



PAIN MANAGEMENT August 2003

Agostoni, E., R. Frigerio, and P. Santoro. "Antiepileptic drugs in the treatment of chronic headaches." *Neurological Sciences*. 24, no. Suppl 2(2003): S128-31 UI 12811611.

In recent years, anticonvulsant drugs (AEDs) have been considered promising drugs in the prevention of migraine and other forms of headache, based on their action on the metabolism of gamma-aminobutyric acid (GABA) and glutamate. To date many AEDs are being evaluated for headache preventive treatment. The results are often encouraging even if not conclusive except for valproate, which has been extensively investigated and has been found to be effective and well tolerated in the preventive therapy of migraine. Other AEDs seem to be important in the treatment of patients with resistant headaches, with both migraine and epilepsy comorbid with mood and anxiety disorders or in neuropathic pain syndromes. [References: 26]

American Pain, S. "American Pain Society releases new guidelines for arthritis pain." *Home Healthcare Nurse*. 21, no. 6(2003): 413-4 UI 12841185.

Andrasik, F. "Behavioral treatment approaches to chronic headache." *Neurological Sciences*. 24, no. Suppl 2(2003): S80-5 UI 12811599.

Over 3 decades of research have shown the utility of a number of behavioral treatments, chiefly relaxation, biofeedback, and cognitive behavior therapy, for uncomplicated forms of migraine and tension-type headache. However, the literature base is much less extensive for chronic, complicated, and refractory forms of headache. This paper reviews extant work on the usefulness of behavioral treatment for headache accompanied by medication overuse; chronic, daily, high intensity headache; refractory headaches; cluster headache; chronic tension-type headache; posttraumatic headache; and headache accompanied by psychiatric comorbidity. It concludes with a discussion of the role of environmental and familial factors in influencing chronic headaches. Suggestions for future research are pointed out along the way.

Anonymous. "Do you give poor care to patients in pain?" *Ed Management*. 15, no. 6(2003): 65-7 UI 12827998.

You'll need strategies to improve care of patients who request pain medications frequently. Use care plans to ensure that patients with conditions such as sickle cell disease will have medications given immediately. Use written agreements to discourage drug-seeking patients. Have a system to alert ED staff to a patient's existing pain management plan.

Anonymous. "Information from your family doctor. Shoulder pain." *American Family Physician*. 67, no. 6(2003): 1319-20 UI 12674461.

Araujo, M. C., C. J. Sinnott, and G. R. Strichartz. "Multiple phases of relief from experimental mechanical allodynia by systemic lidocaine: responses to early and late infusions." *Pain*. 103, no. 1-2(2003): 21-9 UI 12749955.

Systemic lidocaine can relieve various forms of neuropathic pain that develop after nerve injury. Mechanical allodynia, defined by a significant drop in paw withdrawal threshold force following spinal nerve ligation (L5-L6) in rats, can be reversed by one 30min lidocaine infusion at a constant plasma concentration as low as 1-2 microg/ml, an effect that is still present when the rats are tested days and weeks afterwards. In this study, we resolved the detailed time course of reversal of ipsilateral and contralateral allodynia in rats with spinal nerve ligation by a single systemic infusion of lidocaine, to 4 microg/ml, given either 2 days after ligation (POD2) or 7 days after ligation (POD7). Male Sprague-Dawley rats were examined for 21 days after undergoing sham operation or spinal nerve ligation to produce allodynia, which was quantified by a lower force of von Frey hairs at the plantar hind paw just required to produce paw withdrawal (paw withdrawal threshold, PWT). Six experimental protocols were followed: rats were infused with lidocaine on POD2 (L2) or on POD7 (L7), or with saline on POD2 (S2) or on POD7 (S7), and sham operated rats were infused with lidocaine on POD2 or on POD7. PWTs were measured during the last 5min of a single 30min lidocaine infusion; at 30, 60, 90, 120, 240 and 360min, and 24, 48 and 72h after beginning infusion, and then every 1-3 days up to 21 days. Three distinct sequential phases of ipsilateral relief were apparent in both L2 and L7 groups: (1) an acute elevation of PWT during the infusion, returning to the pre-infusion allodynic level within 30-60min after infusion; (2) a second, transient elevation of PWT within the next 360min; (3) a sustained elevation of PWT developing slowly over 24h after infusion and maintained over the next 21 days. A significant, although weaker contralateral allodynia developed more slowly (>POD8) than the ipsilateral condition, and could be delayed for more than 2 weeks by lidocaine infusion on POD2 but for only 1 week by the same treatment on POD7. None of the sham operated animals had any allodynic signs and no saline infusions elevated PWT in ligated, allodynic rats. These results of separate phases imply that there are mechanistic differences between the acute relief and the sustained relief of allodynia after a single infusion of lidocaine, and may present an experimental paradigm for investigating the advantages of earlier rather than late therapeutic intervention.

Barbano, R., et al. "Pharmacotherapy of painful diabetic neuropathy." *Current Pain & Headache Reports*. 7, no. 3(2003): 169-77 UI 12720596.

