Uncharted territory

A baby girl’s rare, life-threatening problem is solved by a highly skilled University team—and a strategic use of glue

When Anna and Brandon Kohler headed to University of Minnesota Medical Center, Fairview in September 2011 to have their child, they weren’t expecting anything other than a normal birth—and that’s just what they got. Normal labor, normal birth, normal baby girl.

“Everything was totally fine,” says Anna Kohler, “except she had a tiny bump on the back of her head that the doctors said was likely from the birth and would go away. So we took her home.”

At little Lydia’s two-week checkup, the doctor was slightly concerned that the bump hadn’t gone away, so he ordered an ultrasound, which revealed an abnormality. An MRI followed, and that’s when they discovered that Lydia had a large, blood-filled sac in the back of her head caused by an arteriovenous fistula, or AVF—basically, a network of abnormal blood vessels that continually flowed into the sac. Anna Kohler says that she and Brandon could actually feel a pulse when they touched the spot on Lydia’s head.

The AVF in Lydia’s head was beyond rare—maybe 100 of these malformations have ever been reported in newborns. So the doctors had no roadmap for a course of treatment.

“We knew what it was, but she was still so small, and she was asymptomatic, so we decided to delay treatment,”

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“Going through the soft spot was radical, but it was that or nothing.”
—Bharathidasan Jagadeesan, M.D., neurointerventional radiologist

says Bharathidasan Jagadeesan, M.D., a neurointerventional radiologist at University of Minnesota Amplatz Children’s Hospital and an assistant professor in the University’s Department of Radiology.

“Because it was so rare, we actually reviewed the case with many, many people,” adds Andrew Grande, M.D., a vascular/endovascular neurosurgeon on Lydia’s medical team, which also included vascular/endovascular neurosurgeon Ramachandra Tummala, M.D. “Everybody agreed that the best thing to do was wait.” So they sent the Kohlers home, cautioning them to stay alert to anything unusual.

“Well, we were brand-new parents,” laughs Anna. “We didn’t know anything about what was typical!”

Emotional ups and downs

When Lydia had a massive seizure at six weeks old—a result of heart failure caused by the strain of pumping huge amounts of blood into the sac in her head—Anna and Brandon Kohler were jolted out of their new normal world into a medical nightmare, which began with a mad race to Amplatz Children’s Hospital.

“We were terrified,” Anna Kohler recalls. “We had no idea what was going on. We just wanted someone to tell us everything would be OK. But the doctors said flat out, ‘We can’t give you a guarantee.’ When she went into the operating room the next day, we weren’t sure we’d ever see her alive again.”

Four grueling surgeries later, each one lasting eight to 10 hours, the Kohlers were numb, going back and forth between grief and hope and despair and faith that everything would be fine. During the fourth surgery, just before Christmas 2011, the extended Kohler clan gathered to wait with Anna and Brandon.

“Our family and friends are so incredibly supportive,” says Anna Kohler. “Our group filled the waiting room that day and, after about 10 hours, Dr. Jagadeesan came out and said, ‘She’s cured.’ Just like that!”

“They gave us a standing ovation,” Jagadeesan says. “This huge group of people on their feet clapping and cheering. It was nice to have such trust and faith from the family.”

A novel approach

The problem from the outset was the tricky combination: the rarity of the condition, the high rate of blood flow into the sac, and Lydia’s young age. While the team knew it had to get inside Lydia’s head and seal off the openings of the abnormal arteries to stop the flow, the approach was risky. The doctors had to thread a catheter through the femoral artery into Lydia’s brain, then inject dye to highlight the network of blood vessels, then inject a glue commonly used to seal off aneurysms.

“During the first surgery, we injected glue into the sac and closed off about 30 percent of the abnormal connections,” explains Jagadeesan. “Then a second surgery got us to about 70 percent. We were chipping away at it, getting closer to shutting them all down.”

Then Lydia experienced seizures and bleeding after the second surgery, and the team knew it had to try a dramatically different approach. Instead of going through the artery to inject glue, the doctors went directly through the soft
spot on Lydia’s head—something that had never been done before.

“Going through the soft spot was radical,” Jagadeesan admits, “but it was that or nothing.”

