

Pain Consult

DEPARTMENT OF PAIN MANAGEMENT | 2018

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Dear Colleagues

This year marked the 20th anniversary of the Cleveland Clinic Pain Management Symposium in February. More than 200 people attended this year's dynamic event, where a number of my Cleveland Clinic colleagues

presented alongside other internationally renowned faculty.

Just as our annual meeting endeavors to promote a better understanding of the pathophysiology of pain and examine current therapeutic advances, this publication highlights the latest insights from our Pain Management team.

As we continue to confront the opioid crisis and gain knowledge on the latest pain management tools available to us, I think there are three objectives to keep in mind. We must:

- Use the medications we know judiciously to help our patients in their struggle with pain.

- Continue to advance diagnostic accuracy and treatment technology so we can treat patients at the right time to produce the best outcomes.
- Work to educate and engage our patients on the importance of altering their personal habits as a means to achieve optimal pain management and quality of life.

I'd like to thank Dr. Jan Van Zundert, who presented at this year's symposium, for joining me in a discussion on the opioid crisis for this issue (starting on the next page). Finally, I would like to extend a personal invitation to attend the 21st Annual Pain Management Symposium, March 16-20, 2019, at the Hard Rock Hotel in San Diego. For more information, be sure to visit ccfcm.org/2019Pain.

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The Opioid Epidemic:

What Can We Learn from Europe?

In 2017, the U.S. Department of Health and Human Services declared the opioid crisis a public health emergency. But the problem began brewing long before last year, with the age-adjusted rate of drug overdose deaths increasing more than three times between 1999 (6.1 per 100,000) and 2016 (19.8 per 100,000), according to the Centers for Disease Control and Prevention.

How does the opioid epidemic in the United States compare with opioid use in other developed nations, such as European countries? Consider the disparity in these statistics:

- 11.5 million people misused prescription opioids in the U.S. in 2016, according to the 2016 National Survey on Drug Use and Health. (The total U.S. population in 2016 was approximately 323 million people.)
- There are 1.3 million high-risk opioid users in Europe, according to a report from the European Monitoring Centre for Drugs and Drug Addiction. (The European population reporting number is 511 million; see map on p. 5.)

A conversation with two leading pain management experts, Richard Rosenquist, MD, and Jan Van Zundert, MD, PhD, provides insight into opioid use and abuse in the U.S. compared with Europe. Dr. Rosenquist is Chairman of Cleveland Clinic's Department of Pain Management. Dr. Van Zundert is an anesthesiologist who heads the Multidisciplinary Pain Center at Ziekenhuis Oost-Limburg in Genk, Belgium.

Q: Given the current opioid epidemic in the United States, are pain management patients today more receptive to other treatments?

Dr. Rosenquist: It's a mixed bag. We have people who hear the message and are worried, some of whom have been taking opioids for a while. Even some people who are taking them legitimately are beginning to have questions. But there are others who are so physically or psychologically dependent on opioids that a cataclysmic event could come along and they would not change their minds: They can't or don't want to imagine life without opioids.

This has been the ongoing battle. Physicians who bought into opioids for chronic pain started people on the medications and were told to just give them more and more if the meds didn't work and eventually the patients would get pain relief. Well, that didn't work. Long-term use of opioids is only partially effective in most cases and is associated with many adverse long-term effects on the body.

Q: Has the same message about upping the dosage to provide pain relief been prevalent in Europe too?

Dr. Van Zundert: In the past 20 or 30 years in Europe, there has been an increase in the treatment of pain just as in the U.S. But opioid treatment is rather limited. We've known since the last decade that opioids don't have the desired effect, and most people stopped using them due to side effects or noneffectiveness. That seems to be a bit different than in the United States, where opioid usage was increasing. If the opioids didn't work, the dosage was increased.



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Jan Van Zundert, MD, PhD

Q: So what other pain treatments can be used instead of opioids?

Dr. Rosenquist: If you look at the things that are good for chronic pain, they are the same things that are generally good for your health: eat a healthy diet, don't smoke, exercise regularly, maintain a healthy weight and get a decent night's rest — all those things help with chronic pain. You can also do things such as mindfulness-based stress reduction, acupuncture, physical therapy and injections, which may help provide some period of relief or reduced pain. But unless you combine those things with the pillars of general health, you don't get better in the long run.

Dr. Van Zundert: In chronic noncancer pain, we try to avoid opioids and prefer minimally invasive percutaneous interventional pain management, such as epidural steroids for subacute radicular pain and radiofrequency and pulsed radiofrequency treatment for a lot of other conditions. We also recommend pain rehabilitation programs that include coping, acceptance and commitment to reduce the pain as much as possible. The programs stress the importance of a realistic approach and goals. I think in Europe we are a bit more careful watching our patients and not thinking we always have to reach the goal of zero pain. I hear from my American colleagues that the "careful watching" approach is very difficult to explain to American patients.

Q: What are we doing at Cleveland Clinic to foster conservative management of pain patients and help eliminate the opioid epidemic?

Dr. Rosenquist: There are a lot of nonopioid-based approaches from an interventional standpoint that we are incorporating into larger, multidisciplinary programs. For example, we have a novel program for treating people with chronic back pain who have not had surgery, called Back on TREK, that is psychology- and physical therapy-based with physician oversight. We also have a long-standing Chronic Pain Rehabilitation Program that consists of a three-week outpatient multidisciplinary program.

In addition, we are providing education to surgical staff, physician assistants, nurses and other healthcare providers all across the system. We are trying to get surgical teams to change expectations: Prescribe the appropriate amount of pain medication after surgery, and tell patients they will get five or six days

Helping Patients Help Themselves

Recognizing the need for complementary pain management strategies, Cleveland Clinic's Department of Pain Management is launching a program called the "Four Pillars of a Healthy Lifestyle for Pain Management." Pain specialists will offer a class that teaches patients ways to improve sleep, diet, exercise habits and stress management, all of which have a substantial impact on inflammation, a primary cause of chronic pain.