The scope of this review is to describe the epidemiology, physiology, symptomatology, and treatment of diabetic painful neuropathy, which is a common complication of diabetes with significant morbidity. This article focuses on treatment options. Various clinical trials of several classes of medications (eg, antidepressants, anticonvulsants, and topical medications) and alternative treatments (eg, acupuncture, electrostimulation, magnets) are reviewed. Physicians have a large panel of medications that can be used effectively solely or in combination at their disposal. However, a number of these treatments have significant side effects, which are noted, that limit their use. As the understanding of the pathophysiologic mechanisms of diabetic neuropathy improves, new medications are under investigation, which are reviewed in this article. There is great hope that the future may hold treatments that would prevent nerve damage. [References: 81]

Barden, J., et al. "Single dose oral celecoxib for postoperative pain." *Cochrane Database of Systematic Reviews*., no. 2(2003): CD004233 UI 12804506.

BACKGROUND: Celecoxib is a selective cyclooxygenase-2 (COX-2) inhibitor prescribed for the relief of chronic pain in osteoarthritis and rheumatoid arthritis. The

drug is believed to be associated with fewer adverse effects than conventional non-steroidal anti-inflammatory drugs (NSAIDs). However, the effectiveness of celecoxib in the treatment of acute pain has not yet been assessed by systematic review. OBJECTIVES: To assess the analgesic efficacy and adverse effects of a single oral dose of celecoxib for moderate to severe postoperative pain. SEARCH STRATEGY: We searched the Cochrane Library Controlled Trials Register, MEDLINE, Biological Abstracts, PubMed and the Oxford Pain database. Date of the most recent search: May 2002. SELECTION CRITERIA: Randomised controlled trials (RCTs) of adults prescribed any dose of oral celecoxib or placebo for acute postoperative pain were included. DATA COLLECTION AND ANALYSIS: Two trials (418 subjects) met the inclusion criteria for this review. The trials were assessed for quality and the data extracted by two independent reviewers. Summed pain relief (TOTPAR) or pain intensity difference (SPID) was extracted and converted into dichotomous information yielding the number of patients with at least 50% pain relief over 4-6 hours. These derived results were used to calculate the relative benefit (RB) and number-needed-to-treat (NNT) for one patient to achieve at least 50% pain relief. MAIN RESULTS: The number-needed-to-treat for celecoxib 200 mg compared with placebo was 4.5 (CI 3.3 to 7.2). For every 4.5 patients experiencing moderate to severe acute pain treated with celecoxib 200 mg one more will experience at least 50% pain relief that would not have done had they received placebo. The median time to remedication over 24 hours was 5.1 hours with celecoxib 200 mg and 1.5 hours with placebo. Quantitative analysis of adverse effects was not possible but no serious or unexpected adverse effects were reported. REVIEWER'S CONCLUSIONS: Single dose oral celecoxib is an effective means of postoperative pain relief, similar in efficacy to aspirin 600/650 mg, and paracetamol 1000 mg. The two trials included used celecoxib 200 mg, a dose 50% less than is recommended for acute pain. More trials are needed to estimate efficacy for recommended dose of 400 mg, and to reinforce current findings for 200 mg, and provide data for pooled quantitative estimates of adverse effects. [References: 33]

Beydoun, A., and M. M. Backonja. "Mechanistic stratification of antineuralgic agents." *Journal of Pain & Symptom Management*. 25, no. 5 Suppl(2003): S18-30 UI 12694989.

Current treatment options in neuropathic pain include antidepressants, antiepileptics, antiarrhythmics, and analgesics. However, stratification of treatments based on their original therapeutic class is inadequate, as drugs belonging to a particular class may have distinct antineuralgic modes of action. It is therefore useful to review the mechanisms of action of these drugs and determine which of these mechanisms is most likely responsible for the drugs' efficacy in the symptomatic treatment of neuropathic pain. Switching from the traditional therapeutic class stratification to one based on putative antineuralgic mechanisms of action will allow more rational selection of therapies, and aid evaluation of the additive or synergistic effects of drugs when used in combination. [References: 68]

Blau, L. A., and J. D. Hoehns. "Analgesic efficacy of calcitonin for vertebral fracture pain." *Annals of Pharmacotherapy*. 37, no. 4(2003): 564-70 UI 12659616.

OBJECTIVE: To evaluate the analgesic efficacy of calcitonin for treating the pain of vertebral fractures associated with osteoporosis. DATA SOURCES: Searches of MEDLINE (1966-July 2002), Cochrane Library, International Pharmaceutical Abstracts (1977-July 2002), and an extensive manual review of journals were performed using the key search terms calcitonin, analgesic, osteoporosis, vertebral fracture, and pain. STUDY SELECTION AND DATA EXTRACTION: All articles identified from the data sources were evaluated and all information deemed relevant was included for this review. DATA SYNTHESIS: Fractures, especially vertebral fractures, are a common complication of osteoporosis, leading to significant pain. Calcitonin

has been studied for its analgesic properties. Fourteen double-blind, placebo-controlled trials that evaluated the analgesic efficacy of calcitonin for osteoporosis-related vertebral fracture pain were identified and reviewed. Thirteen of these studies demonstrated statistically significant improvement in pain or function in calcitonin-treated patients. CONCLUSIONS: Calcitonin has proven efficacy in acute pain associated with osteoporosis-related vertebral fractures. Analgesic effects are seen with intranasal, parenteral, and rectal administration. Future studies comparing calcitonin with other commonly used analgesics are needed to more clearly define its place in therapy. [References: 28]

Boyce, J. R., and G. E. Peters. "Complete vasomotor collapse: an unusual manifestation of the carotid sinus reflex." *Anesthesiology*. 98, no. 5(2003): 1285-7 UI 12717155.

