7th International Conference and Exhibition on

# Pain Research and Management

October 11-12, 2018 | Zurich, Switzerland

# Keynote Forum

## Day 1

Nelson Hendler, J Pain Relief 2018, Volume 7
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## Nelson Hendler

*Johns Hopkins University School of Medicine, USA*

## Evaluating chronic pain patients using methods from Johns Hopkins Hospital physicians

Chronic pain patients are misdiagnosed 40%-80% of the time, according to research from Johns Hopkins Hospital physicians. The most common of these misdiagnoses is sprains or strains, which are listed in medical textbooks as self-limited disorders, which resolve in less than three weeks without treatment. Yet these diagnoses account for over 50% of diagnoses in patients with pain for more than three months. On the other hand, certain diagnoses are overused, and misapplied without attention to published diagnostic criteria. Therefore, complex regional pain syndrome (CRPS) formerly called reflex sympathetic dystrophy (RSD), and fibromyalgia, are over diagnosed 71% to 97% of the time, to the detriment of the patients. The leading causes of these errors in diagnoses are: failure to take a complete history, and using the wrong medical tests. As an example, MRIs fail to detect damaged discs 78% of the time compared to a provocative discogram, and CT fail to detect bony lesions 56% of the time compared to 3D-CT. Two expert system internet questionnaires are discussed. The pain validity test predicts the presence of abnormal medical testing with 95% accuracy, which validates the complaint of pain, and detects drug seeking behavior. Another internet based expert system the diagnostic paradigm, provides diagnoses with a 96% correlation with diagnoses of Johns Hopkins Hospital physicians. The associated treatment algorithm recommends the appropriate tests to use for confirm the correct diagnosis. The value of these two systems is documented by published outcome studies, which demonstrate patient improvement rates far higher than other methods. These publications report cost savings $20,000 to $175,000 a case, with an 89% reduction in narcotic use, and a 45% reduction in doctor visits. Between 50%-63% of patients need surgery to improve.

### Recent Publications

1. Hendler N and Baker A (2008) An Internet questionnaire to predict the presence or absence of organic pathology in chronic back, neck and limb pain patients. Pan Arab Journal of Neurosurgery 12(1):15-24.
2. Davis R, Hendler N and Baker A (2016) Predicting medical test results and intra-operative findings in chronic pain patients using the on-line pain validity test. Journal of Anesthesia and Critical Care: Open Access 5(1):00174.
3. Hendler N and Spurgeon D (2007) Comparison of clinical diagnoses versus computerized test diagnoses using the Maryland clinical diagnostics diagnostic paradigm (expert system) for diagnosing chronic pain in the neck, back and limbs. Journal of Anesthesia & Critical Care 6(5):00242.
4. Hendler N (2017) Facial pain from various sources-diagnoses, and differential diagnoses. Dental, Oral and Craniofacial Research DOI: 10.15761/DOCR.1000220.
5. Hendler N (2017) An internet based questionnaire to identify drug seeking behavior in a patient in the ED and office. Journal of Anesthesia & Critical Care, Open Access 8(3):00306.

### Biography

Nelson Hendler has graduated cum laude from Princeton University. He has an MD and MS in Neurophysiology from University of Maryland School of Medicine. He did his Residency in Psychiatry at Johns Hopkins Hospital and remained as the Faculty at the Medical School for 31 years. He has published 4 books, 33 medical text book chapter, and 65 articles. He has lectured in over 60 hospitals and medical schools in the US and in 10 other countries. He has served as the President of the American Academy of Pain Management and the Reflex Sympathetic Dystrophy Association of America and served on the board of the Lightning Strike and Electric Shock Survivors International.