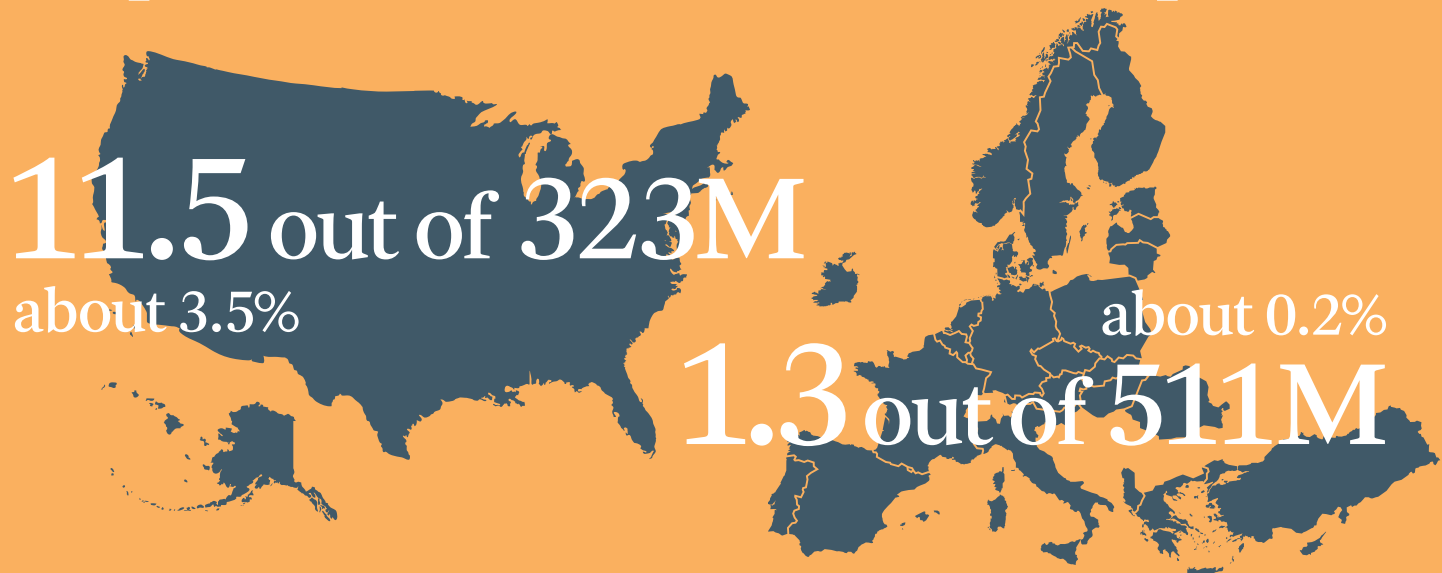
For more on the new program, go to consultqd.clevelandclinic.org/pmtrain.

of opioid medication after selected surgical procedures, followed by a transition to nonopioid-based analgesics, and that pain or discomfort is common as part of the healing process and is not the end of the world. Creating that attitude on a national basis is something we all have to do. There is no magic bullet for complete pain relief.

Q: Why do you think European countries have less of a problem with opioid addiction and are more accepting of conservative approaches to pain management?

Dr. Van Zundert: I think perhaps it's because healthcare is much more regulated in Europe. There are regulatory agencies at the European Union level, as well as national healthcare organizations within each country. Hospitals, general practitioners and pharmacies must follow certain rules and regulations. Take referrals, for instance: Pain patients

Opioid Misuse in the U.S. vs. Europe



The above graphic illustrates the vast disparity in the number of people misusing opioids in the U.S. compared with Europe. “High-risk” is defined as misusing prescription opioids. American stats are from the 2016 National Survey on Drug Use and Health; European stats are from the European Monitoring Centre for Drugs and Drug Addiction. 2016 statistics. Please note, numbers are rounded and approximate.

cannot go directly to a pain center. They must first see a general practitioner or a second-line specialist. Also, regulations forbid advertising by pain centers and pharmaceutical companies in Belgium and other European countries.

Q: What can the U.S. healthcare community learn from Europe’s approach to pain management and addiction?

Dr. Van Zundert: The main message is stop prescribing opioids for chronic pain and practice more evidence-based medicine. Of course, that’s not the cure-all solution. But after 20 years, we see there is no evidence of the effectiveness of opioids on a widespread, long-term basis. A combination of more regulations in healthcare, more emphasis on evidence-based medicine guidelines and a commitment to treating patients only with what they need will prevent a lot of problems. We are all stakeholders in this same issue, and we have to turn this around from a negative story to a positive story.

Q: What can pain management physicians do to change the narrative on opioid abuse?

Dr. Rosenquist: We have to do everything we can to help patients understand that we’re interested in their health and trying to give them the best possible care. We want to work with patients as part of the team — get them engaged in the overall process. We don’t have a crystal ball that we can look into and figure out what’s wrong and how to fix it. I enjoy working with patients to find nonopioid alternatives and promote overall good health and function. And it’s rewarding when you see people succeed. I’ve had many more people thank me for getting them off opioids than I have for putting them on medications.

Dr. Rosenquist is Chairman of Cleveland Clinic’s Department of Pain Management.

Dr. Van Zundert is head of the Multidisciplinary Pain Center at Ziekenhuis Oost-Limburg in Belgium.

A Half Century of Neuromodulation

Today, closed loop stimulation is proving highly effective



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FEATURING NAGY MEKHAIL, MD, PHD

Since the first medical neuromodulation procedure was performed in 1967 in Australia by Dr. Norman Sheely, pain specialists, researchers and industry have been working to improve and perfect this treatment modality.

After more than half a century and dozens of iterations in technology, closed loop stimulation is a breakthrough. It has the propensity to help patients manage their pain. Nagy Mekhail, MD, PhD, Director of Evidence-Based Pain Management Research at Cleveland Clinic, has practiced many therapies over the years and is excited by the promise of closed loop spinal cord stimulation.

“Neuromodulation has been used for many pain conditions, but it has had its limitations,” Dr. Mekhail says. “Patient feedback from the preliminary study done in Australia is telling us that the most recent advances in the technology provide great hope for patients with chronic pain conditions, compared with previous neuromodulation technologies we have used.”

