

# HARTLEY COMMENTARY

Winter 2008

## Welcome

I recently returned from the 14th Annual Napa Pain Conference sponsored by Eric Grigsby, MD, founder and medical director of Spectrum-Care Pain Treatment Center in Napa, CA. While we all value such conferences as opportunities to stay updated on the latest developments in chronic pain care, I congratulate Eric and his colleagues for once again providing a stellar educational experience.

Physicians, physician assistants, and allied health professionals from around the nation participated in the conference's lectures and workshops. These tutorials covered intraspinal techniques in pain diagnosis and treatment as well as treating pain caused by cancer, terminal illness, and neuropathic injury. In addition, the lectures included in-depth information on the effect of opioid therapy on the endocrine system and treating chronic pain in the elderly. An especially valuable exercise was the hands-on training sessions in an intraspinal infusion lab. Further highlights of the conference are included in this issue.

I strongly recommend that all pain physicians and their key staff attend next year's conference. I will look forward to seeing you there.

As we enter 2008, the pain community has the opportunity to build upon the advancements in practice guidelines, scientific research, and public policy gains of the last year. Our colleagues throughout the country, patient advocates, and pain management professional associations have worked to foster greater awareness of the issues surrounding pain management and ever more efficacious treatments.

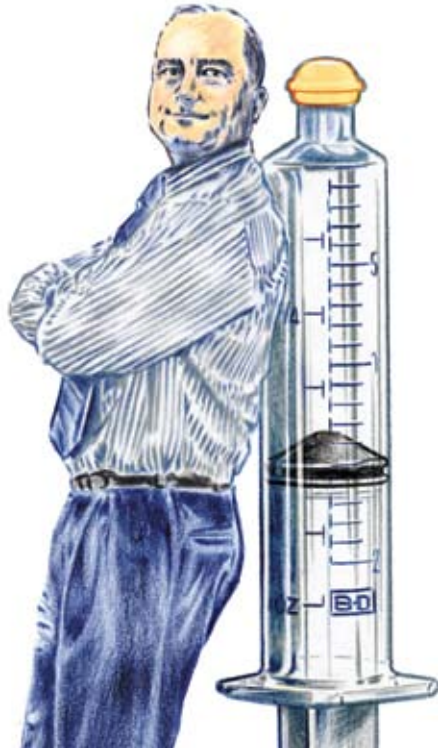
The above activity resulted in the introduction of two Federal pain bills, the National Pain Care Policy Act of 2007 (HR 2994) and the Veterans Pain Care Act of 2007 (S 2160). As these bills are important for our community, I wanted to call your attention to the American Pain Foundation's recommendations for how our profession can advocate for their passage. (Please see page 3.)

I welcome your comments on this issue of *Hartley Commentary*. As always, I am available to you and can be reached via email at [wstuart@hartleymedical.com](mailto:wstuart@hartleymedical.com) or by phone at 888.671.2888.

Best regards,

*William Stuart*

**HM**  
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# Napa Pain Conference Highlights

Dr. Grigsby established the annual Napa Pain Conference in 1990 to inform pain treatment professionals about advances in chronic pain management.

**This year's conference faculty included many of the country's experts in pain management:**

- Lisa Jo Stearns, MD, director of Valley Cancer Pain, Scottsdale, AZ
- David Caraway, MD, PhD, director of the Center for Pain Relief, Tri-State, Huntington, WV
- Michael Stanton-Hicks, MD, vice-chairman, Division of Anesthesiology, Cleveland Clinic Foundation, OH
- Peter Linfoot, MD, PhD, FACP, director of the Diabetes and Endocrine Institute, Lafayette, CA
- Paul Smith, Esq., partner, Davis Wright Tremaine, LLP, San Francisco, CA

Dr. Stearns discussed in depth the treatment of cancer pain with intraspinal drugs. An expert in daily dosing and the clinical effects of specific pharmaceuticals, she will soon publish her latest research on this subject.

A proponent of dosage conservation for treating chronic pain, Dr. Caraway offered his insight into the treatment of non-malignant pain, with an emphasis on prudent drug protocols and daily dosage limits. He detailed several specific drugs, utilizing both common and less known therapies that are suitable for intraspinal administration.

In addition to the clinical seminars, Michelle Byers, MB Business Consulting, and Darla Harrison, SpectrumCare, brought clear and effective principles to life in a highly informative session that focused on the business aspects of private pain management practices.

Dr. Grigsby is also the founder of Napa Surgery Center, Diablo Valley Surgery Center's Pain Management Program, and Napa Medical Resources, Inc. He has also worked as the medical director of the University Pain Service at the University of California, Davis, and was on the staff and faculty of the Mayo Health Clinic's anesthesiology department.

