On the Move

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Parkinson's and Movement Disorders Center

VCU Health™

Moving deeper into multiple movement disorders

Brian D. Berman, MD, MS
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With our recognition last year as a Center of Excellence for Parkinson's disease care, the VCU Parkinson's and Movement Disorders Center (PMDC) has rightly received lots of attention lately for the cutting-edge research we're pursuing into that disease.

As we continue seeking ways to improve the lives of those affected by Parkinson's disease through world-class care and research, we're also continuing to try and improve the lives of those affected by other movement disorders and expanding the number of studies devoted to finding better ways to diagnose and treat them.

You'll hear about some of these efforts in this newsletter, including our growing body of research into dystonia, a disorder characterized by involuntary spasms that lead to abnormal movements and postures.

One of my goals for the PMDC is to grow our portfolio of research studies across the gamut of movement disorders, including dystonia, which I've been researching since medical school. This disabling disorder can take away a patient's sight, speech, limb function and independence. We need better ways to treat it, and VCU is hoping to find answers that will help us improve the quality of life for people living with dystonia, as well as insights into what causes it and better ways to diagnosis it.

With a half-dozen studies into dystonia underway here, PMDC is among a handful of medical centers nationwide pursuing that amount of research into a disorder that's not well understood and is often misdiagnosed.

Researchers at the PMDC are also working hard to find ways to stop the progression of Huntington's disease (HD), an incurable hereditary disorder that causes progressive difficulty in controlling movements as well as changes in cognition and personality.

Our center is participating with several other research hospitals in a trial of a gene therapy that seeks to lower the amount of the disease-causing protein that causes brain cells to die in Huntington's patients. Our researchers are also taking part in a clinical trial of a novel drug that might help improve cognitive symptoms of that disease.

And there are many more studies underway at the PMDC. We're actively seeking patient volunteers (and healthy controls) for our studies into Parkinson's, Huntington's, dystonia, Dementia with Lewy Bodies (DLB), and other neurological conditions as we pursue answers that can lead to better treatments, and better lives, for people living with movement disorders.

ON THE COVER:
Mike Hoyt heads to the top of a climbing wall at Midlothian's Peak Experiences as part of a program offered by Up ENDing Parkinson's. Story on page 7.

Patient studies look to halt Huntington's progression, manage symptoms

Mary* faced a tough decision: Should she undergo an extensive brain surgery as part of patient research to see whether a new gene therapy could keep her existing Huntington's disease (HD) symptoms from worsening?

The catch?

She wouldn't find out for a year whether she actually received the gene therapy during that 14-hour operation (nor would VCU, which is taking part in the clinical trial). At the same time, gene therapy becomes a permanent part of a patient's DNA unlike when an individual can stop taking a drug in a pharmaceutical trial.

Mary chose to participate in the gene therapy trial.

As she waited for official word over the next 12 months, the Virginia mom says her Huntington's disease symptoms remained stable. While intense migraines followed shortly after the surgery, those headaches quickly dissipated while the brief jerking movements she experienced because of the genetic disease remained unchanged — perhaps suggesting the progression of her disease had slowed.

HD is a hereditary disease that progressively destroys brain cells. As the disease advances, individuals living with HD experience difficulties controlling their movements as well as issues with cognition and personality. Most patients begin to experience symptoms in their 30s or 40s.

While studies elsewhere are looking for a cure for HD, this VCU Parkinson's and Movement Disorders Center trial is assessing whether a novel gene therapy can stop symptoms from progressing.

"I was drawn to the fact that it could actually address things like my symptoms straight on compared to a Band-Aid on the issue."

"When I first heard about this study, I thought it was crazy and that I never would do it," says Mary, who is in her mid-40s. She'd participated in earlier research for a drug therapy that proved ineffective. "But what drove me to want to do this study was my own research that I did on the gene therapy. I was drawn to the fact that it could actually address things like my symptoms straight on compared to a Band-Aid on the issue."

Can HD be stopped in its tracks?

VCU is among several academic research hospitals participating in uniQure's trial of an investigational gene therapy known as AMT-130. Its two key components are a vector that acts as a delivery system, and microRNA (miRNA), small pieces of genetic material that will recognize, bind and "non-selectively" lower the human protein that causes HD. That untargeted approach means that both the normal huntingtin protein (HTT) and its disease-causing mutant (mHTT) will decrease. The trial includes study of both low- and high-dosed components.

