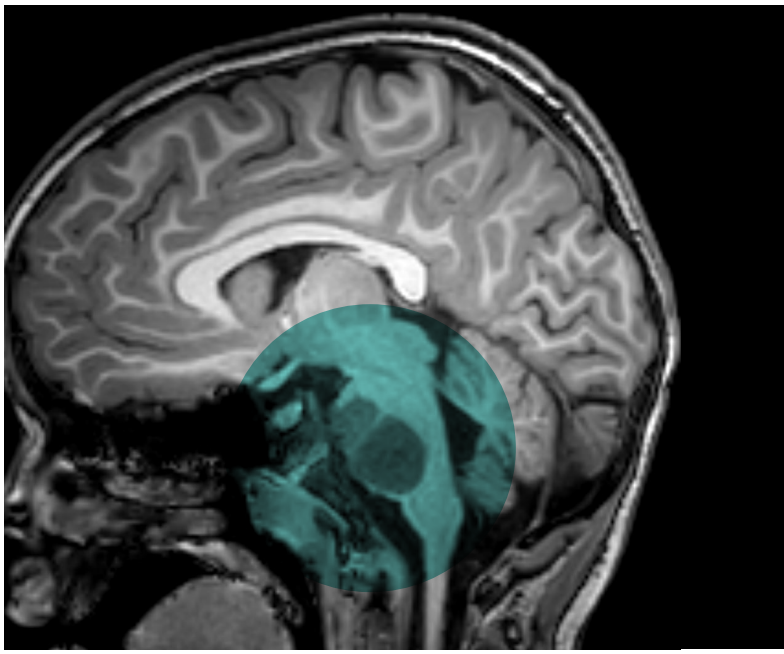
PRECISION MEDICINE

Redefining 'Incurable'



Q: How might the discovery and creation of entirely new treatment routes ignite hope for kids with an incurable form of brain cancer?

More than two decades ago, Sujatha Venkataraman, PhD, met Rajeev Vibhakar, MD. Her son Rishi had been diagnosed with cancer, and Dr. Vibhakar was his bone marrow transplant doctor. When Dr. Venkataraman's son passed away from his disease, Dr. Vibhakar told her that he wished there was more he could have done to save Rishi. From that day on, the two have worked tirelessly on the same goal: saving young kids from the grips of cancer. With their most recent work, they've taken several giant steps toward doing just that.

At the time of Rishi's passing, Dr. Venkataraman was researching adult cancers. Struck by the incredible impact of childhood cancer, she pivoted to join Dr. Vibhakar in his work. Their research focuses on diffuse midline gliomas (DMGs), a class of tumors that are as rare as they are deadly. Most patients are between the ages of 3 and 8 at diagnosis, and because there is currently no curative treatment, the vast majority die within just one year of diagnosis.

Because these tumors are located in the pons — the area of the brain responsible for cardiac functioning, respiratory rate and heart rate — surgery is too dangerous. What's more, chemotherapy is unable to cross the blood-brain barrier, which protects the brain from harmful substances. That leaves radiation, a treatment that buys time, but not much.

