
**4th Scientific Meeting**
**The Australian Chapter**
**International Neuromodulation Society**

# *Neuromodulation: New Frontiers*

**8.00 am Sunday 5th April, 2009**
**Room G06, Ground Floor, Parkside Sydney Convention Centre, Darling Harbour**

**Chaired by: Dr Rick Acland MBChB, FAFRM**
**Consultant Burwood Pain Management Centre & Spinal Unit Christchurch, NZ**

**About the International Neuromodulation Society (INS)**

The International Neuromodulation Society (INS) is a non-profit group of clinicians, scientists and engineers dedicated to the scientific development and awareness of neuromodulation – the alteration of nerve activity through the delivery of electrical stimulation or chemical agents to targeted sites of the body. Founded in 1989 and based in San Francisco, CA, the INS educates and promotes the field through meetings, its quarterly, peer-reviewed journal *Neuromodulation: Technology at the Neural Interface* and chapter websites.

*Neuromodulation: Technology at the Neural Interface* contains articles of the highest scientific caliber. The journal's sole purpose is to advance the basic and clinical science of the field of neuromodulation. It publishes scientific works, scientific reviews, and abstracts of papers accepted for review at national and international congresses.

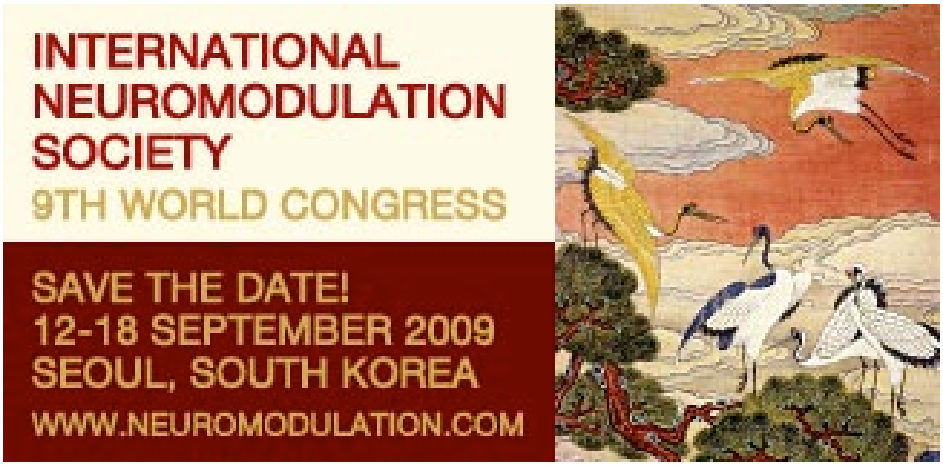
***Mission and Goals of the INS***

**The Mission of the INS** is to promote and disseminate the science, education, practice and accessibility of all aspects of neuromodulation. This multidisciplinary society believes that all scientists, doctors, bioengineers, professions allied to medicine and industry partners who have a specialist interest in neuromodulation can work with this society to share science and encourage best practice for the good of humanity.

**The Goals of the INS** are

- To create a forum for clinicians, basic scientists and bioengineers involved with neuromodulation through a combination of scientific meetings, journal and interactive website
- To create a family of affiliated neuromodulation national chapters to encourage growth and influence at national level
- To encourage research and development into the conditions treated and the devices and techniques used
- To encourage open dialogue with industry partners and health care authorities to improve understanding of these therapies, the needs of patients, service requirements and fair remuneration.

To expand the worldwide access to neuromodulation by raising awareness of the both its clinical efficacy and cost effectiveness.



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## WELCOME

Welcome to the 4th Scientific Meeting of the Australian Chapter, International Neuromodulation Society. The theme of our meeting this year is "New Frontiers" reflecting the increasing awareness and scientific development of Neuromodulation, resulting in a rapidly growing neurotechnology industry offering new treatments for many disorders where more conventional treatments have previously failed to offer relief to patients suffering these ailments.

**The Vision of the INS** is to harness all scientific, clinical and engineering endeavours throughout the world and to brand neuromodulation to encompass all implantable neurological technologies that through electrical or chemical means improve the function of the impaired individual.

Dr Rick Acland, who was excellent at chairing our meeting last year, is returning for a repeat performance as Chair and we are very fortunate to have a very distinguished panel of speakers sharing their research and expertise with us.