Heather Ward, BS, a senior clinical research coordinator in the VCU PMDC, notes HD patients nationwide "are desperate for effective treatments," and she fields regular calls from patients or family members wanting in on the trial. Nationwide, 26 patients have participated in the AMT-130 trial, with 12 in the low-dose cohort and 14 in the high-dose one.

Mary says the prospects of participating were scary and intimidating, "but the surgery was my chance to possibly change my disease projection."

When Mary was born, her family didn't know HD was a hereditary disease. Her father died from HD when he was 50, and she was only 18. Eventually, she and her brother were tested and confirmed to have the disorder.

"I'm lucky to be able to do what I do," says Mary, who still drives and handles full-time mom duties. She and her husband are building a new house with disability features to use should her symptoms worsen. "I've always lived my life knowing this was a possibility."

Improving the moments with HD

Chris Hickok, 40, also sought to participate in the uniQure gene therapy trial. While he didn't meet the criteria for the study, he was a candidate for a new drug aimed at easing the cognitive impacts of HD. "Sometimes I have issues where I can't find the right word. Or I just say it wrong, or I forget what it is I'm reading about," he says.

The clinical trial Hickok is participating in is studying how the Sage Therapeutics investigational drug, SAGE-718, might improve cognitive symptoms including impaired judgment, forgetfulness, difficulty paying attention, and trouble thinking through multiple steps of an activity or complex problems.

— Continued on page 4.

*Mary asked us not to use her real name.

Raised by his grandparents, Hickok learned later in his life that his father had HD. He was already in the U.S. Navy when he decided to get tested. "I could already feel balance issues and memory loss, and just sometimes getting really mad," he says, noting he also needed more time to complete all the paperwork that crossed his desk.

Delays getting tested for HD almost prompted him to abandon the quest. If only one parent has HD, then each child has a 50% chance of inheriting the genetic disorder.

Finally, after getting tested and waiting two months for results, Hickok received his diagnosis. In March, he retired from the military career he loved.

At retirement, he also was three months into the Sage Therapeutics trial, traveling from his home in Suffolk for research appointments.

"My cognition is better when it comes to some stuff, and I feel like I am remembering some things a little bit more," he says. "I definitely feel more myself."

"Our team is committed to participating in clinical trials of therapies that halt or significantly slow the worsening of Huntington's disease," says Matthew Barrett, MD, an associate professor in the Department of Neurology's Division of Movement Disorders. He serves as principal investigator on the AMT-130 and SAGE-178 trials. In the SAGE trial, he is joined by assistant professor Stephanie Bissonnette, DO, as sub-investigator. "Until these therapies are available, we will also be involved in research to identify better treatments for symptoms associated with the disease," he says.

Hickok, who has two children with his wife, Lucy, feels blessed to be in the study. "I worry about my kids having this disease," he says, "and I want there to be more progress by the time they get to be adults."

Volunteers needed for clinical research studies

Volunteers needed for clinical research studies into Parkinson's disease (PD), including investigations exploring Freezing of Gait and cognition symptoms, as well as for clinical research studies investigating Huntington's disease (HD), Dementia with Lewy Bodies (DLB), and dystonia (including cervical dystonia and blepharospasm). People with these neurological disorders are needed as are individuals who can serve as "healthy controls". To volunteer, please contact the study coordinators listed below:

PARKINSON'S DISEASE:

- ***PD GENEration genetic study:*** (Ginger at 804-627-1398)
- ***PD Sleep study:*** (Caileigh at 804-220-0970)
- ***PD-MC Cognition study:*** Istradefylline trial (Kara at 804-828-4788)
- ***PDD Cognition study:*** EEG study (Kara at 804-828-4788)
- ***New dx/untreated:*** Tempo-2 (Ginger at 804-627-1398) and LUMA (Heather at 804-382-0076)
- ***Wearing off:*** Tempo-3 (Ginger at 804-627-1398)
- ***Dyskinesias:*** Bukwang (Gina at 804-921-9990)
- ***Percept DBS and Freezing of Gait (FOG):*** (Gina at 804-921-9990)

DEMENTIA WITH LEWY BODIES: Kara at 804-828-4788 or Heather at 804-382-0076

DYSTONIA: Caileigh at 804-220-0970

HUNTINGTON DISEASE: Heather at 804-382-0076

PMDC partnered with Power Over Parkinson's to host our April 15 Parkinson's Disease Education Day. The event featured speakers who tackled a range of topics, including PD cognition issues, caregiver tips and estate planning.

