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## In the News

### Metformin for Pain

Metformin has been shown to have both anti-inflammatory and antioxidant properties. A number of researchers are investigating its use for pain. In animal models, metformin has been shown to significantly suppress microglial activation successfully decreasing pain hypersensitivity and cold allodynia associated with neuropathic pain. Other reports provide a rationale as to why metformin should have a key role in chronic pain states, particularly those that have centralized and have neuroinflammation. Insulin has a direct effect on CNS mitochondria. Glial cells actively absorb glucose from the blood supply to the CNS. Metformin crosses the blood-brain barrier and seems to have a regulatory and homeostatic effect on glial cells and neuroinflammation. *Practical Pain Management*, Dec. 2016.

### IV Acetaminophen for Burn Pain

Sixty-one patients admitted to a burn intensive care unit, burn step-down, and surgery floors were assigned to receive 1 of 2 pharmacologic treatments after burn related surgery: 4 doses of IV acetaminophen 1000 mg plus opioids or PCA morphine or hydromorphone. No NSAIDs or other forms of acetaminophen were allowed. IV acetaminophen was given prior to surgery or debridement procedures. While the difference in pain scores was not statistically significant, opioid use was reduced by 30% in the acetaminophen group. IV acetaminophen may be a good option to add to a burn pain regimen for those at high risk for opioid sedation, respiratory depression, or those with intolerable opioid side effects.

*IV Acetaminophen Reduces Need for Opioids in Burn Patients*, Subieta, G., Torres, M., Poulakidas, S., Messer, T., Waghray-Pennetcha, T., & Fadayomi, O. 2016. *Practical Pain Management*.

### Yoga Helps Reverse Effects of Pain on the Brain

MRI studies in both rats and humans have shown alterations in gray matter volume and white matter integrity in the brain caused by the effects of chronic pain. Gray matter loss has been demonstrated in those with chronic pain and depression. The impact of this loss depends on where it occurs in the brain. It can also lead to memory impairment, emotional problems, and decreased cognitive functioning. Practicing yoga has the opposite effect on the brain. Yoga practitioners have more gray matter than controls in multiple brain regions, including those involved in pain modulation. Further, gray matter increase corresponds to duration of yoga practice. Gray matter changes in the insula or internal structures of the cerebral cortex are most significant for pain tolerance. Increases in insula gray matter can result from ongoing yoga. *Practical Pain Management*, American Pain Society Meeting Highlights, 2015. Bushnell, C.

### New CDC Opioid Guideline Mobile App Now Available

The CDC has released its free Opioid Guideline app, designed to help providers apply the recommendations of the CDC Guideline for Prescribing Opioids for Chronic Pain into clinical practice. The new app includes the full guideline, as well as tools and resources to help promote the safe and appropriate prescribing of opioids for chronic pain. The app includes a morphine milligram equivalent calculator, summaries of key recommendations and an interactive motivational interviewing feature to help providers practice effective communication skills and "prescribe with confidence," according to the CDC. The new CDC Opioid Guideline app is now available for free download on Google Play (Android devices) and on the App Store (iOS devices). For more information, go to [www.cdc.gov/drugoverdose/prescribing/app.html](http://www.cdc.gov/drugoverdose/prescribing/app.html).

### Risk of Endo's opioid painkiller outweigh benefits: FDA panel

The benefits of Endo International Plc's long-acting opioid painkiller no longer outweigh its risks, an independent panel to the U.S. Food and Drug Administration (FDA) concluded on Tuesday. The advisory committee meeting was called to address the high abuse rate of Endo's Opana ER and other oxymorphone formulations, as the health regulator looks to stem the tide of opioid abuse, overdose and addiction. Initially approved in 2006, a new formulation of Opana ER designed to deter snorting and oral abuse hit the market in 2012. Data shows that while nasal abuse has reduced with the reformulation, intravenous abuse has increased, FDA staff noted in an internal review on Thursday, acknowledging that it was unclear whether that rise was tied directly to the reformulation. This trend was apparent before the reformulation hit the market, and abuse rates are similarly high for oxymorphone generics, they said. Of particular concern is the increased rate of certain rare blood disorders and HIV that are linked to the shift in route of Opana abuse from nasal to intravenous, panelists said on Tuesday. Eighteen panelists recommended that the benefit of the Opana reformulation continues to eclipse the risk of serious side-effects, while eight disagreed and one member abstained from voting. The FDA typically follows the recommendations of the panel but is not obliged to do so.