Neurostimulation over the past 50 years has gone through many phases. Starting with unipolar stimulation of nerves, pain specialists moved to spinal cord stimulation with multiple leads using the following fixed-input technologies:

- Dual leads / Tripolar leads / Paddle leads
- Constant current / Constant voltage
- Wave forms: “Tonic” / Burst / Multiwave Platform
- High frequency of stimulation (“HF10”)

Most recently, stimulation of the dorsal root ganglion has been used to provide pain reduction and improve functional capacity and quality of life for patients with complex regional pain syndromes. However, most of the clinical trials throughout the 2000s have shown that conventional spinal cord stimulation has failed to achieve long-term results. Dr. Mekhail notes that more vigorous study designs have been needed to establish evidence-based applications of

neuromodulation therapy in emerging indications of pain management.

Studies looking more closely at the effectiveness of these technologies and methods have shown a 50-50 response from patients at best, and even when patients reported some therapeutic pain relief, it was very limited. “There has been no way of knowing the real dose of the stimulation. With all the current technology, we assumed we knew better, and sometimes we were correct and other times the new technologies did not work as well,” says Dr. Mekhail.

He says that fixed-input spinal cord stimulation systems may drive patients to use subtherapeutic electrical doses due to overstimulation events. “When we ask patients how they feel, they would say they felt a sensation, yes, but not necessarily pain relief,” Dr. Mekhail says. “And the studies showed that pain relief diminishes by 70 percent over time and ultimately leads to no relief.”

“In hindsight, we missed with these technologies,” says Dr. Mekhail. “We accepted the uncertainty, and patients didn’t get the relief we expected.” In fact, in 2017, the global market showed about 100,000 spinal cord stimulators implanted annually, with about 25 percent of them having unsatisfactory outcomes over time, which frustrates patients and costs millions of dollars.

Neuromodulation in the form of spinal cord stimulation is a growing class of therapies that has been in common use since the 1980s to help restore function and relieve patients’ neurologically based pain symptoms.

CLOSED LOOP STIMULATION

Closed-loop feedback technology was introduced in 2013. The idea came from electrophysiologic studies on the spinal cord neurons, which record the electrically evoked compound action potential (ECAP), which represents the synchronous firing of a population of electrically stimulated nerve fibers. This technology allows the spinal cord stimulation device to communicate with the spinal cord neurons and adjust the dose of stimulation accordingly.

Dr. Mekhail explains that it delivers and maintains a therapeutic electrical dose while preventing overstimulation of the dorsal column. In the preliminary study, when patients crossed over to closed loop control, they used the appropriate stimulation dose for the neurons and maintained pain relief at a therapeutic level 90 percent of the time.

“This is a unique way of dealing with the nervous system. The device is listening to the neurons of the spinal cord. It is interacting with the living nerve structure, and this makes it much more effective,” Dr. Mekhail explains. “With closed loop stimulation,

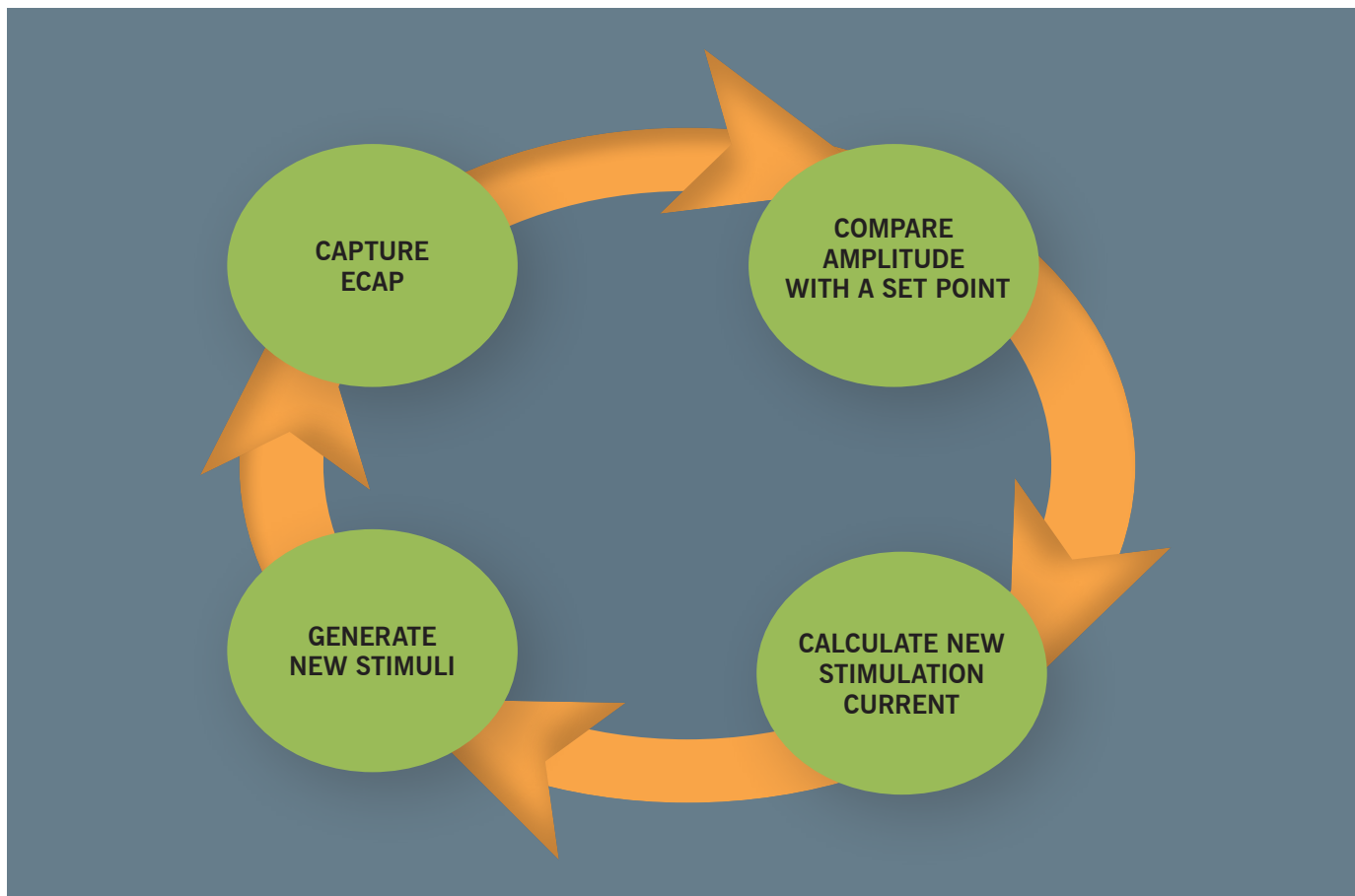
the Australia study showed that 81 percent of patients have good pain relief — this is marvelous. The beauty of this is that there is always contact between the stimulator and the nerves.”

