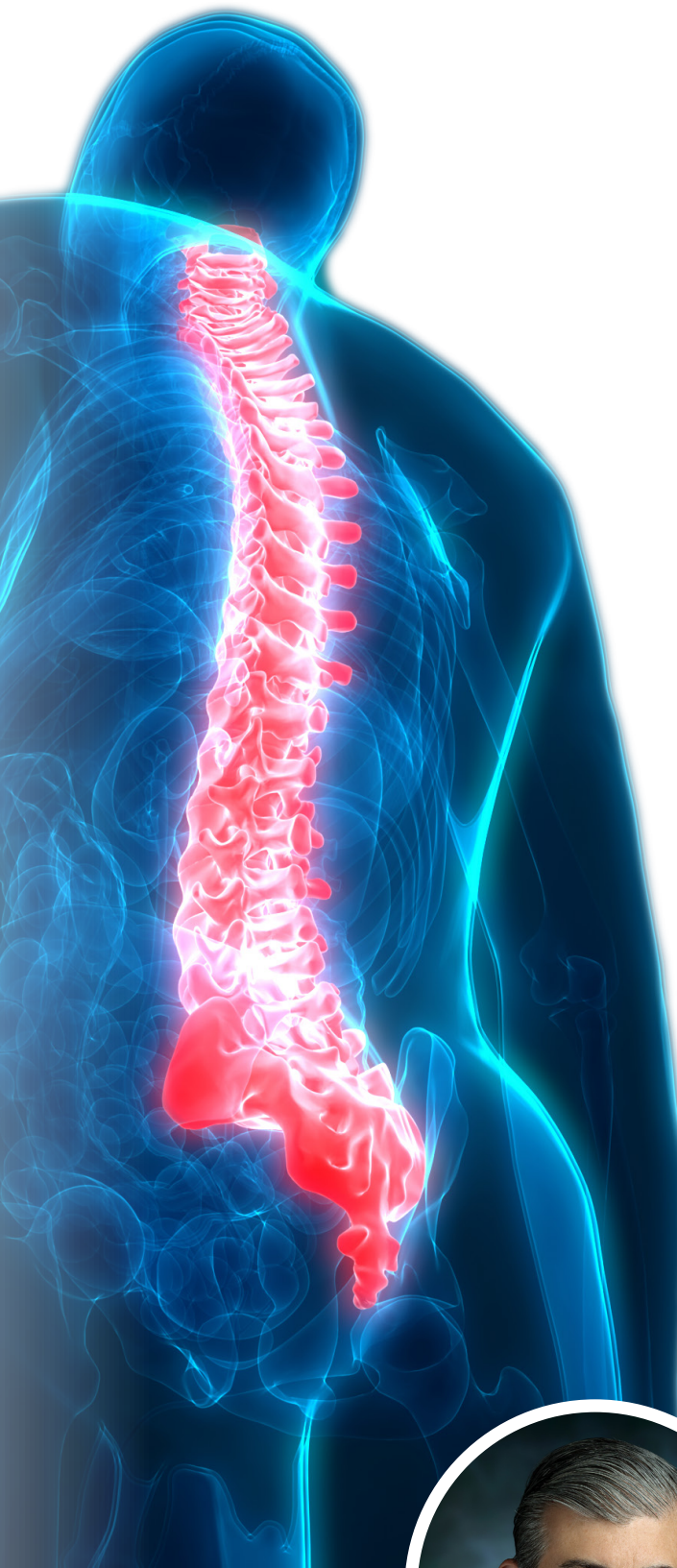


# JOHNS HOPKINS NeuroLogic

WINTER 2020

NEWS FOR PHYSICIANS FROM THE JOHNS HOPKINS  
DEPARTMENTS OF NEUROLOGY AND NEUROSURGERY



## A Clinical Innovation: Shortening the Spinal Column to Loosen Tethered Cords

Johns Hopkins neurosurgeons provide spina bifida patients new option to avoid ongoing detethering operations.

Up to half of children with spina bifida whose defects are surgically repaired shortly after birth develop tethering leading to later symptoms including back and leg pain, weakness, and bowel and bladder dysfunction.

The traditional fix for these problems is an operation that loosens the spinal cord from the tissue that confines it. However, as a child grows taller and taller, this detethering procedure surgery must be performed repeatedly, causing a buildup of scar tissue that eventually causes its own set of issues.