In keeping with Dr. Grigsby's desire to improve the delivery of health services, all proceeds of the conference benefited the Margaret Dunn Grigsby Foundation, a Grigsby family foundation that supports numerous health-related, non-profit organizations in the U.S and Africa.

## Baclofen: A REVIEW

*Each issue of Hartley Commentary provides a discussion of one or more specific therapeutic agents that are administered intraspinally. For some readers this is a helpful review and, for others, an introduction to the drug.*

Baclofen is an agonist of gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter, which acts on receptors in the brainstem and dorsal horn of the spinal cord. The drug is used primarily in the treatment of such conditions as spinal cord injury, cerebral palsy, and multiple sclerosis; however, the chemical also possesses analgesic properties. Intraspinal administration of baclofen was first studied in 1984 by Richard Penn, MD. In the 1990s, baclofen gained FDA approval for intrathecal administration and in 1991 was approved for administration through the implantable infusion pump.

At Hartley Medical, we have extensive experience with this drug and its intraspinal application, having quantitatively analyzed it for more than nine years. Treatment with baclofen must take into consideration that the drug has a very small therapeutic window and presents significant withdrawal issues that must be carefully managed.

The product can be compounded in a vast range of concentrations exceeding 4000mcg/ml. However, some reports have proposed baclofen's instability in concentrations exceeding 2000/mcg/ml. I believe Hartley Medical has perhaps the greatest experience in studying this drug for intraspinal and pump administration, particularly in relation to the enduring storage within an implantable pump for 60 to 90 days. If you would like to discuss this further, please contact me.

## Baclofen in Combination

Baclofen can be safely compounded with many medicinals such as fentanyl, sufentanil, ziconotide, and more commonly, morphine and hydromorphone. Baclofen has a good shelf life and sustained stability within an implantable pump.

## New Recommendations for Intrathecal Delivery

The Polyanalgesic Consensus Conference's report "Recommendations for the Management of Pain by Intrathecal Drug Delivery: Report of an Interdisciplinary Expert Panel" was recently published in the journal *Neuromodulation* (Volume 10, Number 4, 2007).

This report is a broader investigation of the subject than the previous work of the Polyanalgesic Conference. I recommend that you contact *Neuromodulation* or your pain representative regarding these guidelines and obtain a copy for review. If you have any questions regarding this report, contact me by email ([wstuart@hartleymedical.com](mailto:wstuart@hartleymedical.com)) or at 888.671.2888.

A study performed and published in *Hospital Pharmacy* in 2001 showed baclofen and clonidine to be stable in borosilicate test tubes stored at 37° C for 10 weeks. Although the study was not conducted within an implantable device, the results show chemical integrity in combination and resistance to degradation attributed to body temperature.

The stability and compatibility of baclofen and morphine were studied and published in the *International Journal of Pharmaceutics*. This study determined that both drugs maintained structure when introduced into an implantable device, stored at body temperature, for 30 days.

## USP 797 Report: STANDARDS FOR THE COMPOUNDING PHARMACY

At Hartley Medical, we strive to maintain the optimal environment for compounding sterile drugs. Long before the United States Pharmacopeia (USP) Chapter 797's guidelines for sterile compounding were introduced, Hartley Medical had an effective environmental monitoring program that incorporates advanced technology.

The previous issue of *Hartley Commentary* discussed two means of monitoring microbial air quality: our use of passive plates during the last decade and the augmentation of this practice with an active air-sampling program.



Met One laser particle counter is used daily to assess Hartley Medical's air quality.

The third component of Hartley Medical's comprehensive air quality management program is monitoring for very small dust particles, 0.3 to 5.0 microns in dimension, which can transport bacteria. This objective is critical to maintaining air quality, as bacteria attached to minute air particles

may possibly contaminate sterile compounded preparations. Employing a Met One laser particle counter, we assess our air quality daily. On a weekly basis, our extensive evaluation includes sampling the air in seven locations throughout each room in the sterile preparation area. We are trending and analyzing our collected data for future publication.

USP guidelines for pharmacies compounding sterile preparations stipulate that the number of air particles for an ISO 6 compounding room will not exceed 10,000 particles per cubic foot. Hartley Medical's aseptic preparation environment is certified as a Class 1,000 – exceeding the USP Federal guidelines by a factor of 10. Thus, while other pharmacies may adhere to USP regulations by storing and preparing compounds in a room with 10,000 particles per cubic foot, Hartley Medical takes every precaution to protect the sterility of our compounds by operating within a certification of 1,000 particles per cubic foot.

At Hartley Medical, we are proud to integrate the latest environmental testing technology into our leadership in intrathecal medication preparation.