WOMEN GOING FORWARD

Parkinson's Disease Support Group for Women

SEPTEMBER THROUGH MAY
Second Wednesday of the month
10-11:30 a.m.

JOIN US! Contact Ginger Norris at **virginia.norris@vcuhealth.org** to receive email reminders about the date, time and topic each month.

What causes dystonia?

VCU researchers search for answers in a number of studies.

Researchers at the VCU Parkinson's and Movement Disorders Center are seeking to shed light on what causes dystonia, a chronic and frequently disabling and painful neurological disorder that causes muscles to spasm, forcing the body into abnormal movements and postures.

PMDC Director Brian Berman, MD, who has been interested in the disorder since his time in medical school, has worked to increase the center's research portfolio in dystonia.

An estimated 300,000 people have dystonia in the United States, but this number is thought to be an underestimate as it is an often-underdiagnosed disorder. "We think it affects a lot more people than who are diagnosed with it because it's underrecognized," Berman says.

Dystonia is considered the third most common movement disorder, Berman notes. The disorder can be a spontaneous isolated condition, or it can be seen in patients taking anti-psychotic medications as well as those with Parkinson's disease or those who have suffered a stroke or traumatic brain injury. In many cases, the root cause of a patient's dystonia remains a mystery.

"It's clear that current treatment options are pretty poor. We do our best with medications, but they often aren't very effective or require repeated painful injections," Berman says. "Ultimately, we want to have better treatments and hopefully cures."

Berman wrote his first medical paper on botulinum toxin treatments for dystonia. During his neurology residency, he completed a study on how dystonia responds to deep brain stimulation.

"Dystonia can be very disabling," he says. "If it affects the eyelids, it can cause functional blindness. If it affects the neck muscles, it can impact daily functioning and lead to diminished quality of life. If it affects the vocal cords, it can impair speech. If it affects limb muscles, it can impact handwriting and walking."

Caileigh Dintino, BS, a PMDC clinical research assistant working with dystonia patients involved in the center's studies, has learned from them about how the disorder impacts their way of life.

"Beyond the pain, a lot of people with dystonia end up not being able to drive, function at work, or complete daily tasks comfortably on their own," she explains. "That's a huge hit to someone's independence."

This June, Dintino traveled to the International Dystonia Symposium in Dublin, Ireland to present preliminary findings from a PMDC study investigating blepharospasm, which is when dystonia affects the muscles of the eyelids and upper face.

Caileigh Dintino, clinical research assistant

Dozens of patients from around the United States are taking part in a half-dozen dystonia research projects that Berman leads at the PMDC. Those studies seek improved ways to diagnose dystonia and better ways to treat it.

Several VCU PMDC research projects are being conducted through the Dystonia Coalition, a multicenter consortium of academic medical centers from around the globe. One of those projects uses patient surveys and videos of their neurological exams to train software to track symptom severity and gauge how symptoms change over time. Another seeks patient feedback on how botulinum toxin injections are affecting their motor and neuropsychiatric symptoms and impacting their activities of daily living. A third project draws samples of a patient's blood to create a "biobank" for protein biomarker and DNA testing to better understand what causes the disorder.

Developing an effective tool to spot depression and anxiety in dystonia patients is the target of another PMDC study. Further research is examining levels of a major inhibitory chemical in the brain known as GABA (gamma-aminobutyric acid) and whether abnormal levels in patients with dystonia can be used to better diagnose dystonia and track its symptoms.

PMDC researchers are also seeking funding to investigate the use of non-invasive transcranial neurostimulation techniques to alleviate dystonia symptoms. Only a handful of movement disorders centers around the country are undertaking the amount of clinical research into dystonia that the VCU PMDC is conducting.

"Our growing focus on dystonia is another way we're trying to improve the lives of those impacted by movement disorders," Berman says.