“Until recently, this was the best option we could offer patients,” explains Johns Hopkins pediatric neurosurgeon **Mari Groves**. “But every time we go in, we create more problems.”

Recently, Groves and her colleague **Nicholas Theodore**, director of Johns Hopkins’ Neurosurgical Spine Center, teamed up to offer patients a completely new approach: an operation that circumvents the tether completely and decreases tension on the spinal cord by shortening the spinal column instead.

Neurosurgeons have long performed procedures that inadvertently shorten the spinal column, such as partially or fully removing vertebrae when a cancerous tumor arises within the bone. However, to use this type of procedure for spinal cord tethering is new and extremely rare, says Theodore, practiced by just a handful of academic

medical centers across the country. Of these, Johns Hopkins has the largest series of patients, with many such procedures performed here over the past few years.

Their most recent patient exemplifies who would benefit most from this unusual procedure, Theodore explains. By the time they performed the procedure in April 2019, the 20-year-old had already undergone six detethering operations. However, with each subsequent procedure, she benefitted less and less. The pain and weakness wracking the patient’s legs and back severely limited the time she could spend on her feet. Bowel and bladder problems were steadily worsening.

Although the patient qualified for another detethering operation, based on her prior experience, this was only a short-term fix before these problems would come back potentially worse than before, Theodore says. However, shortening the spinal column could offer a more durable solution.

During the four-hour procedure, about 80 percent of the T12 vertebra was removed using image guidance and a robot that precisely places screws even in patients with very small pedicles. Under high resolution ultrasound, Theodore, Groves and colleagues could see the spinal cord relax during the operation, transitioning from a tight stretch to a looser confirmation that pulsed with each heartbeat. Theodore says this patient woke from surgery in tears of joy — although the pain of the procedure lingered, the excruciating pain from the tethered spinal cord had already dissipated.

The patient, says Theodore, is already running and hiking again and recently began nursing school.

“This is a significant departure in how we’ve traditionally treated these patients, but for the first time, it has the potential to be curative,” Theodore says. “It’s really exciting to be able to offer this new option.” ■

“THIS IS A SIGNIFICANT DEPARTURE IN HOW WE’VE TRADITIONALLY TREATED THESE PATIENTS, BUT FOR THE FIRST TIME, IT HAS THE POTENTIAL TO BE CURATIVE.”

— NICHOLAS THEODORE



Recently Johns Hopkins neurosurgeons Mari Groves and Nicholas Theodore teamed up to offer an alternative to spinal cord detethering. The procedure is available at only a handful of centers across U.S.

TO REFER A PATIENT, CALL 410-955-7337.

# For Spinal Fusion: Certain Antihypertensive Drugs May Improve Outcomes

New Johns Hopkins research suggests that blood pressure-lowering medicines can speed or inhibit bone healing.

Each year, doctors prescribe antihypertensive drugs to tens of thousands of Americans, with a large array of options available. These include angiotensin-converting enzyme inhibitors, or ACEIs, and angiotensin II receptor blockers, or ARBs.

Prior evidence in the literature suggests that these drugs can have wide-ranging effects throughout the body, including on the function of bone-building osteoblasts and bone-absorbing osteoclasts. But new research led by Johns Hopkins neurosurgeon **Timothy Witham** and published in *The Spine Journal* in August of this year, suggests that they can either slow or promote rates of spinal fusion clinically.

After Witham's postdoctoral fellow Alexander Perdomo-Pantoja read about these drugs' conflicting consequences on the cells pivotal for bone remodeling — with ARBs promoting the activity of osteoblasts and inhibiting osteoclasts, and the opposite true for ACEIs — they and their colleagues decided to review the records of 200 patients who underwent anterior cervical discectomy and fusion at Johns Hopkins. Of these patients, who had average age of about 54, about 39% were taking an antihypertensive drug: of them, about a third were on ACEIs, another third were on ARBs, and a final third took different

types of blood pressure-lowering medications.

After each of these patients underwent their procedures, their surgeons tracked recovery rates within the bone itself using plain cervical X-rays and other imaging techniques if necessary. Their findings showed a stunning difference between the ACEI and ARB groups: those taking ARB drugs had fusion rates about twice as fast as those taking ACEIs. Those not on antihypertensive drugs had spinal fusion rates between these two extremes, suggesting that the drugs themselves were either helping or harming the fusion process.