Carrazana, E., and I. Mikoshiba. "Rationale and evidence for the use of oxcarbazepine in neuropathic pain." *Journal of Pain & Symptom Management*. 25, no. 5 Suppl(2003): S31-5 UI 12694990.

Oxcarbazepine is a second-generation antiepileptic drug (AED) with proven efficacy in managing partial epileptic seizures, with or without secondary generalization, in adults and children. The overlap between the underlying pathophysiologic mechanisms of some epilepsy models and neuropathic pain models supports the rationale for using certain AEDs in the treatment of neuropathic pain. Several AEDs have reportedly produced analgesia in a range of neuropathic pains, including painful diabetic neuropathy (PDN) and post-herpetic neuralgia. Increasing evidence suggests that oxcarbazepine can provide significant analgesia in several neuropathic pain conditions, including trigeminal neuralgia and PDN, and is also may be effective in treating neuropathic pain refractory to other AEDs, such as carbamazepine and gabapentin. The analgesic effects of oxcarbazepine, and its generally improved safety and tolerability profile compared with other standard AEDs, suggests that oxcarbazepine will be an important addition to the neuropathic pain armamentarium. The rationale and evidence to support the efficacy of oxcarbazepine are presented here. [References: 25]

Casucci, G. "Chronic short-lasting headaches: clinical features and differential diagnosis." *Neurological Sciences*. 24, no. Suppl 2(2003): S101-7 UI 12811604.

Chronic short-lasting headaches are relatively rare, poorly recognized syndromes. The chronic short-lasting headaches are a group of chronic disorders in which the headaches occur for one year or more, either without remission or with remission periods less than two weeks; each attack lasts less than 4 hours. These headache syndromes are divided into those with autonomic activation and those without autonomic activation. This article presents the clinical features and differential diagnosis of the relatively rare and clinically challenging trigeminal autonomic cephalgias (TACs). The article also focuses on the clinical features and differential diagnosis of hypnic headache, a chronic shortlasting, non-unilateral headache of moderate intensity in which there is no autonomic involvement, in order to differentiate this from chronic cluster headache, with which it is often confused.

Chandran, P., and K. A. Sluka. "Development of opioid tolerance with repeated transcutaneous electrical nerve stimulation administration." *Pain*. 102, no. 1-2(2003): 195-201 UI 12620611.

The analgesia produced by low and high frequency transcutaneous electrical nerve stimulation (TENS) is mediated by the release of mu- or delta-opioids, respectively in the central nervous system. Repeated administration of either mu- or delta-opioid agonists induce opioid analgesic tolerance. Thus, we tested if repeated administration of TENS (either low or high frequency) in rats leads to a development

of tolerance to its antihyperalgesic effects with a corresponding cross-tolerance to mu- and delta-opioid agonists. Unilateral knee joint inflammation (3% carrageenan) was induced in adult Sprague-Dawley rats. Either low (4 Hz) or high frequency (100 Hz) TENS was administered for 6 days (20 min daily) to the inflamed knee joint under halothane anesthesia. The no TENS controls were administered anesthesia only for the same period. Withdrawal threshold to mechanical stimuli was measured before and after administration of TENS on each day and also on the sixth day. A separate group of animals was tested for tolerance to either the mu-opioid agonist, morphine (1.32, 3.95, 13.2 nmol/10 ml, intrathecal (i.t.)) or the delta-opioid agonist, SNC-80 (6, 20, 60, 120 nmol/10 ml, i.t.) 30 min after i.t. administration. The reduced mechanical withdrawal threshold following the induction of inflammation was reversed by the application of TENS. However, repeatedly administering either low or high frequency TENS for 6 days, lead to a diminution in its effectiveness in reversing the ipsilateral secondary mechanical hyperalgesia by the fourth day. The effects of morphine in the low and SNC-80 in the high frequency TENS groups were significantly less than the group that did not receive TENS. On the other hand, morphine and SNC-80 were similar to the no TENS control in the high and low frequency TENS groups, respectively. Thus, repeated administration of low and high frequency TENS leads to a development of opioid tolerance with a corresponding cross-tolerance to i.t. administered mu- and delta-opioid agonists, respectively. Clinically, it can be inferred that a treatment schedule of repeated daily TENS administration should be avoided to possibly obviate the induction of tolerance.

Chong, M. S., and Z. H. Bajwa. "Diagnosis and treatment of neuropathic pain." *Journal of Pain & Symptom Management*. 25, no. 5 Suppl(2003): S4-S11 UI 12694987.