Professor Michael Cousins AM will discuss the current concepts of neuropathic pain in relation to neuromodulation and Dr Timothy Deer will update us on recent advances in neuromodulation and share his research and experience in peripheral nerve field stimulation.

Intrathecal drug delivery will be covered by Dr Peter Georgius discussing the non-nociceptive effects of intrathecal agents and Dr Charles Brooker, another repeat performance, focusing on spinal cord injury.

N of 1 trials and their application to neuromodulation will be discussed by Professor Nikolai Bogduk and Dr James O'Callaghan will give an update on the PROCESS Multi-centre Study.

Welcome to Sydney and to our 4th Annual Scientific Meeting, I look forward to sharing with you a rewarding professional experience as we work together to expand the horizons of neuromodulation for the benefit of our patients.

Marc Russo
Secretary, Australian Chapter, INS

# PROGRAM

*Neuromodulation: New Frontiers*

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| **8.00 – 8.30** | **Registration** |
| **8.30 – 9.15** | **"Neuropathic Pain: Current Concepts in Relation to Neuromodulation"**<br>**Professor Michael Cousins AM** |
| **9.15 – 10.15** | **"Advances in Neuromodulation"**<br>**Timothy R Deer MD, DABPM, FAADEP,CIME** |
| **10.15 – 10.45** | **PANEL DISCUSSION** |
| **10.45 – 11.15** | **MORNING TEA** |
| **11.15 - 11.45** | **"Non-Nociceptive Effects of Intrathecal Agents"**<br>**Peter Georgius FFPMANZCA, FAFRM** |
| **11.45 - 12.15** | **"N of 1 Trials and Application to Neuromodulation"**<br>**Professor Nikolai Bogduk MD, PhD, DSc, FFPMANZCA** |
| **12.15 – 12.45** | **"PROCESS Study Results"**<br>**James O'Callaghan FANZCA, FFPMANZCA** |
| **12.45 – 1.15** | **PANEL DISCUSSION** |
| **1.15 – 2.00** | **LUNCH** |
| **2.00 – 2.30** | **"Intrathecal Drug Delivery for Spinal Cord Injury: Current Status & Future Directions"**<br>**Charles Brooker MBChB, MRCP(UK), FFPMANZCA** |
| **2.30 – 3.30** | **"Peripheral Nerve Field Stimulation"**<br>**Timothy R Deer MD** |
| **3.30 – 4.00** | **PANEL DISCUSSION** |
| **4.00 – 4.30** | **INS 2009 Korea Presentation & AGM** |
| **4.30** | **Close** |
| **6.00** | **APS Annual Scientific Meeting - Welcome Reception** |
| **8.00** | **INS Dinner – Coast Restaurant, Darling Harbour** |

**Professor Michael J. Cousins AM MB BS MD DSc FANZCA FRCA FFPMANZCA F A C h P M ( R A C P )**

Michael Cousins is Professor and Head of the Department of Anaesthesia and Pain Management at the Royal North Shore Hospital, University of Sydney, where he is also the Director of the Pain Management Research Institute. A graduate of the University of Sydney, Professor Cousins specialised in anaesthesia and postoperative pain management at the Royal North Shore Hospital and at the Royal Victoria Hospital and McGill University, Montreal, Canada. He is a Fellow of the Australian and New Zealand College of Anaesthetists and a Fellow of the Royal College of Anaesthetists (UK). Professor Cousins was awarded the prestigious Order of Australia for his contribution to anaesthesia and pain management. He is Past-President of the Australian & New Zealand College of Anaesthetists. He is currently Chairman of the College of Presidents of Medical Colleges. He recently became the first Australian to receive the Pugh award for research from the Australian Society of Anaesthetists. Professor Cousins has written over 200 original publications, reviews and book chapters on anaesthesiology and pain research. He has held numerous editorial positions, including the associate editorship of *Pain* and membership of the editorial boards of *Anesthesia and Analgesia*, the *Journal of Clinical Anesthesia*, the *Journal of Pain and Symptom Management* and *Current Reviews in Anesthesiology*. His current research interests include causes and treatment of acute, chronic and cancer pain; post spinal cord injury pain; opioid and non-opioid drug administration by novel routes; injury response, and general pain management.

**Dr Tim Deer, M.D.**

Dr. Deer is the President and Chief Executive Officer of The Center for Pain Relief in Charleston, West Virginia. He is a clinical professor of anesthesiology at the West Virginia University School of Medicine, where he also received his medical degree. He completed his training in anesthesiology and pain medicine at the University of Virginia.