Today, closed loop spinal cord stimulation is being studied in the U.S. in a large multicenter double-blind randomized trial. Ideally, it will gain approval from the FDA in the near future.

Dr. Mekhail is Director of Evidence-based Pain Management Research in Cleveland Clinic’s Department of Pain Management.

Figure

In closed loop stimulation, the spinal cord stimulation (SCS) generator measures the response of neurons to stimulation ECAP (electrically evoked compound action potential) and makes real-time adjustments to stimulation. Such adjustments are designed to keep patients within the individual therapeutic window.



Can Stem Cells ‘Stem’ the Use of Opioids? Study Shows Great Promise



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Addressing the challenge of opioid tolerance and overdose, Cleveland Clinic research finds stem cells may improve opioid therapy.

Stem cell therapy may prevent and even reverse opioid tolerance, according to Cleveland Clinic research. The recently published findings demonstrate that “this emerging therapeutic strategy has shown promise to impact clinical practice and improve the efficacy and safety of opioid therapy.”

The widespread chronic use of opioids in pain management often leads to opioid tolerance (OT) and worsened pain, an effect known as opioid-induced hyperalgesia (OIH). The amount of opioids prescribed increased by three times between 1999 and 2015 in the U.S., and opioid-related deaths claimed more than 42,000 lives nationwide in 2016.

There is a “need to find new solutions for OT and OIH as part of a national effort to combat chronic pain as a public health issue and the opioid epidemic as a national crisis,” writes the research team.

PRECLINICAL TRIALS

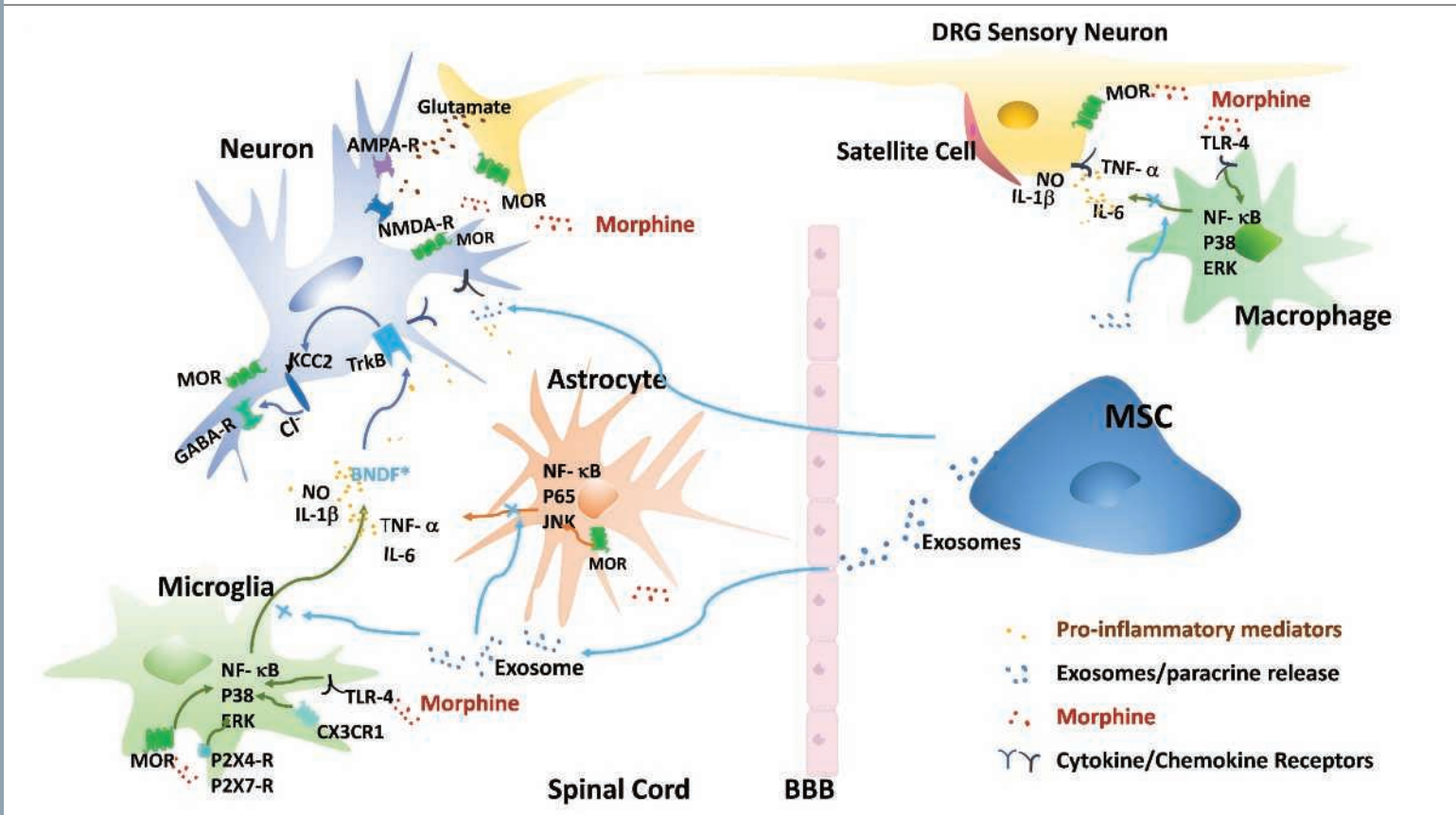
In preclinical trials, the researchers found that mesenchymal stem cells (MSCs) had “powerful therapeutic effects on OT and OIH.” The MSC therapy effectively prevented and reversed OT and OIH in rats and mice and suppressed neuroinflammation in the spinal cord. The research found that using both intrathecal and intravenous transplantations were safe and that “the preventive and therapeutic effects were long-lasting and consistent across different assessment schemes.”