Currently, no consensus on the optimal management of neuropathic pain exists and practices vary greatly worldwide. Possible explanations for this include difficulties in developing agreed diagnostic protocols and the coexistence of neuropathic, nociceptive and, occasionally, idiopathic pain in the same patient. Also, neuropathic pain has historically been classified according to its etiology (e.g., painful diabetic neuropathy, trigeminal neuralgia, spinal cord injury) without regard for the presumed mechanism(s) underlying the specific symptoms. A combined etiologic/mechanistic classification might improve neuropathic pain management. The treatment of neuropathic pain is largely empirical, often relying heavily on data from small, generally poorly-designed clinical trials or anecdotal evidence. Consequently, diverse treatments are used, including non-invasive drug therapies (antidepressants, antiepileptic drugs and membrane stabilizing drugs), invasive therapies (nerve blocks, ablative surgery), and alternative therapies (e.g., acupuncture). This article reviews the current and historical practices in the diagnosis and treatment of neuropathic pain, and focuses on the USA, Europe and Japan. [References: 29]

Colombo, B., P. O. Annovazzi, and G. Comi. "Neuropathic cranial pain." *Neurological Sciences*. 24, no. Suppl 2(2003): S132-7 UI 12811612.

Neuropathic cranial pain, i.e. pain due to central or peripheral nervous system damage localized in cranial area, is a clinical challenge for the neurologist. Despite major advances in knowledge of physiology and biochemistry of pain, relief for many patients suffering from neuropathic pain remains incomplete. Adjuvant analgesics play a key role in the management of neuropathic pain. The introduction in the therapeutical armamentarium of antiepileptic drugs and the results derived from clinical studies indicate that some of these compounds show promise in the treatment of neuropathic pain. [References: 51]

Conti, C. R. "Partial fatty acid oxidation (pFOX) inhibition: a new therapy for chronic stable angina." *Clinical Cardiology*. 26, no. 4(2003): 161-2 UI 12708620.

During myocardial ischemia, fatty acids are the principal source of energy, increasing myocardial oxygen consumption and making a decrease in coronary blood flow less well tolerated. Increasing glucose oxidation during myocardial ischemia may improve cardiac efficiency. The pFOX inhibitors have the potential to accomplish this. In 2003, I think we can look forward to learning more about this class of compounds called pFOX inhibitors. Perhaps they will provide us alternative therapies in our patients who have persistent chronic stable angina pectoris despite aggressive medical therapy and/or revascularization. It seems to me that this is an increasing problem, and it is particularly common in older patients who want to remain active, but whose chronic stable angina interferes with that lifestyle.

Coomaraswamy, R. P. "End-of life care." *Connecticut Medicine*. 67, no. 1(2003): 49 UI 12630187.

Craft, R. M. "Sex differences in opioid analgesia: "from mouse to man"." *Clinical Journal of Pain*. 19, no. 3(2003): 175-86 UI 12792556.

BACKGROUND: Numerous experimental studies, conducted primarily over the past 10 years, show that there are sex differences in opioid analgesia. This review summarizes the published literature on sex differences in analgesia produced by acute administration of drugs acting at mu-, kappa-, and delta-opioid receptors, in animals and humans. Additionally, methodological issues in research into opioid sex differences are discussed. CONCLUSIONS: Procedural variables that may influence the outcome of studies examining sex differences in opioid analgesia include modality and intensity of the noxious stimulus used in the pain test, opioid type (efficacy and selectivity), and experimental design and data analytic techniques. Subject variables that may be important to consider include subject genotype and gonadal steroid hormone state of the subject at the time of analgesia testing. Evidence is provided for multiple mechanisms underlying sex differences in opioid analgesia, including both pharmacokinetic and pharmacodynamic factors. Future research directions are suggested, such as examining sex differences in opioid tolerance development, sex differences in opioid analgesia using models of acute inflammatory pain and chronic pain, and sex differences in effects of opioids other than analgesia, which may limit their therapeutic use. [References: 106]

Davy, T. A., C. Sharp, and S. Lynch. "Perioperative pain control." *Clinics in Podiatric Medicine & Surgery*. 20, no. 2(2003): 257-67 UI 12776980.

There are many options for perioperative pain control available to surgeons. Given these options, adequate levels of analgesia should be achieved and maintained in all surgical patients. Data suggest that analgesia may be improved by combining different analgesic approaches. To avoid high-dose requirements, dose-dependent adverse effects, and potential toxicity associated with reliance on one agent or technique, "balanced" or multimodal analgesic regimens have been advocated. A multimodal recovery program consists of three major components: (1) early mobilization, (2) complete perioperative analgesia, and (3) early oral nutrition. The goal of multimodal programs is to accelerate patient rehabilitation and reduce hospital stays. Balanced multimodal programs are the present and future of perioperative pain control and will enhance patient care. [References: 28]

de Kleuver, M., F. C. Oner, and W. C. Jacobs. "Total disc replacement for chronic low back pain: background and a systematic review of the literature." *European Spine Journal*. 12, no. 2(2003): 108-16 UI 12709847.