Dr. Deer has published on a range of topics, including injection techniques, minimally invasive disc procedures, intrathecal drug delivery, and spinal cord and peripheral nerve stimulation. He has lectured at many national and international symposiums and has been involved in the hands-on training of more than a thousand interventional pain specialists. He serves on the board of Directors of the North American Neuromodulation Society and American Academy of Pain Medicine. He is the immediate past chair of the committee on pain medicine of the American Society of Anesthesiologists, a member of the editorial board of the Journal Neuromodulation, President of the West Virginia Society of Interventional Pain Physicians, and serves

on several other boards and committees. Dr. Deer has authored numerous journal articles, chapters, and review articles

**Dr Charles Brooker MB ChB MRCP (UK) FANZCA, FFPMANZCA**

Doctor Brooker trained in anaesthesia and pain medicine in Sydney and is now the Director of the Chronic and Cancer Pain Program at Royal North Shore Hospital. He is involved in a range of clinical activities including procedural pain management. The unit at Royal North Shore provides a procedural service to spinal cord injury patients requiring intrathecal pump implants as well as being involved in the research and general pain management for these patients.

**Dr Peter Georgius**

Dr Peter Georgius MBBS, BMedSc, FFPMANZCA and FAFRM is a Rehabilitation Physician and Pain Specialist who is currently working full time in private practice in Queensland on the Sunshine Coast, servicing three private hospitals at Noosa, Nambour and Buderim. He specializes in the medical management of patients with complex needs such as patients with acquired brain injury, spinal injuries; as well as complex orthopaedic and neurological conditions. His expertise is pain interventions in a multidisciplinary setting which facilitates patient participation in therapy to make functional gains. His current focus is on pulsed radiofrequency and peripheral and central neuromodulation. He previously held an appointment as a sessional lecturer at Victoria University (Melbourne) in Neuroanatomy and Clinical Neurology and currently provides sessional lecturing in Pain, Neuroanatomy and Clinical Neurology at the University of Queensland, Brisbane.

**Professor Nikolai Bogduk**

Professor Bogduk is Conjoint Professor of Pain Medicine at the University of Newcastle and the Royal Newcastle Centre, in Newcastle Australia. His research has addressed the anatomical basis, diagnosis, and treatment of spinal pain and headache. He has for 10 years taught the Master of Pain Medicine course at the University of Newcastle.

His relevance to our present meeting is twofold. He was the first Australian to engage in neuromodulation, having studied with CN Shealy, and at Johns Hopkins Hospital, in 1975. More recently he has championed the application of critical reasoning and biostatistics to studies of interventions for spinal pain.

**Dr Jim O'Callaghan**

Doctor O'Callaghan is an Anaesthetist and Pain Management Specialist working at Axxon Pain Medicine in Brisbane.

**8.45 – 9.15**
**Professor Michael Cousins**
**NEUROPATHIC PAIN: CURRENT CONCEPTS IN RELATION TO NEUROMODULATION**

Much progress has been made in the understanding of neuropathic pain, using a wide range of animal models including nerve compression, nerve section, 'spared nerve lesions' (some fibres spared), loose ligatures around nerves to create inflammatory reactions, spinal cord compression, contusion and section. [1,2,3]

However although animal models have some overlap with clinical neuropathic pain presentations, results of drug treatments in animal models do not reliably predict outcomes in patients. Also there is a lack of appropriate animal models for example for CRPS type I and CRPS type II and for post stroke neuropathic pain, postherpetic neuralgia, etc.

An important development in 2008 was an initiative of the American Academy of Pain Medicine (AAPM) in conjunction with the American Medical Association (AMA) [4] Resolution 528 proposed:

- That AMA prepare a report based on current scientific literature which addresses the pathophysiology of neuropathic pain ("maldynia") as a *neurobiological disease*
- That such a report address the therapeutic scope of practice for non-pharmacologic therapies for maldynia, including interventional and non-interventional modalities.

These proposals will be considered by AMA Council in 2009. The AMA Council on Science and Public Health carried out the review of neurobiology of neuropathic pain (maldynia) by reviewing reports of 274 studies of human subjects (see AMA USA website).