### Beta-Blocker Use Correlated With Less Joint Pain, Opioid Use in Patients With Osteoarthritis

The use of beta-adrenergic blockers has been negatively associated with increased joint pain and opioid use, as well as analgesic use, in patients with osteoarthritis (OA), according to a team of investigators in Britain. Publishing in *Arthritis Care & Research* (2016 Oct 1. [Epub ahead of print]), the investigators reported that their results echo other recent findings, from animal models and human studies, that suggest that beta blockers are effective against pain. The investigators assessed joint pain in 873 patients with symptomatic OA in their hips and/or knees and hypertension, and who were taking at least one prescription antihypertensive medication. They assessed the patients' joint pain using the Western Ontario and McMaster Universities Arthritis Index (WOMAC), and used binary logistic regression analysis to analyze the association between beta-blocker use and moderate or higher joint pain (WOMAC <75) and the use of prescription analgesics. The investigators also adjusted their analyses for age, sex, body mass index, knee or hip OA, history of joint replacement (at other joints), anxiety and depression. The investigators found that beta-blocker use was associated with lower WOMAC pain scores and prevalence of joint pain (adjusted odds ratio [aORpain], 0.68 [95% CI, 0.51-0.92; P<0.011]), as well as with less opioid use (aORopioids, 0.73 [95% CI, 0.54-0.98; P<0.037]) and less use of analgesics in general (aORanalgesics, 0.74 [95% CI, 0.56-0.94; P<0.032]). The study was carried out based on the hypothesis that adrenergic signaling would be involved in OA pain. The results suggest the hypothesis that beta adrenoreceptors are involved in OA pain is true.

*Pain Medicine News*, March 20, 2017.

### CDC: Painkillers No Longer Driving Opioid Epidemic

A top official for the Centers for Disease Control and Prevention has acknowledged that prescription painkillers are no longer the driving force behind the nation's so-called opioid epidemic. In testimony last week at a congressional hearing, Debra Houry, MD, Director of the CDC's National Center for Injury Prevention and Control, said that heroin and illicit fentanyl were primarily to blame for the soaring rate of drug overdoses.

"Although prescription opioids were driving the increase in overdose deaths for many years, more recently, the large increase in overdose deaths has been due mainly to increases in heroin and synthetic opioid overdose deaths, not prescription opioids. Importantly, the available data indicate these increases are largely due to illicitly manufactured fentanyl," Debra Houry, MD, said in her prepared testimony before the House Energy and Commerce Committee's Oversight and Investigations Subcommittee.

The CDC blamed over 33,000 deaths on opioids in 2015, less than half of which were linked to pain medication. While painkillers may be playing less of a role in the overdose epidemic, Houry believes pain medication is still a gateway drug for many abusers. She cited statistics from Ohio showing that nearly two-thirds of the people who overdosed on heroin or fentanyl received at least one opioid prescription in the seven years before their deaths. Houry also disputed reports that efforts to reduce opioid prescribing have led to increased use of illegal drugs. It was her office that oversaw the development of controversial CDC guidelines that discourage doctors from prescribing opioids for chronic pain. According to a recent

survey of over 3,100 patients by Pain News Network and the International Pain Foundation, the CDC guidelines have reduced access to pain care, harmed many patients and caused some to turn to illegal drugs for pain relief. Over 70 percent said their opioid doses have been reduced or cutoff by their doctors in the past year. And one out of ten patients (11%) said they had obtained opioids illegally for pain relief since the guidelines came out. The DEA says illicit batches of fentanyl are being made in China and exported to Mexico, where drug dealers mix it with heroin or turn it into counterfeit medication before smuggling it into the U.S.