In this paper the rationale for total disc replacement is discussed, and the authors suggest seven requirements that should be met before the implantation of

these devices can be accepted as regular procedures. In an attempt to answer the questions raised, a systematic literature search was performed. The search yielded no controlled trials and nine case series with a total of 564 arthroplasties in 411 patients. The devices used were SB Charite in eight and Acroflex in one study. The percentage results classified as "good" or "excellent" in the studies varied from 50 to 81%. Complications were observed in 3-50% of the patients. Twenty-two of the operated levels were fused either spontaneously or after additional surgery. A meta-analysis to compare the results with other treatments could not be performed due to the lack of comparative studies. Despite the fact that these devices have been implanted for almost 15 years, on the basis of this literature survey there are currently insufficient data to assess the performance of total disc replacement adequately. There is no evidence that disc replacement reliably, reproducibly, and over longer periods of time fulfils the three primary aims of clinical efficacy, continued motion, and few adjacent segment degenerative problems. Total disc replacement seems to be associated with a high rate of re-operations, and the potential problems that may occur with longer follow-up have not been addressed. Therefore, total disc replacements should be considered experimental procedures and should only be used in strict clinical trials. [References: 40]

Dionne, R. A., and J. Witter. "NIH-FDA Analgesic Drug Development Workshop: translating scientific advances into improved pain relief." *Clinical Journal of Pain*. 19, no. 3(2003): 139-47 UI 12792552.

Analgesic drug development as currently undertaken is limited by a number of factors that contribute to the paucity of new analgesics introduced into clinical practice despite marked advances in delineating of the molecular-genetic mechanisms contributing to acute and chronic pain. The participants in this workshop explored the unmet need in analgesia and recommended strategies for enhancing analgesic drug development in the future. The workshop concluded that translating scientific advances into improved pain relief will require new thinking and a cooperative effort among the pharmaceutical industry, regulatory agencies, funding agencies, the biomedical research community, professional societies and clinicians. The workshop also recommended that a better understanding of the epidemiology of pain could contribute to improvement in clinical trial methodology and outcome measures. [References: 2]

Ettinger, S. M. "Myocardial infarction and unstable angina: gender differences in therapy and outcomes." *Current Women's Health Reports*. 3, no. 2(2003): 140-8 UI 12628084.

In the United States, coronary heart disease (CHD) is the leading cause of death for women. Combined with hypertension, stroke, and other vascular conditions, one in every two women dies annually owing to a cardiovascular condition. During the past 20 years, overall death rate from CHD has declined, but the rate of decline has been lower for women compared with men. Trials and studies have demonstrated that CHD might be preventable; however, optimal treatment strategies for women are still in question. It is, therefore, essential that the medical profession continues its current efforts to focus on the development of clinical practice guidelines that critically evaluate both diagnostic and therapeutic treatment options for women with CHD. [References: 47]

Fakata, K. L., and A. G. Lipman. "Pharmacotherapy for pain in rheumatologic conditions: the neuropathic component." *Current Pain & Headache Reports*. 7, no. 3(2003): 197-205 UI 12720599.

Nociceptive and neuropathic types of pain occur in rheumatologic conditions. Most clinicians are familiar with the former, but many are not aware of the prevalence of the latter. The literature reports numerous examples of the occurrence

of rheumatologic neuropathic pain, but little has been published on its management. In this article, neuropathic and nociceptive pain in rheumatologic conditions are differentiated and treatment recommendations are discussed. Common rheumatologic conditions and their pathophysiology in relation to pain mechanisms also are described. Pharmacotherapeutic recommendations for the treatment of both types of pain in the common rheumatologic conditions are presented. [References: 52]

Frediani, F., et al. "The patient with medication overuse: clinical management problems." *Neurological Sciences*. 24, no. Suppl 2(2003): S108-11 UI 12811605.

Patients with chronic headache arise many problems in clinical management, often strictly related to medication overuse. IHS classification did not clear the different clinical presentation and a chapter dedicated to this problem is lacking. This condition is very frequently associated with psychiatric illness, so that the clinical features become more complex over the years. Most of patients share a past clinical condition of episodic migraine; this aspect is very important facing the therapeutical phase, because after discontinuing medication overuse, if present, the treatment must be direct toward this disease. To treat a patient with analgesic, or ergotamine, or triptan abuse, require much caution because stopping the drug may arise new problems, such as different headache, abstinence syndrome, epileptic seizures etc. We review the different possibility that we have to manage the overuser patient.

Frerichs, J. A., and L. R. Janis. "Preemptive analgesia in foot and ankle surgery." *Clinics in Podiatric Medicine & Surgery*. 20, no. 2(2003): 237-56 UI 12776979.

Central neuroplasticity, or changes in CNS processing due to surgical nociception. can amplify postoperative pain. As a result, a hyperalgesic state called wind-up can occur, having debilitating effects on postoperative patients. Preemptive analgesia works to prevent this process and results in a more positive surgical experience. Inhibition of afferent pain pathways by use of local anesthetic blocks, altered perception of pain with opioid use, and inhibition of pain pathways by NMDA receptor antagonists are examples of preemptive analgesia. Using a combination of preemptive modalities and addressing patients' perceptions can aid in interrupting pathologic pain cycles. Positive and modest results have been obtained from animal and human preemptive trials, yet basic pathophysiology demonstrates the validity and importance of preemptive analgesia. Future studies are needed to test effective blockade of afferent input while controlling perception, hyperalgesia, and NMDA receptor activity. The Agency for Health Care Policy and Research now recommends a multifaceted approach to postoperative pain. The goal in pain management is to inhibit destructive pain pathways, maintain intraoperative analgesia, and prevent central sensitization. Preliminary results of multimodal preemptive analgesia trials continue to be promising. [References: 54]

Fujii, M., and M. Saitou. "Factors influencing the progress and prognosis of angina pectoris." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 5(2003): 79-86 UI 12808929.

