ASRA NEWS

A PUBLICATION OF THE AMERICAN SOCIETY OF REGIONAL ANESTHESIA AND PAIN MEDICINE

NOVEMBER 2016

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ASRA PAIN MEDICINE EDUCATION RESEARCH

Advancing the Science and Practice of Regional Anesthesia and Pain Medicine

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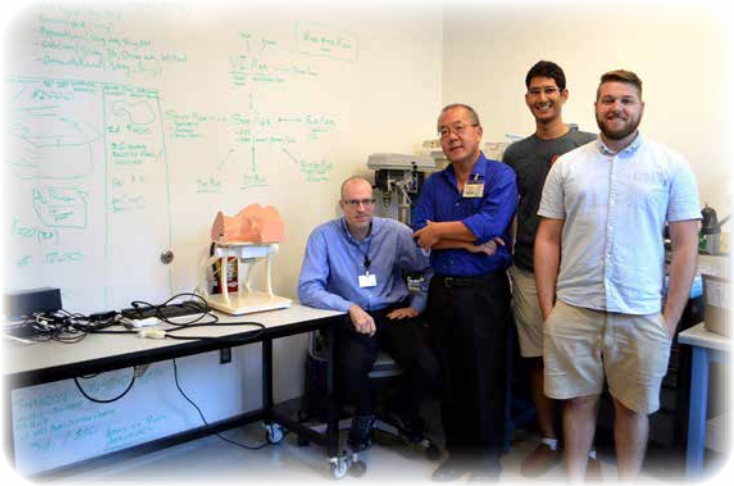

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President's Message

Information You Must Have . . . and Use

This message is about our ASRA Website features. Members of the ASRA staff and savvy volunteers have worked together to bring you a cornucopia of services that places us at the forefront of informatics for members. Some of them are available only to members; once you use them, you will understand why we made the decision to restrict these services to members only.

If you are about my age, you may remember receiving telegrams: short, no more than five words, one idea or concept at a time. The excitement of getting a special delivery telegram was part of the glamour. I hope that you will get the same feeling when you read this message, which, because of the number of issues that I need to cover, will be in a telegram style.

Webcasts: With the 2016 Annual Regional Anesthesiology and Acute Pain Medicine Meeting in New Orleans, Louisiana, we have started to archive webcasts of lectures presented at our meetings. This is a member-only benefit, and they can be accessed by clicking on Resources – Meeting Materials – Archived Webcasts. The quality is very good, and you can scroll through the content. Stay tuned for new postings after the Annual Pain Medicine Meeting in November 2016 as well as future meetings.

Regional Anesthesia and Pain Podcast (RAPP): I have to acknowledge the work of Dr Raj Gupta in creating this resource. Dr Gupta hosts, along with ASRA Website and Social Media Committee Chair Eric Schwenk, MD. Podcasts link to other ASRA products or programs such as *ASRA News* articles, advocacy initiatives, meetings, and so on. So far, we have six podcasts in the series. The last one, recorded on August 10, 2016, deals with the very hot topic of point-of-care ultrasound. You can access RAPP by clicking on Journal & News – Listen to a podcast.

RAPM Journal Podcasts: Dr Marc Huntoon, editor-in-chief of our journal, *Regional Anesthesia and Pain Medicine*, will soon restart the RAPM podcasts featuring highlights of each issue of the journal. This is a great resource to help you stay up to date with the latest articles.

Poll Questions: Give us your opinion on different issues affecting our practice. We recently asked a poll question on point-of-care ultrasound and learned that 64% of the respondents felt that it had a great potential but were not currently using. Registration is now open for our new workshop, "Introduction to Perioperative Point-of-Care Ultrasound," which will take place in San Diego in February 25–26, 2017.

Oscar de Leon-Casasola, MD
ASRA President

How I Do It: We have archived a collection of "How I Do It" articles that have appeared in past issues of the *ASRA News* on pain and regional anesthesia. These are excellent resources for continued education. For example, if you are planning to attend an ASRA workshop on ultrasound-guided shoulder injections and want to gain knowledge prior to participating in it, follow the pain link to read the excellent articles by Dr Philip Peng.

"Readers are encouraged to submit letters to the editor in response to published articles/topics published in the newsletter."

Advocacy: Part of your member dues goes toward our regulatory advocacy work. Stay informed on the different ASRA advocacy initiatives by clicking on Journal & News – News Announcements – Advocacy.

ASRA News: Full *ASRA News* issues since February 2012 are now online and fully searchable. Readers are encouraged to submit letters to the editor in response to published articles/topics published in the newsletter. Please e-mail your letters to ASRAEditor@asra.com

ASRA Blog: Have you read the ASRA Blog? You can find blog posts by clicking on ASRA & News – Read the ASRA Blog. Moreover, ASRA members are invited to submit blog entries for consideration for publication. Check out our tips for writing blog entries. That is it for now. Hope to see you in San Diego at our Pain Meeting!

Editorial – in Nabil's Corner

Why Should You Get Involved?

At the time of writing this editorial, a call for committee membership nominations was released by ASRA (the deadline has since passed). I forwarded this call to my partners. Some of them welcomed the opportunity and were eager to serve. Others were not as open to the idea. I had a discussion with one of my partners, who is relatively new to practice, and the conversation went like this:

Me: Did you see the call for nominations for committee membership?

Dr X: Yes I did. I do not think I will go for it.

Me: OK. Can I ask why?

Dr X: Well, this is the type of thankless work that you do, and it has very low yield.

Me: I disagree. Getting involved gives you a sense of giving back to the regional anesthesia and pain medicine subspecialty and gives you a platform through which you can express your values in meaningful activities. Additionally, you will learn new skills through networking with other knowledgeable peers and mentors. This may be a very good opportunity to enhance your career and gain prestige by building relationships with new and old contacts.

Having said that, committee membership is not the only way for you to get involved. Perhaps you can submit an abstract or educational contents for the meeting or state your opinion when asked. Your input provides great benefit to the larger profession.

Now, I have to go do this block. Let's talk later or e-mail me at: ASRAEditor@asranews.com

In this issue of the newsletter, we present to you a new feature based on the problem-based learning discussion concept. We will present a case and invite experts to comment on the case and discuss pros and cons of different management strategies. We will display the details of the case scenario on the ASRA Blog, post a summary of the case on Twitter, and run a straw poll for 5 days.

Have you had an interesting case recently that stirred a lot of discussion among your colleagues in the regional anesthesia section? Are you willing to share the details of the case? Send the de-identified case you would like to see discussed within this format to the *ASRA News* at ASRAEditor@asra.com We will choose the most suitable cases for discussion. Let us know if we can count on you as a contact to reply to cases, and provide your opinion on how you would manage said case. Please send your name, practice setting, and contact information to ASRAEditor@asra.com

Nabil Elkassabany, MD MSCE
ASRA News Editor

I am excited to read the welcome message for the 15th Annual Pain Medicine Meeting from Dr Ricardo Vallejo and to learn about all the exciting learning activities available to ASRA meeting attendees. Every year, the CME and Scientific/Educational Planning committees come up with new sessions and educational venues that make both the spring and fall meetings nothing short of a spectacular display of the latest and greatest in practice, academia, and cutting-edge science. I am looking forward to another wonderful meeting in San Diego in November.

Are you interested in other applications for perioperative ultrasound? In this issue, we introduce to you the Point of Care Ultrasound (PoCUS) Special Interest Group (SIG). Drs Jan Boublik and Stephen Haskins discuss the goal, objectives, and the future of the SIG. This is an exciting time for PoCUS. Sign up at http://www.asra.com/pocus.

The advocacy effort of ASRA is always on display in *your* ASRA News. ASRA leadership have put together a task force to address the challenges that society members will face with implementation of the Medicare Access and Chip Reauthorization Act (MACRA) and to appropriately provide comments to Centers for Medicare and Medicaid Services as new legislation is being developed. Drs David Provenzano and Alexandru Visan discuss the mission of this task force in detail.

I enjoyed learning about alternative tools for postoperative pain management, use of regional anesthesia for organ transplant, and the future of telemedicine in pain medicine. However, this is not everything. You have to read it all to learn it all.

15th Annual Pain Medicine Meeting in San Diego: Cutting-Edge Information for Your Practice

As chair of the Scientific/Educational Planning Committee, it is my pleasure to invite you to ASRA's 15th Annual Pain Medicine Meeting to be held November 17–19, 2016, at the Hilton San Diego Bayfront Hotel in San Diego, California.

Based on positive feedback from previous educational programs, our committee has worked diligently to develop an educational program that integrates basic science with the most common and advanced treatment options available in the pain medicine field today. Particular emphasis has been placed on recent challenges associated with commonly used pharmacologic and interventional therapies. Our goal is to create the best possible learning environment that gathers together academic and private pain practitioners learning valuable information that helps all of us in our daily practice.

MAIN MEETING

On Thursday, November 19, **refresher courses** feature internationally recognized speakers covering fundamental aspects of pain medicine extending from novel analgesics, the renaissance of the dorsal root ganglion (DRG) as a target for neuropathic pain, a practical approach to migraines and headaches for pain physicians, and the value of different imaging techniques to guide our therapies.

"We are proud of this exceptional scientific program and are confident that the ASRA Pain Medicine Meeting will be a remarkable experience for all."

On Friday, **parallel sessions** include a discussion of the implications of the Quality Payment Program on practice reimbursement with valuable information on demonstrating the value of your performance. Other hot topics include the use of cannabinoids, from the available clinical evidence to the regulatory, legal, and public health issues related to its use. Sessions will cover cancer pain as well as novel options to decrease the need for surgical interventions, such as regenerative therapies, minimally invasive lumbar decompression, and biacuplasty. A session on integrative medicine will provide a critical vision of its value in the field of chronic pain. As an example of our multidisciplinary vision of pain medicine, we also offer a panel session headed by the North America Neuromodulation Society in which the newest therapies in spinal neuromodulation will be reviewed.

Saturday **plenary sessions** include an in-depth review of regenerative medicine, from the fundamentals of stem cells, growth factors, and proteins to a critical appraisal of the evidence and regulatory concerns. A session on neuromodulation will address new data on high-frequency stimulation, DRG stimulation, and burst stimulation with the potential to convince payers of the benefits of these therapies. An afternoon session will address the deadly opioid epidemic, including a revision of the Centers for Disease Control and Prevention guidelines, potential implications for patients and physicians, as well as the consequences of the concomitant use of opioids and marijuana.

Ricardo Vallejo, MD
Chair, Scientific/Educational Planning Committee

ASK THE EXPERT INTERACTIVE SESSIONS

Our innovative "Ask the Expert Interactive Sessions" allow attendees to connect with world experts in a small and friendly environment, addressing useful topics for daily practice. On Thursday, these sessions will cover complications in pain medicine and tips to prevent them, data outcomes collection and their influence in reimbursement, how to read and interpret spinal imaging, and management of complex cancer cases. Friday sessions will include topics such as alternative treatments for patients with headaches that do not respond to conventional therapy, an in-depth review of musculoskeletal and neurological physical examination, and how to transition your practice from fluoroscopy to ultrasound-based procedures. Saturday sessions will focus on practice management, with emphasis on the new Medicare Access and CHIP Reauthorization Act of 2015 (MACRA); how to successfully grow your pain program, whether academic or private practice; and economics, compliance, and human resources.

PROBLEM-BASED LEARNING DISCUSSIONS AND WORKSHOPS

On Thursday, enjoy lunch with an expert as you choose from **25 Problem-Based Learning Discussions** covering a broad variety of topics, from brain effects of long-term marijuana use, regenerative medicine, intrathecal drug combinations, new spinal cord stimulation waveforms, Botulinum toxin, interventional procedures for headaches, and much more.

We also are offering **20 hands-on cadaver and model workshops** using fluoroscopy or ultrasound. These workshops include a full-day special session on ultrasound in pain medicine; cervical, thoracic, lumbar, and sacroiliac nerve blocks; sympathetic blocks; radiofrequency for knee and hip pain; botulinum toxin for headache management; minimally invasive lumbar decompression; vertebral augmentation techniques; and two fusion workshops in which fluoroscopy and ultrasound may be explored for head and neck blocks and soft-tissue injections.

RESIDENTS AND FELLOWS

One of the most important traditions of ASRA's meeting is its focus on education for residents and fellows. In addition to the main meeting and Ask the Expert Interactive Sessions, we invite residents and fellows to join us for an outstanding parallel program on Friday, November 18, with topics such as basic neuroimaging and its interpretation, tips to interpret results of urine toxicology, controversies about the use of epidural steroid injections, and contract negotiations and interpretation. Two workshops specifically for residents and fellows will be held on Saturday as well, covering fluoroscopy and ultrasound. These fill quickly, so don't put off registering.

PHYSICIAN ASSISTANT/NURSE PRACTITIONER PROGRAM

In addition to attending the main meeting on Thursday and Friday, physician assistants (PAs) and nurse practitioners (NPs) are invited to join us for a full day of specially designed programming on Saturday. Topics include management of terminally ill patients, diagnosis and treatment of commonly seen painful conditions such as chronic low-back pain and complex regional pain syndrome, and a review of the evidence and legal implications of the concomitant use of opioids and marijuana and interpretation of the toxicology results. Encourage your colleagues to attend and join us for the PA/NP Meet and Greet on Friday at 4 p.m. in the Exhibit Hall.

SPECIAL EVENTS

At the end of the first meeting day, join us at 6:30 p.m. for the **Wine and Bubbly Networking Reception** at the Exhibit Hall. Come meet new people, see old friends, and share wine and hors d'oeuvres in a pleasant and relaxing environment while supporting our exhibitors who make the meeting possible.

Please join us on Saturday, November 19, for the **Excellence in ASRA Award Luncheon,** featuring the President's Address by Dr Oscar De Leon-Casasola, the Best of Meeting Abstracts awards and presentations, the Chronic Pain Medicine Research Grant Update, and this year's John J. Bonica Lecture, presented by award winner Dr Honorio Benzon for his exceptional contributions to regional anesthesia and pain management.

On Saturday, cap off a successful meeting with our not-to-be-missed **Fiesta on the Bay** with food, drinks, and dancing on board the *Admiral Hornblower* yacht, and celebrate with new and old friends as we bring this exciting meeting to a close.

We are proud of this exceptional scientific program and are confident that the ASRA Pain Medicine Meeting will be a remarkable experience for all. We look forward to welcoming you to beautiful San Diego!

The Future of Health Care: The Medicare Access and Chip Reauthorization Act (MACRA)

In April 2016, the Centers for Medicare and Medicaid Services (CMS) published the proposed rule implementing the Medicare Access and Chip Reauthorization Act (MACRA) of 2015. MACRA is not a stand-alone act as it builds on years of transformative health care legislative efforts including the Tax Relief and Health Care Act of 2006 (which established the physician quality reporting systems [PQRS]); the Medicare Improvements for Patients and Provider Act of 2008 (MIPPA); the Health Information Technology for Economic and Clinical Health (HITECH) Act of 2009, which is part of the American Recovery and Reinvestment Act (which established incentive payments to eligible professionals to promote the adoption and meaningful use of certified electronic health record technology); and the Affordable Care Act of 2010 (which established the value-based payment modifier). At the same time, MACRA received significant bipartisan support within both chambers of U.S. Congress and the White House. As such, this does represent a strong signal of bipartisan support from the executive and legislative branches of the U.S. government for a transition toward value-based payments within the health care system.