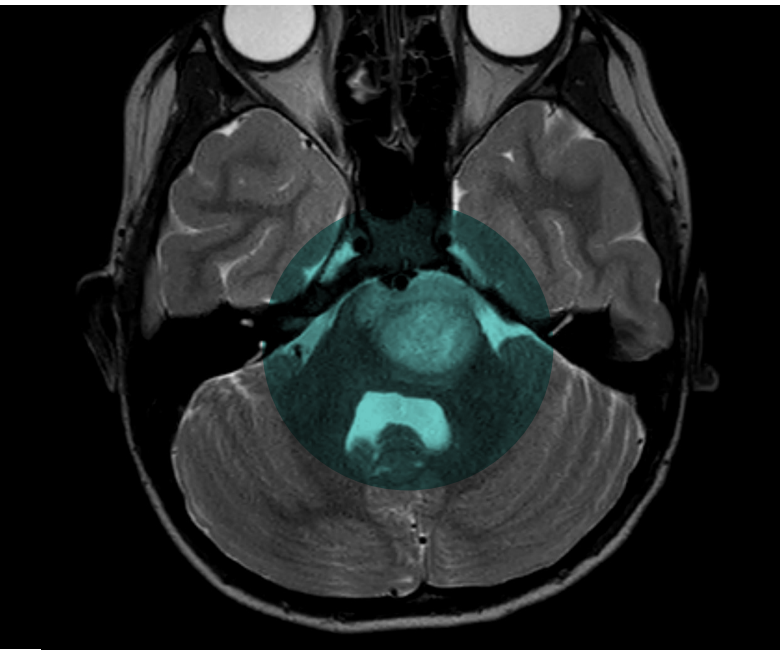
UNLOCKING NEW AVENUES

Over the years, there have been hundreds of clinical trials that have thrown every tool in a researcher's arsenal from all angles at DMGs. But those approaches were missing a critical piece of information. In 2016, as biopsies of DMGs became safer and more widely available, researchers found the genetic change responsible: the H3K27M mutation. Upon investigation, they discovered that this mutation was present in 85% to 95% of these tumors, opening up a new area of focus for Drs. Venkataraman and Vibhakar.

The pair reached out to researchers around the world for tumor specimens and have been focused on DMGs ever since. Their first order of business was to try to better understand how the H3K27M mutation operated and the fundamental biology behind DMGs.

"Unfortunately, learning all of that was great, but it didn't really help us understand how we target it or how we attack this tumor," Dr. Vibhakar says.

The solution was there all along, but at first, Drs. Venkataraman and Vibhakar didn't know where to look.



"Everything that I have done, everything that I've published, every grant that I've gotten, every award that I've had is all nice. And you could stack all of it together, and it would not even compare close to what this is."

RAJEEV VIBHAKAR, MD, PHD

FINDING THE KEY

"We were doing RNA sequencing to look at the gene expression of what was changing. We were really interested in trying to understand what happens in the nucleus, because that's where the mutation is," Dr. Vibhakar recalls. "We started seeing no matter what experiment we did, if we put the mutation into a tumor cell, CD99 went up. If we took the mutation out of a tumor cell, CD99 went down. It was the gene that changed the most of everything that we had done."

CD99 is a protein that shows up on normal cells but is highly present on the surface of DMG tumor cells. Drs. Venkataraman and Vibhakar found that when they knocked down, or gene edited, CD99, tumor cells stopped growing, indicating that the protein plays an important role in tumor growth. With this new knowledge, the team had found its target.

The first step in developing a treatment was to synthesize a new antibody to target CD99. In preclinical models, they found that the antibody cleared a DMG known as diffuse intrinsic pontine glioma, or DIPG. But there was a catch: Once the animal models stopped receiving the antibody, the tumors came back.

With this in mind, Dr. Venkataraman got to work on a secondary approach that could provide a much-needed one-two punch. Using the antibody they synthesized as a base, she created a chimeric antigen receptor-T cell (CAR-T cell), which successfully targeted DIPG cells. The team has since iterated on the original CAR-T cell design through gene editing. This next-generation approach takes T cells from a patient's own body and edits them such that they can target two proteins that are expressed together on the tumor cells. This logic gate allows the CAR-T cells to target tumor cells with precision, while leaving healthy cells untouched.

"We found it very effective in preclinical models, and it completely cleared the tumor," Dr. Venkataraman says. "There was no relapse, and we did not see off-target toxicities against normal cells."

Both the antibody and the CAR-T cell are able to cross the blood-brain barrier thanks to an Ommaya reservoir, a plastic bubble implanted under a patient's skin that offers direct access to the pons.

Though these two therapies are only in preclinical models, Drs. Venkataraman and Vibhakar already have a treatment plan in mind for the hopeful day these therapies make it through the approval process and into a clinical setting.

Kids with a suspected DIPG would get a dose of the antibody before getting a biopsy. If the biopsy confirmed the diagnosis, the team would then harvest the patient's T cells and send them to be edited. While that's happening, the patient would receive more infusions of the antibody as well as radiation, before finally getting access to the CAR-T cells.