It worked. Using the new technique, the team completely shut down the malformed connections, which caused the sac to shrink and Lydia’s brain to rebound into the space once filled by the sac. Eventually, says Jagadeesan, they expect the sac to go away completely.

**Triumph of teamwork**

Today Lydia is a running, talking, 2-year-old whirlwind who will never remember days spent in lifesaving surgery. That’s the first happy ending.

And what the doctors learned from treating Lydia’s AVF has also given them new tools to use on other patients afflicted with abnormal blood vessel connections; the team has already contributed to heart, brain, and lung procedures using techniques it honed with Lydia. So when, defying the odds, a second baby girl was born this year in the Twin Cities with the same rare AVF, the doctors knew what to do.

Finally, the triumph of teamwork remains a lasting legacy of Lydia’s treatment. Grande sums it up like this: “By working together we were able to understand the problem and gain the confidence to treat it. That’s a unique theme here at the U; we work together on all our cases, arguing, debating, asking—and, as a result, everything we do is better.”

“If we hadn’t thought out of the box,” adds Jagadeesan, “and had this kind of team cooperation, I don’t think either of these girls would have lived.”

And, thankfully, for the Kohlers, today that is so far from their reality.

“I can’t say enough about these doctors,” says Anna Kohler. “We are so grateful to them. I look at Lydia now, so happy and cheerful, talking like crazy—you’d never know anything was ever wrong. How can you ever say ‘thank you’ for that?”

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—Anna Kohler
In its 10th year of supporting muscular dystrophy research at the University, the Greg Marzolf Jr. Foundation holds hope for a cure

Research at the University of Minnesota’s Paul and Sheila Wellstone Muscular Dystrophy Center has flourished with 10 years of support from the Greg Marzolf Jr. Foundation—the legacy of a boy who yearned for a cure for MD.

“Gregory always felt he didn’t want other kids to have to go through what he had gone through,” says his father, Gregory Marzolf Sr.

Gregory Jr. was just 2 years old when he was diagnosed with MD. In the years that followed, Gregory, with his mischievous wit, good-natured persistence, and prodigious problem-solving ability, advocated for himself and others with the disease, won many friends, and helped raise thousands of dollars for MD-related causes.

Gregory’s mother, Patricia Marzolf, says it was his personality and strength of character that galvanized his community. Friends and strangers alike saw beyond Gregory’s disability. “He was not ‘the kid in the wheelchair,’” she says. His high school principal told Patricia presciently, “He can do more for us than we can do for him.”

Not long after Gregory died—in 2000 at age 20—the Marzolf family was approached by friends determined to keep his spirit and mission alive. They asked if they could start a foundation in his name.

“A lot of times when families lose someone, they tend to fall off the radar,” says Gregory Sr. “Our community pushed us to stay involved. We wanted to stay involved.”

Now, more than a decade later, the Greg Marzolf Jr. Foundation and its committed group of volunteers are still going strong. At the U, the group created the Greg Marzolf Jr. MD Trainee Program, which distributes competitive research stipends to undergraduate, graduate, and postdoctoral trainees focused on muscle diseases. University leaders told the Marzolfs that this support would help to cultivate and nurture young scientists’ bold new ideas about how to cure MD—and that the funding also could be leveraged to attract larger grants from the National Institutes of Health and other research-funding bodies.

“The trainee program was entirely different than anything we’d ever heard of,” says Patricia Marzolf. “It lets us focus [our donations] locally, with a mission that says research for a cure.”

Since 2002, the Greg Marzolf Jr. Foundation has raised more than $1 million for research. Of that, the organization has designated more than $250,000 to the Greg Marzolf Jr. MD Trainee Program at the University, which in turn has attracted $12.6 million in additional funding for the MD Center.

The Marzolfs say they are particularly excited about the work being done by Joseph Metzger, Ph.D., chair of the University’s Department of Integrative Biology and Physiology and holder of the Maurice B. Visscher Endowed Chair in Physiology. The Metzger lab is testing a “molecular Band-Aid” it designed to help repair weakened heart muscle that occurs in conjunction with Duchenne muscular dystrophy and other conditions.