“MSC therapy has enormous potential to profoundly impact clinical practice and improve opioid efficacy and safety,” says principal investigator Jianguo Cheng, MD, PhD, of Cleveland Clinic’s Departments of Pain Management and Neurosciences.

Using stem cell transplantation may allow for opioids to be more effective at lower doses in the treatment of pain, thus minimizing the risk of overdosing and improving patient safety. Dr. Cheng says he and his team see plausible reasons that this treatment could be practical: its efficacy, safety, cost-effectiveness and the ease of clinical application. The team is hoping to get FDA approval and to secure funding by the end of the year in order to translate the laboratory findings into clinical trials and applications.

Dr. Cheng is on the staff of the Pain Management Department, a Professor of Anesthesiology and Director of the Cleveland Clinic Multidisciplinary Pain Medicine Fellowship Program.

The research team noted: “There is a need to find new solutions for opioid tolerance and opioid-induced hyperalgesia as part of a national effort to combat chronic pain as a public health issue and the opioid epidemic as a national crisis.”



Figure

Postulated mechanisms of the therapeutic and preventive effects of MSC-TP. MSCs inhibit OT and OIH through suppression of neuroinflammation. Repeated administration of morphine leads to activation of microglia and astrocytes in the spinal cord and macrophage and satellite cells in the dorsal root ganglion (DRG). Morphine directly activates a Toll-like receptor (TLR-4) and leads to development of opioid tolerance. Morphine also leads to MOR-mediated expression of purinergic receptors P2X4R and release of brain-derived neurotropic factor (BDNF) from microglia. OIH develops as a result of sensitization of lamina I

neurons mediated by microglia-to-neurons signaling through the P2X4–BDNF–TrkB pathway. Mesenchymal stem cells may inhibit neuroinflammation by paracrine secretion of a multitude of exosomes, microvesicles and soluble factors that include indolamine 2,3-dioxygenase (IDO), prostaglandin (PGE)2, interleukin (IL)-10, transforming growth factor (TGF)-b, leukemia inhibitory factor (LIF), human leukocyte antigen-G5 (HLA-G5) and tumor necrosis factor (TNF)-a-induced gene/protein 6 (TSG-6), among others. MSCs interact with microglia, astrocytes, macrophages and other immune cells through these mediators and various intracellular signaling pathways to inhibit

the production and release of interleukin 1b (IL-1b), IL-6, TNF-a, BDNF, nitric oxide (NO), and other pro-inflammatory mediators that are critical to the development of OT and OIH. BBB, blood-brain barrier; ERK, extracellular signal-regulated kinase; GABA, gamma- aminobutyric acid; JNK, c-Jun N-terminal kinase; KCC2, potassium-chloride co-transporter 2; MOR, mu-opioid receptor; NF-jB, nuclear factor kappa B; NMDA-R, N-methyl-D-aspartic acid receptor; TrkB, tyrosine kinase B.

From Li F, Liu LP, Cheng K, Chen ZB, Cheng J. The use of stem cell therapy to reverse opioid tolerance. *Clinical Pharmacology & Therapeutics*. 2018;103(6):971-4. DOI:10.1002/cpt.959.)

Guiding Research for Ketamine

Use for CRPS



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FEATURING JIJUN XU, MD, PHD

As physicians look for nonopioid treatments to manage pain, various types of infusion therapies are being reassessed for efficacy. Intravenous ketamine infusion therapy has been used for difficult-to-treat chronic pain syndromes such as complex regional pain syndrome (CRPS). But it has been used cautiously because of a number of side effects, including dissociative phenomena, hallucinations, elevated blood pressure and possible liver and bladder injury.

Since the 1970s, ketamine's primary medical use has been for general anesthesia, and it is now being used in intensive care and pediatric procedures, in emergency medicine, and as a secondary treatment for certain psychiatric conditions, including depression.

"This medicine has been used before for pain, but because of its adverse effect profile, it was discouraged for a while," says pain specialist Jijun Xu, MD, PhD. "In recent years it has come back as an option for refractory chronic neuropathic pain because it works on one of the key receptors that mediates nerve pain."

CRPS is one of the most challenging clinical pain syndromes to treat, with amplification of pain signals in the central nerve system (or central sensitization). Dr. Xu says ketamine has been used around the world in different ways to treat CRPS, but to date there has been little research and no consensus protocol. Over the past two years, Dr. Xu has been doing extensive research on the drug with support from the Reflex Sympathetic Dystrophy Syndrome Association. CRPS was formerly known as reflex sympathetic dystrophy (or RSD).

The objective of his research has been to come to a consensus on the use of ketamine for the treatment of CRPS and to develop a reference protocol for future studies.

RESULTS OF THE RECENT RESEARCH

Dr. Xu's research included a survey of 351 medical professionals from around the world on how they use ketamine to treat pain associated with CRPS. The survey asked questions about inpatient and outpatient treatment, children versus

adults, safety, and basic demographic information. In most cases, ketamine was used at subanesthetic doses with close management by nurses to avoid adverse events and improve outcomes for patients.

In Dr. Xu's study, participants were titrated to "drowsy to moderate sedation" or pain reduction by 50 percent using a numeric pain rating scale. Study participants agreed that pain rating was the primary measurement used to assess how fast the infusion should happen and its impact. The majority of study participants reported pain relief lasting between one and six months.

Dr. Xu says this consensus statement for inpatient and outpatient care serves as a starting point for statistical validation of formal guidelines and a more uniform approach to research protocols. "Ketamine has great promise as a treatment for CRPS, but we need to be cautious," says Dr. Xu. "We have

Current evidence indicates that short-term use of subanesthetic ketamine infusion under clinical supervision is safe.

to be careful about the dose, the duration of use and the side effects. Current evidence indicates that short-term use of subanesthetic ketamine infusion under clinical supervision is safe, but we don't know the long-term cognitive effects it could have. We need more data and must gather more extensive outcome measurements."