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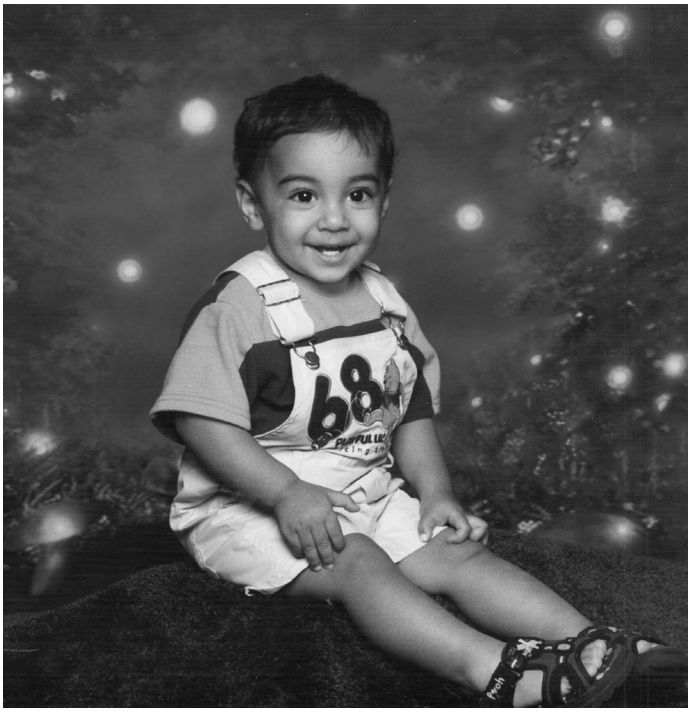
Redefining 'Incurable' continued



Dr. Venkataraman's son Rishi, who passed away from cancer.

This, Drs. Venkataraman and Vibhakar say, could increase survival by 50%, if not more.

BRINGING A PROMISE TO LIFE

These therapies promise to revolutionize the treatment of this insidious class of tumors, but the work behind them could reach far beyond this single indication.

"We now have a CAR platform we're able to use to target multiple different tumors, and Sujatha is well on the way to doing that," Dr. Vibhakar says. "We've created several other CARs for other tumors, and we're in much earlier phases compared to this, but we've actually now developed the expertise and tools to do this, which is a big deal."

But even though these new treatments could help treat patients of any age and a wide variety of tumors, the pair is laser-focused on ensuring their first application is children. That's why instead of selling their drug patents, they are holding them close, even if it means lengthening the timeline to treatment.

"It is very, very difficult to get drugs into kids, because most drugs are developed for adults, and drug companies are very reluctant to provide drugs for trials in kids," Dr. Vibhakar says. "This is a little bit crazy, but Sujatha and I are doing what a drug company normally would do. ... We both know that if we were to license this thing to any pharma company, it would never get to kids. So, we will do what it takes to make it all happen."

It's worth it to make good on the promise they made to each other all those years ago, and to kids fighting cancer.

"Everything that I have done, everything that I've published, every grant that I've gotten, every award that I've had is all nice. And you could stack all of it together, and it would not even compare close to what this is," Dr. Vibhakar says. "I mean, honestly, the day the first patient gets this antibody, if I disappear, I will be perfectly happy."

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Enriching the Source

NEONATOLOGY

In early 2022, Children's Hospital Colorado's lactation team began using a milk analyzer program to support babies in the neonatal intensive care unit (NICU). The goal of the device, called a Miris HMA, is to analyze macronutrients in human milk to allow for tailored fortification for preterm and undernourished babies. This is just one of the many tools currently used to ensure babies in the Children's Colorado NICU get the nutrition and support they need to thrive.

By using the milk analyzer, the team can pinpoint the macronutrient content of an individual's breast milk to better understand the amount of fat, carbohydrates and protein present in that sample. This allows the medical team to fortify the milk to best suit a baby's needs.

While this was the original goal of the milk analyzer, over time, the team has found that it can be helpful in diagnosing babies with underlying growth issues, according to Amy Hill, MSN.