Docnelse@aol.com

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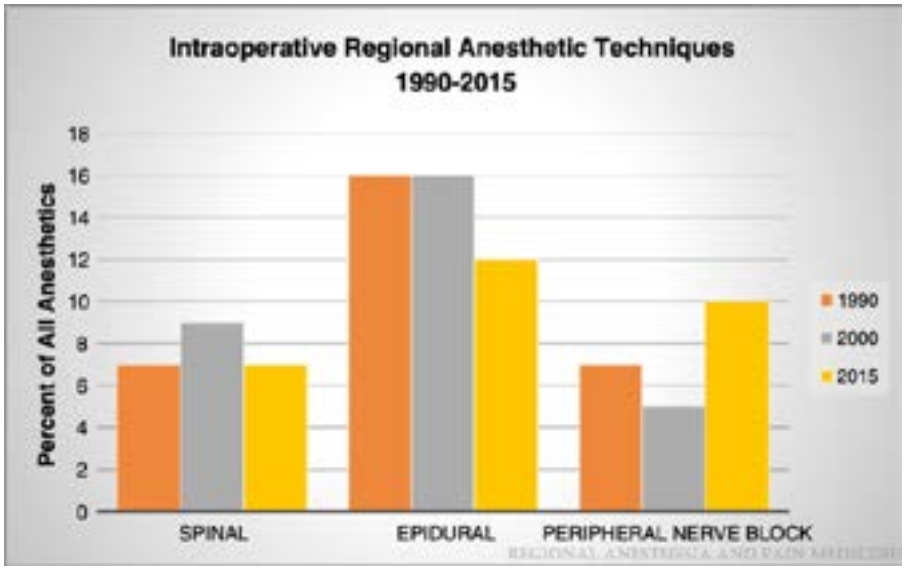
*Jeff L Xu*

*Westchester Medical Center & New York Medical College, USA*

## Paraneuraxial nerve blocks: Can they replace neuraxial nerve blocks?

Over the past 10-15 years, the quick development of ultrasound technique has rapidly changed the practice of regional anesthesia including the greater use of truncal nerve blocks. Some of the truncal blocks are performed just outside of neuraxial region, such as deep cervical plexus block (dCPB), paravertebral nerve block (PVB) and lumbar plexus block (LPB), in addition to Thoracolumbar Interfascial Plane (TLIP),1 retrolaminar block (RLB), erector spinae plane (ESP) block, and cervical columnar interfascial plane (CCIP) block, quadratus lumborum block III (QL, III), which are new techniques. These techniques are comparable to neuraxial nerve blocks in terms of analgesic efficacy and may confer many of advantages over neuraxial nerve blocks.2Specifically, neuraxial blocks are not site-specific, they cause hypotension, and some of them may lead urinary retention, the placement of Foley catheters, limited mobility.2-3 We have proposed the use of the new terminology "Paraneuraxial Nerve Block (ParaNXB)".4 This new term provides a direct pictorial anatomy of the nerve block and would help clinicians develop clinical insights.5-7 The ParaNXB family may include the dCPB, PVB and the LPB, as well as ESP, RLB, TLIP block, CCIP block, QL III block and sympathetic chain block. We believe that ParaNXB will become even more popular clinically, due to its clinical and anatomical characteristics. It is thus clinically significant and beneficial in the practice, teaching, and training aspects of regional anesthesia. Study has shown that since 1990, wherein the relative percentage of spinal and epidural techniques has declined, and peripheral nerve blocks have increased.8 ParaNXBs will challenge the clinical role of the traditional neuraxial nerve blocks fundamentally.



## Recent Publications

1. Hironobu Ueshima, Hiroshi Otake. Clinical Experiences of the Continuous Thoracolumbar Interfascial Plane (TLIP) Block. Journal of Clinical Anesthesia 2016; 34, 555–556
2. Davies RG, Myles PS, Graham JM. A comparison of the analgesic efficacy and side-effects of paravertebral vs epidural blockade for thoracotomy—a systematic review and meta-analysis of randomized trials. Br J Anaesth 2006;96:418–26.
3. Powell ES, Cook D, Pearce AC, et al. A prospective, multicentre, observational cohort study of analgesia and outcome after pneumonectomy. Br J Anaesth 2011;106:364–70.
4. Jeff L. Xu. Paraneuraxial Nerve Blocks: A well-defined novel terminology that is clinically essential for regional anesthesia. J Clin Anesth. 2017 Sep 13;43:14
5. Alan David Kaye, Richard D. Urman, Nalini. Essentials of Regional Anesthesia. New York, NY: Springer Science+Business Media, LLC, 2012. Page 585
6. L. Brown. Atlas of Regional Anesthesia.4th ed. Philadelphia, PA: Sunders, 2010. Page 254
7. Andrea Toufexis Esch, Andrew Esch, John L. Knorr, Andre P. Boezaart. Long-Term Ambulatory Continuous Nerve Blocks for Terminally Ill Patients: A Case Series. Pain Medicine 2010; 11:1299–1302
8. Joseph M. Neal, Anne Gravel Sullivan, Richard W. Rosenquist, Dan J. Kopacz. Regional Anesthesia and Pain Medicine US Anesthesiology Resident Training—The Year 2015. Regional Anesthesia and Pain Medicine, 2017; 42:437-441