## Advocating for Improved Public Policy

The American Pain Foundation is encouraging the pain community to raise public awareness of the issues surrounding pain and promote improved pain policy, legislation, and practice. More than 76 million Americans suffer pain and the majority of them do not receive appropriate care. Together, we can eliminate this public health crisis.

The foundation points to four critical actions we can take that will support the advancement of pain care. Each is listed below, along with the links to further information. (*continued on page 4*)

# Hydromorphone's Role in Pain Management

Hydromorphone is a semi-synthetic opioid discovered in Germany in 1921 and introduced into clinical practice in 1926. Hydromorphone is structurally similar to morphine acting on  $\mu$  receptors and, to a lesser extent, delta receptors. This drug is often considered a second-line drug for pain management. Hydromorphone is four to five times more potent than morphine sulfate, with a maximum solubility of one gram in 4 mlf. of water. This high solubility enables the drug to be administered subcutaneously as well as intrathecally. While the compound is not FDA-approved for intrathecal administration, the drug's use as such is well documented. Clinically, hydromorphone is administered with many common intrathecal drugs with no loss of potency noted. Hydromorphone is more lipophilic than morphine-sulfate and, because of less rostral spread, a clinician could expect less narcotic to reach the vomiting center.

A landmark study published in the *Journal of Pain and Symptom Management* in 2001 established the stability of hydromorphone<sup>1</sup>. Keith Hildebrand, DVM, PhD, and his colleagues documented the drug's stability when contained in a SynchroMed infusion device maintained at 37 degrees C. The authors found hydromorphone to be stable for four months within the infusion device.

A case report published in *Journal of Neurosurgery* in 1986<sup>2</sup> by Dennis W. Coombs, MD, et al., presented a case study of a 49- year-old woman with stage 1 uterine carcinoma. Due to the metastasis and subsequent radiation and chemotherapy, her pain required aggressive treatment. This patient was implanted with an infusion device and began to receive intrathecal hydromor-

phone. Two months post-implantation, a trial of 0.3mg clonidine was administered IT with almost complete relief of pain. A new drug regimen of hydromorphone and clonidine was very effective and stable. Coombs' unpublished data substantiate stability of clonidine and hydromorphone at 37° C within an infusion device.

A dosing of hydromorphone, as I stated, is four to five times more potent than morphine; however, at Hartley Medical we suggest a conservative, one to five hydromorphone to morphine conversion. Initial dosages of intrathecal hydromorphone in opiate-naïve patients should start out at 0.1 to 0.2mg per day.

Equianalgesic opioid conversion (mg)				
Drug	Oral	Parenteral	Epidural	Intrathecal
Morphine	300	100	10	1
Hydromorphone	60	20	2	0.25
Meperidine	3000	1000	00	10
Fentanyl	-	1	0.1	0.01
Sufentanil	-	0.1	0.01	0.001

Ref: Krames, Elliot S. *Pain Reviews*, 1995, 2: 243-267. Implantable intraspinal infusional analgesia.

The reimbursement of hydromorphone involves a paradoxical effect. In low concentrations, 1-5mg/ml, most insurance claims are reimbursed less than pharmacy charge. However, for concentrations exceeding 5mg/ml, insurance reimbursements should cover the cost of the drug, depending on pharmacy providers.

1 Keith R Hildebrand, DVM, PhD, Dennis E. Elsberry, DVM, PhD, and Valerie C Anderson, PhD. *Journal of Pain and Symptom Management*, Vol. 22, No. 6, Dec. 2001.

2 Dennis W. Coombs, MD, Richard L. Saunders, MD, Jonathan D. Fratkin MD, Lawrence E Jensen, MS, and Carol A. Murphy, RN. *Journal of Neurosurgery*, Vol. 64, June 1986.

## Advocating for Improved Public Policy (continued from page 3)

- Ask your Congressional representative to co-sponsor the
- National Pain Care Policy Act of 2007 (HR 2994) - [CLICK HERE](#).
- Ask your Senator to co-sponsor the Veterans Pain Care Act of 2007 (S 2160) - [CLICK HERE](#).
- Ask your organization to endorse the Consensus Statement for the National Pain Care Policy Act of 2007 - [CLICK HERE](#).
- California Residents: Send a thank you letter to Representative Capps for co-introducing the National Pain Care Policy Act of 2007- [CLICK HERE](#).

William Stuart cheers on participants in the USC Pain Center's Quench the Fire 5K Run/Walk in December. Hartley Medical was a sponsor of the event that raises awareness of chronic pain associated with Reflex Sympathetic Dystrophy and Complex Regional Pain Syndrome. Funds raised from the Run/Walk support clinical research and trials, patient education and community outreach activities.



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