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Implementation of MACRA will have a significant impact on the future direction and structure of health care regardless of practice type (i.e., academics, hospital based, and private practice). The new legislation will replace the sustainable growth rate formula with goals of paying health care providers based on the value and quality of care provided to covered participants. Under MACRA, two new payment systems will coexist: the Merit-Based Incentive Payment System (MIPS) and Advanced Alternative Payment Models (Advanced APMs). These new reimbursement platforms will significantly affect health care delivery and reimbursement. In addition, implementation of MACRA will result in major challenges for physicians as they integrate into these new payment models and program requirements.

"Implementation of MACRA will have a significant impact on the future direction and structure of health care regardless of practice type."

ASRA, recognizing the challenges that society members are facing, developed a special task force to assist in educating members and to appropriately provide comments to CMS as new legislation is being developed. The task force, which was developed under the direction of ASRA president Dr Oscar De Leon-Casasola, consists of both regional anesthesia/acute pain medicine and chronic pain medicine teams. The two-team model was created based on the understanding that each sector of pain management may face different challenges under the new legislation. Chronic pain members are Drs David Provenzano, Carlos Pino, and Kevin Vorenkamp. Regional anesthesia/acute pain members are Drs Alexandru Visan, Arthur Atchabahian, Douglas Jaffe, and Sanjay Sinha. The executive director of ASRA (Angie Stengel, MS, CAE) has also been instrumental in ASRA's ability to respond to MACRA.

Throughout the months of May and June, ASRA worked with six other organizations (American Academy of Pain Medicine, American Academy of Physical Medicine and Rehabilitation, American Society of Anesthesiologists, American Society of Interventional Pain Physicians, North American Neuromodulation Society, and Spine Intervention Society) to provide comments to CMS. In the letter, 11 specific points were outlined for CMS.

CHRONIC PAIN MANAGEMENT AND MACRA

Under the quality payment program, most chronic pain physicians will participate in MIPS unless they are part of an organization that has a well-developed Advanced APM that is approved by CMS. The MIPS program is **budget neutral** and will score physicians in four performance categories (Table 1): (1) cost, (2) quality, (3) clinical practice improvement activities, and (4) advancing care information. The program will provide adjustments to fee-for-service payments that range from ±4% in 2019 (reflecting 2017 reporting year data) to ±9% in 2022 and beyond. The calculated composite MIPS score will be used to compute a positive or negative or neutral adjustment to a health care provider's Medicare payments. Participation in an APM (Table 2) exempts a provider from the MIPS payment program and allows the health care provider to qualify for a 5% Medicare part B incentive payment from 2009 to 2014.

Of the 11 points made to CMS by the multisociety letter, areas specific to chronic pain management include MIPS low-volume threshold and participation by solo practitioners and small group practices, Advanced APMs, MIPS quality performance measurement, MIPS resource use measurement, facility-

Table 1: *MACRA four MIPS performance categories. EHR = electronic health record; PQRS = physician quality reporting system.*

MIPS category	% Of total score for year 1	Program replacing
Resource use (ie, cost)	10	Cost component of value base-payment modifier program
Quality	50	PQRS and quality component of the value-based payment modifier program
Clinical practice improvement activities	15	
Advancing care information	25	Medicare EHR incentive program (meaningful use)

Table 2: *Requirements for participation in Advanced Alternative Payment Model*

Participation in a risk-sharing model
Receive a sufficient share of their revenue from an alternative payment model. Proposed threshold in 2019 of 25% of Medicare part B payments or 20% of patients constituting Medicare Part B patients.[a]
Uses certified electronic health record technology
Pays for physician services using quality measures comparable to MIPS
Bear financial risk "in excess of a nominal amount" or be a CMS Innovation Center "Medical Home Phase 2 Expansion Model"

[a] The share of revenue and patients will increase in future years and include revenue and patients from other payers.

based MIPS eligible clinicians and group, MIPS advancing care information measurement, MIPS clinical practice improvement activities measurement, and MIPS Composite Performance Score reweighting. Please refer to the multisociety letter for further detail on recommendations. The letter comments directly on CMS's proposed rule to implement MACRA. CMS will take recommendations from ASRA and other stakeholders into consideration when writing the final rule expected for release around November 1, 2016.

CMS will continue to release multiple rules in future years related to MACRA and as implementation policy issues arise when the program becomes effective. In August, ASRA responded to the physician-patient relationship categories and code guidance, which will inform CMS in its development of episode and patient condition groups for which physicians could be measured for purposes of meeting MACRA requirements.

ACUTE PAIN MANAGEMENT AND REGIONAL ANESTHESIA AND MACRA

While we urge you to read the multisociety comment letter, we would like to bring to your attention some essential comments that our group provided to CMS for consideration.

1. We strongly urge and request that CMS establish an interim, shortened process for developing subspecialty-specific measure sets until CMS formally adopts subspecialty-specific quality measures.
2. MACRA implementation, in its current form, will have a significant impact on individual and small practices, from a regulatory and financial perspective.
3. There is limited opportunity for specialists in our field to participate in APMs. In current form, it is estimated that most of our specialty members will participate in MIPS. Given the current definitions, they will also be considered non–patient-facing clinicians. That creates a degree of complexity regarding reporting and reweighting of various components within the reporting system.
4. The societies support considering the Comprehensive Care for Joint Replacement (CCJR) as an Advanced APM. At the time of this letter, CMS is requesting comments on a separate proposal that would consider CCJR an Advanced APM. The date and many details of the implementation phase are under review by CMS.

CONCLUSION

In conclusion, MACRA is just one of the many current regulatory efforts that create a very dynamic and challenging health care environment. New payment models proposed through MACRA will have significant consequences for all health care providers. ASRA will continue to work both independently and with the other societies to provide substantive recommendations to CMS. Education will be provided continuously on MACRA through our educational meetings. We recommended that all members involved in chronic pain management check out the educational opportunities offered at 2016 Fall Pain Meeting in San Diego. In addition, the 2017 Spring Acute Pain meeting in San Francisco includes a specific Practice Management Portfolio where you will be able to find answers to many of the health care challenges, including the current regulatory environment. Furthermore, if you have specific concerns regarding MACRA, please email us at asraassistant@asra.com.

Introducing the Perioperative Point-of-Care Ultrasound (PoCUS) Special Interest Group (SIG)

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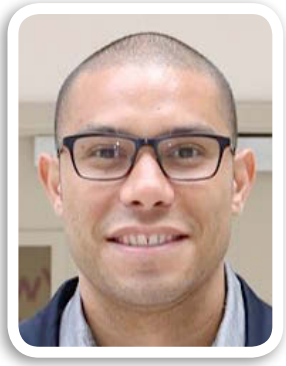

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Section Editor: Melanie Donnelly, MD

At a casual glance, one may wonder, "What does point-of-care ultrasound (PoCUS) have to do with ASRA?" Well, two important pieces of information make it clear that PoCUS is a "natural" extension of regional anesthesiology and ASRA's mission:

1. Ultrasound (US) guidance has transformed regional anesthesia from the practice of relatively few academic experts to an "everyday" tool widely used by most anesthesiologists. US imaging is now used in virtually every anesthesiology practice in the United States to guide interventions such as regional anesthesia procedures (both central neuraxial and peripheral nerve blocks) and vascular access.
2. ASRA has been a powerful advocate for improving patient safety and care related to regional anesthesia (e.g., management of local anesthetic toxicity and anticoagulation guidelines). In addition, ASRA has successfully collaborated with the American Society of Anesthesiologists to create guidelines and a certification process in the POC use of ultrasound-guided regional anesthesia.

ASRA's longtime commitment to expanding the use of ultrasound by regional anesthesiologists, in addition to a strong track record on improving safety and outcomes in regional anesthesia, has led to the creation of a special interest group (SIG) that melds those two missions. This SIG, therefore, represents an opportunity for ASRA to stay at the forefront as a leader in anesthesiology when it comes to the ever-evolving use of US in the perioperative setting!

"The perioperative PoCUS SIG encourages regional anesthesiologists with an interest in perioperative ultrasound to advance the knowledge and expand the scientific body of perioperative PoCUS."

WHAT IS PoCUS?

By definition, PoCUS applications involve a focused or limited examination aimed at answering a simple, well-defined clinical question to guide patient management with the intention of improving patient outcomes. The examination is performed at the bedside by the physician providing patient care. Many studies have shown that minimal training is required to become proficient at basic, yet potentially life-saving POCUS skills.[1,2]

WHY A PoCUS SIG?

The perioperative PoCUS SIG encourages regional anesthesiologists with an interest in perioperative ultrasound to advance the knowledge and expand the scientific body of perioperative PoCUS, with the aims of improving care and outcomes of patients undergoing regional anesthesia. For example, PoCUS will allow regionalists to more accurately diagnose and manage adverse events related to regional anesthesia such as pneumothorax, hemidiaphragmatic paresis, and hemodynamic instability in the setting of high spinal/epidural. Of note, PoCUS diagnostic applications relevant to regional anesthesia practice are, in many cases, superior to traditional imaging modalities and clinical assessment tools. In addition, many PoCUS applications, such as pulmonary assessment of acute respiratory events, are well-established in intensive care and emergency medicine practices.

- Ultrasound is superior to chest X-ray to rule out pneumothorax and better than fluoroscopy to diagnose hemidiaphragmatic paresis.[3,4] Lung ultrasound is also an excellent tool to diagnose other lung pathology such as chronic obstructive pulmonary disease (COPD) and interstitial syndromes including congestive heart failure (CHF), acute respiratory distress syndrome (ARDS), and pneumonia.[5]
- Focused transthoracic echocardiography (TTE; also called focused cardiac ultrasound) is an important tool in the hands of anesthesiologists and critical care physicians to supplement clinical evaluation and optimize cardiopulmonary resuscitation in the perioperative setting.[6] As opposed to transesophageal echocardiography (TEE), TTE allows for assessment without a general anesthetic, making it more accessible and amenable to a regional anesthesiologist.

- Other relevant PoCUS applications include use of (1) abdominal ultrasonography to identify patients at increased risk for postoperative pain following hip arthroscopy due to intra-abdominal fluid extravasation, (2) airway assessment, (3) gastric content and aspiration risk evaluation, and (4) assessment of intracranial pressure.[7–11]

HISTORY OF THE PoCUS SIG (SO FAR)

The ASRA Board approved the creation of the PoCUS SIG in September 2015, and our first meeting was held at the 41st annual spring meeting in 2016 in New Orleans, Louisiana. After starting with our 20 founding members committed to support and growth, the SIG has since seen tremendous membership growth to more than 600 members and counting.

Current stated goals from our mission statement are as follows.

Educational:

- Define and prioritize educational needs and dissemination of educational material pertaining to perioperative ultrasonography.
- Define and integrate perioperative ultrasonography topics relevant to anesthesiology residents as well as the regional anesthesia and acute pain fellows.

Science:

- Identify current gaps and encourage clinical and outcomes research in the area of perioperative ultrasonography.
- Advance the body of knowledge in perioperative ultrasonography and creation of publications relevant to ASRA members with an interest in the area.

Practice:

- Integrate perioperative ultrasonography into the practice of regional anesthesiologists to improve patient care and outcomes.
- Develop and standardize of indications, approaches, and techniques of perioperative ultrasonography.

We have proposed the following activities.

I. Recommend perioperative PoCUS modules to the annual meeting scientific/education planning committee for incorporation into the annual meeting curricula or other educational venues as decided by ASRA leadership.
II. Offer advice and provide support for implementation of educational activities.
III. Publish an article in the *ASRA News* every 12–18 months pertaining to a topic relevant to the practice of perioperative PoCUS for the regional anesthesiologist.

HOW CAN I JOIN THE PoCUS SIG?

Members can join the PoCUS SIG during renewal or upon becoming an ASRA member.

Current members are able to join by contacting membership services at 855-795-ASRA or by e-mail: asramembership@asra.com. Or simply press the Join button on the ASRA POCUS SIG webpage [LINK TO https://www.asra.com/page/189/perioperative-point-of-care-ultrasound-sig].

HOW MUCH DOES IT COST TO JOIN THE PoCUS SIG?

Nothing! There is no cost other than regular society dues.

WHEN WILL THE PoCUS SIG MEET?

The PoCUS SIG will meet at the 42nd Annual Regional Anesthesiology and Acute Pain Meeting, which will be held April 6–8, 2017, at the Marriott Marquis in San Francisco, CA.

HOW CAN I GET INVOLVED AND PROVIDE INPUT?

Feedback and suggestions can be directed to the PoCUS SIG at pocus@asra.com.

We look forward to your suggestions, comments, and participation in this exciting, growing area of ASRA!

IV. Create a dedicated page for perioperative PoCUS on the ASRA website.
V. Provide a communication platform for ASRA members interested in perioperative PoCUS.
VI. Create a curriculum of perioperative PoCUS for residents and fellows in regional anesthesia and acute pain medicine to recommend to fellowship directors.

To date, we have implemented the following.

1. Created a stand-alone, 2-day course separate from the annual meeting, “Introduction to Perioperative Point-of-Care Ultrasound.” For all interested, we would like to cordially invite you to join us at the inaugural course on February 25–26, 2017, in San Diego! Click here to register and take advantage of the early bird rates (Figure 1).
2. Integration of several perioperative ultrasound modules at the past spring meeting in New Orleans as well as the upcoming 42nd Annual Regional Anesthesiology and Acute Pain Meeting in San Francisco, California, on April 6–8, 2017.
3. Our SIG PoCUS website is a work in progress, with content to be added.
4. Publication of an article on Lung Ultrasonography for the Regional Anesthesiologist in the November 2015 issue of the *ASRA News*, publication of a Gastric Ultrasound article in the upcoming February 2017 issue of the *ASRA News*, with more in the works.

Figure 1

Although we believe this is a solid start, there are several other projects in the pipeline, and we welcome you to join and participate in this exciting and meaningful work!

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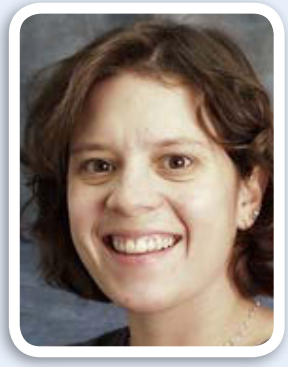
Problem-Based Learning: A Real Case of Local Anesthetic Toxicity and Perspectives on Management

We hope you enjoy this first problem-based discussion (PBLD) article. The case described here was provided by one of our colleagues. We contacted some of the readership and experts in the field to comment on the case and contribute to the discussion. We also posted the case on Twitter to get the response of the broader regional anesthesia community on social media.

Let us know if you like this feature. *In order to keep this feature going, we need your help!*

1. Please send de-identified cases you would like to see discussed within this format to the *ASRA News* at ASRAEditor@asra.com. We will collectively choose the most suitable cases for discussion.
2. Please let us know if we can count on you as a contact to reply to cases and provide your opinion on how you would manage the case. Send your name, practice setting, and contact information to ASRAEditor@asra.com.

Thanks, and enjoy!



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CASE STUDY: PART 1

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An 82-year-old woman with a body mass index of 29 and a medical history of hypertension, hyperlipidemia, tobacco use, and atrial fibrillation presented for a total knee arthroplasty. Her atrial fibrillation was well controlled, but she remained in that rhythm. Nurses prepared the patient, and she provided consent for her anesthetic. Although she desired a spinal anesthetic, she had last taken her apixaban 2 days prior. Thus, the patient and her anesthesia team settled on general endotracheal anesthesia and a single-shot adductor canal block (ACB) for postoperative analgesia.