"Through analyzing samples, we found that it wasn't always the mom's milk that was the issue. Their milk was doing a great job meeting their infant's nutritional needs, and in many cases, there was more that we needed to investigate with the infant," Hill says. "For instance, there may have been an unknown genetic component or condition affecting nutrient absorption and causing them not to grow appropriately. The beautiful part about the data we receive is that it improves patient outcomes by better equipping our staff to create tailored feeding plans based on reliable information."

In addition to the milk analyzer, the team uses a centrifuge to remove fat from milk, providing a higher level of care for infants in need of a low-fat diet. This is particularly useful for babies with a condition called chylothorax, which is an accumulation of lymphatic fluid within the pleural space. Fat can add to this problem, so providers needed a way to remove it. This allows infants to drink breast milk rather than transitioning to a low-fat formula.

Together with the skilled care of the lactation team and carefully developed protocols, these tools are improving outcomes. ●

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Pain Points

Q: Can a nonhormonal treatment work to alleviate pain and reduce health disparities for adolescents with endometriosis?

From gender discrimination to period poverty, global health inequities persist between those who menstruate and those who don't. This divide is exemplified by treatment for endometriosis. In this chronic pain condition, tissue mimicking the endometrium spreads outside the uterus, causing lesions throughout the pelvic region — including on the fallopian tubes, ovaries and uterosacral ligaments — and, more rarely, the bowel, intestines or bladder. This tissue thickens, breaks down and bleeds with each menstrual cycle, causing inflammation and extreme pain. Half of all adolescents with chronic pelvic pain eventually receive an endometriosis diagnosis, but before that, their healthcare providers and families affirm that painful periods are normal. When the answer finally comes, endometriosis has already exacted its physical, social and emotional toll.

At Children's Hospital Colorado, clinicians and researchers are working to break the silence on endometriosis pain. The team includes pediatric and adolescent gynecologists Tricia Huguelet, MD, and Stephen Scott, MD, along with Kendra Hutchens, PhD, Co-Director of Research for Pediatric and Adolescent Gynecology at the University of Colorado School of Medicine. Drs. Huguelet, Scott and Hutchens are collaborating with researchers across the country to study a nonhormonal treatment option that may help alleviate the severe pain of endometriosis.

"Endometriosis is another level of unrelenting pain that makes it really hard for teens to engage in school or outside activities with friends," Dr. Huguelet says. "It can have a negative impact on emotional well-being as well as their physical health."