Witham points out that, like most initial findings, more studies will be necessary to confirm these results in larger populations and with more diverse groups of patients, such as those undergoing similar procedures in other areas of the spine. His team is already working on the next phase of this research in lumbar fusion patients.

However, if the findings continue to hold true, they could have broad consequences both within his and other specialties. For example, he says, doctors may eventually take a patient's blood pressure medication into consideration before performing spinal fusion as well as other types of orthopaedic bone surgeries. It could be advantageous to switch a patient on ACEIs to ARBs to encourage bone healing. Someday, he suggests, doctors could even prescribe ARBs

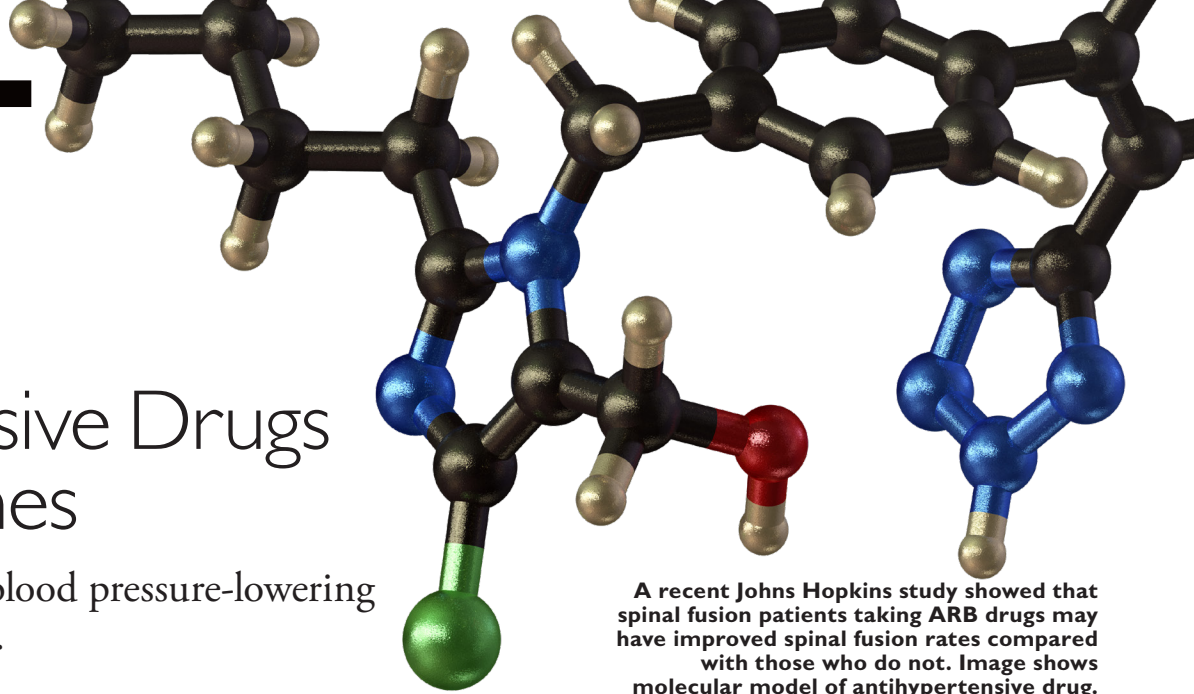
to patients who aren't currently taking an antihypertensive drug purely for a boost in healing rates.

"Tens of thousands of patients in the U.S. are on these medications that we've had no idea affected bone healing," Witham says. "Our research is showing that we should pay attention to these off-target effects that could make a real difference in recovery from spinal fusion procedures." ■

☎ TO REFER A PATIENT, [CALL 410-955-4424](tel:410-955-4424).

"OUR RESEARCH IS SHOWING THAT WE SHOULD PAY ATTENTION TO THESE OFF-TARGET EFFECTS THAT COULD MAKE A REAL DIFFERENCE IN RECOVERY FROM SPINAL FUSION PROCEDURES."

— TIMOTHY WITHAM



A recent Johns Hopkins study showed that spinal fusion patients taking ARB drugs may have improved spinal fusion rates compared with those who do not. Image shows molecular model of antihypertensive drug.