## Biography

Jeff L. Xu, MD, chief of Regional Anesthesia & Acute Pain Management, Program Director of Regional Anesthesiology & Acute Pain Medicine Fellowship. As the founder of the Regional Anesthesia & Acute Pain Services at Westchester Medical Center, he initiated and developed the regional anesthesia program for the anesthesia residents. He also is the founder of the fellowship program for Regional Anesthesiology & Acute Pain Medicine at Westchester Medical Center/New York Medical College, New York, USA, and served as fellowship program director. He served as principal investigator on multiple clinical studies, reviewer for peer review journals, faculty for regional anesthesia workshops, speaker for national and international conferences.

jeff.xu@wmchealth.org

**Notes:**

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## William P Gallagher Jr

*American Academy of Motor Vehicle Injuries, USA*

## Understanding the mechanism of injury: A means to provide better direction for proper diagnoses in motor vehicle collisions

**Statement of the Problem**: Diagnosing any disease or injury can be a challenge even for the most experienced physicians. Studies dating back to the 1999 Institute of Health report, To Err is Human estimated up to 98,000 die each year in the US due to medical errors and to death by medicine in 2011 that calculated 784,936 deaths, making medical errors the leading cause of death in the US. Unfortunately, the all too common lack of proper diagnosis not only exposes the doctor to malpractice but it also leaves the patient with inappropriate treatment and quite often a failure to recover. With motor vehicle collisions, understanding the mechanism of injury is an essential tool toward a better diagnosis.

**Literature Review**: Past studies with live subjects offer a better understanding of spinal motion and what structures can be injured. Unfortunately, knowing the probability of injury it is difficult to do additional live testing today to observe injuries that were overlooked in past studies. This is of particular concern with concussions/traumatic brain injuries that until recently were commonly overlooked. Testing on these injuries today is primarily with athletes and military personnel with little information on motor vehicle collisions. What we lack in knowledge of the mechanism of injury becomes evident in our failure to diagnose so many conditions.

**Conclusion & Significance**: Live subject studies can in part be replaced by digital modeling. Coupled with existing knowledge of biomechanics this can be a useful resource. For the most part the ability to diagnose injuries still goes back to the basic foundation of a good history. Understanding the mechanism of injury is an essential starting point for that history and in turn the means to a better diagnosis.


Factors to consider in making a diagnosis

### Recent Publications

1. Hendler et al. (1993) Overlooked Physical diagnoses in chronic pain patients involved in litigation. Psychosomatics 34(6):494-501.
2. Nelson W G, Rosen A and Pronovost P J (2016) Reengineering the physical examination for the new millennium? JAMA 315(22):2391–2392.
3. Kirkwood Graham, Hughes Thomas C and Pollock Allyson M (2014) Injury surveillance in Europe and the UK. BMJ DOI: https://doi.org/10.1136/bmj.g5337.
4. Erin P Balogh and B T (2015) Improving Diagnosis in Healthcare. New York: National Academies DOI: 10.17226/21794.

## Biography

William P Gallagher Jr has practiced chiropractic in Arizona and California for the past 30 years. As someone who has survived several motor vehicle collisions, this is an area of particular concern to him. In order to learn and teach about motor vehicle injuries he created the American Academy of motor vehicle injuries. The academies 150 hour certificate program teaches doctors how to diagnose, document, and manage a personal injury case. Half of the core curriculum is on exam and diagnosis and all of that is based on understanding first the mechanism of injury. He publishes a personal-injury quarterly for the Arizona Association of chiropractic and is a contributing Editor to attorney at law magazine.