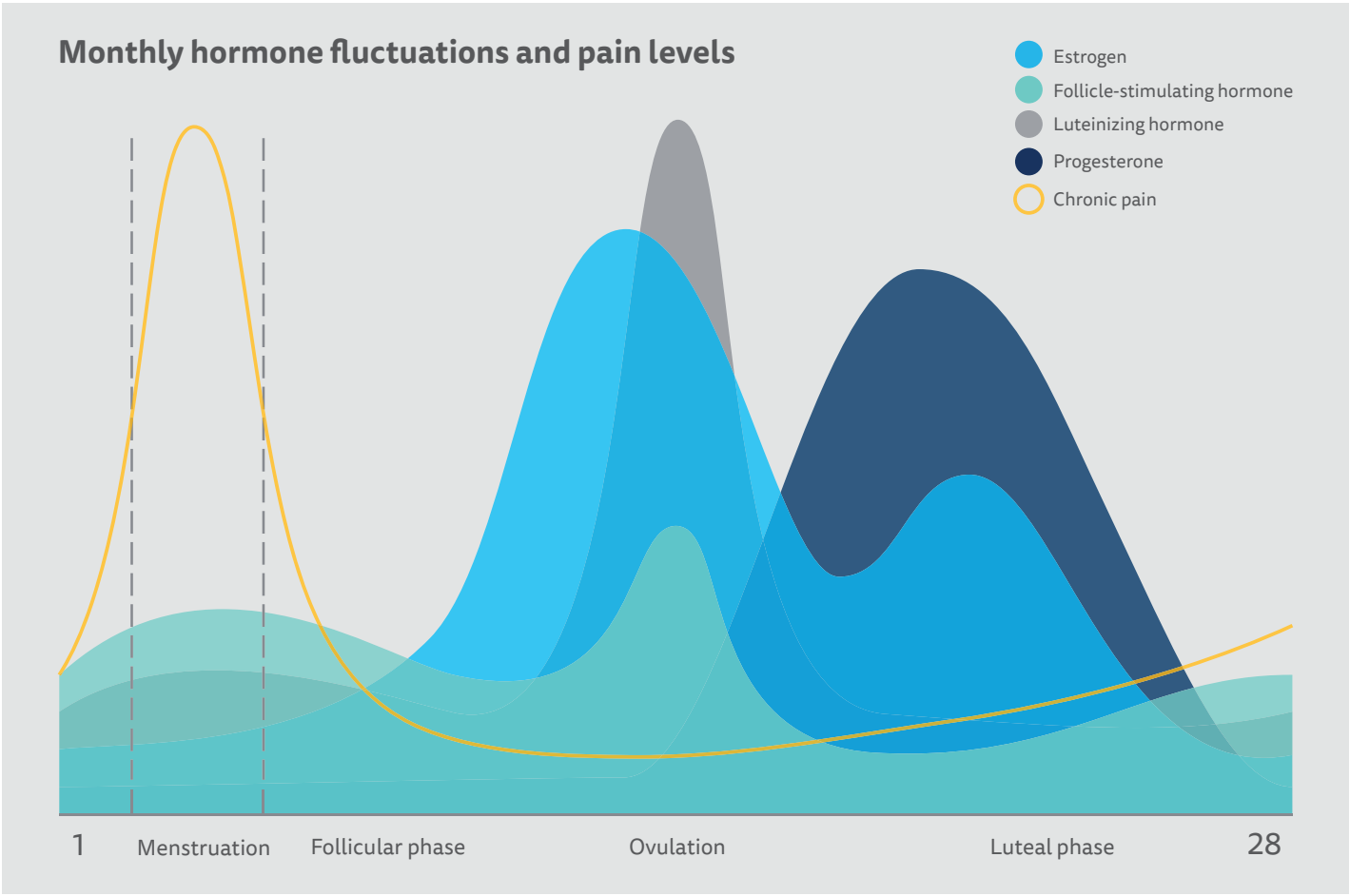
The Novel Treatment for Endometriosis (NOTE) Expansion study, funded by the J. Willard and Alice S. Marriott Foundation, unites multiple institutions — including Children's Colorado, Boston Children's Hospital, Stanford University Hospital, Beth Israel Deaconess Medical Center and Thomas Jefferson University Hospital — to study the drug cabergoline. There is no treatment approved by the United States Food and Drug Administration (FDA) for endometriosis-associated pain in adolescents, but by recruiting participants at multiple sites, the NOTE study will confirm to researchers if this novel, nonhormonal drug could be the first.

"Endometriosis is a common condition, but many people don't know pediatric gynecologists exist," Dr. Huguelet says. "We're excited to partner with other institutions because it allows us to bring attention to our field and find substantial research data that will support better treatments."

The trial at Children's Colorado will begin enrolling participants with endometriosis in summer 2024, with a focus on people assigned female at birth between the ages of 15 and 40. Individuals may be eligible if they have had a surgical diagnosis of endometriosis in the past three years, experience chronic pain from the condition and are currently using a hormonal treatment. Over six months, participants will take either a placebo or cabergoline, a dopamine receptor agonist approved by the FDA in adults to treat a variety of other hormonal conditions, including infertility that results from hyperprolactinemia (high prolactin levels). Participants will also be asked to engage in sensory tests, and to complete questionnaires and symptom diaries throughout the study's duration.

TARGETING PAIN

Pain is the primary symptom of endometriosis, and the goal of this research is to help treat and reduce that pain. Currently, patients are treated with hormonal medications that regulate the menstrual cycle and slow or prevent the growth of endometrial tissue. In more serious cases, a hormone-based approach involves shutting down hormonal stimulation to induce a menopause-like state.