## Improving the Efficiency of Clinical Trials

Johns Hopkins neurologist Daniel Hanley co-leads Trial Innovation Center, helping researchers solve roadblocks to efficacy and lower costs.

Clinical trials are an incredible vehicle for introducing innovation in pharmaceuticals, medical devices and technology. However, they're also notoriously inefficient, with multiple factors slowing progress from the bench to the bedside and increasing costs.

A decade ago, the Institute of Medicine convened a public workshop titled "Transforming Clinical Research in the United States," which focused on identifying challenges in planning and implementing trials and developing strategies to improve efficiency. Seven years later, that discussion resulted in the formation of the Trial Innovation Network, an initiative sponsored

by the National Center for Advancing Translational Sciences (NCATS) and led by five institutions tasked with helping researchers overcome such hurdles, saving time and money in the process.

As leaders in NIH funding and two of just 65 institutions that have received coveted Clinical and Translational Science Awards (CTSAs) — a program run by NCATS to speed translation of research discovery into improved patient care — The Johns Hopkins University and Tufts University were natural choices to be part of this network, says Johns Hopkins neurologist **Daniel Hanley**. In 2016, he

became one of three principal investigators (PIs) to lead the Johns Hopkins-Tufts Trial Innovation Center.

The center, which recently received a new \$8 million grant from NCATS, helps PIs from CTSA institutions develop protocols, enhance study operations and improve recruitment and retention. "The program is specialty and disease agnostic," explains Hanley, "helping researchers with trials covering any conceivable area or illness."

Although the center's work extends to institutions across the country, he says, it's assisted several researchers within Johns Hopkins. For example, the center recently



# A Rare Diagnosis of Spinal Cord Stroke and the Road to Recovery

Under the care of experts at the Johns Hopkins Transverse Myelitis Center, a patient overcomes odds to walk again after rare and devastating neurological event.

The morning of February 7, 2014 was supposed to be an uneventful one for Arlene Whitmore, a 62-year-old kindergarten teaching assistant in Anne Arundel County, Maryland. But when she swung her legs out of bed, she immediately noticed something strange: her right leg heavy and numb, like it was asleep. The feeling persisted over the next several days.

“I thought I must have pinched a nerve,” Whitmore remembers.

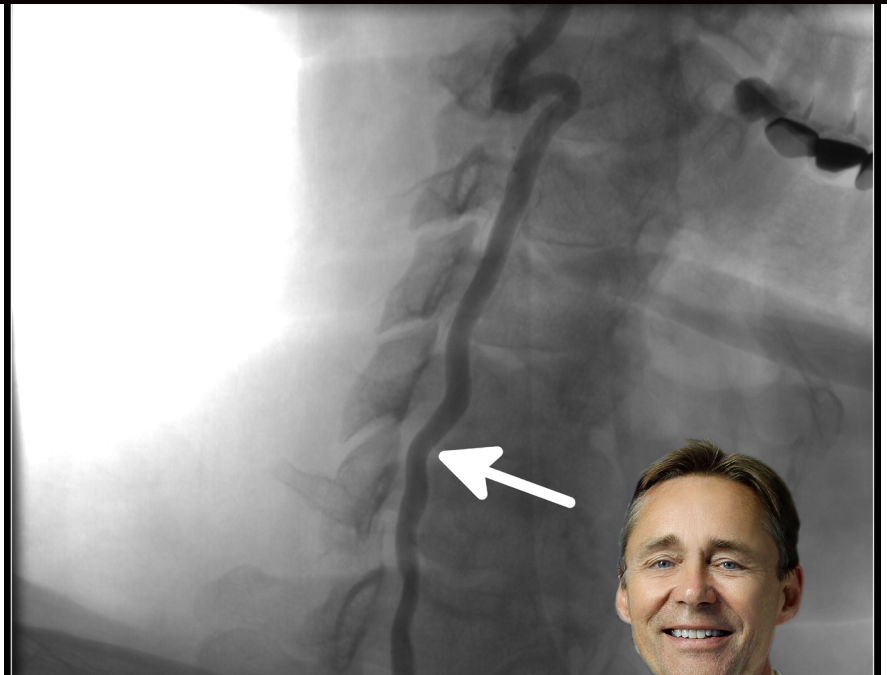
But the problem was much more serious. Over the next several months, she bounced from provider to provider, including her family physician, chiropractor and a local neurologist. Her providers ran numerous exams, including blood tests for Lyme disease and markers of multiple sclerosis, and imaging tests including multiple MRIs. None turned up anything suspicious.