The patient was scheduled for an 8:00 a.m. start, as the first case in the second room for the orthopedic surgeon. At around 7:50 a.m., the acute pain fellow started an ultrasound-guided ACB. Because of the patient's age, the regional anesthesia team chose to avoid sedation. An injection of 30 mL of 0.5% ropivacaine with 75 µg of epinephrine and 100 µg of clonidine (preservative free) was prepared and ready for injection into the canal. Upon ultrasound examination, the superficial femoral artery was noted to be quite deep (around 5 cm). The needle was placed in plane. Once the approximate area was reached, following a negative aspiration, 1 mL of the injectate was given, with an unsatisfactory spread of local anesthetic. The needle was redirected, followed by another negative aspiration. At that time, 1 mL of the local anesthetic was injected with satisfactory spread. This was followed by injection of 5 mL of the mixture. During the next aspiration, bright-red blood was easily aspirated through the 10-cm, 21-gauge echogenic needle. At this point, the needle was withdrawn.

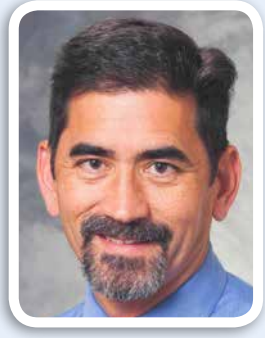
Around 10 seconds later, the patient began to have a generalized tonic-clonic seizure. The attending physician was emergently called to the bedside for a local anesthetic systemic toxicity (LAST) event.

The patient continued to show seizure activity after 2 mg of midazolam was administered. The fellow and preoperative nurse were preparing lipid emulsion. The patient had a strong irregular radial pulse and normal blood pressure. On the monitor screen, the patient remained in atrial fibrillation, with near baseline blood pressure. An additional 2 mg of midazolam was administered. At this point, seizure activity stopped. The patient maintained her airway and adequate oxygenation throughout. The Code cart, multiple nursing staff, anesthesia residents, and fellow were prepared to perform advanced cardiac lipid support (ACLS) and administer lipid emulsion.

How would you proceed at this point and why? Specifically, would you administer lipid emulsion? Why or why not?

KM: This patient is hemodynamically stable and maintaining her airway. She has had cessation of her seizure activity with administration of additional midazolam, and she is arousable. This patient also has received a small dose of local anesthetic from a known intravascular injection. In this instance, I would not proceed with lipid emulsion. I think it is prudent to have lipid emulsion within reach and perhaps even prepare it. Some would say that giving lipid emulsion "can't hurt" or that you should start it "just in case the worst is yet to come." I do not agree with these views as there are reported cases of severe side effects of lipid emulsion (possible links to adult respiratory distress syndrome and

Commentators:



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Twitter Poll:

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pancreatitis). In addition, at what point do you decide to administer lipids? If a hemodynamically stable patient states that he or she has a metallic taste or tinnitus, would I give lipid emulsion "just in case?" No, I would not. There is always a chance that the seizure is just the tip of the iceberg and cardiovascular collapse is next. I would observe hemodynamics closely and consider her response to midazolam. If the patient shows any changes in hemodynamics, I would proceed with lipid emulsion. As that was not the case here, I would not administer.

JS: I would immediately administer the bolus dose of 1.5 mL/kg of lipid emulsion and start a continuous infusion of 0.25 mL/kg per minute. Although the patient seems stable, she may develop an additional arrhythmia and rapidly become unstable. The benefit of getting an initial dose of lipid emulsion far outweighs the risk of administering it as soon as possible during local anesthetic toxicity. I would also administer oxygen and follow the ASRA checklist. I would discuss with the team that vasopressin, calcium channel blockers, and beta blockers should not be administered, as well as using lower doses of epinephrine if the patient requires ACLS.

RJ: I would consider this a significant LAST event with central nervous system (CNS) toxicity. Although the patient remained hemodynamically stable, the unsuccessful initial dose of benzodiazepine would make me very concerned that the patient's condition could rapidly deteriorate. Therefore, I would initiate lipid emulsion therapy along with the second dose of midazolam. As described, CNS toxicity often precedes cardiac toxicity. With this patient's preexisting cardiac disease, I feel that the theoretical risks of lipid emulsion therapy are outweighed by the benefit.

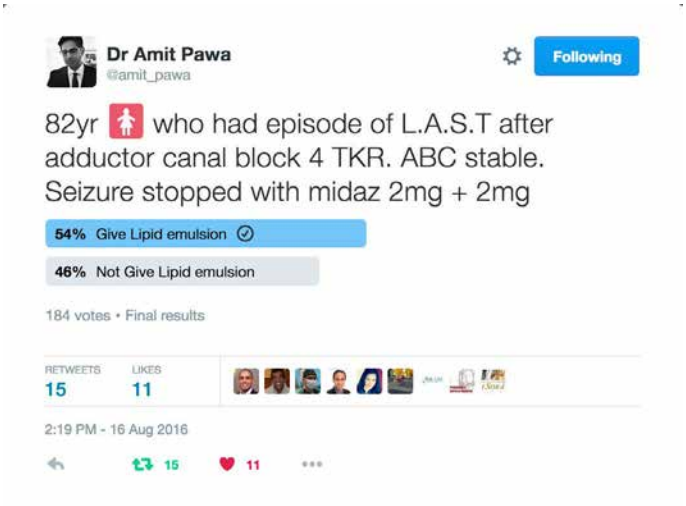
CM: At this point, I would continue to monitor the patient and give her supplemental oxygen. I would not administer lipid emulsion. Although atypical presentations of LAST can occur, the majority of patients with LAST present with CNS signs prior to cardiovascular instability. Current guidelines recommend prompt administration of benzodiazepines upon the onset of seizure activity, and this appears to have been effective in this case. Since there were no signs of airway compromise or cardiovascular instability, the seizure activity had ceased, and the intravascular dose was relatively small, I would remain prepared to administer the lipid emulsion but would not give it at that moment.

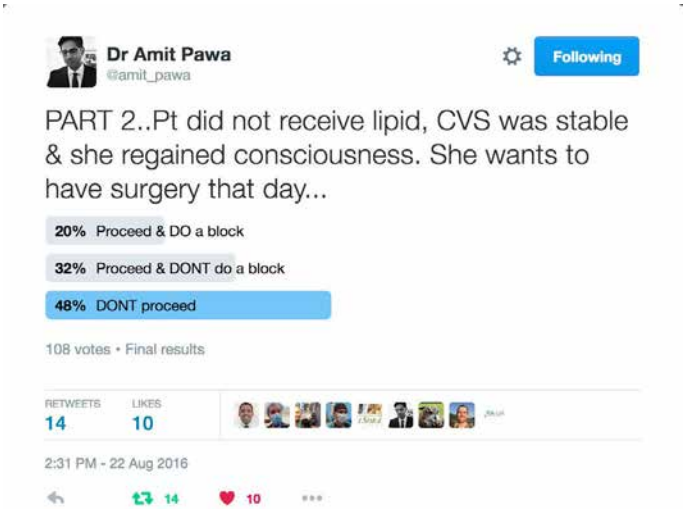
GW: This case presentation is pathognomonic for LAST, and one can make a reasonable argument for either giving or not giving lipid emulsion at this stage. The case for giving lipid early in the course of LAST is based on the potential for progression to cardiovascular toxicity and recognizing that giving lipid emulsion could lessen both the probability and the severity of hemodynamic compromise. Unfortunately, it is impossible to predict who will progress to cardiovascular compromise, and this fact strengthens the argument for earlier treatment with lipids.

TWITTER POLL

The full case scenario (part 1) was posted on the ASRA Blog by Dr Amit Pawa.

A 140-character summary of part 1 of the case was posted on Twitter. The poll was open for voting for 48 hours. Figure 1 displays the poll results: 184 votes came in, with 54% of respondents electing to give lipid emulsion and the remaining 46% of respondents deciding against it. For a complete list of all the tweets





and comments and to read the discussion, follow the link: https://twitter.com/amit_pawa/status/765659324429533186.

CASE STUDY: PART 2

The patient did not receive lipid emulsion. She remained hemodynamically stable and, within a couple of minutes, was responding to her name and opened her eyes. Around 5 minutes after the event, the patient was sleepy but oriented and able to answer questions.

Thirty minutes later, and despite 4 mg of midazolam, the patient seemed to be alert and awake. In the hours following this event, the patient repeatedly stated her desire to proceed with surgery, despite the LAST event, saying that she felt well. Her husband and daughter were summoned to the bedside. The event was described entirely to the patient and her family. They collectively deferred to your judgment on the question of whether to proceed with surgery.

Would you proceed with the case? Why or why not?

KM: Given the fact that the family, surgeon, and patient are comfortable proceeding, I would move forward with this case. The patient has had an iatrogenic seizure after a low dose of local anesthetic, which has completely resolved. She remains absent of signs or symptoms of the adverse event. She is reportedly at her baseline regarding both mental status and vital signs, according to the patient and her family. She has received midazolam, which may impair her decision making/memory and must be considered. As far as the potential of recurring LAST, I see no reason to cancel her case after having an iatrogenic, limited, and resolved neurologic event. This is a judgment call, and I would move forward with this case.

JS: The patient had suffered an episode of LAST, and I would not proceed with the case. She needs to be closely monitored for at least 12 hours since she had symptoms of LAST, which can persist or recur after initial treatment. In addition, the patient received 4 mg of midazolam and is likely unable to provide consent. If she did not have midazolam and was aware of the potential severity of proceeding with the case, she may not wish to proceed.

RJ: I would feel uncomfortable proceeding with the procedure as planned. I know that I'm likely in the minority and most would proceed, but I feel that the risk (as small as it may be) outweighs the benefit. This is a completely elective procedure. She has already shown that, for whatever reason, she has a very low seizure threshold, so why push it? Her best chance of a good outcome is to mitigate the anesthetic and surgical risk as much as possible. Postponing would also allow more options to optimize her pain management strategy. This would include a subarachnoid block for the surgical anesthetic (greater than 3 days from last dose of apixaban as per the ASRA coagulation guidelines) as well as an adductor canal catheter with a surgeon-administered posterior capsule injection.

CM: I would not proceed with this case for several reasons. First of all, this is an entirely elective case and, due to her anticoagulation status, she is ineligible for the preferred anesthetic. Avoidance of inhaled anesthetic and perioperative opioids is clearly a better choice for this woman given her advanced age and comorbidities. Furthermore, I wouldn't be comfortable administering a general anesthetic to a postictal patient who is already at risk of having some postoperative cognitive dysfunction. Current guidelines recommend that any patient who has had a significant LAST event be observed for at least 12 hours. Admittedly, it is unlikely that, after the stated period of time without any further signs of toxicity, this patient will have any further sequelae of LAST. General anesthesia would complicate assessment of this patient. Finally, although the patient appears alert and awake, one should assume that after 4

mg of IV midazolam, she may have some amnesia and should not be making important decisions regarding consent for anesthesia and surgery following this event.

GW: I think it is reasonable to proceed with the planned operation. The episode of LAST was brief and limited to CNS involvement. Progression to symptomatic cardiovascular instability after resolution of CNS toxicity can occur but generally does so by 15 minutes. In brief, we know what happened, after a sufficient interval we're confident it's self-limited, and nothing done in the operating room is likely to exacerbate LAST. Moreover, she will be monitored in the operating room and afterward in the postanesthesia care unit, so if LAST does recur, it will be recognized and treated quickly.

If so, would you do a block for this patient? Why or why not?

KM: As this patient has returned to her baseline after a known intravascular injection, I would not be too concerned that this patient has any increased sensitivity to local anesthetics. Since the situation has resolved with stable vital signs, I would be willing to reblock the patient. Again, this patient has received a low dose of local, directly into the vasculature. Obviously, "low dose" is relative, as the "toxic" doses of local anesthetics are considerably lower than stated doses administered intravascularly, and there are potentially even vast differences between intra-arterial and intravenous injection. I would consider a lower dose of local anesthetic than usual in case of increased uptake by the previously punctured vessel (unlikely from a 21G needle). I would also attempt to place a new block in a more proximal or distal position from the previous block.

JS: Absolutely not, since administering more local anesthetics to the patient who just suffered a seizure from LAST could cause worsening symptoms leading to cardiac arrest and death.

RJ: With the potential for an unknown percentage of the myocardial receptor sites to be bound with local anesthetic, I would be hesitant to perform an additional block. However, a total knee arthroplasty comes with a considerable amount of postoperative pain, and the use of a multimodal approach to this 82-year-old's pain management would be very beneficial—specifically, to try and limit the amount of narcotics she requires and the associated side effects in her age group. Therefore, after assessing her saphenous nerve distribution for signs of a previously successful block, I would feel comfortable placing an adductor canal catheter using the lowest necessary volume. If the sonoanatomy at the adductor canal were ambiguous or "deep," as previously described, I would opt for a traditional femoral nerve block.

CM: I would not repeat a block for this patient. When considering a repeat ACB, I see no reason to believe that visualization of the needle and artery at a depth of 5 cm would be any easier the second time around. Furthermore, to inject again at the same site in an anticoagulated patient, who may now be developing a hematoma after arterial puncture, seems unwise. A femoral nerve block in the inguinal region might be easier to perform under ultrasound guidance but at the expense of possible prolonged quadriceps weakness. Postponement of the case until a spinal anesthetic and an ACB can be done (perhaps by a more experienced staff member) is the best course of action. To proceed with the case and simply not provide a block for postoperative analgesia would be doing a disservice to this patient.

GW: Doing a block for postoperative analgesia is reasonable given the episode was brief and the patient had no evidence of cardiovascular compromise. However, I would defer doing it until after the operation when the risk of LAST has presumably returned to baseline. The small dose of local anesthetic is largely redistributed, metabolized, and excreted at this point. Furthermore, since extreme sensitivity to LAST presents as hemodynamic compromise, having CNS symptoms alone does not make the case that her response was exaggerated and supports the safety of doing a subsequent nerve block, of course with standard monitors and dosing.

TWITTER POLL, PART 2

Part 2 of the case scenario was posted on the ASRA blog by Dr Amit Pawa. Similarly, part 2 of the case was posted on Twitter. The poll was open for voting for 48 hours. Figure 2 displays the poll results. A total of 108 votes came in, with 48% of respondents electing to defer the case, 20% voting to proceed but redo the block, and the remaining 32% deciding to proceed with the case but not to reblock the patient. For a complete list of all the Tweets/comments and to read the discussion, follow the link https://twitter.com/amit_pawa/status/767836733685792768.

ADDITIONAL COMMENTS/PERSPECTIVES ON CASE

KM: Clearly, this was a unique case. The patient, family, surgeon, and intraoperative anesthesiologist were all prepared to proceed. More often than not, one will balk at continuing and the procedure will be canceled. A question I would ask myself: Would I admit this patient after this particular LAST event? In this case, I would not. That would factor into my decision making for proceeding to surgery. If we had administered fat emulsion, it would have been hard to discharge the patient or proceed with the surgery. The idea of causing or avoiding admission should obviously not be weighed in the decision of whether or not to give lipid emulsion.

LAST is a spectrum of symptoms. It can range from neurologic excitability (tinnitus, perioral numbness) to seizure to cardiac conduction issues/arrhythmias to cardiovascular collapse refractory to typical ACLS. Despite LAST being a "spectrum" of symptoms,

signs of severe cardiovascular LAST do not have to be preceded by lesser neurologic symptoms. However, if lesser signs and symptoms are handled by lesser interventions, it may not be necessary to proceed to lipid emulsion.

