In errata

The published letter PubMed citation is missing the second author's name.Integrating Clinical Pharmacokinetics, Pharmacogenetics, and Quantitative Cytochrome P450 Polymorphic Gene Drug-Drug Interactions (DDIs)
authors are: Oscar A. Linares, MD, Tod Michel, PharmD, PhD , Jeffrey Fudin, PharmD, Raymond C. Boston, PhD, and Annemarie L. Daly, MD, JD.

In errata

The manuscript titled "Feasibility of spinal cord stimulation in a patient with a cardiac pacemaker." Pain Physician 9.3 (2006): 249 published in Pain Physician 2006 has been flagged for plagiarized portions of certain text.
In order to be in compliance with the Journal's revision policies all authors must agree with the revisions that are to be included in the errata sheet.

Feasibility of Spinal Cord Stimulation in a Patient with a Cardiac Pacemaker.
Kosharskyy B, Rozen D. *Pain Physician*. 2006 Jul; 9 (3):249-51.

***Introduction*: p. 249, par. 1, sentences 3-5; par. 2, sentence 3; par. 4, sentence 2**

However, because spinal cord stimulation could potentially interfere with the cardiac pacemaker, individual testing is warranted to prevent significant side effects.]

Several case reports demonstrated the concomitant use of SCS and implantable cardiac pacemakers. Nonetheless, most authors raised concerns about possible interference between both devices (1, 3). Romano et al. (2) published a case series describing the use of SCS in 10 patients with pacemakers. Pacemaker malfunction was noted in one patient and the authors concluded that the use of SCS in patients with the existing cardiac pacemaker might be hazardous. Incidentally, SCS and PPM were in the unipolar mode, thus explaining the potential for interference (3).

In the recent past, SCS in patients with PPM were relatively contraindicated due to the concern of false inhibition of the pacemaker (3).

The concordant use of SCS and PPM in our patient yielded no interference. This case report demonstrated the safety and efficacy of SCS in a patient with painful diabetic neuropathy.

***Case description*: p. 249-250, par. 6, sentence 2; par. 7, sentences 2-5, 7-10; p. 250, par. 3, sentences 2-4**
The proper electrode placement was confirmed with fluoroscopy and adequate stimulation in bilateral feet. Appropriate coverage was achieved in all areas of patient's habitual pain.

In collaboration with the department of electrophysiology we tested various modes of stimulation to evaluate the possibility of interference under different conditions. Using continuous monitoring, IPM unipolar mode of ventricular sensing was implemented with the lowest acceptable threshold. Pulse width and amplitude were increased well beyond the necessary therapeutic levels to reach the maximally tolerated stimulation.

Continuous electrocardiography was used throughout the entire patient's hospitalization. Once tested for the highest output, SCS was reprogrammed to assure the appropriate coverage with the amplitude restricted to the safe range previously tested.

After the SCS leads placement the entire system, including the implantable generator was internalized. The patient was then educated on remote programming of the SCS.

***Discussion*:**
p. 250, par. 5, sentence 1-2; par. 6, sentences 1-2; par. 7, sentences 1-2;
p. 250, par. 8, sentence 2 – p. 251, par. 1, sentences 1-6

Historically, due to a potential for severe cardiac complications SCS was not offered to patients with PPM. Alternatively, patients with existing SCS who have also been implanted with PPM could be at significant risk for arrhythmias.

Understanding most probable causes of interference between SCS and PPM is crucial. SCS impulses could be "mistaken" by PPM as R-waves. This could occur with either unipolar or bipolar sensing mode of the PPM (6). The preset PPM threshold (6), the

In errata (cont.)

output mode (bipolar or unipolar), frequency, as well as the pulse amplitude and the pulse duration of the SCS could all lead to device interference (2,3,6).One study reported PPM derangements in a patient with SCS and PPM being used in the unipolar mode (2). This was an expected occurrence since both devices used in the unipolar mode would significantly increase the risk of device interference (3).

In the clinical case presentation from our institution SCS was used in bipolar mode and no interference with PPM was noted. Therefore, SCS in patients with PPM could be indicated, providing that extensive cardiac testing is completed and found no interference between devices.

Since some patients are pacemaker dependent, SCS has to remain turned off until the testing for inter devices interference is completed. SCS implantation in patients with PPM should only be performed in centers with electrophysiological testing capabilities. With any SCS reprograming a new test is warranted (3). Using SCS in bipolar mode appears significantly safer in patients with PPM. Alternatively, in SCS patients requiring PPM implantation the pacemaker should use bipolar sensing. Appropriate patient education about signs of pacemaker malfunction (such as light headiness, rapid heart rate, etc.) is of paramount importance (3).

Intravenous Infusions in Chronic Pain Management. Kosharskyy B, Almonte W, Shaparin N, Pappagallo M, Smith H. *Pain Physician*. 2013 May-Jun; 16(3):231-49.