The next step is to validate the safety and efficacy of ketamine through controlled clinical trials. "With more feedback, we can make it a treatment modality that is a safe and effective treatment for CRPS," Dr. Xu concludes.

Dr. Xu is a pain management specialist in Cleveland Clinic's Department of Pain Management. He served as chief fellow in 2014.



KETAMINE FOR CRPS: A BRIEF CASE STUDY

Faith Modic, 35, of Cleveland has suffered from chronic regional pain syndrome (CRPS) in her right arm since 2005 and uses a wheelchair to get around due to chronic neurofibromatosis. For six years, she has been coming to Cleveland Clinic for intermittent ketamine infusions to relieve her pain.

She receives five days of ketamine infusion for six hours each day. (Dosage: ketamine 500 mg in 1,000 ml 0.9 percent normal saline at 20-70 mg/hour.) Following treatments, she has pain relief for about four months.

“The strongest clinical evidence of ketamine infusion’s effectiveness for chronic pain comes from CRPS patients,” says Jijun Xu, MD, PhD. “Ms. Modic is one of the example patients who responds well to this treatment. By titrating the infusion dose, we have been able to reduce her overall pain level from about

10 to 3 out of 10. Her general functionality is improving as well.”

Ms. Modic reports having “amazing results.” Following infusions, she is able to use her arm, feed herself and be touched without having excruciating pain. She is no longer bedridden and can get around more easily in her wheelchair.

She says ketamine treatment provides the added benefit of reducing her joint pain and the pain caused by her neurofibromatosis.

To keep the hallucinations that arise during treatment at bay, she watches DVDs of familiar television shows during the infusion process.

Improving Centralized Pain Management



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FEATURING ROBERT BOLASH, MD

Historically, the medical community has exclusively approached pain management by targeting the source location of the pain. However, physicians are now learning the importance of attacking the central component of pain as well as the peripheral target.

Centralized pain indicates that there is some hypersensitivity that the patient has developed, which has either been amplified by a peripheral pain problem or has originated from a source within the central nervous system. Classic centralized pain disorders include fibromyalgia, some temporomandibular joint disorders and irritable bowel syndrome.

“Even peripheral pain conditions can have varying degrees of centralization. If you’re struggling to address what appears to be a peripheral pain diagnosis, consideration should be given to central sensitization as the missing link,” explains pain specialist Robert Bolash, MD. “For example, if you’re treating a nociceptive pain complaint such as osteoarthritis and the patient still has unmanageable pain, consider the other factors that may be involved.”

WAYS TO MEASURE PAIN

Pain scale: Physicians historically requested patients to rate the intensity of their pain using a numerical scale (0 to 10 or 0 to 100). While these scales are convenient to administer, they offer no opportunity to assess function. There’s also a lack of standardization across populations.

Impact on daily life and function: Function scales (e.g., Oswestry Disability Index and Pain Disability Index) allow patients to measure pain by indicating how much their pain impacts their ability to perform daily activities. Patients may be asked to rate how much their pain interferes with their ability to do household chores, socialize with friends, maintain personal hygiene and sustain an active sex life. The Cleveland Clinic Pain Management team considers a treatment successful if the patient is able to do something they couldn’t do before, regardless of the change in pain levels.

CHALLENGES IN TREATING CENTRALIZED PAIN

When centralized pain is involved, physicians need to take a whole-person, broad perspective by treating the brain and nervous system as well as the peripheral target. Physicians are beginning to understand that centralized pain requires unique treatment strategies, which vary in number and type when compared with peripheral pain treatments. In turn, physicians need to educate their patients on centralized pain and how the brain is involved in pain processing.

Central sensitization, or a centralized pain state, may represent a number of conditions that interact to amplify pain signals. These originate from upregulated peripheral input but are facilitated by a heightening of pain amplification from the brain. Successful pain management is achieved by addressing both components.

We must recognize the importance of addressing both the central and peripheral components of pain. For example, osteoarthritis of the knee is a prototypical peripheral nociceptive pain complaint manifesting in sharp, use-related pain and inflammation. “Although the initial pain is peripheral, we’ve discovered that some patients also experience heightened centralized pain resulting from the constant barrage of painful inputs,” notes Dr. Bolash. “It has been demonstrated that patients who have high pain intensity before knee replacement and low pain thresholds are more likely to report constant, ongoing pain after knee replacement.” This suggests an opportunity to address centralized pain by using a comprehensive treatment strategy that not only targets the peripheral inflammation but also the central sensitization.

Cleveland Clinic pain experts are evaluating how to best optimize a patient’s centralized pain before surgery, during recovery or before being treated by other physicians for other conditions. “If we identify a patient with heightened preoperative pain, we often suspect that they may also have a lot of challenges during recovery, require an extended hospital stay and need additional therapy,” says

Dr. Bolash. “Getting the baseline pain addressed as much as possible before surgery helps improve surgical outcomes.”