It is important to always review ASRA's guidelines for management of LAST. Special attention should be focused on ACLS during LAST as it varies considerably from traditional ACLS.

RJ: Considering the patient's age, even the small (5–7 mL) intravascular dose of 0.5% ropivacaine was likely the cause of her CNS toxicity. I suspect that the patient was on a heart rate–controlling medication for her atrial fibrillation, which could have contributed to the negative epinephrine response with initial injection.

In my institution, and I assume in most, surgical outcomes (especially total joint replacements) are monitored closely. With the recent emphasis by the Centers for Medicare and Medicaid Services regarding joint replacement in Medicare patients, I am very confident that the surgeon would agree with postponing the procedure.

LAST is a life-threatening condition with a widely variable presentation. We, as regionalists, must always keep it high on our differential diagnoses list when patients have odd or unusual symptoms around the time of local anesthetic administration. Luckily, we've discovered lipid emulsion therapy.

I am concerned, however, by the theoretical risks of lipid therapy including acute lung injury and pancreatitis. Assuming I'm not alone, this fear could potentially delay therapy and increase morbidity and mortality. Should lipid emulsion therapy be limited to use with cardiovascular collapse? It would be nice to have a decisive answer as to when to institute therapy. Should we wait until cardiovascular collapse and failed CPR, or should we institute it as soon as we see early neurologic signs such as tinnitus? Until this question is answered, I will continue to have a low threshold for it use.

GW: Although LAST is rare, it is likely that busy regionalists will see several such events over the course of a career. This case is particularly good to consider since most examples of LAST are self-limited and the questions addressed here are quite relevant. The availability of an effective treatment[1] makes it important to (1) consider LAST in anyone experiencing neurological symptoms or cardiovascular compromise after receiving local anesthetic in the course of regional anesthesia or by a nonanesthesiologist (e.g., local infiltration, field block, nerve block) and (2) be prepared to treat LAST (i.e., familiarity or availability of the ASRA advisory).[2] One of the most important safety measures we can take is to identify in advance patients with higher-than-normal susceptibility to LAST. Patients with preexisting heart disease (as in this patient), extremes of age, and significant comorbidities are well-known examples. However, small size and especially small muscle mass are also risk factors for LAST. It is reasonable to consider reducing the total dose of local anesthetic in these patients. Recent research has identified the mechanisms of lipid resuscitation as a combination of pharmacokinetic effects[3] and direct inotropy.[4] The net effect of lipid infusion is accelerated redistribution of local anesthetic, which decreases its tissue concentration in target organs. Thus, lipid functions as a shuttle, carrying local anesthetic away from target sites to reservoir organs (the true "sinks"), the mechanism of which may involve activation of the intracellular insulin-signaling cascade.[5]

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2014 Winner of the Carl Koller Grant: Towards a Transferable Curriculum in the Training of Thoracic Epidural and Thoracic Paravertebral Blockade Using a Mixed Reality Simulator

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Nearly 10 years ago, we came up with a novel idea to build a simulator for training on procedures in regional anesthesia (RA). This idea was inspired by a navigation and image fusion technology used by the Neurosurgery and Ear, Nose, and Throat departments. We believed that by using a similar tracking device, we could track needle movements in a high-fidelity phantom (based on real patient imaging), similar to the way a neurosurgeon can track his instrument in a patient while watching the virtual counterpart of the instrument on the virtual image of the patient's anatomy.

At the beginning, our ambition was to build a comprehensive simulator for all RA procedures, but we narrowed our focus to one region owing to the immensity of the task. We decided to focus on anesthesia and analgesia of the thorax. At the time, the University of Florida (UF) Health hospital system had just become a level I trauma center and we had a clinical need to provide good analgesia for patients with multiple rib fractures.

We initially received a local grant from the I. Heermann Anesthesia Foundation to create a prototype in collaboration with our UF engineering team (UF has a very strong tradition in simulation training in anesthesia), which has been instrumental in the undertaking of this project. We created a physical phantom of part of the upper back by using the chest computed tomography (CT) scan of one of our UF physicians. We constructed the bony structures of the T2–9 bony spine and ribs by using a 3D printer and soft tissues out of ballistic gel. We then fused the physical phantom with a 3D virtual image of the bony anatomy, manually adding additional virtual structures of interest such as lung, ligaments, spinal cord, and dural sac, with a focus on keeping the 3D virtual image anatomically correct.

"Our current work is only the beginning of the use of mixed reality simulators with structured curriculums in clinical education."

Thus, we created our first version of the mixed reality simulator for thoracic RA. It had both a physical component (needle and phantom) and a virtual component (virtual 3D anatomy image, virtual needle). When the trainee advances a physical needle into the phantom and "lands" on the transverse process (TP), for example, he or she experiences a realistic feeling of hitting bone while simultaneously seeing on the screen an image of the virtual needle touching the virtual TP. If the trainee physically advances the needle past the TP into the area where we programmed our virtual superior costotransverse ligament (SCTL), he or she would notice a thump as the needle engages in ligament and a realistic loss of resistance (LOR) as he or she penetrates the virtual SCTL. The thump and LOR would be triggered at the moment when the physical needle is advanced to the spots in the physical phantom that correspond to the correlating virtual anatomic structure.

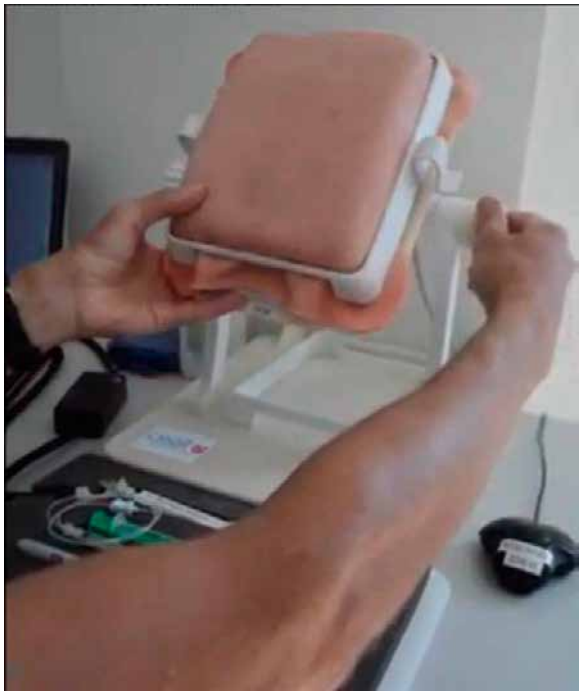
With time, our engineers added a greater number of features to the simulator. Early on, we equipped the simulator with a tangible user interface, such as a camera, that allowed the user to view the virtual anatomy or procedure from different perspectives. One of the greatest additions to the simulator was a mixed reality ultrasound (US) consisting of a physical "dummy" US transducer, whose position is tracked in space, and its virtual counterpart, a virtual US probe with a semitransparent insonating plane displayed in real-time on the computer screen that interacts with the 3D virtual anatomic structures, producing a virtual US image. Another cool feature is the ability to replay the procedure with "inside look," observing and analyzing procedural steps such as US-image acquisition and needling, as if one can see through the skin. Later on, our engineers also added the effect of angle of incidence on US visualization of anatomic structures (such as pleura) and needle. See Figures 1 and 2 for links to videos showing the simulator and its features.

Our mixed reality simulator has been extremely well received. We received a first-place prize for best scientific exhibit from the American Society of Anesthesiologists in 2014 as well as excellent feedback from many national and international experts in the field of regional anesthesia and acute pain medicine.

We began using the simulator to teach thoracic paravertebral blockade (TPVB) and thoracic epidural (TE) blockade. All techniques could be taught in several patient positions (sitting, prone, lateral) and in three versions (landmark based, US assisted, and US guided).

Figure 1: *Ultrasound (US)–assisted thoracic paravertebral blockade (TPVB): right side TH6.*

Figure 2: *Basic setup–Test Mode: no visualization.*



Still, we lacked a curriculum to optimize trainee learning using the simulator. We therefore applied for and were awarded the prestigious ASRA Carl Koller Memorial Research Grant in 2014 to further develop the simulator, create a teaching curriculum, and conduct outcomes-based research on the use of simulation in clinical education.

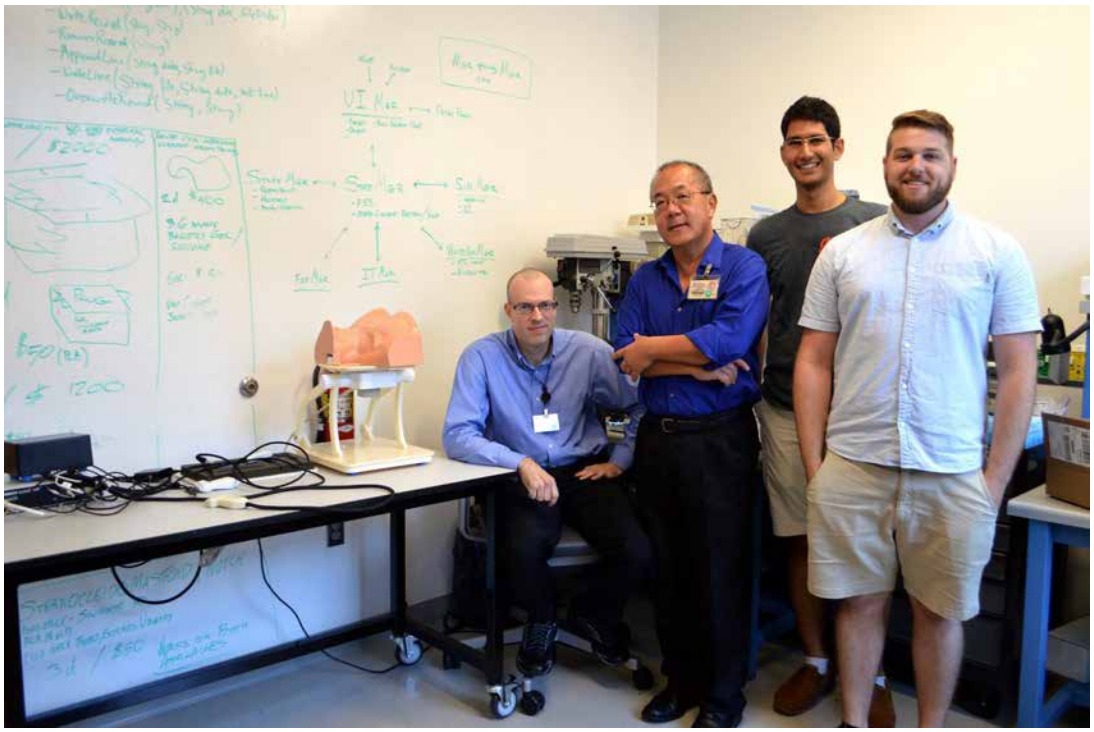
In the past 2 years, our work on this project can be divided into the following categories:

1. **Further simulator development**
2. **Technique refinement** for TPVB and TE
3. **Curriculum development** for TPVB and TE with the creation of an integrated tutor and a focus on transferability of procedural skills into real practice
4. **Data acquisition on outcomes** with our simulator-based training, which includes development of a testing algorithm to assess technical competence.

SIMULATOR DEVELOPMENT

Simulator improvements were based on the following three goals: to improve clinical utility, to enhance educational experience, and to improve product features.

Upgrades to the clinical utility of our simulator included the addition of hydrolocation with US-guidance (ability to visualize



anterior pleural displacement when the needle tip is correctly placed in the thoracic paravertebral space), the addition of more anatomic structures such as the internal intercostal membrane and intercostal muscles for the study of more lateral approaches to the TPVB, the creation of two levels of difficulty by decreasing the dimensions of the epidural and paravertebral spaces, and the addition of the presence of a false LOR when the epidural needle exits the interspinous ligament.

To enhance the educational experience of our trainee, we built a new physical simulator (and its virtual correlate) with different anatomic dimensions. This version is intended for testing and was developed in order to assess the trainee more accurately by avoiding biased scoring due to the trainee's increasing familiarity with the simulator during the learning phase. We also added multiple cognitive aids to help the trainee improve precision when manipulating the US transducer and the needle. These cognitive aids include probe perpendicularity indicator, needle trajectory projection and depth marker, needle and US beam alignment indicator, and labeling of anatomic structures. We created a scoring algorithm based on the different approaches to TPVB and TE in order to help the trainee recognize inadequacies or errors that require attention. For the simulator use, we designated two modes of function (training and testing) with new, more user-friendly interfaces for instructors and trainees.

Product feature improvements were aimed at increasing durability, portability, and dependability of our simulator units so that we can ship the simulator across the country and even across the ocean, allowing us to run workshops with potentially hundreds of simulated procedures in any given day with less hardware and software malfunction.

TECHNIQUE REFINEMENT

To refine our procedural techniques for both TPVB and TE, we had to update our knowledge of the published literature. In addition, we initiated several studies to clarify important anatomic questions and merits/pitfalls of previously described techniques in TPVB/TE that have not been clearly defined in the current body of literature. Our study of CT scans examining the dimensions and distances of the thoracic paravertebral space earned us a first place in category out of 725 abstracts at the International Anesthesia Research Society's 2016 meeting. We are in the process of completing two other studies that will help us refine our techniques for TPVB and TE placement.

We incorporated our findings into our teachings to improve accuracy of needle placement as well as safety (avoiding inadvertent dural or pleural puncture). We tested our revised techniques and elicited feedback from novice and expert learners. We generated multiple hours of lecture material that was eventually condensed into a basic curriculum and a bonus curriculum. We created a multimedia library of videos, photos, drawings, animations, and images to aid in explaining our refined procedural techniques. We ran multiple pilot studies to test our approach for failures and inaccuracies.

CURRICULUM DEVELOPMENT

We believe that discovery learning is not as effective as an organized curriculum when trying to master complicated procedures such as TPVB and TE placement. We have made great progress in the development of our integrated tutor (virtual instructor with some basic components of intelligent tutor). The integrated tutor deconstructs these complicated procedures into the basic component steps and helps the learners understand the best way to fine-tune their technique, step-by-step.

The integrated tutor allows for independent learning in the most efficient way possible. Our integrated tutor not only disseminates information by using multimedia (videos/photos/animations) but also is intelligent enough to give feedback to the learner. In addition, the use of a virtual tutor allows learners to study at their own pace without the need to invite experts to their institution, which can be time-consuming for the expert and costly for the learner.

The curriculum developed is a fusion of multimedia-based presentations combined with sets of drills and tests designed to constantly educate and assess the learners for their mastery of each of the steps. Owing to the depth and breadth of the material, the presentations were divided into more easily digestible blocks:

1. The Fundamentals (overview in clinical practice, anatomy, basics of ultrasound-guided regional anesthesia)
2. Entry-Level Techniques (description and demonstration)
3. Troubleshooting (difficult procedures)
4. Skills and Drills (description of basic skills in needle manipulation and US image acquisition including drills for skill mastery)
5. Tests (understanding theory and principles and technical skills practice and assessment of competence).