Currently available basic and clinical data point to the following maladaptive changes in the nervous system at the levels [1,2]:

- peripheral nerve terminals
- peripheral nerves (nociceptive and non-nociceptive)
- dorsal root ganglion
- sympathetic nerve
- spinal cord
- brain

Phenotypic changes may occur, alterations in gene expression may play a part as well as fundamental changes in properties of neurons and neuronal pathways at various levels (neuroplasticity changes). Glial cells may be involved and recent evidence points to a small family of genes that determine likelihood of progression from an acute phase to persistent neuropathic pain [5]

In the case of CRPS type I and II additional mechanisms may include [3]:

- motor abnormalities; immune cell-mediated inflammation and cytokine release; auto-immune mechanisms; sensitisation to adrenergic stimuli [5].

Neuroplasticity changes in brain have now been reported in humans in association with

amputation pain [6]; neuropathic pain of spinal cord injury (SCI) [7]; and in association with motor disturbances and CRPS [8]. In SCI pain a correlation has been shown between severity of pain and brain neuroplasticity changes [7] – perhaps the strongest evidence yet that neuropathic pain is a disease entity [7,9].

Neuromodulation has evolved in a major way over the past 10 years as an important non-pharmacologic *and* pharmacologic option for management of neuropathic pain.

Spinal opioid and non-opioid drug administration promises to have a resurgence as a result of new non-opioid drugs that target spinal neuroplasticity changes [10].

Non-pharmacologic neuromodulation by neurostimulation continues to evolve [11] at the level of peripheral 'field'; peripheral nerve (PNS); spinal nerve; dorsal root ganglia; spinal cord (SCS); brain. Much new evidence has become available concerning mechanisms of SCS [12] and PNS analgesia (eg greater occipital nerve stimulation) [13,14]including the strong role of GABA [12]

With respect to SCS a recent evidence based review has summarised the evidence for SCS in chronic pain of neuropathic or ischaemic origin [15].

**REFERENCES**


1. Siddall PJ, Cousins MJ. Introduction of Pain Mechanisms: Implications for Neural Blockade. In: Cousins MJ, Carr DB, Horlocker TT, Bridenbaugh PO (Eds) *Neural Blockade in Clinical Anesthesia and Pain Medicine 4th Ed. 2008 Wolters Kluwer Lippincott Williams & Wilkins. Pp 661-692*
2. Yaksh TL. Physiologic and Pharmacologic Substrates of Nociception after Tissue and Nerve Injury. In: Cousins MJ, Carr DB, Horlocker TT, Bridenbaugh PO (Eds) *Neural Blockade in Clinical Anesthesia and Pain Medicine 4th Ed. 2008 Wolters Kluwer Lippincott Williams & Wilkins. Pp 661-692*
3. Binder A, Baron R. Complex Regional Pain syndrome, Including Applicatins of Neural Blockade. In: Cousins MJ, Carr DB, Horlocker TT, Bridenbaugh PO (Eds) *Neural Blockade in Clinical Anesthesia and Pain Medicine 4th Ed. 2008 Wolters Kluwer Lippincott Williams & Wilkins. Pp 661-692*
4. American Medical Association and Academy of Pain Medicine. Maldynia: Pathophysiology and Non-Pharmacologic treatments. (See AMA (USA) website)
5. Tegeder I, Costigan M, Griffin RS et al. GTP cyclohydrolase and tetrahydro-biopterin regulate pain sensitivity and persistence. Nat Med 2006;12:1269-127
6. Flor H, Elbert T, Knecht S et al. Phantom limb pain as a perceptual correlate of cortical reorganisation following arm amputation. Nature 1995;375:482-4
7. Wrigley PJ, Press SR, Gustin SM et al. Neuropathic pain and primary somatosensory cortex reorganisation following spinal cord injury. Pain 2009;141:52-59
8. Maihofner C, Baron R, DeCol R et al. The motor system shows adaptive changes in complex regional pain syndrome. Brain 2007;130:2671-87
9. Siddall PJ, Cousins MJ. Persistent pain as a disease entity: Implications for clinical management. Anesth Analg 2004;99:510-20
10. Carr DB, Cousins MJ. Spinal route of Analgesia: Opioids and Future Options for Spinal Analgesic Chemotherapy. In: Cousins MJ, Carr DB, Horlocker TT, Bridenbaugh PO (Eds) *Neural Blockade in Clinical Anesthesia and Pain Medicine 4th Ed. 2008 Wolters Kluwer Lippincott Williams & Wilkins. Pp 661-692*
11. Prager JP, Stanton-Hicks M. Neurostimulation. In: Cousins MJ, Carr DB, Horlocker TT, Bridenbaugh PO (Eds) *Neural Blockade in Clinical Anesthesia and Pain Medicine 4th Ed. 2008 Wolters Kluwer Lippincott Williams & Wilkins. Pp 661-692*
12. Myerson Ba, Linderoth B, Mechanisms of spinal cord stimulation in neuropathic pain. Neurol Res 2000;22:285-92
13. Goadsby PJ, Hoskin KL, Knight YE. Stimulation of the greater occipital nerve increases metabolic activity in the trigeminal nucleus caudalis and cervical dorsal horn of the cat. Pain 1997;73:23.8
14. Bartsch T, Goadsby PJ. Stimulation of the greater occipital nerve induces increased central excitability of dural afferent input. Brain 2002;125:1496-1509
15. National Institute for Clinical Excellence.UK. Pain (chronic neuropathic or ischemic) – spinal cord stimulation. www.nice.org.uk/TA159