Lidocaine: **p. 232, par. 1, sentences 1-3; par. 2, sentences 1-2; par. 3, sentences 1-6; par. 4, sentences 1-2**

The ability of sodium channels to provide analgesia has been known for many centuries. Historically, Western colonists in Latin America were combating toothaches with coca leaves (1). In 1962, Bartlett and Hutaserani (2) were able to show that lidocaine used as an intravenous infusion can relieve postoperative pain. A landmark study by Groudine in 1998 presented clear evidence that intravenous (IV) lidocaine is effective in treating postoperative pain and decreasing the length of stay in patients after radical prostatectomy (3) (Table2).

Despite this strong evidence of efficacy, IV lidocaine use initially declined due to significant side effects and discovery of new analgesic medications that possess better safety profiles. In the 1980's, Boas and his colleagues demonstrated that IV lidocaine decreases the central nervous system's response to painful stimuli. This discovery bolstered interest in IV lidocaine especially since other treatment modalities were usually not effective in alleviating this painful condition (4).

Neuropathic and inflammatory pain is mediated among several other receptors through voltage gated, tetrodotoxin-sensitive (Na 1.3 and 1.7) and -resistant (1.8 and 1.9) sodium channels. They are heterometric protein complexes found in the cell membrane with a [alpha] subunit and one or two ancillary [beta] subunits. Substantial research to date indicates that a nerve injury as well as carrageenan-induced inflammatory pain produces ectopic discharges, all of which originate from the injured nerve, dorsal root ganglia and potentially from adjoining intact neurons (5-7). These discharges were discovered in myelinated as well as unmyelinated nerve fibers, indicating that ectopic impulses are present in both nociceptors and low-threshold mechanoreceptors (8).

Furthermore, tetrodotoxine- sensitive and –resistant sodium ion channels were shown to play a significant role not only in spontaneous but also in evoked pain (9, 10).

Several controlled clinical studies established clear efficacy of systemic lidocaine for treatment of neuropathic and acute nociceptive pain irrespective of the route of its administration (11-14). Most researchers and clinicians agree that a lidocaine plasma concentration of 5-10μm is required to achieve adequate pain relief. A much higher concentration is needed to interrupt nerve conduction (15).

Ketamine: **p. 237, par. 1, sentences 1-3;**
par. 2, sentences 1-4; par. 3, sentences 1-7

There is a strong pharmacological, physiological and behavioral evidence that the excitatory transmitter glutamate plays a critical role in pain pathways. Once the tissue injury occurs, the excitatory signals are conducted via afferent neurons in the spinal cord and peripheral nervous system. The fast-inactivated kainite and α-amino-3hydroxyl-5-methyl-4-isoxazole-propionate (AMPA) subtypes of the glutamate receptors facilitate the propagation of excitatory impulses. Chronic painful stimuli lead to the buildup of prolonged, slowly depolarizing action potentials. The outcome of this process is the cessation of the tonic Mg2+blockade from the N-methyl-d-aspartate (NMDA) glutamate receptor (7).

Excitatory transmission via afferent pain pathways in the dorsal horn of the spinal cord, mediated by the activation of the NMDA

In errata (cont.)

receptor (NMDA-R) is often referred to as "wind up phenomenon". The development of pathophysiological processes such as opioid tolerance, neuroplasticity and long term potentiation is being largely attributed to the NMDA-R (40-42). Persistent stimulation of NMDA-R receptor results in change and interruption of the cell signaling. This in turn could trigger the central sensitization; a phenomenon describing amplified sensitivity of nociceptive neurons. The stimulation NMDA-R of prolonged duration could potentially abolish analgesic effect of opioids.

The NMDA-R is a ligand-gated ion channel and once stimulated enables not only the diffusion of sodium and potassium channels, but also the passage of calcium ions thereby deranging cell signaling (43). The NMDA-R ion channel has heterotetrametric configuration with up to 7 subunits, comprising a pore-forming NR-1 subunit capable of binding glycine, NR-2 subunit that binds glutamate and occasionally present glycine-binding NR-3 complex (44). NMDA-R complex has several allosteric binding sites for zinc, a proton sensor, a polyamine site, which protects the proton sensor. Using another important binding site of the NMDA-R ion channel magnesium is able to block the receptor in the resting state. Multiple binding sites are identified as targets for clinically relevant NMDA antagonists: ketamine, dextromethorphan, amantadine and, memantine (19).

Adrenergic agents: **p. 242, par. 1, sentences 1-6**

Chronic pain is often associated with derangements of the autonomic nervous system. Sympathetic nervous system blockade frequently presents an effective symptomatic treatment of several painful conditions including CRPS, central pain, neuropathic pain, fibromyalgia and phantom limb pain (63-69). Disease states amendable to attenuation of sympathetic nervous system are defined as sympathetically maintained pain (SMP). Multiple pathophysiological processes are responsible for worsening of chronic pain: endogenous cathecholamines are capable of hypersensitizing damaged sensory neurons (70, 71), overexpression of α 1 adrenoreceptors on afferent nociceptors (72,73), dermal hyperalgisia in patients with CRPS (74), central sensitization via A-β-mechanoreceptors (75), as well as sympathetic sprouting and increased release in the dorsal root ganglia (76, 77).