This curriculum allows flexibility for the learner to repeatedly practice specific skills for his or her level of training and based on feedback from the integrated tutor. The test component of this curriculum includes both a knowledge test and a procedural skills test with immediate feedback to the learner. A score is given to him or her for both test components. The knowledge test is a series of multiple-choice questions that assess the learner's grasp of anatomy, procedural technique, block indications/contraindications, and complications. The technical skills test is conducted on a different physical phantom to avoid falsely high scores due to familiarity with the training phantom. The technical skills test is equipped with a scoring algorithm that has been checked for accuracy, using experts in the field of RA. Algorithms were tailored to specific techniques (landmark based vs ultrasound assisted vs ultrasound guided).

DATA ACQUISITION

We are in the early phase of data collection acquisition as we are working hard to smooth out glitches and validate our scoring algorithm. Most of the data gathered currently are on test subjects. Enrollment has begun on our Institutional Review Board–approved study. In our study, we have divided subjects into three groups.

1. Group A has access only to traditional lecture material and the simulator without visualization of the 3D virtual anatomy and without the immediate feedback on the quality of performed blocks (discovery learning).
2. Group B has access to visualization of the 3D anatomy, cognitive aids, and immediate feedback but still uses discovery learning without the assistance of the integrated tutor (IT).
3. Group C has access to all the same features as group B but with the addition of the IT.

All subjects regardless of group designation learn TPVB and TE placement without the assistance of an expert in regional anesthesia.

We propose that a curriculum with the IT will be superior to discovery learning without specific objectives and without

feedback on skill mastery. We also eventually will test the clinical transferability of the knowledge and skills obtained through this curriculum by asking subjects who had independently trained with our simulator (even novices without previous training in RA) to perform blocks on cadavers and compare their competency with those individuals trained on cadavers by experts in TPVB and TE block performance.

Ultimately, we hope to obtain data on learning curves for TPVB and TE procedures as well as long-term knowledge and skill retention. For those who have mastered basic techniques in TPVB and TE placement, we are in the process of creating a bonus curriculum that covers techniques not covered in the basic curriculum, which includes several variations of US-guided TPVB and of TE placement with patients in different positions (eg, lateral). Our bonus curriculum also covers the fundamentals for out-of-plane US-guided technique.

CONCLUSION

While we embarked on a journey to instruct trainees in the acquisition of the complex skills of TPVB and TE placement, we as educators and researchers have gathered new insight into WHAT we teach and HOW we teach it. More specifically, we found that it is much harder to teach US-based TPVB techniques (especially US-guided procedures) than landmark-based techniques, more so in individuals with "US dyslexia." We discovered that while US was a harder skill to acquire, its mastery helped complete more complicated tasks more successfully. And we learned that even in the advanced practitioner, it takes at least 1–2 hours of practice on the simulator to enhance the ability to efficiently manipulate the needle and to effectively use US as a tool to improve RA success and safety.

We thank ASRA for its generous support, our engineering team for its endless labor and ingenuity, and all of our residents/fellows/faculty for their feedback and data points! We intend to share our educational materials for free with all ASRA members and will be happy to help with courses and workshops for those who are interested in using our simulator in teaching and learning thoracic regional anesthesia. We also believe that our current work is only the beginning of the use of mixed reality simulators with structured curriculums in clinical education and are open for collaboration and further research.

Regional Anesthesia in Abdominal Transplant: What's the Hold up?

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Abdominal organ transplantation has become increasingly common over the last several decades with improvement in outcomes for kidney and liver transplant recipients. Nearly 26,000 were performed in 2015 alone[1] (Figure 1). Advances in immunosuppression, surgical, and anesthetic techniques have all played important roles. Typically, these procedures are performed under general anesthesia, using intravenous agents for intraoperative and postoperative pain control. Regional anesthesia techniques, whether neuraxial or peripheral, are rarely used. Why is this?

Some answers immediately come to mind. First, neuraxial analgesia can cause hypotension, which may have an adverse effect on graft function. Second, these patients are at higher risk for coagulopathy during the perioperative period, putting them at higher risk for bleeding complications associated with regional anesthesia. Third, a priority is placed on the survival of the patient and the graft, making pain control a secondary concern. Finally, these procedures are often performed on a semiurgent basis during overnight or weekend hours when a skilled regional anesthesia provider may not be immediately available.

The literature is lacking in regard to regional anesthesia, especially neuraxial techniques, for abdominal transplant. A few studies in the 2000s investigated neuraxial anesthesia versus general anesthesia for kidney transplant and found no significant differences in intraoperative hemodynamic stability or postoperative outcomes.[2–5] Although two studies used combined spinal epidurals and maintained the epidural catheters with infusions of morphine or buprenorphine for postoperative pain control, there were no comparisons to other methods of postoperative pain control.[2–4] Interestingly, the study of Dauri et al[5] from 2003 found improved postoperative pain control and oxygenation when comparing general anesthesia with epidural to general anesthesia alone. However, intravenous tramadol appears to be the only analgesic method used in the general anesthesia group.[5]

"There are opportunities for the growth of regional techniques in the abdominal transplant population."

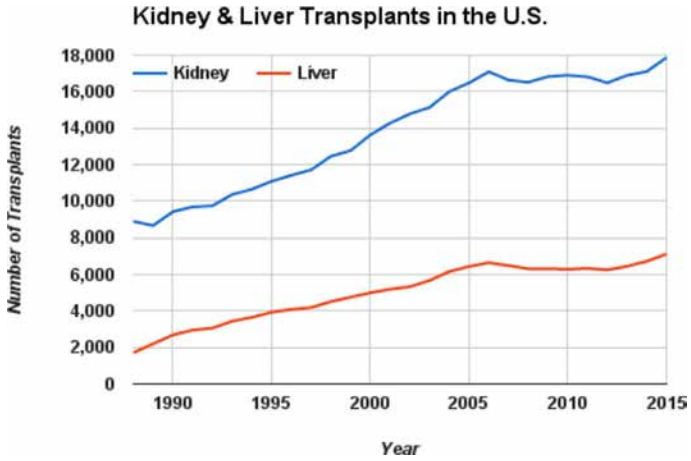
Posterior transversus abdominis plane (TAP) blocks for renal transplant have been investigated more extensively but with variable results. A retrospective study from Farag et al[6] in 2015 demonstrated a reduction in 24-hour morphine consumption with continuous TAP catheters (Figure 2). However, studies using a single injection technique have returned both positive and negative results.[7–9] This makes it difficult to make a strong case for TAP blocks for renal transplant surgery, with the possible exception of continuous TAP blocks, given the current evidence.

Other trunk block techniques such as paravertebral and quadratus lumborum blocks have produced favorable results for other abdominal procedures, specifically hernia repair (inguinal and ventral) and cesarean section[10,11] (Figure 2). However, a thorough literature search yielded no articles on their use in transplant procedures. These techniques may be worth investigation in the renal transplant population.

Liver transplant poses more difficulties for regional anesthesia given that these patients can often be quite coagulopathic. However, despite these perceived risks, there have been attempts at using neuraxial and peripheral nerve blockade for pain control. In the largest study, published in 2010, Trzebicki and colleagues[12] retrospectively examined a series of 67 patients receiving thoracic epidurals for liver transplant. To screen patients, they used cutoffs of international normalized ratio < 1.5, activated partial thromboplastin time < 45 seconds, and platelets > 70 G/L. Only 24% of their patients met these criteria. Of these 67 patients, 56 were extubated immediately postoperatively and there were no bleeding complications reported. Unfortunately, there were no comparisons made to the other 212 patients regarding early extubation or pain control.[12] Other reports by Hussain et al[13] in 2003 and Milan and Rewari[14] in 2011 show similar results without complications in well-selected patients. While there is no conclusive evidence that epidural analgesia for liver transplant is necessarily beneficial, these reports do show that epidural analgesia may be safe in relatively healthy liver transplant recipients.

There are, of course, peripheral alternatives to neuraxial techniques for liver transplant surgery. In a pilot study of 17 patients, Milan

Figure 1: *Number of kidney and liver transplants in the United States from 1988–2015. Data collected from the US Department of Health and Human Services. Available at: https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/. Accessed September 2016.*



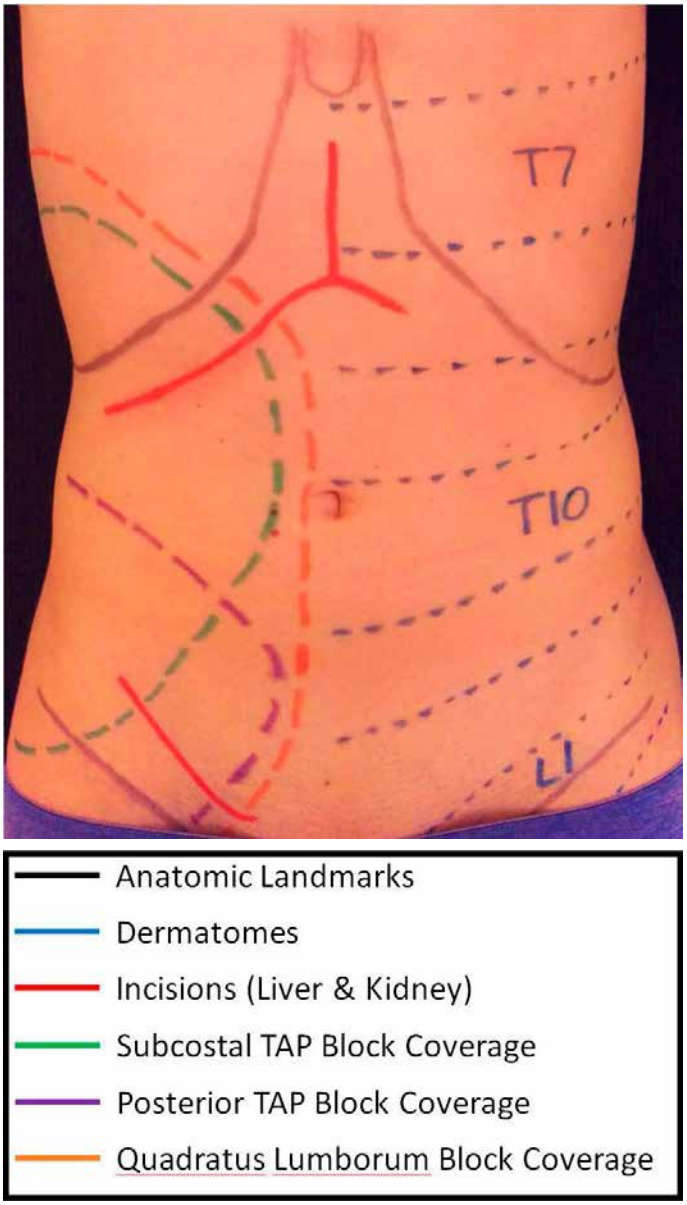
et al[15] in 2011 saw a reduction in morphine consumption and a trend toward earlier extubation after bilateral subcostal transversus abdominis plane blocks in liver recipients (Figure 2). This block could be performed with less concern for bleeding in coagulopathic patients, but there is a need for additional evidence before it can be confidently recommended for this population. The previously mentioned paravertebral and quadratus lumborum blocks could provide other options, albeit unstudied in liver transplant at this point.

Interestingly, decreased opioid requirements have been reported after liver transplant surgery when compared to other abdominal surgeries. This may be due in part to central and peripheral effects of modulated endogenous opioids in liver disease.[16–18] However, in a retrospective study, Chen et al[19] found that patients undergoing liver transplant required less morphine on only postoperative day 1 when compared to patients undergoing either hepatectomy or living liver donation. Perhaps this could be related to ongoing sedation post liver transplant or large doses of steroids and immunomodulating agents that patients receive postoperatively.

Another point worth mention in a discussion of regional anesthesia for liver transplant is the decreased metabolism of amide local anesthetics in patients with poor hepatic function. Lauprecht et al[20] compared plasma levobupivacaine levels in patients with epidurals undergoing liver transplant versus those undergoing anterior rectal resection. Liver transplant patients showed significantly higher concentrations of levobupivacaine by comparison both intraoperatively and postoperatively, but not to a degree that would warrant dose reduction.[20]

Finally, it is important to note that many of the studies surrounding regional anesthesia in transplant surgery are based outside of

Figure 2: *Expected area of analgesia for posterior transversus abdominis plane (TAP), subcostal TAP, and quadratus lumborum blocks in relation to incisions for hepatic and renal transplant. Dermatome levels and anatomic landmarks are shown for reference. Please note: All markings are approximations.*



the United States. Because of possible regional variability in approaches to acute pain management and patient's cultural responses to pain, care needs to be taken when applying these studies to individual populations. With the overall increase in abdominal organ transplant surgery, as perioperative providers, we are faced with the challenge of providing quality pain control while weighing the risks and benefits these methods carry. Clearly,

there are opportunities for the growth of regional techniques in the abdominal transplant population. We look forward to future studies to provide us additional tools to aid in our clinical decision making.

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Telemedicine in Pain Management: A New Frontier in Patient Care

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Chronic pain affects a significant portion of the United States population, more than even diabetes mellitus. Effective management of these patients is hampered by several barriers, the most common being geographic distance to the clinic, functional limitations of patients, stigma associated with hospitals or seeking treatment, economic limitations, and lack of knowledge/education on pain conditions and treatment options. There are also issues of long wait times to see a specialist, particularly for initial diagnosis. The inherent flexibility in telemedicine can remove many of these barriers. Although not new, telemedicine is relatively underused in the pain field currently.

Telemedicine has grown to encompass various modalities and implementations, such as two-way video/videoconferencing; e-mail; short message service; use of mobile technologies such as smart phones, tablets, and wearables; e-health including patient portals; remote monitoring of vital signs (eg, remote cardiac monitors); and continuing medical education. Telemedicine is currently growing at a rate of 2.5% annually in the United States and over half of all United States hospitals now use some form of telemedicine. In the field of pain, telemedicine may be used for pain assessment, pain consultation, and certain pain treatments such as behavior modification and pain education. Telemedicine has been shown to be effective in pain assessment and diagnosis as well as in telehealth-based pain management education.[1,2]

Telemedicine can be defined as the exchange of health-related information or services between geographically distinct sites through electronic communications (telecommunications). The terms "telehealth" and "telemedicine" may have slightly different interpretations, similar to the difference between electronic medical records and electronic health records where use of the term "health" is more encompassing (including preventative measures) than the term "medical," which refers to clinically oriented information such as procedures, monitoring, and diagnosis. For simplicity, most organizations consider telemedicine and telehealth to be interchangeable terms, encompassing a whole range of remote health care interpretations.

"Telemedicine has the ability to surpass current pain mitigation strategies, not only in access to care but also in catering toward more personalized medicine."

In general, telemedicine delivery can be structured in one of two ways: store and forward technologies or direct communication via telecommunications (usually person-to-person). In the store and forward method, information is collected and stored for later retrieval. Several examples of this are web-based educational sessions, physician training/education, and some web-based automated interactive training modules. In the field of pain medicine, Palermo et al[3] showed that web-based, cognitive-behavioral interactive sessions for pediatric pain were more effective than a control condition without sessions. Also, Harris et al[4] showed that online clinician education on chronic pain management was just as effective as in-person education sessions. The store and forward methodology is relatively simple to set up and can be operated at a very low overhead cost, allowing increased dissemination. However, issues of quality and accuracy have emerged partially owing to the ease of implementation. There have been a plethora of these types of services, and many have been haphazardly created or modified from old material without much thought to content and presentation, leading to possibly diminished effectiveness, if not outright biasing patients against these technologies.[5] Another issue with store and forward technology is that there is no direct reimbursement by insurance despite the potential improvement in patient satisfaction that comes at modest investment.