**9.15am - 10.15am**

**ADVANCES IN NEUROMODULATION**

**Dr Timothy Deer MD, DABPM, FAADEP, CIME**

President & CEO, The Center of Pain Relief Charleston, West Virginia, USA

The field of Neurostimulation has grown dramatically in recent decades, with as many as 75,000 neurostimulators implanted worldwide each year for a variety of indications. These indications include pain treatment, neurological diseases such as Parkinson's, and visceral syndromes such as gastric dysmotility, and angina. With tremendous advances in technology over the past few years and newer indications for Neurostimulation, the discussion will focus on the current uses of Neurostimulation and the disease states that are currently amendable to this therapy including failed back surgery syndrome, complex regional pain syndromes, ischemic pain, angina, peripheral neuropathy, and neuropathic foot pain. As we review these disease states we will focus on the impact of technology on the outcome. The advances have been in multiple areas that impact patient care. These include: 1. Lead Technology 2. Generator Technology 3. Computer Technology Platforms 4. Patient Selection and 5. Physician Education.

Unfortunately some areas have still not made a clinical impact that could change the future of the field. These include: 1. MRI compatible systems 2. Wireless technology 3. Self contained systems that include the computer source and lead in a compact small device. 4. Percutaneous Paddle lead technology 5. Multi-electrode computer arrays that will improve programming and patient coverage to improve outcomes 6. Peripheral nerve implants that allow for successful and specific electrical current delivery to the periphery without the need for a generator.

We will review what each of these "unfulfilled" advances could mean to the physician, to the patient and to the society.

This discussion will review the past advancements in spinal cord stimulation that have changed the overall view of this therapy, and we will also review the probable developments that may occur over the next decade in the arena of Neurostimulation.

**Intrathecal Granuloma Formation:**

This discussion will review the past advancements in spinal cord stimulation that have changed the overall view of this therapy, and we will also review the probable developments that may occur over the next decade in the arena of Neurostimulation.

**A look at Intrathecal Drug Delivery**

Advances in intrathecal drug delivery can be identified into different categories. These include drug delivery expansions and technology advances. This lecture will focus on new pump technologies, improved patient safety issues, granuloma formation reduction and future drug options for our patients.

**Current State Of The Literature:**

This segment of the literature will focus on the current evidence to support the use of intrathecal drug delivery. We will examine both cancer and non-cancerous disease states as causes of pain.

This segment will focus on the causes of granuloma and possible reduction in this potentially devastating complication. We will review the current recommendations to avoid granuloma, diagnose granuloma and treat granuloma. These comments will focus on the recent consensus on the current state of literature on this topic.

**New Pump Technology:**

There are currently two studies ongoing to determine if new pump technologies will be efficacious for our patients. We will review the new potential pump options, and look at new advances in multi-chamber pumps, new catheter materials, and new features to improve patient safety.

**New Drug Options:**

We will review newly researched drugs and look at the future of neurotoxins in the treatment of pain.

***Octreotide:*** The use of this growth hormone analog has been promising, safe in humans and has seen some efficacy in neuropathic pain. Future research is needed to determine effective dose, and ideal patient populations.