“It’s nice to see all of this happen here in our own backyard,” Patricia Marzolf says.
Two years in, promise of new research fund pays off

When Brad Wallin helped to announce his family’s generous gift to create the Winston and Maxine Wallin Neuroscience Discovery Fund at the University of Minnesota in 2011, he said, “It will be exciting to see what unfolds.”

Two years later, we can see exactly what’s unfolded—and it is quite remarkable.

The Wallin Neuroscience Discovery Fund, made possible by an annually recurring gift of $500,000, was designed to spur pioneering brain research at the U. Winston (who died in 2010) and Maxine Wallin and their family hoped that the seed money they provided would help scientists gather the data they need to move their research to the next level, where they could obtain larger, longer-term grants.

Looking at two of the four projects funded in the first year, for example, shows just how successful that strategy was.

**Understanding crucial brain interactions**

Disturbances in the interactions between the thalamus and the cortex can result in serious disorders like schizophrenia and autism. But what causes those disturbances? With his Wallin award, associate professor in the Department of Neuroscience Yasushi Nakagawa, M.D., Ph.D., produced results that led to an additional grant from the Brain & Behavior Research Foundation, and a critical portion of his team’s findings were published in May in the *Journal of Neuroscience*.

**Getting inside the mind**

Understanding how the brain processes information—or fails to do so—can help scientists understand diseases like Alzheimer’s, Parkinson’s, and depression. Using his Wallin grant, A. David Redish, Ph.D., professor in the Department of Neuroscience, developed a new nanowire technology that allowed his team to record from inside the brain of a laboratory rat. That work led to a new grant from the National Science Foundation that will help the team delve further into its investigation.

In 2012, Institute for Translational Neuroscience director Harry Orr, Ph.D., was one of five scientists chosen to receive a Wallin grant for work he’s now doing with colleague Marc Jenkins, Ph.D., a Distinguished McKnight University Professor in the Department of Microbiology. Their research looks at communication between the brain and the nervous system, exploring what role it plays in neurodegenerative diseases like Alzheimer’s and Parkinson’s.

“The Wallin Fund is so helpful to both junior investigators and more senior people who have many ideas for new research but not enough money to get them going,” says Orr. “Grants like these allow us to move from the talking phase to the doing phase, and that’s how important discoveries are made.”

*Two years in, promise of new research fund pays off*

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Yasushi Nakagawa, M.D., Ph.D., is investigating what causes disturbances in the way parts of the brain interact and how those disruptions can lead to disease.
IRA charitable giving opportunity extended for 2013

Thanks to recent legislation, you can again benefit from a popular tax-advantaged giving option.

Make a gift of up to $100,000 directly from your IRA to the University of Minnesota Foundation (UMF) to support research into brain, nerve, and muscle diseases before December 31, and avoid paying federal income tax on the amount of your gift.

These rules apply:
• Only IRAs are eligible (other types of retirement accounts are not).
• You must be age 70 1/2 or older at the time you make your gift.
• Your gift must come directly from the IRA custodian to UMF.
• You can give up to $100,000 from your IRA to one or more qualified charities in 2013 (and if your spouse has a separate IRA, you can each give up to $100,000).
• Your gift must be outright; it cannot be used to fund a charitable gift annuity or charitable remainder trust.

While you will not be able to claim a charitable deduction for your IRA rollover gift, you also won’t owe federal income tax on any amount up to $100,000 that you distribute to a qualified charity.

To make a gift or learn more, contact us at plgiving@umn.edu, 612-624-3333, or 800-775-2187.

Save the date for the ninth annual Diamond Awards

Thursday, January 23, 2014
Target Field

Don’t miss Minnesota’s premier baseball charity event and the chance to celebrate with Twins baseball icons at Target Field. Be part of a televised awards dinner featuring current and former Twins players, bid on rare baseball memorabilia, and more.

Proceeds support the University of Minnesota’s innovative research and patient care in ALS (Lou Gehrig’s disease), ataxia, multiple sclerosis, muscular dystrophy, and Parkinson’s disease.

Learn more or purchase your tickets today at minnesotadiamondawards.org.