Gaertner, J., et al. "Encapsulation of an intrathecal catheter." *Pain*. 103, no. 1-2(2003): 217-20 UI 12749977.

A 47-year-old patient with cancer pain underwent implantation of an intrathecal drug delivery device. When the patient suffered from an infection with fever, pain on injection into the catheter and an elevated number of granulocytes in the cerebrospinal fluid 7 weeks later, radiologic examination showed an encapsulation of the catheter tip. Concentrations of morphine and morphine-6-glucuronide in the cerebrospinal fluid suggested transport of morphine into the systemic circulation via the vascularisation of the encapsulating membrane. After antibiotic therapy and

removal of the catheter, morphine was administered intravenously with a one to one conversion ratio.

Gazewood, J. D., and S. Meadows. "What is the prognosis of postherpetic neuralgia?" *Journal of Family Practice*. 52, no. 6(2003): 496-7; discussion 497 UI 12791234.

Postherpetic neuralgia occurs rarely among patients aged <50 years with herpes zoster. The incidence, duration, and severity of postherpetic neuralgia increases with age, but older patients usually have only mild pain. Most cases resolve spontaneously within 3 months. Even in the highest-risk group, people aged >70 years, 25% had some pain at 3 months, but only 10% had pain at 1 year, and none had severe pain. Only a few patients have pain that persists for years (strength of recommendation: A, based on a well-done prospective cohort study). [References: 10]

Gilron, I., et al. "Gabapentin blocks and reverses antinociceptive morphine tolerance in the rat paw-pressure and tail-flick tests." *Anesthesiology*. 98, no. 5(2003): 1288-92 UI 12717156.

Goucke, C. R. "The management of persistent pain." *Medical Journal of Australia*. 178, no. 9(2003): 444-7 UI 12720511.

Persistent pain is a complex mix of physical and psychological symptoms and is ideally managed by a biopsychosocial approach. Often the relative contributions of family and personal relationships, finances, work, past pain experiences and personality outweigh those of the nociceptive or neuropathic processes from which most pain originates. Recent advances in our understanding of the pathophysiology of pain may lead to improved drug treatments; however, non-drug treatments--education, lifestyle modification, exercise and reassurance--should be used routinely to improve patients' quality of life. Patients with persistent pain that is difficult to control or has complex psychosocial influences, or who have a history of medication misuse, should be referred to a multidisciplinary pain centre. Selected patients may be offered invasive options such as nerve blocks or spinal-cord stimulation. The best outcomes are achieved in patients treated in group-based pain-management programs using cognitive-behavioural therapy to improve physical function, change unhelpful thinking and improve patients' understanding of their situation. [References: 35]

Green, S., R. Buchbinder, and S. Hetrick. "Physiotherapy interventions for shoulder pain." *Cochrane Database of Systematic Reviews*., no. 2(2003): CD004258 UI 12804509.

BACKGROUND: The prevalence of shoulder disorders has been reported to range from seven to 36% of the population (Lundberg 1969) accounting for 1.2% of all General Practitioner encounters in Australia (Bridges Webb 1992). Substantial disability and significant morbidity can result from shoulder disorders. While many treatments have been employed in the treatment of shoulder disorders, few have been proven in randomised controlled trials. Physiotherapy is often the first line of management for shoulder pain and to date its efficacy has not been established. This review is one in a series of reviews of varying interventions for shoulder disorders, updated from an earlier Cochrane review of all interventions for shoulder disorder. **OBJECTIVES:** To determine the efficacy of physiotherapy interventions for disorders resulting in pain, stiffness and/or disability of the shoulder. **SEARCH STRATEGY:** MEDLINE, EMBASE, the Cochrane Clinical Trials Register and CINAHL were searched 1966 to June 2002. The Cochrane Musculoskeletal Review Group's search strategy was used and key words gained from previous reviews and all relevant articles were used as text terms in the search. **SELECTION CRITERIA:** Each identified study was assessed for possible inclusion by two independent reviewers. The determinants for