Both instances alter levels of estrogen — a hormone that's essential for bone accrual during adolescence. Peak bone mass isn't established until age 18, so interfering with this process earlier in life could have long-term implications on bone health. Furthermore, hormone therapy is not a cure for endometriosis, and pain returns when treatment is stopped.

"Unfortunately, there's very little research in the adolescent population with regard to optimal hormonal therapy," Dr. Huguelet says. "There also aren't a lot of long-term studies looking at surgical intervention in adolescents, and then how that translates into long-term reproductive health and fertility outcomes for them as adults."

Another barrier to treating endometriosis pain effectively is that the condition can only be officially diagnosed via surgery. Imaging tests may help detect lesions, but in most cases, doctors can't see abnormalities in an adolescent on an MRI or ultrasound. This means that the main form of diagnosis results from patients self-reporting their pain to providers. Listening to teens in pain is always important, but it especially matters with endometriosis, where it's often the lone signpost that something is wrong.

UPLIFTING VOICES, STIFLING STIGMA

Unfortunately, a growing body of research shows that the pain of girls, women and gender expansive individuals is often dismissed, though they are more likely to experience chronic pain conditions such as endometriosis (1). This phenomenon isn't only frustrating; it also furthers health disparities. Adolescents with endometriosis frequently experience debilitating pain that causes them to miss school, work and social activities. "When the pain of adolescent girls, women and gender expansive patients is not taken seriously or treated aggressively, those disparities widen and have implications for patients' immediate and long-term health and well-being," Dr. Hutchens explains. "It is important to also consider

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Pain Points continued

SOCIAL ISOLATION
Low self-esteem
Painful periods
Infertility
Nausea and vomiting
CHRONIC PAIN
DECREASED BONE HEALTH
Delayed access to care
Anxiety and depression
Days missed at school

Endometriosis affects more than 6.5 million women nationwide.

these issues from an intersectional lens, as these disparities are often compounded by other factors. For instance, evidence from other studies shows that Black women's pain is treated less aggressively than white women's pain."

Left untreated, endometrial tissue can also spread to new areas of the body, causing further pain and irreversible complications, such as infertility. It's common for patients to grow so exasperated with the lack of effective treatment that they reach a breaking point. "A lot of patients as young adults will say, 'I'm done. Just do a hysterectomy,'" Dr. Huguelet says. "It's so heartbreaking that they feel that way, and a hysterectomy is not always curative, especially if there's a late diagnosis and they already have chronic pain from lesions outside the uterus that have triggered muscle and nerve pain."

This is why, in addition to ameliorating the pain and associated symptoms of endometriosis, Drs. Huguelet, Scott and Hutchens hope the study will draw attention to abnormal periods and put a stop to the normalization of pain for teens. "This provides us with an opportunity to reassure young people that their pain is not normal and that there are treatments available to them," Dr. Hutchens explains. "The earlier that we can begin to treat some of these issues, the better outcomes people are going to have throughout their entire life course."

Dr. Huguelet, who works with patients daily, says an important part of this work involves fostering healthy discussions about vaginas, sex and menstruation, and why these topics matter. "Combating the stigma around sexual and reproductive health for young people will also help us to take that more preventative approach," she says. She hopes that someday, in addition to having better nonhormonal treatments, standard care for endometriosis will echo the multidisciplinary approach at Children's Colorado, where chronic pain teams, pelvic floor therapists and behavioral health specialists work together with OB/GYN providers to address the full scope of the impact of living with endometriosis.

"What I'd like to see is earlier diagnosis and clear treatment regimens that are approved for adolescents," Dr. Huguelet says, "and for this to then translate into better outcomes — long-term, their pain decreases, their fertility improves and so does their quality of life."

1. eClinicalMedicine. "Gendered pain: a call for recognition and health equity." EClinicalMedicine vol. 69 102558. 7 Mar. 2024, doi:10.1016/j.eclinm.2024.102558.

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A New Chapter in Treatment

FETAL CARE

For decades, there have been no new advancements in doctors' ability to treat hemolytic disease of the fetus and newborn, or HDFN. The condition, in which a pregnant patient has antibodies that attack fetal red blood cells in utero, typically causes fetal anemia and requires blood transfusion. A new drug aims to change this.