EFFECTIVE PAIN MANAGEMENT STRATEGIES

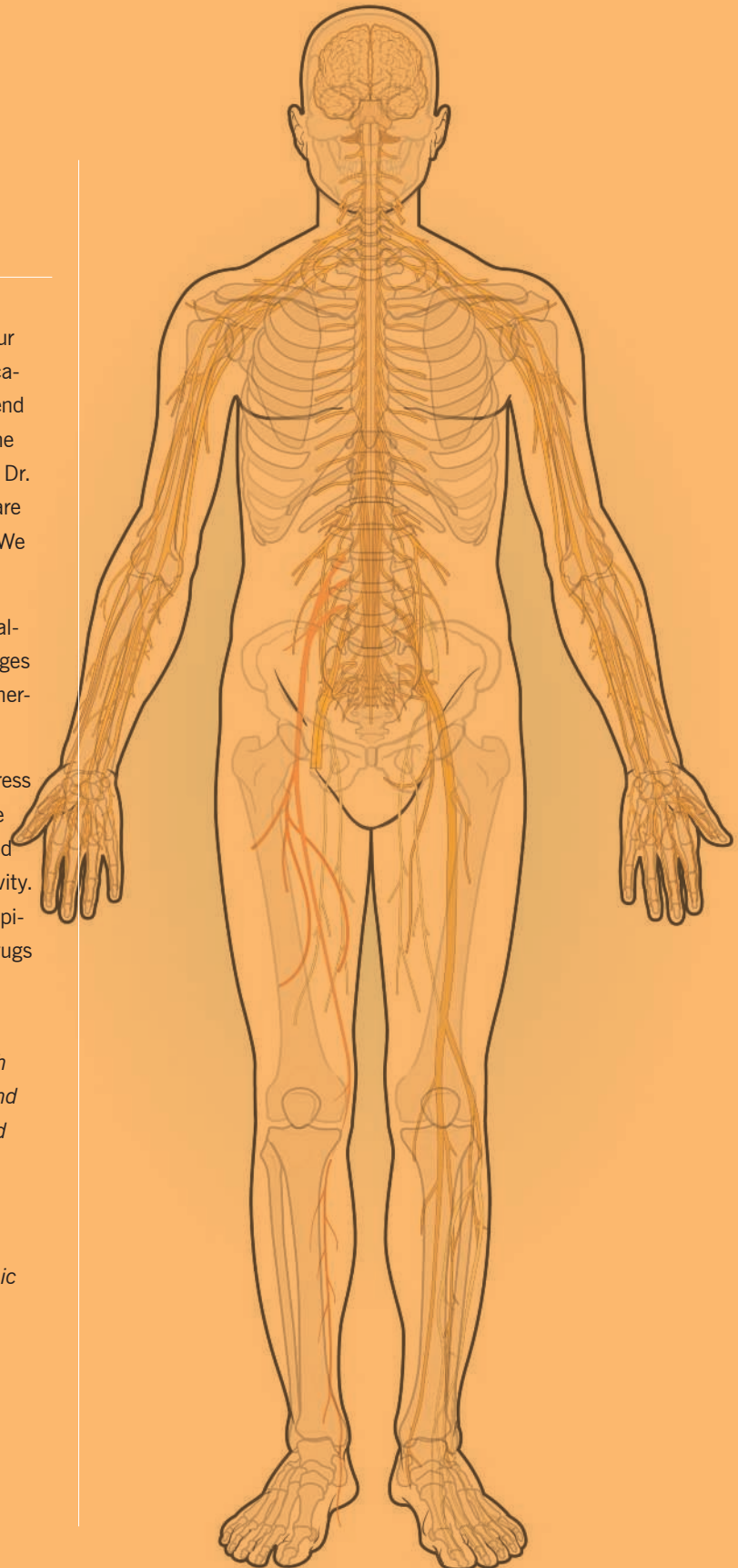
We employ various treatment strategies, including medical, cognitive and physical therapies, to address centralized pain. Our physicians work with patients to identify the appropriate medications and physical therapies while pain psychologists recommend effective cognitive strategies. “Each strategy will likely help the patient’s pain level improve by a certain percentage,” explains Dr. Bolash. “The exciting part is that pain management therapies are often stronger and more effective when used in combination. We call this phenomenon therapeutic synergy.”

An effective centralized pain treatment plan must be individualized. It’s important to discuss the advantages and disadvantages of each therapy, highlighting the benefits of using multiple synergistic therapies.

While anti-inflammatory drugs and opioid medications can address peripheral pain generators, these medications are ineffective in treating centralized pain. In fact, using opioids for centralized pain could be harmful to patients by exacerbating pain sensitivity. According to Dr. Bolash, membrane stabilizers, selective norepinephrine reuptake inhibitors and ketamine can be effective drugs for centralized pain management.

Cleveland Clinic pain management specialists often work with primary care providers or surgeons to help patients understand their unique comfort zone and recommend basic or advanced management strategies as needed.

Dr. Bolash is a staff physician with the Department of Pain Management. He completed his fellowship with Cleveland Clinic in 2013.



Introducing **Digital Health** for Pain Management



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FEATURING BENJAMIN ABRAHAM, MD

Using telehealth to provide care is No. 5 on Cleveland Clinic's list of the top 10 medical innovations for 2018, and with good reason: The service is booming, with 7 million patients nationwide expected to use telehealth in 2018.

Cleveland Clinic Express Care® Online is the moniker for virtual outpatient visits, and each institute in the system is enabling physicians to make these visits available to the appropriate subset of patients, whether it be for follow-up care or consultations for certain conditions or procedures.

Since 2017, 43 pain management specialists have been trained on using the Express Care Online platform and each has designated weekly times on their schedule for virtual appointments. The physicians and patients can choose to have the appointment via their smartphone, tablet or computer. Pain Management telehealth visits are available for:

- Follow-up to procedures/therapy.
- Non-narcotic medication refills.
- Questions that are challenging to answer via email.
- Clarification of a treatment plan.
- Consultations on a procedure.

Pain Management Specialist Benjamin Abraham, MD, says telehealth visits have been helpful for consulting with patients considering vascular surgery. Specifically, he has consulted with patients with the rare median arcuate ligament syndrome, which is treated only at a few centers in the U.S. He says these virtual appointments help him get acquainted with patients and saves them travel time. He also finds telehealth visits useful for follow-up care — specifically for patients with chronic pain conditions such as fibromyalgia.

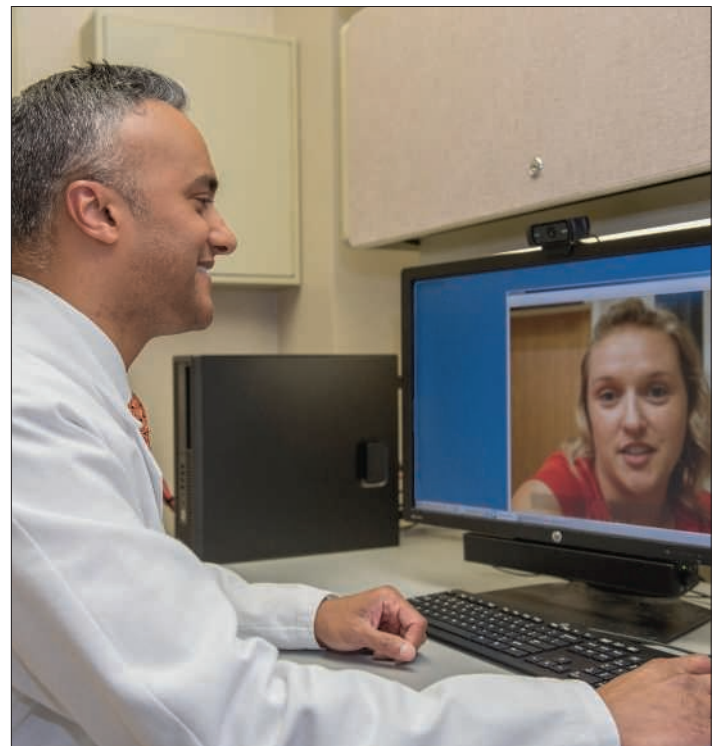
“In the past I may have had a phone call with the patient, but now virtual visits allow for a much