New PMDC physician brings focus on healthcare disparities and DEI

Stephanie Bissonnette, DO, MPH, recently joined the VCU Department of Neurology, bringing a commitment to addressing the healthcare disparities many patients with movement disorders face.

Bissonnette started in January as a new movement disorders specialist and core member of the VCU Parkinson's and Movement Disorders Center. She also leads efforts directed toward promoting equal care of all neurologic patients as associate vice chair for Diversity, Equity and Inclusion (DEI) within the department.

"I'm really interested in Parkinson's disease disparities and looking at how language and health literacy affect a PD patient's ability to understand their disease and to follow complex treatment plans and engage in things like physical therapy and exercise programs," Bissonnette says.

Stephanie Bissonnette, DO, MPH, assistant professor of neurology

She's very familiar with the area.

In a prior role at Boston Medical Center, Bissonnette continued work on a project launched by a colleague that explored the social determinants of health and such disparities. While that medical center had a patient population that was one-third Caucasian, one-third Black, and one-third Hispanic, its movement disorders clinic was about 90% white, she says.

"It became clear as I transitioned into an attending physician that my patients who had poorer health literacy or just poorer literacy or did not speak English were at a disadvantage in terms of being able to obtain essential information about their disease," Bissonnette says.

As she pursued research, Bissonnette also noticed that the way trials were set up excluded many patients because they required English language literacy as well as access to email and the Internet.

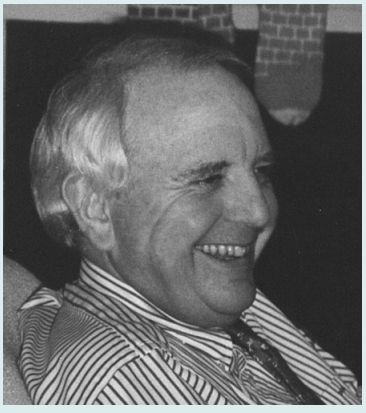
"Parkinson's affects everyone — not just white older males," Bissonnette says. "We also see many many younger, non-white patients, and female patients."

In addition to focusing on Parkinson's, Bissonnette is particularly interested in working with individuals who have ataxia (loss of muscle control and impaired balance) and Huntington's disease, and she'll be transitioning into the role of director of the Huntington's clinic. VCU is a Huntington's Disease Society of America Center of Excellence for treating that disease, an inherited neurological disorder where the brain's cells degenerate over time, causing abnormal movements, emotional changes and cognitive decline.

"Huntington's is one of the most unique diseases out there because it has such a strong family link," Bissonnette says. "People who are at risk for Huntington's have their own experience with what the disease means. There is a dedication to cure and treatment and improvement in quality of life in the community that I don't see with any other disease."

Bissonnette defines success in her new roles as delivering excellent clinical care to all her patients and expanding the VCU PMDC's outreach into the community.

"One of the things that really brought me to Virginia was how diverse it is and how much work we could do to improve patient care and quality of life," she says.



IN MEMORIAM: **DAVID CALDWELL REYNOLDS**

We were saddened by the passing of David Caldwell Reynolds, a driven business leader in Richmond who played a lead role in the formation of the VCU Parkinson's and Movement Disorders Center.

His life of service and compassion had a tremendous and enduring impact on patients at VCU and beyond. Like many patients under our care, Reynolds lived with Parkinson's disease, but his life was not defined by it.

We greatly respect his dedication to and support in creating a comprehensive movement disorders center at VCU and advanced care for individuals with Parkinson's disease and other movement disorders. We hope to honor his inspirational legacy as we continue to pursue the mission of the center Reynolds helped establish.

PD patients hit the wall to improve mind and body

Mike Hoyt ties a rope into his harness connecting him to the top of a wall some 50 feet high. He places one foot on the wall, then one hand, the other foot, now the other hand, and maneuvers his way to the top before letting go and being brought slowly down to earth by a belayer.

You would never know Hoyt is a face of Parkinson's disease (PD), and has been one since December 2013.

On diagnosis then, "I tried not to look at what I couldn't be doing," the now 67-year-old says, standing on the floor of Midlothian's Peak Experiences rock climbing gym. At home in Williamsburg, he began exercising more and working with a personal trainer before actually becoming a certified personal trainer himself as a retirement gig. The former Newport News engineer trained numerous clients and even a few with PD.