### Novel, non-addictive opioid proves safe and effective in monkeys

Researchers have identified a novel opioid drug that offers long-lasting pain relief but doesn't cause addiction or respiratory arrest like other opioids. Results of this study, which used a primate model, were published online August 29, 2016 in the Proceedings of the National Academy of Sciences. However, recent research on the nociceptin/orphanin FQ peptide (NOP) receptor has opened the door for developing novel analgesics. Even more recently, scientists have sought to develop agonists with an affinity for both MOP (mu-opioid peptide) and NOP receptors. Among these, BU08028 demonstrated a similar binding profile to buprenorphine (a partial MOP receptor agonist) but with better binding affinity and efficacy at NOP receptors. For this study, Dr. Ko and colleagues tested BU08028 in 12 rhesus monkeys to determine its efficacy as an analgesic and whether it causes physical dependence. They also investigated its effects on physiological functions, including pruritus, respiration, and cardiovascular activities. In a pain test, BU08028 produced antinociceptive effects in a dose- and time-dependent manner. In addition, pain relief lasted up to 30 hours and repeated administration did not cause physical dependence. The results also showed that BU08028 didn't cause itching or inhibit respiratory and cardiovascular activities. The researchers concluded that BU08028 is an effective and safe analgesic without the likelihood of abuse or other opioid-associated side effects. Further research will determine whether BU08028 itself or a related drug will be a candidate for clinical trials in humans.

### Specialized compound could lead to chronic pain relief without the use of opioids

Purdue researchers have discovered a compound that could lead to the treatment of chronic pain without the need for patients to rely on opioids. A team led by Val Watts, associate head and professor of medicinal chemistry and molecular pharmacology in Purdue's College of Pharmacy, said the compound shows unparalleled selectivity in inhibiting the adenylyl cyclase 1 (AC1). Adenylyl cyclases are enzymes that organize the production of cyclic adenosine monophosphate, an important biological messenger in numerous organisms. There are 10 isoforms of adenylyl cyclases found in humans. Numerous studies have suggested that AC1 could be used as a drug target for chronic pain. The compound identified at Purdue has shown selectivity for inhibiting AC1 versus the other nine isoforms. The Watts group is the first to identify a compound that is selective for AC1 only. Findings from the study were published in a research paper by Watts' group that recently appeared in the journal *Science Signaling*. There is also a recent news feature about the research in the journal *Science*. While the research is still in its early stages, another potential application for the compound is the possibility of reducing opioid dependence. Separate research has shown that completely deleting the AC1 enzyme reduces the signs of dependence.

## Chapter News

Meeting dates:

4/6/2017 Coping Skills for Dealing with Pain. Jennifer Surprise presenter

6/1/2017 Conference Planning Meeting

8/3/2017 An Evening with Neurostimulation. Laura Textor will coordinate with St. Jude Medical, Medtronic, Boston Scientific and Nevro.

10/21/2017 Fall Conference.

12/7/2017 Wrap Up the Year!

Dates are set but educational programs may change.

***Unless otherwise specified, meetings are held at North Kansas City Hospital in the Pavilion. Meeting is from 1800-1830 with educational program from 1830-1930.***

#### 2017 Officers

President	Alan Reschke
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## Laughter Does Good Like Medicine

Why don't some couples go to the gym? Because some relationships don't work out.

I'd tell you a chemistry joke but I know I wouldn't get a reaction.

A friend of mine tried to annoy me with bird puns, but I soon realized that toucan play at that game.

Did you hear about the guy who got hit in the head with a can of soda? He was lucky it was a soft drink.

A man just assaulted me with milk, cream and butter. How dairy.

What is the difference between a nicely dressed man on a tricycle and a poorly dressed man on a bicycle? A tire.

Police were called to a daycare where a three-year-old was resisting a rest.

Spring