better connection,” says Dr. Abraham. “They can show me where the pain is, and I can show them charts or pictures when necessary. And for those considering coming for surgery, we can cover their CAT scans and surgical test results. We can make sure they have everything they need before they make the trip to Cleveland.”

Based on a patient's history and/or diagnosis, physicians help patients in determining the length of appointment they need, which corresponds to its cost. The Pain Management Department offers three levels of appointment: simple, moderate and complex.

“Interest in telehealth varies, but often once patients see how it works, they are satisfied and want to come back,” he says. If Dr. Abraham's virtual appointment slot on Tuesdays is not taken as an online appointment, it switches to a conventional in-person appointment.

Dr. Abraham is a pain specialist in Cleveland Clinic's Department of Pain Management.



At right,
Dr. Abraham
conducts a
virtual visit
with a
fibromyalgia
patient.

Staff Awards and Achievements

Richard W. Rosenquist, MD, serves in the following leadership roles:

- Chairman, American Board of Anesthesiology Pain Medicine Examination Committee
- American Society of Anesthesiology (ASA) — Member of Committee on Pain Medicine and Committee on Economics and an Advisor for the Relative Value Scale Update Committee
- American Society of Regional Anesthesia and Pain Medicine (ASRA) — Vice Chair of Faculty Development Committee
- American College of Surgeons Pain Education Project member
- National Committee for Quality Assurance Opioids and Pain Management Measurement Advisory Panel member

Robert Bolash, MD, is the recipient of the 2018 Pain Medicine Staff of the Year Award. He is the Scientific Abstract Co-Chair for the American Academy of Pain Medicine and was appointed as a full faculty member with the American Society of Regional Anesthesia and Pain Medicine.

Jianguo Cheng, MD, PhD, was elected President of the American Academy of Pain Medicine (2018-2019). He is a member of the Health and Human Services Pain Management Best Practices Interagency Task Force (PMTF) and the Centers for Medicare & Medicaid Services (CMS) Expert Work Group, which is developing clinical quality measures.

Nagy Mekhail, MD, PhD, is Chair of the Interventional Pain Practice Examination Board, a member of the Pain Committee of the American Society of Anesthesiologists, and a Member of the World Institute of Pain Executive Board.

Beth Minzter, MD, is President of the Ohio Society of Anesthesiologists.

Jijun Xu, MD, PhD, received a MENTR scholar award from Cleveland Clinic Lerner Research Institute, an innovative two-year professional staff development program to support his study on chemotherapy-induced peripheral neuropathy.

Select Pain Management Trials Now Enrolling

Cleveland Clinic’s Department of Pain Management is enrolling patients in a range of ongoing clinical studies, including those listed here. For more trial listings, visit clevelandclinic.org/paintrials.

| Study Overview | Investigator and Contact | Key Inclusion Criteria |
|---|--|---|
| <p>HI-FI Comparing ultra-high versus traditional pulse widths using the ALGOVITA® SCS system high-fidelity stimulation in the treatment of chronic back and/or leg pain.</p> | <p>PI: Robert Bolash, MD Call: 216.444.3134</p> | <p>Patients 18-65 diagnosed with chronic, intractable pain of the back and/or legs that has been refractory for 3 months after previous conservative therapy.</p> |
| <p>MOTION™ Examining functional improvement (defined by increased activity levels) in lumbar spinal stenosis patients with neurogenic claudication who are treated with the MILD® procedure.</p> | <p>PI: Shrif Costandi, MD Call: 440.695.4000</p> | <p>Patients age 50-80 experiencing symptoms for at least 3 months with comorbid conditions commonly associated with spinal stenosis.</p> |
| <p>NEVRO Evaluating the effectiveness of 10 kHz SCS plus medical therapy to medical therapy alone for the treatment of chronic lower limb pain from diabetic neuropathy.</p> | <p>PI: Jijun Xu, MD, PhD Call: 216.445.0466</p> | <p>Patients with painful diabetic neuropathy of the lower limbs who remain symptomatic despite therapy with pregabalin and ≥ 1 other class of analgesic.</p> |



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clevelandclinic.org/refer123

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View Outcomes books at
clevelandclinic.org/outcomes.

CME OPPORTUNITIES

Visit ccfcme.org for live and online offerings from Cleveland Clinic's Center for Continuing Education.

OUR STAFF

For a full list of Pain Management staff, go to
clevelandclinic.org/painmanagementdoctors.

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WE WANT TO HEAR FROM YOU Please visit clevelandclinic.org/painsurvey to take a brief survey about *Pain Consult*, and you will be entered into a drawing for a chance to win one of two \$100 Amazon gift cards.

Cleveland Clinic is an integrated healthcare delivery system with local, national and international reach. At Cleveland Clinic, more than 3,500 physicians and researchers represent 140 medical specialties and subspecialties. We are a main campus, more than 150 northern Ohio outpatient locations (including 18 full-service family health centers and three health and wellness centers), Cleveland Clinic Florida, Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas, Cleveland Clinic Canada and Cleveland Clinic Abu Dhabi. In 2018, Cleveland Clinic was ranked the No. 2 hospital in America in *U.S. News & World Report's* "Best Hospitals" survey. The survey ranks Cleveland Clinic among the nation's top five hospitals in 12 specialty areas, and the top hospital in heart care (for the 24th consecutive year) and urologic care.