An investment in MnDRIVE: Boosting U research and the economy

Gov. Mark Dayton and policymakers supported University of Minnesota initiatives aimed at advancing research and boosting the state’s economy during the 2013 Legislative session.

The Legislature made a two-year, $35.6 million investment in MnDRIVE—Minnesota Discovery, Research, and InnoVation Economy—to fund research initiatives in four key industries: food production, robotics, water quality, and neuromodulation.

Neuromodulation, a growing field of research centered around changing the activity of brain circuits, offers the potential to improve stroke recovery and address other debilitating disorders such as Parkinson’s disease, Alzheimer’s disease, and schizophrenia, says Department of Neuroscience head Timothy Ebner, M.D., Ph.D.

“Depression and obsessive compulsive disorder are incredibly hard to treat, and [researchers] are now turning to neuromodulation,” he says. “If we could intervene in these diseases, we could make a major impact.”

Learn more about MnDRIVE at z.umn.edu/cod.
A perfect match

With help from a challenge grant, U advances research on a first-ever treatment for ataxia

There are no real treatment options for people who have ataxia—no real course of action other than coping with symptoms of the neurodegenerative condition, which can include difficulties with balance, coordination, speech, and sometimes vision.

But today researchers at the University of Minnesota are on a path to change that reality. Working with colleagues at the University of Iowa and Rush University in Chicago, U scientists are developing what could be the first-ever gene therapy for people who have spinocerebellar ataxia type 1 (SCA1).

Gene-based treatment approaches are potential alternatives to drug-based therapies for some conditions. In the case of SCA1, a specific gene therapy already has been shown to be effective in mice. Now a team led by renowned U of M ataxia researcher Harry Orr, Ph.D., is taking the next steps toward determining whether the therapy could also be transferable to people.

The University has a rich history of “firsts” in ataxia research. In the 1990s, Orr and his colleagues discovered the gene and mutation that cause SCA1 and developed the first mouse model of the disease. (Investigators also discovered that the genetic mutation that causes SCA1 causes Huntington’s disease as well as five other ataxias: SCA2, SCA3, SCA6, SCA7, and SCA17). Research centers around the world have used this knowledge in their own studies.

Through experiments funded by the generosity of donors, Orr and his collaborators proved that this new gene therapy works in mice. And now they’re relying on that generosity to take the work to the next level—and, eventually, to patients through clinical studies.

Philanthropists Richard and Maureen Schulze have offered to match all gifts to advance this gene therapy research project dollar for dollar, up to $50,000.

It’s a significant opportunity to make a difference—not only for people who deal with SCA1 every day of their lives, but also for people suffering from Huntington’s disease and other forms of ataxia who stand to benefit from this therapy.

Make your gift online today at www.give.umn.edu/giveto/schulzechallenge. Or to learn more about the research, contact Tracy Ketchem of the University of Minnesota Foundation at 612-625-1906 or tketchem@umn.edu.
Department of Neuroscience professor A. David Redish, Ph.D., discusses his new book, *The Mind Within the Brain: How We Make Decisions and How Those Decisions Go Wrong*. It’s available through Amazon and Oxford University Press.

**Q: How do the decision-making systems in our brains work?**

**A:** There are multiple decision-making systems that work in tandem with each other. They can be separated based on the information processing that they do. In the book, I lay out four action-selection systems—a deliberation system, a procedural (think sports) system, a Pavlovian or emotional system, and (since any action is a decision) your reflexes.

**Q: How did you find these insights?**

**A:** A large part for me personally has been the work that’s been done in my lab and others over the last few years looking at how nonhuman animals, rats in our case, make decisions. These animals make decisions in ways that are remarkably close to humans. For example, we now know that rats can deliberate over choices, imagining the possibilities and evaluating those possibilities. Because we’ve been able to see the actual information processing happening in these animals, we’ve been able to connect that to how humans seem to be making decisions.

**Q: How did using multiple disciplines help lead to these conclusions?**

**A:** Decision-making is a very large field, with contributions from fields including psychology, robotics, economics, neuroscience, neuroeconomics, and computational psychiatry. Each of these fields has a different set of tools that allows a different perspective on the problem. What’s remarkable (I think) is how similar the conclusions have been from these different perspectives.

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