The other major category of telemedicine is direct contact via telecommunications. This category can be further subdivided into two more: (1) assessment and measurement and (2) therapeutics.

Pain assessment and measurement can be performed through videoconferencing software, as can some therapies such as cognitive behavioral therapy (CBT). Additionally, web-based and mobile devices can be easily used for pain assessment, as

their primary function is to record and transmit information. Cell phone and tablet applications can keep logs of pain level, mood, activity, and other related pain symptoms and health indicators, all important information in assessing the status of patients and their pain condition. The data can be used in real time to provide feedback and remote monitoring or can be stored and transmitted to the clinician to evaluate at appropriate time points. These methods would provide more rigorous data on the pain condition than would office visit questionnaires. While off-based questionnaires can involve recall (memory) biases and reflect only a single point in time, mobile devices can record multiple measurements across time and occasions.

Telemedicine therapeutics is the area with the greatest potential benefits. Psychological services can help in several ways with chronic pain management. The most obvious are psychological therapy sessions and coping methods education. A Cochrane review on web-based psychological therapies for the management of chronic pain in adults by Eccleston et al[6] showed that telemedicine-delivered psychological therapies reduced pain, disability, depression, and anxiety for patients other than those with primarily headache pain. For headache patients, pain and disability were reduced, but no clear benefit was found for depression and anxiety.[6] More research still needs to be done but the telemedicine-delivered therapies seem to be as effective as face-to-face therapies for chronic pain. With the addition of monitoring and feedback, these therapies could be better tailored to individual patients' needs.

Similar to the traditional, in-person office visit, telecommunications can be fully reimbursed if certain conditions are met. Implementation of this technology in the areas of psychological treatment and management has blossomed. Psychological consults, visits, and CBT can all be accomplished rather easily and effectively with modern videoconferencing software. Implementation is simplified owing to the nature of these interactions largely not requiring a physical examination.

There have been issues with reimbursement from Medicare/Medicaid with the provision of psychological therapy via telehealth. To be reimbursed, the clinician and the patients must both be physically located in a health care environment. For example, the clinician can be at the hospital making the call in the city and the patient may be in a rural clinic that has been set up to receive the teleconference. Although the conditions and limitations vary by state, new legislation is attempting to relax these limitations (eg, Medicare Telehealth Parity Act). Information on reimbursement in different states can be found in American Telemedicine Association report on the topic.[7] In their analysis of telemedicine policies by state, they found only five states with an "A" grade based on their criteria (Figure 1).

Another interesting use of telemedicine is in the area of risk identification and mitigation. Chronic pain, particularly postoperative, persistent pain (PPP), has been associated with pain catastrophizing. Pain catastrophizing is the psychological predilection to focus on and worry about the experience of pain. The scale contains three factors further defining subjects' psychological state: rumination (fixating on the pain), magnification (magnifying the experience of pain), and helplessness (lack of control over their pain).

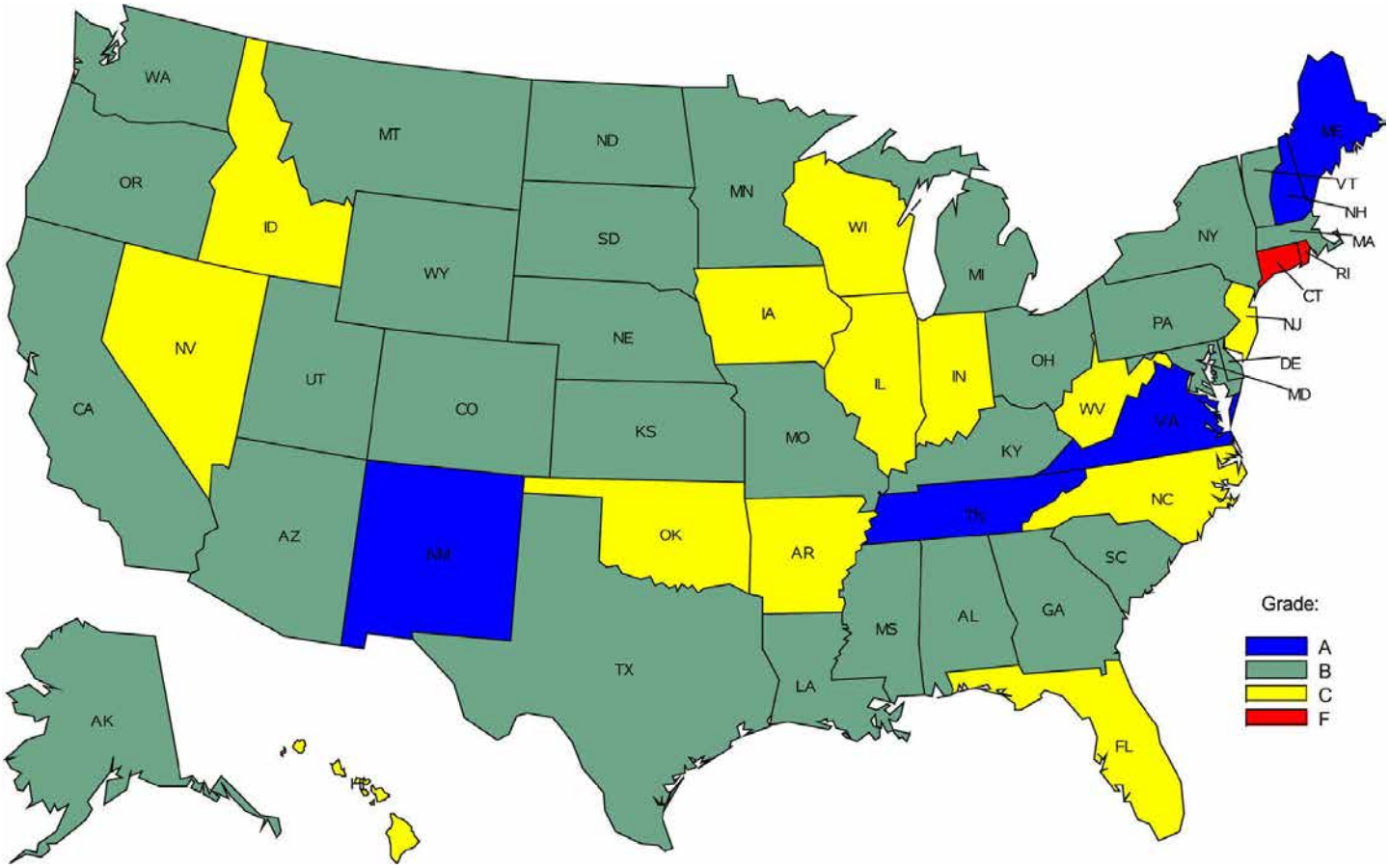
Use of CBT has been shown to reduce pain catastrophizing. It may be possible to curtail the development of PPP through the reduction of pain catastrophizing. Using telemedicine for the application of CBT is becoming more common, and use of this technology would make application of programs to mitigate PPP through CBT far more feasible. We are currently conducting a study at the Rush University Medical Center to evaluate the viability of such a model on total knee arthroplasty patients. In this study, we measure pain catastrophizing through use of questionnaires and select subjects with the highest reported level of pain catastrophizing. We then randomize them to either CBT delivered through traditional in-person visits, telemedicine-delivered CBT, or a control condition. We hypothesize that both telemedicine and traditional in-person CBT for pain catastrophizing will result in a lower incidence of PPP than in the control condition.

If our hypothesis is validated, the use of telemedicine to deliver CBT to address high pain catastrophizing can be inserted in our workflow, along with a system to evaluate the risk factors for PPP so that a scoring system for PPP vulnerability can be created. Use of vulnerability detection, CBT, and telemedicine together can lead to an efficient system to reduce incidence of PPP and increase quality of life of the chronic pain population.

The future of pain management through telemedicine has exciting new developments in virtual reality (VR), augmented reality (AR), and sensing technologies such as global positioning systems (GPSs). VR and AR for pain management have been used for pain distraction in children and adolescents with burn injuries while undergoing dressing changes[8,9] and resulted in lower pain levels and reduced analgesic use. GPSs have been used to monitor and motivate chronic pain patients through wearables.

Telemedicine, particularly in the field of pain, is a nascent health care technology. In this article, we outlined some of the positive signs of its utility. With further study and optimization, telemedicine has the ability to surpass current pain mitigation strategies, not only in access to care but also in catering toward a more personalized medicine. Clinicians' interactions with patients will improve and patients' interactions with other patients through social networks and outreach organizations will empower them to improve their well-being. Better patient outcomes and improved efficiency will lower health care costs for both patients and providers. Telemedicine is the future of pain management. Well-designed research in this

Figure 1: *American Telemedicine Association grading of states' telemedicine policies from "A" to "F."*



area and proper implementation will lead to improved quality of life for patients and better efficiency for clinicians.

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Stimulation of the Dorsal Root Ganglion: A Breakthrough in the Treatment of Focal Neuropathic Pain

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INTRODUCTION

Spinal cord stimulation (SCS) has been a widely adopted therapy for treatment in neuropathic pain syndromes such as failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS). Historically, SCS has referred to stimulation of the dorsal columns of the spinal cord via the posterior epidural space. Even with significant evidence suggesting its efficacy, traditional SCS has several shortcomings including paresthesias in unwanted areas, position-related changes in the perception of neurostimulation, decreased efficacy over time, and the inability to consistently selectively isolate regions, such as the groin, hip, pelvis, and foot.[1,2] These shortcomings have led to interest in stimulating new targets within the central nervous system to address these issues and provide optimal pain relief for those suffering from focal neuropathic pain states. The dorsal root ganglion (DRG) is a neural structure containing cell bodies responsible for transducing and modulating sensory information from the periphery to the spinal cord.[3] The DRG has historically been thought to be a passive neural structure with minimal involvement in the development and maintenance of neuropathic pain.[3] Significant clinical evidence now exists that the DRG is a robust structure that, when focally stimulated, can result in dramatic pain relief.[4,5] The St. Jude's Axium stimulation system was approved for use by the Federal Drug Administration (FDA) in the United States this year. It is the first device specifically designed to access the DRG and is now widely available to physicians and patients searching for treatment options in the most difficult of neuropathic pain states such as CRPS.[6]

ANATOMY

The DRG is located in the lateral epidural space within the spinal foramen and houses the cell bodies of the primary sensory neurons. The DRG is involved in the transduction of pain to the central nervous system and exhibits a number of pathophysiologic changes during chronic pain states.[5] The DRG houses several types of neurons, including Type A and B DRG neurons. Type A DRG neurons are responsible for touch, vibration, and proprioception, while the smaller type B neurons are responsible for nociception.[7] Historically, the DRG was thought to be a support structure with no clear role in the transmission or perpetuation of chronic pain. Although its precise role is still not known, many have long held that the DRG plays a role in pain transmission.[8] Because of this, the DRG has been a target of many interventions, such as injection of steroids, radiofrequency ablation (pulsed and thermal), surgical resection and, most recently, neuromodulation. Evidence suggest that in certain neuropathic pain states, significant hyperexcitability develops in the DRG, leading to spontaneous firing and resulting in central sensitization and allodynia.[3] The hyperexcitability in pathological states, along with its role in pain processing, makes the DRG a highly intuitive target for neuromodulation.[9–11]

"The DRG is a robust structure that, when focally stimulated, can result in dramatic pain relief."

PATIENT SELECTION, INDICATIONS, AND CONTRAINDICATIONS

As is the case with traditional SCS, patients being considered for this therapy should typically have failed less invasive modalities, such as physical therapy, medications, and conventional interventional pain injections. Currently, the FDA "on-label" usage of the commercially available Axium (St. Jude Medical, St. Paul, MN) DRG stimulator is limited to CRPS I and CRPS II of the lower trunk and extremities.[6] The literature also suggests that DRG stimulation is effective in a variety of other neuropathic pain states, such as phantom limb pain, postinguinal herniorrhaphy pain, postherpetic neuralgia, post-thoracotomy pain, postmastectomy pain, and peripheral neuropathy (Figure 1).[5,12] DRG stimulation seems poised to play a pivotal role in many focal neuropathic pain states in which discrete and focal coverage is needed without unwanted stimulation of other regions, which commonly occurs in traditional SCS.

The most compelling data for DRG stimulation is for CRPS. Outcomes data at 12-month follow-up was recently presented at the North American Neuromodulation Society for a pivotal trial performed in the United States that compared DRG stimulation to conventional SCS in patients with CRPS of the lower extremity. The primary endpoint of the study was achieving a reduction in

Figure 1: *Indications for DRG stimulation.*

Indications
CRPS I*
CRPS II*
Phantom limb pain
Postherpetic neuralgia
Peripheral neuropathy
Post-thoracotomy pain
Postmastectomy pain
Ilioinguinal neuralgia
Intercostal neuralgia
Groin pain (postherniorrhaphy neuralgia)
Lumbar radiculopathy
Discogenic pain
Neuropathy pain from peripheral neuropathy
Neuropathic chest wall pain
Lumbar stenosis
Chronic postsurgical pain

*Current on-label FDA approved indication

pain score by 50%. The modified intent-to-treat analysis (those who received a trial of a device) suggested that 81% of patients trialed with DRG stimulation had at least 50% improvement in their affected extremity at 3 months and 74.2% at 12 months, compared to traditional SCS of 55% and 53%, respectively.

Contraindications for DRG stimulation again mirror those associated with traditional SCS.

Relative Contraindications

- Infection, systemic or localized
- Abnormally high or uncontrolled daily opioid regimen
- Patients with metastatic cancer pain who may have local masses in the region
- Anatomic barriers for placement of the lead
- Major psychiatric comorbidity
- Presence of demand pacemaker or defibrillator
- Risk of falls
- Anticoagulant or antiplatelet therapy
- Difficulty maintaining prone position for procedure
- Unresolved secondary gain

Absolute Contraindications

- Inability to control the device
- Spine instability that could potentially cause neurological damage
- Coagulopathy or immunosuppression associated with unacceptable surgical risk
- Patient refusal

Specific mention should be made of anatomical barriers for placement. For instance, the postsurgical spine and extensive neuroforaminal narrowing can make deployment of the DRG electrode technically challenging. A comprehensive review of the patient's surgical history and baseline imaging of the patient's spine should be part of the evaluation process when considering patients for DRG stimulation. Decision of imaging modality to utilize (eg, X-ray, CT, MRI) should be made on a case-by-case basis. If spinal pathology is likely, MRI can be helpful to evaluate for neuroforaminal stenosis, as this can make deployment of lead technically challenging.[13] It should be noted that if a specific DRG is not accessible for anatomical reasons, adjacent ipsilateral DRGs can be targeted to achieve appropriate coverage because of redundancy from afferent DRGs.

PROCEDURE TECHNIQUE

The tenants of DRG stimulation are consistent with the standard practice utilized in conventional SCS. Patients are typically trialed for a period of 5–10 days with the externalized leads implanted based on significant improvements in pain and function. Overall, the DRG is an easily accessible structure with a predictable location in the intervertebral foramen.

Lead placement is a percutaneous procedure performed via a 14 ga Touhy needle, epidural sheath, guidewire, and stimulator lead (Figure 2). Needle entry through the skin is typically two levels below the target DRG on the contralateral side. The epidural needle should enter at a shallow angle, directed toward the anatomical midline. After this point, the procedure differs significantly from traditional SCS. Once epidural access is obtained, a curved sheath is then advanced toward the target neuroforaminal opening (Figure 3). A semi-firm guidewire can be inserted within the sheath providing added rigidity to aid in advancing the tip out of the neuroforaminal opening while avoiding damage to the apparatus. Once the epidural sheath is appropriately positioned inferior to the pedicle, the DRG lead is then advanced out of the sheath with the contacts placed underneath the pedicle, presumably dorsal to the DRG. Strain relief loops are then added by retracting the sheath and advancing the lead superiorly as well as inferiorly (Figure 4); these serve to provide stability and prevent lead migration. As a result, anchoring of the lead is rarely required.