All the while, the function in her right leg, and then her left, gradually declined. She transitioned from a walker to a rollator to a wheelchair, eventually becoming bedridden. Edema crept into both affected limbs, ballooning them both into extreme proportions. In the meantime, she says, no one could figure out why any of it was happening.

She finally had a breakthrough nearly a year and a half later after a friend suggested she see Johns Hopkins neurologist **Justin McArthur**, director of the hospital’s Department of Neurology. After a thorough review of Whitmore’s substantial medical records, McArthur says he had a strong suspicion of what might have caused her paralyzing cascade.

He referred her to the Johns Hopkins Transverse Myelitis Center, a hub for experts in the disease of transverse myelitis itself, but also for a variety of other conditions that affect the spinal cord. Under the guidance of McArthur’s colleagues **Carlos Pardo-Villamizar** and **Phillipe Gailloud**, Whitmore underwent a spinal angiogram, showing concretely that she’d undergone a spinal cord stroke — a rare manifestation of neurologic ischemia. The extreme infrequency of this condition, affecting only a few patients in the U.S. per year, and Whitmore’s unconventional presentation of gradual decline stymied her timely diagnosis, McArthur explains.

But now that they had an answer, McArthur and Whitmore worked together to create a plan to improve her function and stave off further



After diagnosis of spinal cord stroke — a rare manifestation of neurologic ischemia affecting only a few patients in the U.S. per year— patient Arlene Whitmore and neurologist Justin McArthur worked together to create a plan to improve her function and stave off further complications. Image shows normal vertebral artery on angiography.



“WE WANT TO SEND THE MESSAGE TO PATIENTS TO NEVER GIVE UP. THERE IS ALWAYS SOMETHING THAT CAN BE DONE, WHETHER IT’S REHABILITATION OR SYMPTOMATIC TREATMENTS.”

—JUSTIN MCARTHUR

TO REFER A PATIENT, CALL 410-502-7099.

assisted physician-researchers **Ellen Mowry** and **Scott Newsome** with their TREAT-MS trial, a multicenter study of multiple sclerosis that aims to understand whether an “early aggressive” therapy approach, versus starting with a traditional, first-line therapy, influences the intermediate-term risk of disability. The trial’s 44 sites presented a site activation challenge, with unique legal requirements in their different states, different levels of trained staff at each medical center and the need to execute contracts at each site for participating researchers. The center helped develop a path to work through these challenges, including establishing weekly and monthly goals for each institution to complete.

They also helped Johns Hopkins pediatric surgeon **Eric Jelin** plan a study that was recently submitted to the National Institute of Child Health and Human Development to test a novel fetal therapy for a condition



in which the fetus is absent amniotic fluid — previously considered universally fatal. The center helped him establish a consortium to implement the procedure in a standardized manner, a must for producing comparable results.