inclusion were that the trial be of an intervention generally delivered by a physiotherapist, that treatment allocation was randomised; and that the study population be suffering from a shoulder disorder, excluding trauma and systemic inflammatory diseases such as rheumatoid arthritis. DATA COLLECTION AND ANALYSIS: The methodological quality of the included trials was assessed by two independent reviewers according to a list of predetermined criteria, which were based on the PEDro scale specifically designed for the assessment of validity of trials of physiotherapy interventions. Outcome data was extracted and entered into Revman 4.1. Means and standard deviations for continuous outcomes and number of events for binary outcomes were extracted where available from the published reports. All standard errors of the mean were converted to standard deviation. For trials where the required data was not reported or not able to be calculated, further details were requested from first authors. If no further details were provided, the trial was included in the review and fully described, but not included in the meta-analysis. Results were presented for each diagnostic sub group (rotator cuff disease, adhesive capsulitis, anterior instability etc) and, where possible, combined in meta-analysis to give a treatment effect across all trials. MAIN RESULTS: Twenty six trials met inclusion criteria. Methodological quality was variable and trial populations were generally small (median sample size = 48, range 14 to 180). Exercise was demonstrated to be effective in terms of short term recovery in rotator cuff disease (RR 7.74 (1.97, 30.32), and longer term benefit with respect to function (RR 2.45 (1.24, 4.86). Combining mobilisation with exercise resulted in additional benefit when compared to exercise alone for rotator cuff disease. Laser therapy was demonstrated to be more effective than placebo (RR 3.71 (1.89, 7.28) for adhesive capsulitis but not for rotator cuff tendinitis. Both ultrasound and pulsed electromagnetic field therapy resulted in improvement compared to placebo in pain in calcific tendinitis (RR 1.81 (1.26, 2.60) and RR 19 (1.16, 12.43) respectively). There is no evidence of the effect of ultrasound in shoulder pain (mixed diagnosis), adhesive capsulitis or rotator cuff tendinitis. When compared to exercises, ultrasound is of no additional benefit over and above exercise alone. There is some evidence that for rotator cuff disease, corticosteroid injections are superior to physiotherapy and no evidence that physiotherapy alone is of benefit for Adhesive Capsulitis REVIEWER'S CONCLUSIONS: The small sample sizes, variable methodological quality and heterogeneity in terms of population studied, physiotherapy intervention employed and length

Gruber, T., et al. "The Hawthorne effect in the assessment of pain by house staff." *American Journal of Hospice & Palliative Care*. 20, no. 3(2003): 231-4 UI 12785046.

Internal medicine residents are one component of the healthcare delivery team in the hospital setting. Their ability to assess and treat pain should be considered in quality improvement efforts. We surveyed our residents, using a 0 to 10 scale to determine how well they assessed their patients' level of pain. We then asked half of these residents to write down their patients' pain score as a fifth vital sign in the medical record. We repeated the house staff survey three weeks later. The residents improved their assessment as a whole, with the nonintervention group faring better on the follow-up surveys. We believe that the residents' improvement can be attributed to the Hawthorne effect, in which a group that is singled out for special study or consideration has its performance positively affected. The residents' ability to accurately rate patients with moderate and severe pain is still an area for further development. Improvements in our palliative care curriculum have been implemented to enhance our residents' education and performance in this area.

Hao, S., et al. "Transgene-mediated enkephalin release enhances the effect of morphine and evades tolerance to produce a sustained antiallodynic effect in neuropathic pain." *Pain*. 102, no. 1-2(2003): 135-42 UI 12620604.

We examined the pharmacologic characteristics of herpes simplex virus (HSV) vector-mediated expression of proenkephalin in the dorsal root ganglion in a rodent model of neuropathic pain. We found that: (i). vector-mediated enkephalin produced an antiallodynic effect that was reversed by naloxone; (ii). vector-mediated enkephalin production in animals with spinal nerve ligation prevented the induction of c-fos expression in second order sensory neurons in the dorsal horn of spinal cord; (iii). the effect of vector-mediated enkephalin enhanced the effect of morphine, reducing the ED(50) of morphine 10-fold; (iv). animals did not develop tolerance to the continued production of vector-mediated enkephalin over a period of several weeks; and, (v). vector transduction continued to provide an analgesic effect despite the induction of tolerance to morphine. This is the first demonstration of gene transfer to provide an analgesic effect in neuropathic pain. The pharmacologic analysis demonstrates that transgene-mediated expression and local release of opioid peptides produce some effects that are distinct from peptide analogues delivered pharmacologically.

Harden, N., and M. Cohen. "Unmet needs in the management of neuropathic pain." *Journal of Pain & Symptom Management*. 25, no. 5 Suppl(2003): S12-7 UI 12694988.

Neuropathic pain is a challenging condition to treat. It is heterogeneous in nature and largely resistant to treatment with commonly prescribed analgesics. Current management strategies fail to achieve adequate or satisfactory pain relief in a high proportion of patients. The four main reasons that treatments for neuropathic pain fail are: inadequate diagnosis and a lack of appreciation of the mechanisms involved; insufficient management of comorbid conditions; incorrect understanding or selection of treatment options; and the use of inappropriate outcomes measures. These unmet needs in the current management of neuropathic pain are reviewed in this article. The review focuses on the need for a methodical and mechanistic approach to diagnosis, and a flexible, interdisciplinary approach to treatment of neuropathic pain conditions, in order to improve pain relief and quality of life in patients with neuropathic pain. [References: 36]

Harris, M. H. "Pain barriers." *South Dakota Journal of Medicine*. 56, no. 6(2003): 219-20 UI 12827936.

Hayashi, F., and H. Kambara. "Vasospastic angina and serious ventricular arrhythmia." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 5(2003): 137-9 UI 12808937.

Haze, K., and A. Itoh. "Refractory unstable angina." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 5(2003): 222-31 UI 12808951.

Hildebrand, K. R., D. D. Elsberry, and S. J. Hassenbusch. "Stability and compatibility of morphine-clonidine admixtures in an implantable infusion system." *Journal of Pain & Symptom Management*. 25, no. 5(2003): 464-71 UI 12727045.