Nipocalimab is designed to lower the pregnant patient's antibodies and stop them from crossing the placenta so they can't attack the fetus's red blood cells. The Colorado Fetal Care Center at Children's Hospital Colorado is one of a small number of participating centers worldwide testing the drug's efficacy and safety as part of a phase 3 randomized trial sponsored by Johnson and Johnson.

Though the condition is relatively rare, its impacts can be devastating. The blood transfusions carry a roughly 1% fetal loss rate each time they are performed and can increase the risk of early labor or emergent delivery. The goal of nipocalimab is to delay, limit or eliminate the need for transfusions.

The project, also known as the Azalea study, will last three years in total, and is enrolling patients who have a history of HDFN, are over 18 and have tested positive for the concerning red cell antibodies. Participants receive a weekly dose of nipocalimab between 13 and 35 weeks' gestation. From there, the plan is to follow babies for the first two years of their life to ensure the long-term safety of the drug.

"The interesting thing about this disease is that even if a baby gets successfully transfused, after delivery their blood volume may drop again, because the antibodies remain there for quite some time," explains maternal fetal medicine specialist Michael Zaretsky, MD. Additionally, because the drug lowers antibodies, babies may experience a higher risk for certain infections.

If the study proves nipocalimab safe and effective, it will mark a monumental moment in HDFN treatment.

"The history of the disease is pretty profound. I mean, they were doing the first fetal transfusion in the 1960s without the use of ultrasound, and it wasn't until the early 1980s when the first ultrasound-guided needle procedure was done on the umbilical cord," he says. "It's been really the same procedure over the last 40 years. And if this actually works, it will be another huge step in the evolution of HDFN treatment that will further prevent both morbidity and mortality." ●

MICHAEL ZARETSKY, MD

Director of Research, Colorado Fetal Care Center, Maternal Fetal Medicine, Children's Hospital Colorado

Professor, OB-GYN-Maternal Fetal Medicine, University of Colorado School of Medicine

Mindful Machines Intervene

MENTAL HEALTH

Over the last few years, Patrick Romani, PhD, BCBA-D, began noticing a troubling trend in mental health. Kids with neurodevelopmental disorders, such as autism, were being admitted to Children's Hospital Colorado's neuropsychiatric special care inpatient unit with high-acuity cases and increasingly severe behaviors. Often, their families would bring them to the emergency department (ED) in crisis, seeking a lifeline.

Current care standards see these kids admitted from the ED to inpatient care, which can be stressful for both the child and their family members.

"I think that a lot of families are going without support, and so they try to maintain at home, and eventually they're not able to any longer," Dr. Romani says. "That's really where we're trying to intervene — with those families that are hanging on."

To do this, Dr. Romani reached out to Sidney D'Mello, PhD, and Bobby Moulder, colleagues at the University of Colorado Boulder who focus on artificial intelligence (AI) and machine learning. Working together, their goal is to map the subtle physical signs that a child might be about to engage in severe behaviors, such as hitting, biting and kicking themselves or others.

"We are using biosensors to get a sense of kids' motion — the way they move their arms, their torsos, their bodies, their heart rate, as well as even facial expression changes or things like that," he explains. "We're relating that to when they exhibit severe behavior here in the hospital. We are collecting all this biological data to then be able to develop a model that predicts when these things will happen."

The team is using a tool that takes videos of kids who are working with staff and color codes each body part so that researchers can see how they move in relation to each other and what movements might be precursors to behavioral events.