***Gabapentin:***

Gabapentin is a GABA analog originally developed to treat epilepsy and is thought to work at the voltage gates, N-Type calcium Ion Channels. The drug has shown great promise in the area of neuropathic pain of the limbs. Currently the drug is being studied in both open label and randomized blinded prospective studies. If successful this drug may be the next drug approved in the United States for intrathecal use.

Conotoxins are a group of neurotoxic peptides derived from the venom of the marine cone snail, genus Conus, of which there are an estimated 500 species. Conotoxins have a variety of mechanisms of actions, most which have not yet been determined; Omega-conotoxin peptides block voltage-sensitive Ca2+-channels to suppress neurotransmitter release. Other groups of Conus based protein toxins include sigma-conotoxins which act on the serotonin 5HT-3 receptor,

kappa-conotoxins which block voltage-sensitive K+-channels, and gamma-conotoxins which target voltage-sensitive nonspecific calcium ion channels.

The following analgesics represent the most promising agents for the treatment of chronic intractable pain in this group.

**Current Therapies**

*Ziconotide (Prialt)* - The Polyanalgesic Consensus Conference recommended Ziconotide (Prialt) as a first line drug in its consensus algorithm. Ziconotide (Prialt), a non-opioid, non-NSAID, non-local anesthetic analgesic, derived from the cone snail Conus magus, is the synthetic form of the cone snail peptide conotoxin, M-VII-A, an N-type calcium channel blocker. Although Ziconotide has been associated with serious adverse affects in some patients, it did receive approval from the Food and Drug Administration in 2004 for the treatment of chronic intractable pain. Ziconotide is approved for use only as an IT therapeutic agent. It is non-addictive, and is 1000 times stronger than morphine as an analgesic.

**Future IT Agents:** A number of promising new experimental agents are currently being developed. They may be considered for occasional clinical use only under special circumstances and should be utilized at the discretion of physicians knowledgeable in the treatment of intractable chronic and malignant pain.

***Xen2174 -*** Xen2174 is a chemically modified, synthetic version of a venom peptide that the marine cone snail uses to immobilize prey. It is a structural analogue of Mr1A, also a chi-conopeptide, isolated from Conus marmoreus, but has higher chemical stability than Mr1A. Chi-conopeptides are potent, non-competitive selective inhibitors of the norepinephrine transporter (NET), a subgroup of monoamine transporters. Preclinical research suggests that IT Xen2174 may be a novel therapeutic agent for treatment of chronic neuropathic pain. A study compared the effects of Xen2174 with those of tricyclic antidepressants and clonidine, an alpha (2)-adrenoreceptor agonist, on mechanical allodynia in rats with either a chronic constriction injury (CCI) of the sciatic nerve or an L5/L6 spinal-nerve injury. Xen2174 administered via IT bolus doses results in dose-dependent anti-allodynia in two rat models of neuropathic pain, while producing mild side-effect profiles. The findings suggest that the wider antiallodynic, anti-hyperalgesic, and antinociceptive responses elicited by IT Xen2174a and Mr1A may contribute to upregulation of descending noradrenergic inhibitory inputs to the ipsilateral spinal dorsal horn.

***CGX-1160 -*** CGX-1160 is a broad spectrum non-opioid com analgesic in clinical development. This conopeptide-based drug acts on the neurotensin, NTR1 receptor to induce analgesia. It has a stronger activation of the NTR1 receptor when compared to neurotensin, thus giving CGX-1160 a uniquely high level of efficacy for the relief of pain. To assess nociceptive activity of contulakin-

G, Allen et al delivered Contulakin-G as a bolus intrathecally (0.03, 0.1, 0.3, 3 nmol) or epidurally (10, 30, 89 nmol) in rats. Intrathecal Contulakin G significantly decreased Phase II and, to a lesser degree, Phase I paw flinching produced by intradermal formalin. The ED50s of intrathecal and epidural doses of were 0.07 nmol and 45 nmol, respectively, giving an epidural/intrathecal ED50 ratio of 647. In dogs, intrathecal Contulakin-G (50-500 nmoL) produced a dose-dependent increase in the thermally evoked skin twitch latency by 30 min after administration as did morphine (150 and 450 nmol). Epidural morphine (750 and 7500 nmol), but not epidural Contulakin-G (1000 nmol), also significantly decreased skin twitch in dogs. No changes in motor function were seen in any rats or dogs receiving these doses of Contulakin-G.