drbillgallagher@yahoo.com

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## Peter W. Schiller

*Montreal Clinical Research Institute, Canada*

*University of Montreal, Canada*

## Bi- or multifunctional opioid analgesics

Acute pain typically responds well to treatment with opioids and NSAIDs, whereas neuropathic pain is difficult to treat with only 40-60% of patients achieving pain relief. Currently used treatments, including tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors, anticonvulsants and morphine are either ineffective or produce major, limiting side effects. Our goal is to develop opioids with novel bi- or multifunctional activity profiles for treatment of chronic pain with minimal side effects. [Dmt1]DALDA (SS-02), a tetrapeptide with excellent drug-like properties, is a potent mu opioid analgesic and also is a mitochondria-targeted antioxidant. Mitochondrial reactive oxygen species (ROS) play a key role in mechanisms of neuropathic pain and there is evidence that ROS quenchers synergize with opiates in alleviating neuropathic pain. As expected, SS-02 turned out to be more effective than morphine in a rat model of neuropathic pain. Similarly, in a rat model of complex regional pain syndrome (CRPS-1), SS-02 and one of its analogues produced an up to 70-fold more potent and longer-lasting analgesic effect as compared to morphine. A structurally related peptide (SS-20) capable of promoting mitochondrial energetics had a protective effect against the development of chemotherapy-induced peripheral neuropathy in mice. Thus, these compounds are excellent drug candidates for neuropathic pain treatment. In a different approach we developed bifunctional compounds that target two distinct receptors. On the basis of a strong pharmacological rationale compounds were designed that act as agonists at the mu opioid receptor (MOR) and as antagonists at the delta opioid receptor (DOR). Such MOR agonist/DOR antagonists turned out to be potent analgesics in the rat tail flick test with low propensity to produce analgesic tolerance and dependence. Furthermore, bifunctional MOR agonist/NK1 receptor antagonists and opioid agonist/nociceptin antagonists were more potent than morphine in a neuropathic pain model and in one case did not produce respiratory depression.

### Recent Publications

1. Schiller P W, Nguyen TM-D, Saray A, Poon A W H, Laferrière A and Coderre T J (2015) The bifunctional μ opioid agonist/antioxidant [Dmt1]DALDA is a superior analgesic in an animal model of complex regional pain syndrome-type 1. ACS Chemical Neuroscience 6:1789-1793.
2. Toyama S, Shimoyama N, Szeto H H, Schiller P W and Shimoyama M (2018) Protective effect of a mitochondria-targeted peptide against the development of chemotherapy-induced peripheral neuropathy in mice. ACS Chemical Neuroscience DOI: 10.1021/acschemneuro.8b00013.
3. Ballet S, Betti C, Novoa A, Tömböly C, Nielsen C U, Helms H C, Lesniak A, Kleczkowska P, Chung N N, Lipkowski A W, Brodin B, Tourwé D and Schiller W (2014) *In vitro* membrane permeation studies and *in vivo* antinociception of glycosylated Dmt1-DALDA analogues. ACS Medicinal Chemistry Letters 5:352-357.
4. Betti C, Mika J, Dyniewicz J, Frankiewicz L, Novoa A, Keresztes A, Kosson P, Van Duppen J, Chung N N, Vandenbroeck J, Lipkowski A W, Schiller P W, Przewlocka B, Tourwé D and Ballet S (2015) Dual alleviation of acute and neuropathic pain by fused opioid agonist-neurokinin 1 antagonist peptidomimetics. ACS Medicinal Chemistry Letters 6:1209-1214.
5. Guillemyn K, Starnowska J, Lagard C, Dyniewicz J, Chung NN, Kosson P, Lipkowski A W, Chevillard L, Megarbane B, Tourwé D, Simonin F, Przewlocka B, Schiller P W and Ballet S (2016) Bifunctional and peptide-based opioid agonist-nociceptin antagonist ligands for dual treatment of acute and neuropathic pain. Journal of Medicinal Chemistry 59:3777-3792.

## Biography

Peter W. Schiller is a Medicinal Chemist and Pharmacologist. He is a research Professor in the Department of Pharmacology and Physiology of the University of Montreal and at the Montreal Clinical Research Institute (Canadian Pacific Chair in Pain Research). His research in the opioid field resulted in the discovery of highly receptor-specific agonists and antagonists and of opioids with novel bi-or multifunctional activity profiles. Some of his compounds are widely used as pharmacological tools or are being pursued as analgesic drug candidates. He has published over 400 scientific articles and holds 17 patents. He was elected Fellow of the Royal Society of Canada (Academy of Science) and of the American Association for the Advancement of Science (AAAS). His numerous awards include the Prix Galien of Canada for excellence in pharmaceutical research, a NIH MERIT Award and the Vincent du Vigneaud Award from the American Peptide Society.

schillp@ircm.qc.ca

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