For Hanley, a veteran researcher who’s been continuously funded for more than

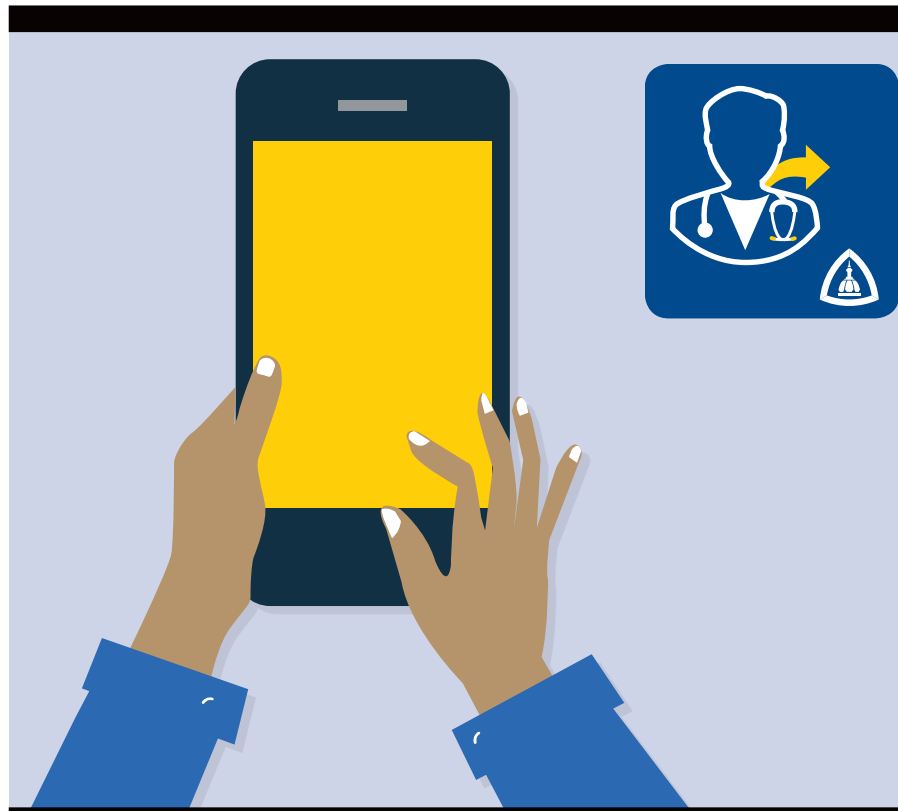
35 years and won more than 60 National Institutes of Health grants, the center represents an unprecedented and invaluable tool that has the power to transform clinical trials in the U.S.

“When I started my own multisite clinical trial work, there were no resources like this, so I had to build up expertise in

“THE PROGRAM IS SPECIALTY AND DISEASE AGNOSTIC, HELPING RESEARCHERS WITH TRIALS COVERING ANY CONCEIVABLE AREA OR ILLNESS.”

—DANIEL HANLEY

patient recruitment, ethical approval and FDA protocols over the years,” Hanley says. “Now we have the ability to provide clinical trial researchers a team to solve these problems with them.”



## Introducing the Johns Hopkins Doctor Referral App

The Johns Hopkins Doctor Referral app is a pilot program that offers referring providers a simple and quick way to identify the appropriate Johns Hopkins Medicine physician to contact to make a referral, schedule a consultation or discuss research.

Available for free in the Google Play Store and Apple App Store, the app also enables you to text information to your patients about how they can make an appointment with the Johns Hopkins physician to whom you are referring their case.

At this time, only full-time Johns Hopkins faculty members in the departments of surgery, neurosurgery, urology, orthopaedics, otolaryngology-head and neck surgery, plastic and reconstructive surgery, as well as the division of cardiology are listed in the app.

Visit [bit.ly/hopkinsapp](https://bit.ly/hopkinsapp)

# NeuroLogic

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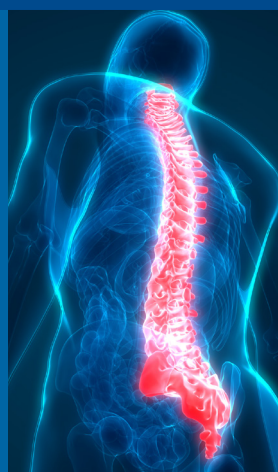
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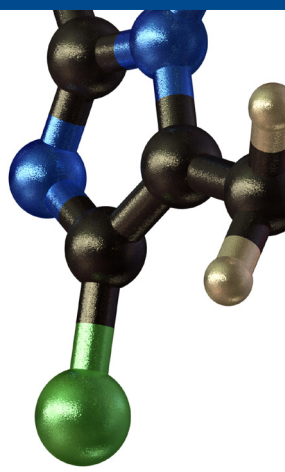
NEWS FROM THE JOHNS HOPKINS DEPARTMENTS OF NEUROLOGY AND NEUROSURGERY

Inside



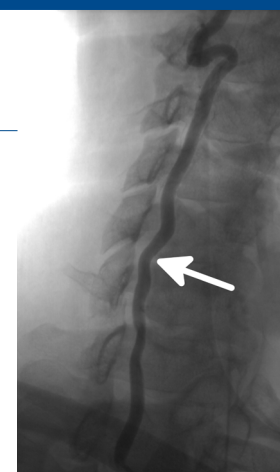
1

A Clinical Innovation: Shortening the Spinal Column to Loosen Tethered Cords



2

For Spinal Fusion: Certain Antihypertensive Drugs May Improve Outcomes



3

A Rare Diagnosis of Spinal Cord Stroke and the Road to Recovery