A phase 1b clinical trial of CGX-1160 for the treatment of chronic intractable pain was completed at Brigham and Women's Hospital in Boston. The trial was conducted in a limited population of spinal cord injured patients, and, the results supported the Company's position that CGX-1160 will be a safe and effective drug for the treatment of chronic intractable pain.

***AM336 -*** AM336 (CVID) is a synthetic analogue conotoxin first isolated from the venom of Conus catus. The compound is a novel peptidic, N-type, calcium channel blocker. Intrathecal bolus dosing of AM336 produces dose-dependent antinociception with adjuvant-induced chronic inflammatory pain of the right hind paw in rats. N-type calcium channels regulate the release of important pro-nociceptive neurotransmitters, including substance P and glutamate. Both AM336 and MVIIA (a conotoxin originally isolated from the venom of the fish-hunting cone snail, Conus magus, is a blocker of voltage-sensitive Ca2+ channels in neurons) showed antinociceptive effects via inhibition of the release of substance P from rat spinal cord slices in a concentration-dependent manner (EC50 values=21.1 and 62.9 nM, respectively). Acute dosing of IT AM336 induces dose-dependent antinociception (ED50 approximately 0.110 nmol).

**Conclusion**

These agents appear to be very promising in their indications for IT use. The continual development of these, and future agents, will provide effective treatment options for the pain physician.

**References**

Deer, T, Krames, E, Hassenbusch, S, et. al. Polyanalgesic Consensus Conference 2007: Recommendations for the Management of Pain By Intrathecal (Intraspinal) Drug Delivery: Report of an Interdisciplinary Expert Panel. Neuromodulation, 10;4, Pages 300-328.

Deer, T, Krames, E, Hassenbusch, S, et. al. Future directions for Intrathecal Pain Management: A review and Update from the Interdispiplanry Polyanalgesic Consensus Conference 2007. Neuromodulation, 11;2, Pages 92-97

**11.15 am – 11.45am**

**NON-NOCICEPTIVE EFFECTS OF INTRATHECAL AGENTS**

**Dr Peter Georgius**

**FFPMANZCA,FAFRM**

Pain Medicine Specialist & Rehabilitation Physician

Noosa Private, Salangor & Nambour Private Hospitals, Qld.

Intrathecal agents have a significant role in pain management; however the non-nociceptive effects are complex and involve multiple systems. The non-nociceptive effects of intrathecal morphine can be profound and are considered to be side effects which are in general reversed by naloxone. Additionally, there are more subtle effects from short- and long-term intrathecal agents that can alter the homeostasis of the endocrine, autonomic and immune systems. These changes can also have a significant effect on modulation of pain.

Furthermore, there is a significant relationship between the non-nociceptive effects of multiple agents and the stress response. The stress response to trauma and more specifically to pain, involves the autonomic, immune and endocrine systems. The main changes are seen within the sympathetic nervous system, the pro-inflammatory cytokines and lymphocytes as well as the hypothalamic-pituitary-adrenal axis, all of which are inter-related. Other hypothalamic responses can affect the hypothalamic-pituitary-gonadal-axis and hypothalamic-pituitary-thyroid axis. Some of the non-opioid intrathecal agents can reverse elements of opioid-related tolerance by modulation of the elements of the autonomics, immune and endocrine systems.

The degree to which intrathecal agents have a clinical significance is complex and has yet to be quantified.

**11.45 am – 12.15pm**

**N OF 1 TRIALS & APPLICATION TO NEUROMODULATION**

**Professor Nikolai Bogduk MD, PhD, DSc, FFPMANZCA**

University of Newcastle, Newcastle Bone & Joint Institute

Royal Newcastle Centre, NSW

The question is: is the response reported by a given patient attributable to the active competent of the intervention? The answer comes from N of 1 trials. In such trials there is one participant – the patient – who is treated, under double-blind or single-blind conditions, with active or sham versions of the intervention, allocated randomly. If the patient's response is attributable to a specific effect of the intervention, they will respond consistently whenever treated with the active intervention, but will not respond to the sham intervention.

A single alternation of treatment is not sufficient to overcome chance variations in response. Multiple iterations are required.

The number of iterations required is not fixed. It depends on the magnitude of response and the difference in magnitudes of responses to active or sham treatment. The larger the differences in response, the fewer the number of iterations required to ensure that differences are statistically significant and therefore, that conclusions are sound.