CONCLUSION

DRG stimulation appears primed to become a powerful and effective tool in neuropathic pain. Traditional SCS will continue

Figure 2: *Illustration of curved sheath (lead contained within) used to position the lead under the pedicle (A). Sheath (with lead inside) is inserted through the Touhy needle into the epidural space (B). Sheath is withdrawn, leaving the lead in position under the pedicle (C). Illustrations courtesy of St. Jude Medical.*

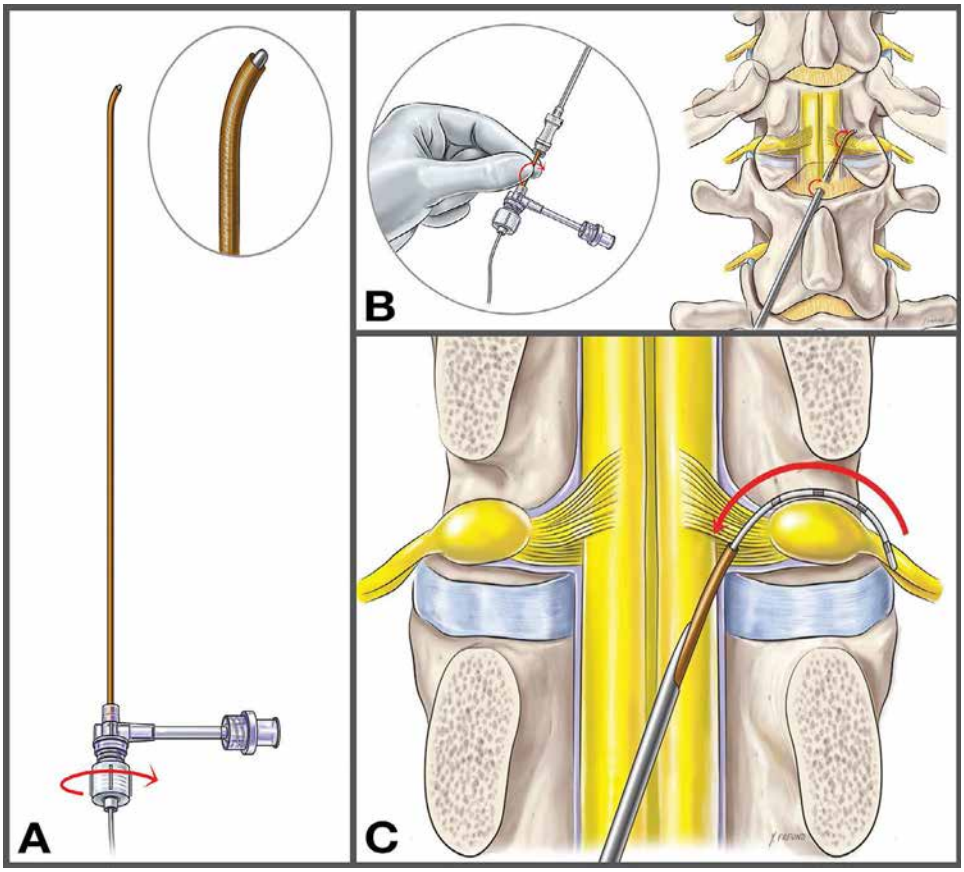


Figure 3: *Touhy needle entering at midline of L2/L3 epidural space with epidural sheath loaded with guidewire at the left L2 neuroforaminal opening.*

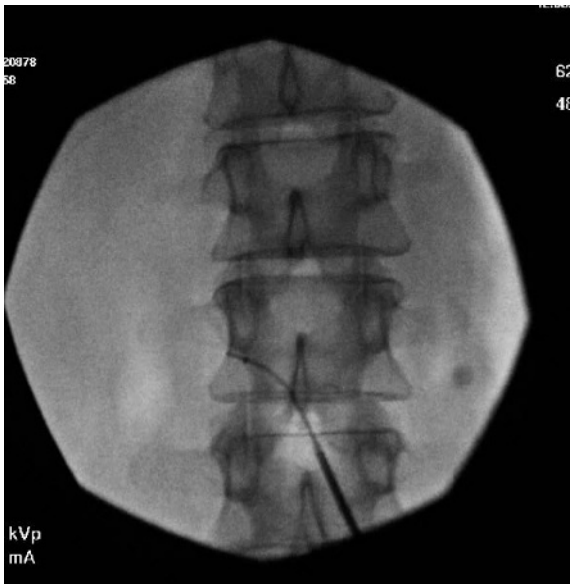
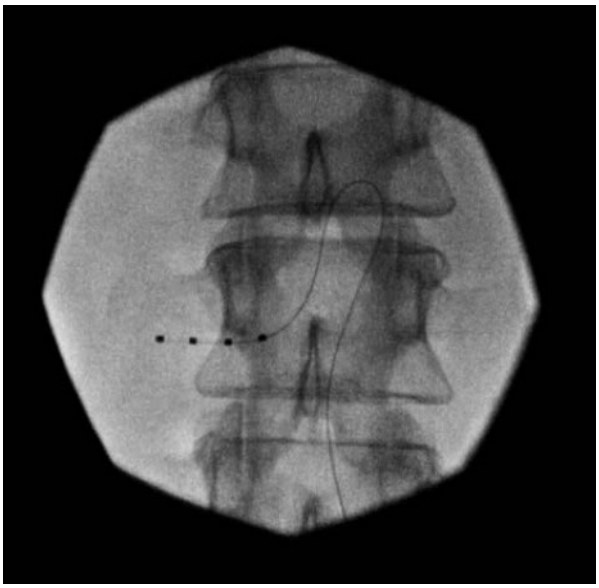


Figure 4: *Lead deployed at the left L2 DRG with superior epidural strain relief loop placed to increase stability and decrease lead migration.*



to play a significant role in a majority of neuropathic pain states, especially those involving spinal pathology or pain in a more dispersed distribution. DRG stimulation has limited but impressive evidence in its favor for CRPS and other focal neuropathic syndromes.[4,5,12] Selective stimulation of the DRG provides targeted coverage of specific areas such as the foot, hip, groin, and knee simple, thereby eliminating paresthesias in nonpainful or unwanted areas. DRG stimulation is a true breakthrough in the field of pain management; in appropriately selected patients, there is the potential to dramatically reduce pain even further than previously possible with conventional neuromodulation.

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Role of Opioids in Tumor Recurrence: An Update

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Cancer is the second most common cause of death in the United States.[1] This year marks a decade of studying the relationship between opioids and cancer recurrence, and some consider its study "one of the most important research questions in the specialty."[2,3] Multiple medications and anesthetic techniques have been evaluated for their effects on cancer recurrence, but none has been studied more than opioids.

Cancerous tumors evolve from single cells that undergo multiple cycles of division and mutation.[3] The tumor microenvironment includes blood vessels, immune cells, fibroblasts, inflammatory cells, signaling molecules, and an extracellular matrix.[4] Tumors larger than 2 mm cannot survive without angiogenesis. To access the systemic circulation, tumors release chemicals to penetrate vessels and lymphatics. Inflammation assists in tumor formation. Leukocytes make up the nonspecific, or innate, immune response. These cells phagocytize abnormal cells. Lymphocytes and natural killer (NK) cells mediate humoral and cell-mediated responses. Inflammatory cells secrete cytokines (Table 1), which assist in tissue turnover, cellular proliferation, and angiogenesis.[5]

During an inflammatory response, cells undergo multiple cycles of division and repair, creating the perfect opportunity for mutation and cancer formation. Thankfully, the immune system successfully destroys most cancer cells, and less than 0.1% are viable after 24 hours. The most widely accepted theory for destruction is immune-editing.[6] Surgery and pain elevate stress hormones and cytokine production, increasing the inflammatory response and weakening the immune response for 3 to 5 days postoperatively.[7] The effect of opioids on tumor progression or recurrence is currently unclear (Table 2). Opioids interact with tumor cells directly via mu receptors expressed by the tumor cells, or indirectly by altering immune cell function and angiogenesis.

"Multiple medications and anesthetic techniques have been evaluated for their effects on cancer recurrence, but none has been studied more than opioids."

OPIOIDS AND TUMOR CELLS

Mu-opioid receptors (MORs) are expressed by many tumor cells. Activation of MORs in vitro induces DNA cleavage in human lung cancer cells and activates various signaling pathways, cycloxygenase-2 (COX-2), and transactivates receptor tyrosine kinases (RTKs) in cells.[8] MOR antagonists reverse the protumoral effect of opioids in vitro.[9] Overexpression of MOR has correlated with greater tumor progression in a lung cancer mouse model.[9] Under different experimental conditions, high-dose morphine slowed tumor growth[10] and promoted apoptosis in lung tumor cells.[11] The antitumor properties of opioids were not always reversed by the use of opioid antagonists, indicating a potential MOR-independent effect.[12]

OPIOIDS AND ANGIOGENESIS

Tumor-induced proliferation of endothelial cells is mediated by angiogenic growth factors (eg, vascular endothelial growth factor [VEGF]). Upregulation is caused by hypoxia in the microenvironment of the tumor. Opioids directly stimulate VEGF via MOR. In vitro and in rats, morphine has stimulated endothelial cell proliferation and angiogenesis.[13,14] However, kappa opioid receptor suppresses angiogenesis by suppressing VEFG signaling.[15]

OPIOIDS AND TUMOR METASTASIS

Tumor metastasis requires degradation of the surrounding extracellular matrix and breach of the basement membrane mediated by release of urokinases and different metalloproteinases. Morphine augments the release of urokinases.[16]

OPIOIDS AND APOPTOSIS

Opioid receptor-mediated apoptosis has been demonstrated in breast cancer cells[17] and in small cell lung cancer cells.[13] Morphine (via MORs) induces expression of Fas (a receptor for the tumor necrosis factor family) in immune cells, priming them for Fas ligand-mediated apoptosis.

OPIOIDS AND IMMUNE CELLS

NK cells are key to eliminating tumor cells. They contact the target cells directly and release cytotoxic mediators that alter membrane permeability.[18] In animal models and in humans, opioids decreased NK cell activity for several days,[19] but chronic administration of opioids has had no effect. Intrathecal doses suppressed immune cells via MOR present in the central nervous system.[20] Opioids retard migration of immune cells to the tumor, potentiate inhibitory regulatory T cells, resulting in a weaker immune response that promotes tumor spread, reducing the activities of macrophages and cytokines. The function of IFNγ is decreased with opioid administration.[21]

HUMAN CLINICAL DATA

Four retrospective studies have shown an association between the use of opioids and poor recurrence-free or overall survival.[22] Three of the studies evaluated the use of opioids in the perioperative period, and one was conducted in patients with advanced disease.

Table 1: *Important inflammatory mediators.*

Cytokines	Action
TNF-α	Found in macrophages/monocytes, increases tumor adhesion to endothelial cells
IL-1	Released locally at injured site, alters pain perception
IL-2	Increases T lymphocyte proliferation, enhances NK cell activity
IL-6	Induces neutrophil activation
IL-12	Induces cytokine production by NK cells; enhances NK cell activity and migration
INF-α	Enhances NK activity, inhibits cell growth and proliferation
IFN-γ	Activates macrophages, potentially inducing acute lung inflammation and enhances NK cell activity
GM-CSF	Delays macrophage and neutrophil apoptosis
VEGF	Increases microvascular permeability and stimulates endothelial cell growth and angiogenesis

GM-CSF = granulocyte macrophage-colony stimulating factor; IFN = interferon gamma; IL = interleukin; NK = natural killer cell; TNF = tumor necrosis factor; VEGF = vascular endothelial growth factor

Table modified from Le-Wendling L, Nino O, Capdevila X. Cancer recurrence and regional anesthesia; the theories, the data, and the future in outcomes. Pain Medicine 2016;17(4):756–775.

Still others have found that the use of opioids for palliative care was not a predictor of survival in patients with lung cancer.[23]

In a study of patients who had radical prostatectomy, reducing amounts of fentanyl perioperatively was not associated with better recurrence-free survival.[24] The use of sufentanil during radical prostatectomy was associated with a seven-fold increase in the risk of cancer recurrence.[25] MOR expression on tumor cells is an independent risk factor for metastases to lymph nodes in esophageal cancer. When the opioid in epidural analgesia was reduced, survival rates did not improve after esophageal cancer surgery.

Three different groups evaluated opioids and tumor recurrence in the context of breast surgery. Of the three, one group found no benefit from reduced opioid use. Patients with colon cancer did not have better survival rates with epidural analgesia, whereas patients with rectal cancer did.[26]

In a population-based study of more than 40,377 patients undergoing surgery for colon cancer, patients receiving epidural analgesia were compared to patients receiving traditional analgesia.[27] There was no difference in recurrence-free survival but a significant benefit for overall survival with epidural analgesia.

In a posthoc analysis of 503 patients who had curative resection of colon cancer, survival was similar in both epidural and control groups (hazard ratio 0.95, 95% confidence interval [CI] 0.76–1.17;

Table 2: *Direct interaction of opioids on tumor cells.*

Cancer type	Opioids in vitro	Opioids in vivo animal data
Breast	Both pro- and antitumor effects	Pro- and antitumor effects
Gastrointestinal	Antitumor effect in esophageal cancer and gastric cancer, but no effect on liver and pancreatic cell lines	Pro- and antitumor effects
Glioblastoma	Antiproliferative effect	Antiproliferative effect
Lung	Increase proliferation and invasion	Short-term exposure causes tumor growth, but long-term exposure suppresses growth.
Ovarian	No effect on cell proliferation	No study data
Prostate	Antitumor effect in some lines	Pro- and antitumor effects

$p = 0.61$).[28] The median morphine use in the epidural group was 0; in the nonepidural group, 107 mg.

In a study of 4,329 patients whose melanoma was removed, the probability of survival was 85% in patients given local anesthesia and 78% in patients given general anesthesia.[29]

Epidural anesthesia and analgesia may improve overall survival in patients with operable colorectal cancer, but survival is not recurrence-free.[30] Survival improved with the use of peripheral mu antagonism when opioids were administered.[31]

CONCLUSION

Given that current data are primarily observational, it is impossible to determine definite associations at this time. The future of cancer pain management must rely heavily on prospective randomized trials. Cancer patients should not be denied pain relief, and until further research is completed, opioids will continue to be used in their treatment.