In the last year, Hoyt added rock climbing to his daily exercise regimen.

"When you're on the wall, there's a focus…you don't think…," he says, his voice breaking, "you don't think about your limitations. You set goals for yourself and work to achieve them."

The Richmond rock climbing program is a chapter of the growing Virginia-based nonprofit Up ENDing Parkinson's. The group, which promotes the benefits of climbing for those with PD, was started by Molly Cupka, a climbing instructor and director at Sportrock Climbing Centers in Northern Virginia who began climbing with PD patients in 2012.

"I am convinced that rock climbing is the most comprehensive exercise a person with Parkinson's disease can do," she says. She cites recommendations from the Parkinson's Foundation and American College of Sports Medicine on the best types of exercise for PD — aerobic activity, strength training, balance/agility/multitasking and stretching — and notes climbing "checks all the boxes."

Hoyt found Cupka via Google in February 2022. He travelled to Sportrock in Alexandria for several months before they connected with Margaret Preston, president of Richmond-based Power Over Parkinson's (a VCU Parkinson's and Movement Disorders Center partner), to replicate the climbing program in Richmond. Weekly events are now held at Peak Experiences under an additional partnership with a team from Beyond Boundaries, a Central Virginia nonprofit helping individuals with disabilities, underserved youth and those in recovery to get active. Richmond is Up ENDing Parkinson's second outpost, and it has added others in Asheville, N.C., Ohio and Italy.

For those living with PD, exercise is vital to maintaining balance, mobility and activities of daily living. The Parkinson's Foundation notes research supports that people with PD who start exercising earlier in their disease course for a minimum of 2.5 hours per week experience a slowed decline in quality of life compared to those who start later.

Exercise and physical activity cannot only maintain and improve mobility, flexibility and balance, but can also ease non-motor PD symptoms, such as depression or constipation.

"It is the only thing we believe that has been proven to slow disease progression," says Leslie Cloud, MD, an associate professor of neurology and director of the Parkinson's Disease Program at the VCU PMDC.

Whether rock climbing or boxing — as many with Parkinson's take up — the key is getting the heart rate up with aerobic exercise. "You can't mosey along and walk the dog, you have to be sweating, and get your cardiac output up," says Cloud, who has been Hoyt's PD specialist since 2014. "By getting your heart rate up, you increase blood flow to the brain, and that brings all sorts of good downstream benefits that keep brain cells happy and healthy and alive for longer."

There are benefits specific to rock climbing, Cloud says — at least in theory. Climbing requires large-amplitude movements with all four limbs. Fingers must move in novel ways to grasp colorful holds of random size and shape that are bolted to the wall. Balance and core strength are critical to success.

"And then there's kind of a meditative, mind-over-matter element," Cloud says.

Indeed for Hoyt, rock climbing is but one element in his life to take his mind off the disease — he eats well, gets in his exercise and stays positive. "The encouragement, support and friendships you develop with your fellow climbers, the individuals who volunteer their time to belay and coach you, and people you meet in the climbing community motivate you to continue to challenge yourself and to keep moving," Hoyt says, "in spite of what your PD symptoms are telling you."

Congratulations to Karishma Popli, MD '22, who presented on a research project she worked on at the VCU Parkinson's and Movement Disorders Center. She spoke during the American Academy of Neurology's Annual Meeting in Boston earlier this spring.

Follow us at vcupdcenter

PMDC held a Huntington's Disease Education Day on May 6 for patients and caregivers. The event covered topics such as "HD 101," "Research Round Up," "Developing Your Care Team," "Behavioral Issues in HD" and many more. Thank you to all the speakers, organizers, attendees and sponsors who made this event possible.

Support the PMDC

Find all the ways you can support our work to transform current treatment models for movement disorders.

Philanthropy plays an important role in bolstering our multidisciplinary clinical team, funding innovative research and supporting our training and outreach efforts. For information about how you can support the VCU PMDC, please contact the Neuroscience Development Team at 804-628-8287 or vcuhealthdevelopment@vcuhealth.org.

parkinsons.vcu.edu/donate

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