**12.15pm – 12.45pm**

**PROCESS STUDY RESULTS**

**Dr Jim O'Callaghan FANZCA, FFPMANZCA**

Anaesthetist & Pain Medicine Specialist

Axxon Pain Management, Brisbane, Qld

Patients with failed back surgery syndrome (FBSS) experience persistent or recurrent pain, reduced functionality, and reduced quality of life despite anatomically successful lumbosacral spine surgery. In selected candidates, spinal cord stimulation (SCS) can reduce pain, improve quality of life, reduce the consumption of analgesics, improve the ability to perform activities of daily living, improve sleep and may allow some patients to return to work. To evaluate the clinical effectiveness of spinal cord stimulation, the PROCESS study randomised 100 patients with FBSS to receive either conventional medical management (CMM ) alone or SCS plus CMM . Clinical outcomes were evaluated over a period of 24 months. Results after treatment for 6 months have been reported previously.

CONCLUSIONS

In selected patients with FBSS, treatment with SCS results in pain relief that is sustained at 24 months and is associated with clinically important improvement in functional capacity, health-related quality of life, and patient satisfaction.

**2.00pm – 2.30pm**

**INTRATHECAL DRUG DELIVERY FOR SPINAL CORD INJURY: CURRENT STATUS & FUTURE DIRECTIONS**

**Dr Charles Brooker MBChB, MRCP(UK), FFPMANZCA** Director, Chronic & Cancer Pain Program

Royal North Shore Hospital, NSW

Intrathecal Drug Delivery for Spinal Cord Injury: Current Status & Future Directions

In this presentation I will summarise the status of our spinal cord injury and multiple sclerosis patients who currently have an implanted intrathecal drug pump. We will discuss the current evidence for the use of different drugs in the management of these patients and also allow time to discuss the interesting technical issues relating to implantable pumps in these patients.

**2.30pm – 3.30pm**

**PERIPHERAL NERVE STIMULATION (PNS) AND PERIPHERAL NERVE FIELD STIMULATION (PNFS)**

**Dr Timothy Deer MD, DAPM, FAADEP, CIME**

The Center of Pain Relief, Charleston, West Virginia, USA

***Scientific Principle:*** In some disease states the nerve that is involved in the generation of pain is easily stimulated in the periphery. This may be performed by placing the lead directly over the nerve or by stimulating the fibers of the nerve as it courses in the tissue. The theory of this technique is that the device can effect the transmission of pain signals via A delta and C fibers.

***PNS*:** Peripheral nerve stimulation is performed by identifying the nerve involved in the pain transmission and directly applying electrical current to the structure. In order to perform PNS, the surgeon has to dissect and identify the nerve. At this point a fascial graft is placed over the nerve to insulate the fibers from direct stimulation. This technique is technically challenging and fraught with problems. In most clinical disease states the use on PNFS has become more common**.**

***PNF:*** The occipital nerve, ilioinguinal nerve, cluneal nerve, and intercostal nerves are receptive to stimulation of their peripheral fibers in lieu of stimulating the entire nerve.

In order to perform this technique, the nerve field is mapped out by exam, the tissue is prepped and draped, local anesthesia is applied and the needle is placed just below the dermis in the subcutaneous tissue. If the needle is too superficial the lead can erode. If the lead is too deep, the nerve fibers are missed. Table 2 shows the potential targets for peripheral nerve stimulation.

**Complications of PNS and PFNS:** The risks of these techniques are limited. They include cellulitis, peripheral nerve injury and mechanical dysfunction of the leads and generator.

**Table. Targets for PNS & PNFS Placement**

| Disease | Nerve Target |
|---|---|
| Occipital Neuralgia | C2 Fibers at the Occiput |
| Neuritis of the Face | Supraorbital, Infraorbital Temporo-Auricular, Trigeminal |
| Upper Extremity Pain | Median, Ulnar, Radial, Axillary |
| Pain of Torso | Intercostal and Thoracoabdominal |
| Pain of Pelvis | Ilioinguinal, Ilioypogastric |
| Pain of Lower Extremity | Common Peroneal, Superificial Peroneal, Lateral Femoral Cutaneous, Tibial, Saphenous |

**Conclusion:** This lecture will focus on the nerve targets for stimulation of the periphery with a focus on patient selection, lead placement and clinical pearls to achieve an optimal clinical outcome.

**Notes:**