While Dr. Romani is currently analyzing data from 61 children and plans to develop further studies, the goal is to one day create an app that utilizes a database of information to predict when a child might act out with precision, giving parents time to use evidence-based strategies to intervene. One day, the team hopes that using tools like this, families can avoid the need for emergency mental health care altogether. ●

PATRICK ROMANI, PHD, BCBA-D

Licensed Psychologist, Neuropsychiatric Special Care Unit, Children's Hospital Colorado

Associate Professor, Department of Psychiatry, University of Colorado School of Medicine

A(:) List **Recent awards and accolades**

The Heart Institute

Silver accreditation milestone for 25 years of excellence in pediatric echocardiography

In 2024, the Heart Institute is celebrating 25 years of excellence in pediatric echocardiography, as recognized by the Intersocietal Accreditation Committee (IAC). Founded in 1991, IAC is a nationally recognized nonprofit with a goal to improve healthcare by setting rigorous standards and evaluation methods for diagnostic imaging, interventional programs and therapeutic procedures. In 1999, the Heart Institute at Children's Hospital Colorado became one of the first facilities accredited by IAC in pediatric echocardiography. Since then, it has maintained IAC's benchmarks for quality imaging, patient safety and process improvement.

Luis De La Torre, MD

COLORECTAL

Ibero-American Association of Pediatric Surgery Award

The Ibero-American Association of Pediatric Surgery is a nonprofit organization that unites pediatric surgeons across Latin America, the Caribbean and Spain. In 2020, the association changed the Dr. Gupta medal award to the Alberto Peña medal. The first recipient of this new award will be given to Dr. Peña's colleague, Children's Colorado surgeon Luis De La Torre, MD, who is known for his innovations in procedures for Hirschsprung disease, anorectal malformations, idiopathic constipation and rectal prolapse. Dr. De la Torre's pull-through technique is used throughout the world to treat patients with Hirschsprung disease. The ceremony for Dr. De La Torre was held in Guayaquil, Ecuador in July 2024.

Lori Sussel, PhD

NEPHROLOGY

Albert Renold Prize

In September 2024, Lori Sussel, PhD, Research Director of the Barbara Davis Center for Diabetes, will travel to Madrid, Spain, to accept the 18th Albert Renold Prize at the European Association for the Study of Diabetes's annual meeting. The prize recognizes her contributions to pancreatic islet biology and acknowledges her more than 30 years of research investigating the development of the pancreas and differentiation and function of the pancreatic islet cells. Her work also identified regulatory factors essential for pancreas development and led to the identification of mutations that contribute to pancreatic agenesis and neonatal diabetes in humans. Her research has informed the scientific community on genetic risks for Type 1 and Type 2 diabetes. As an awardee, Dr. Sussel will have the opportunity to deliver a lecture on her work at the annual meeting and will receive a monetary award.

Lorna Browne, MD
Alex Baker, PhD

RADIOLOGY

Caffey Award for Best Clinical Science or Education Paper

The Caffey Award for Best Clinical Science or Education Paper is the Society for Pediatric Radiology's highest scientific honor. This year it was awarded to a team of Children's Hospital Colorado researchers from radiology, cardiology and the Colorado Fetal Care Center, including Lorna Browne, MD, and Alex Barker, PhD, for a paper, titled, "Predictive Capability of Fetal 4D Flow and Black Blood Slice to Volume Reconstruction for Prenatal Diagnosis of Coarctation of the Aorta." The report describes the team's development of a new method for diagnosing aortic coarctation, a heart defect that is sometimes called the "Achilles' heel" of fetal cardiology. The research showed the technique can predict this disease's presence with a high sensitivity and specificity, which will help children receive essential care sooner.

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School of Medicine
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Connected through care

We partner with neighboring University of Colorado School of Medicine, where many of our care providers serve as faculty. The school's Department of Pediatrics is ranked eighth in the nation by U.S. News & World Report, and is among the National Institutes of Health's top-funded research institutions.

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BEST CHILDREN'S HOSPITALS U.S.News & WORLD REPORT RANKED IN 10 SPECIALTIES 2023-2024

Exceptional care counts

Here, it all adds up. From the lifesaving studies we design and the boundary-breaking treatments we offer, to the moments we spend brightening a child's day, every extra second we dedicate to improving care for kids makes a difference. This year, those combined efforts have earned us a spot among the best children's hospitals in the nation with four specialties ranked in the Top 10. And we are proud to continue serving as pediatric leaders right here in our own community, with #1 rankings in both the region and the state.

Here, it's different.