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Thinking Outside the Pharmacologic Toolbox: Integrative Therapies for Postoperative Pain

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Pain is more than just a sensory experience. It has multiple dimensions including affective, cognitive, behavioral, sociocultural, and spiritual components. The use of analgesic medications alone is insufficient to address all dimensions of the pain experience, whether pain is acute or chronic. An integrative approach involves bringing conventional and complementary interventions together in a coordinated manner. Use of cognitive–behavioral and physical modalities as part of a multimodal strategy is a major recommendation with moderate quality evidence in the American Pain Society, American Society of Regional Anesthesia and Pain Medicine, and American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council Guidelines on Postoperative Pain.[1]

COGNITIVE–BEHAVIORAL TECHNIQUES

Cognitive and behavioral strategies for pain management help to change one's interpretation and experience of pain by modifying thoughts and behaviors that exacerbate pain or interfere with coping efforts. In the perioperative setting, psychological factors that may impact pain include anxiety, depression, posttraumatic stress disorder, and pain catastrophizing. Pain catastrophizing is a strong predictor for poor outcomes, including acute and chronic pain intensity, greater use and poor response to opioids, misuse of opioids, and persistent use of opioids after surgery.[2] Brief interventions by a staff psychologist or other mental health provider may help alleviate patterns of negative cognitive–emotional responses, although the most effective timing and format for interventions are as yet undetermined.[3] Some potential interventions are briefly discussed below, including distraction, relaxation, guided imagery, and hypnosis.

"An integrative approach involves bringing conventional and complementary interventions together in a coordinated manner."

Many activities can be used for distraction including listening to music, reading, watching television, doing puzzles, drawing/coloring, or playing video games. The activity should be appropriate to the patient's energy level and ability to concentrate. For example, a patient who is a musician may be unable to physically play his or her instrument but can listen to musical recordings or read a musical score and imagine the activity of playing the instrument. Distraction activities are also more engaging if they stimulate multiple major senses, including hearing, sight, touch, and kinesthetic movement. Distractive tasks that get more complex or difficult as they are practiced, such as video games, may be helpful in maintaining the individual's attention.

Music therapy alone has been a subject of interest and can be considered either as a distraction tool or as part of relaxation. There is moderate evidence from several trials—including patients undergoing hip or knee surgery, nasal surgery, and coronary artery bypass grafting, among others—that use of music after the postanesthesia care unit (PACU) period is associated with reduced pain, analgesic use, and anxiety, when compared to nonmusic controls.[4–6] Prescribed music in studies has ranged from one hour of lullaby music four times daily starting at wakeup from anesthesia to just 20 minutes of easy listening, classical, or jazz, per the patient's preference, twice a day.

Relaxation and guided imagery may be used independently or in tandem. Relaxation interventions decrease autonomic nervous system activity, resulting in reduced oxygen consumption, slowing of heart rate and breathing, reduction in blood pressure, and release of muscle tension. Examples of techniques include jaw relaxation and diaphragmatic breathing. Meditation and prayer may be useful in some patients. Relaxation may have a similar effect to music on pain through postoperative day two.[7,8] Guided imagery involves the use of one's imagination to create and experience mental images that may distract attention from pain or change the pain experience. This process is thought to trigger a physiologic reaction, as though the imagined scenario is actually taking place. Pain-focused imagery uses mental images of the pain itself or of objects that may alter the pain sensation. For example, a patient may imagine his or her pain to feel like a raging fire and create images of a cold rainstorm dousing the fire to change the burning pain sensation. In one of the larger, higher-quality studies on guided imagery in patients undergoing colorectal surgery, it was

associated with significantly reduced opioid use, postoperative pain intensity, and anxiety.[9] The guided-imagery group started techniques with assistance of guided-imagery tapes three days prior to surgery and continued them upon anesthesia induction, in the PACU, and for six days after surgery, resulting in 50% less opioid use after surgery.

Nursing personnel can be trained to provide basic behavioral pain management interventions such as distraction, relaxation (eg, visualization, diaphragmatic breathing), and other techniques. Chaplaincy services may also provide social, emotional, and spiritual support to patients and families. Many chaplains have training in guided meditation.

Hypnosis has shown inconsistent results in studies. Patients are typically taught to practice self-hypnosis preoperatively and use the techniques in the postoperative period. In one higher-quality study of patients undergoing mitral valve surgery, no difference was seen in pain, anxiety, or depression scores.[10] In another higher-quality study of patients undergoing breast biopsy/lumpectomy, hypnosis was associated with reduced pain scores and emotional upset, though this did not translate to reduced analgesic use.[11]

PHYSICAL MODALITIES

Physical techniques provide comfort, correct physical dysfunction, and alter physiologic responses to pain. The use of cold/heat application, transcutaneous electrical nerve stimulators (TENS), and acupuncture postoperatively are discussed below. Massage and physical activity (such as with use of continuous passive motion) also have roles in reducing edema, releasing muscle spasms, and stimulating relaxation.

Application of cold may reduce or relieve pain by decreasing sensitivity to pain, reducing muscle spasms, and providing a competing sensory experience. Interestingly, evidence on application of cold by ice packs or cool compresses at or near the surgical site has been inconsistent in showing reduced postsurgical pain, though it has been studied in anterior cruciate ligament reconstruction as well as caesarean section and inguinal hernia repair.[12–14] Heat can be delivered through simple devices available in most settings, such as hot water bottles, commercial heat wraps, and warm damp towels (compresses). Moist heat has been found to penetrate deeper into tissues than dry heat.[15,16] Heat application is contraindicated over areas of bleeding, over topical menthol or other medicated ointments, and over burned or radiated skin. Topical heat should be used with caution in patients with impaired circulation, reduced sensation, or impaired communication that would prevent reporting when the heat source has become uncomfortable. These factors may limit use of heat immediately postoperatively but can be considered for concurrent pain not related to the surgical site.

TENS are small portable devices that deliver low-voltage electrical currents through the skin. TENS are thought to activate endogenous-descending inhibitory pathways, activating opioid receptors to reduce central excitability and reduce pain. TENS can be used for acute or chronic pain and pose little risk for safety, though consultation should be sought from an electrophysiologist prior to use in patients with implanted pacemakers or defibrillators. A systematic review of over 20 randomized trials found use of TENS associated with approximately 25% less postoperative analgesic use compared to no TENS.[17] Although many hospitals utilize physical therapists to administer TENS, nurses can be trained to deliver TENS in the hospital. Electrodes can be placed on either side of an incisional area on intact skin with recommendation to use during activity for 30–60 minutes several times a day.

Acupuncture stems from traditional Chinese medicine and involves a trained practitioner inserting very thin needles (30–40 gauge) at specific acupuncture points along the body's meridians (pathways) to assist the free flow of Qi (a form of energy). The physiologic basis for acupuncture-induced analgesia is complex: Release of endogenous opioids; modulation of the NMDA, adrenergic, and 5-hydroxytryptamine systems; and anti-inflammation effects have all been proposed as mechanisms. Traditional needle acupuncture, electroacupuncture, capsaicin or TENS unit over acupressure points, auricular acupuncture, and acupressure alone have all been examined without any standard timing, method, or frequency of delivery. A systematic review across all approaches by Sun et al. revealed reduced postoperative opioid consumption and opioid-related side effects at 8 hours, 24 hours, and 72 hours (opioid-sparing effect of 21%, 23%, and 29%, respectively) with reduced pain intensity at 8 hours and 72 hours when compared to sham treatment.[18] A recent review of studies specifically on acupuncture for acute pain following back surgery concludes "encouraging" results with regard to reduced pain intensity and opioid use 24 hours after surgery.[19] However, more trials are indicated as studies in acupuncture overall tend to be inconsistent and insufficient to fully support acupuncture for general acute postoperative pain.[20]

CONCLUSION

In summary, the techniques described above should be considered as part of multimodal analgesic approach for acute postoperative pain. Aside from literature supportive of integrative interventions—such as distraction/relaxation, guided imagery, TENS, and acupuncture—the methods introduce minimal risk to the patient and can be accomplished at low cost with education of nursing personnel and use of an interdisciplinary pain team. As with many areas in medicine, more research is needed, but it is reasonable to conclude that appropriate application in selected patients has potential to improve pain control, reduce analgesic consumption, and reduce medication side effects.

RESOURCE SITE

National Center for Complementary and Alternative Medicine (NCCAM), http://nccam.nih.gov/

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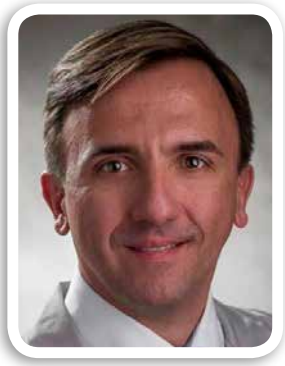
New Therapeutic Options in Perspective for Patients with Chronic Low Back Pain



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The current treatment of back pain, the second leading cause of disability in adults in the United States, according to the Centers for Disease Control and Prevention (CDC),[1] includes conservative management and invasive treatments. Conservative treatments usually improve back pain symptoms in the majority of patients[2–4]; however, in some cases, even more invasive treatments (epidural steroid injections, facet injections, or radiofrequency ablation) have not been found to decrease the need for subsequent surgeries in patients with chronic pain secondary to herniated intervertebral discs.

The question arises whether physicians have other options for patients who fail both conservative therapy and interventional procedures, before considering a surgical approach. The purpose of this article is to review new developing therapies on the horizon to better treat chronic low back pain (Table 1).

CHEMONUCLEOLYISIS: PAST OR FUTURE?

Chemonucleolysis consists of injecting proteolytic enzymes into the intervertebral disc in an attempt to dissolve the herniated nucleus pulposus. Chymopapain, the nonspecific proteoglycanase derived from papaya, has been shown to be effective in dissolving cartilaginous tissue from displaced intervertebral discs without affecting surrounding collagen or nervous tissues.[5] Many studies and meta-analysis showed that chymonucleolysis with chemopapain was superior to placebo and had around 80% success rate in reducing pain caused by a herniated disc.[6–8] It was discovered, however, through 20 years of experience with chymopapin, that careful selection of patients for chemonucleolysis was crucial for the success of the treatment.[9,10] Unfortunately, it is not in use today due to the very allergenic potential of chymopapain (50 per 100,000 patients had serious anaphylactic reactions).[5,8,10,11]

"These new approaches to treatments will prove beneficial for patients suffering from chronic back pain who have failed conservative and interventional procedures."

Due to these safety concerns, other enzymes have been studied, such as collagenase, chondroitinase ABC, and matrix metalloproteinases. Collagenase is fairly specific for type II collagen fibers, which are mainly found in the nucleus pulposus. Collagenase has lower allergic potential than chymopapain[12] and has a similar success rate even at five-year follow up.[12,13] However, there are some reports of end plate erosion on adjacent vertebra, hemorrhage, or even paraplegia after collagenase injections.[14] Chondroitinase ABC cleaves the side chains of proteoglycans, and animal studies have shown that it is safer than chymopapain and collagenase.[15] No human studies have been published, however, testing chondroitinase. Matrix metalloproteinases (MMPs) are zinc proteases that degrade various portions of the extracellular matrix, especially the nucleus pulposus.[16] MMP-3 and MMP-7 have been shown to have an important role in the natural resorption of herniated discs.[17] In vitro–treated human herniated discs showed that MMP-7 degraded mainly the structures of the nucleus, while chymopapain degraded both the nucleus and the annulus.[18] Furthermore, since recombinant human MMP-7 is a human protein, it should not cause anaphylaxis and should be safer than chymopapain in its clinical use.[16]

Ethanol gel is another alternative to chymopapain. Patients with cervical and lumbar disc herniations[19] and those who failed conservative treatments[20] were found to have significant benefit when treated with ethanol gel. A randomized open-labeled study with 300 patients is currently underway, testing the efficacy of ethanol gel in patients with sciatica pain resistant to conservative and interventional treatments.[21]

ARTEMIN

Artemin is a neurotropic growth factor in the glial cell line-derived neurotropic factor (GDNF) family that acts on sensory neurons. In rats, it was found to promote regeneration of nerve fibers and reestablish spinal connections.[22] When disc herniation occurs, it causes direct pressure and damage to the nerves adjacent to the spinal cord. Since artemin is very specific for sensory nerves, it

Table 1. *New Therapeutic Options for the Treatment of Chronic Low Back Pain in Different Phases of Clinical Research.*

Product	Therapeutic area	Phase 1	Phase 2	Phase 3
Intradiscal Injections				
Matrix metalloproteinase	Chemonucleolysis	X		
Ethanol gel	Chemonucleolysis		0	
Platelet rich plasma	Disc regeneration		X	
Stem cell therapy	Disc regeneration	0		
Subcutaneous injection				
Tanezumab	Nociceptor modulation	0		
Intravenous injection				
Artemin	Neuronal regrowth		X	

0=Ongoing clinical trials X=Completed clinical trial

was thought that it could facilitate repair of the damaged nerves, leading to decreased pain. A phase I study examining the safety and tolerability of escalating doses of an intravenous artemin-containing medication has supported the future development of the drug secondary to favorable results.[23] A phase II study completed in 2015 compared intravenous artemin administration to placebo for patients with lumbar radiculopathy; however, these results are yet to be published.[24]

TANEZUMAB

Tanezumab is a monoclonal antibody that has a high affinity for nerve growth factor (NGF). NGF modulates nociceptive neuronal activity and is present when there is nerve damage.[25] High levels are seen in patients with chronic pain conditions, as well as administrating exogenous NGF results in hyperalgesia.[26] Furthermore, human studies blocking NGF have shown decreased pain in some chronic pain conditions.[27,28] Katz et al showed that tanezumab caused a greater reduction in low back pain index than did naproxen.[29] A phase III trial is currently underway to study subcutaneous administration of tanezumab over a 56-week time span in patients with chronic low back pain.[30]

GROWTH FACTORS

Growth factors have also been studied. It was hoped that growth factors would upregulate anabolic pathways and cell proliferation, thereby stimulating disc cells to produce more cell matrix and result in a healthier nucleus pulpous with increased proteoglycan production and water content. Unfortunately, individual growth factor therapy has had limited success for several reasons, including high cost, short half-life of the factors resulting in the need for many repeat injections, and severely decreased amounts of viable cells in degenerative discs for the growth factors to act on, thus limiting matrix synthesis.[31]

Platelet rich plasma (PRP) may, however, be beneficial. It is high in many growth factors, and its safety and relative ease to obtain has been well studied. PRP has already been used for many orthopedic conditions. There have been several small studies demonstrating significant pain relief after injection of PRP directly into the intervertebral disc.[32,33]

STEM CELL THERAPY

Similar to growth factors, stem cell research is aimed at healing the degenerate intervertebral discs by focusing on cell replacement, thus leading to an increased cell matrix. However, there are many obstacles in regards to developing stem cell therapy for treatment of disc disease. Aside from ethical issues clouding the stem cells approach, it has been challenging to preserve the right kind of cell that is able to survive in the unusual environment of the intervertebral disc (low pH, low blood supply). In addition, the most effective source of the stem cells (allogenic vs autogenic or adipose vs bone marrow vs umbilical cells) has not yet been well studied. Smaller human trials have been executed with some success. One study involved patients who failed to respond to conservative therapy; stem cells were harvested from their iliac crests, resulting in reduction of lumbar pain.[34] A phase III trial is currently underway evaluating the administration of stem cells injected into the intervertebral discs in patients with chronic low back pain.[35]

CONCLUSION

Even though chemonucleolysis with chymopapain has been abandoned for more than 10 years, it may re-emerge as a treatment option for patients with herniated intervertebral discs

by using different dissolving agents. Ethanol gel and MMP-7 are currently being tested in human studies. Artemin showed successful nerve regeneration in animal models; however, we are still waiting for results from the Phase II study. Tanezumab is currently being studied in a large, multicenter, phase III, international study. Initial promising results of small studies using PRP and mesenchymal stem cells should be confirmed in larger, prospective, randomized controlled studies. We believe that these new approaches to treatments will prove beneficial for patients suffering from chronic back pain who have failed conservative and interventional procedures and decrease the need for surgery.

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