Nonopioid analgesics are often coadministered with intrathecal morphine to increase efficacy. The purpose of this study was to evaluate stability and compatibility of morphine-clonidine admixtures with an implantable infusion system that is commonly used to treat pain patients. Infusion systems were filled with admixture and maintained at 37 degrees C for 90 days. Samples were collected monthly. Drug concentrations were determined using stability-indicating, high-performance liquid chromatography. For compatibility testing, individual materials

comprising the fluid pathway of the device were immersed in clonidine solution and stored at 37 degrees C for various periods through 64 weeks and mechanical performance evaluated. After 3 months of containment in the infusion system, morphine and clonidine concentrations remained at > or = 94% of the theoretical starting concentrations. All device materials retained acceptable mechanical performance following clonidine exposure. These results demonstrate that morphine and clonidine are stable when combined in aqueous solution maintained at body temperature in an implantable infusion system for at least 3 months.

Holland, S. M. "Dysesthetic vulvodynia. Management strategies to improve quality of life." *Advance for Nurse Practitioners*. 11, no. 5(2003): 42-6 UI 12754982.

Holmes, F. E., et al. "Transgenic overexpression of galanin in the dorsal root ganglia modulates pain-related behavior." *Proceedings of the National Academy of Sciences of the United States of America*. 100, no. 10(2003): 6180-5 UI 12721371.

The neuropeptide galanin is expressed in the dorsal root ganglia (DRG) and spinal cord and is thought to be involved in the modulation of pain processing. However, its mechanisms of action are complex and poorly understood, as both facilitatory and inhibitory effects have been described. To understand further the role played by galanin in nociception, we have generated two transgenic lines that overexpress galanin in specific populations of primary afferent DRG neurons in either an inducible or constitutive manner. In the first line, a previously defined enhancer region from the galanin locus was used to target galanin to the DRG (Gal-OE). Transgene expression recapitulates the spatial endogenous galanin distribution pattern in DRG neurons and markedly overexpresses the peptide in the DRG after nerve injury but not in the uninjured state. In the second line, an enhancer region of the c-Ret gene was used to constitutively and ectopically target galanin overexpression to the DRG (Ret-OE). The expression of this second transgene does not alter significantly after nerve injury. Here, we report that intact Ret-OE, but not Gal-OE, animals have significantly elevated mechanical and thermal thresholds. After nerve damage, using a spared nerve-injury model, mechanical allodynia is attenuated markedly in both the Gal-OE and Ret-OE mice compared with WT controls. These results support an inhibitory role for galanin in the modulation of nociception both in intact animals and in neuropathic pain states.

Horrigan, B., and B. Block. "Planning grant awarded to study CAM in treatment of migraines and lower back pain." *Alternative Therapies in Health & Medicine*. 9, no. 3(2003): 22 UI 12776472.

Hruby, V. J., et al. "Design of novel peptide ligands which have opioid agonist activity and CCK antagonist activity for the treatment of pain." *Life Sciences*. 73, no. 6(2003): 699-704 UI 12801591.

Disease states such as neuropathic pain offer special challenges in drug design due to the system changes which accompany these diseases. In this manuscript we provide an example of a new approach to drug design in which we have modified a potent and selective peptide ligand for the CCK-2 receptor to a peptide which has potent agonist binding affinity and bioactivity at delta and mu opioid receptors, and simultaneous antagonist activity at CCK receptors. De novo design based on the concept of overlapping pharmacophores was a central hypothesis of this design, and led to compounds such as H-Tyr-DPhe-Gly-DTrp-NMeNle-Asp-Phe-NH(2) (i.e., RSA 601) which have the designed properties.

Ishikawa, K. "Medical treatment of acute coronary syndromes." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 5(2003): 312-21 UI 12808963.

Isshiki, T., and N. Suzuki. "Diagnosis of stable effort angina pectoris." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 5(2003): 245-50 UI 12808954.

Ito, Y., et al. "Efficacy of chemoradiotherapy on pain relief in patients with intrapelvic recurrence of rectal cancer." *Japanese Journal of Clinical Oncology*. 33, no. 4(2003): 180-5 UI 12810832.

PURPOSE: To assess the efficacy of chemoradiotherapy on pain relief in patients with intrapelvic recurrence of rectal cancer. METHODS: The records of 30 patients treated with radiotherapy with or without chemotherapy for intrapelvic recurrence of rectal cancer between September 1993 and February 1999 were retrospectively reviewed. There were 17 patients in the chemoradiotherapy (CRT) group and 13 patients in the radiotherapy alone (RTA) group. Simultaneous extrapelvic distant metastases were found in 11 patients in the CRT group and in seven patients in the RTA group. Radiotherapy was administered with a median total dose of 50 Gy in both groups. In the CRT group, 15 patients received 5-fluorouracil by continuous infusion and two patients received irinotecan in a biweekly infusion schedule during the course of radiotherapy. The response rate and duration of pain relief were evaluated and were compared between the two groups. RESULTS: The response rate of pain relief in the CRT and RTA was 100 and 77%, respectively. The median duration of pain relief in the CRT and RTA groups was 7.8 and 4.0 months, respectively and there was a significant difference between the two groups ($P = 0.019$). The median survival time from the start of radiotherapy was 15.1 and 9.3 months in the CRT and RTA groups, respectively, and there was a significant difference between the two groups ($P = 0.046$). CONCLUSIONS: The results suggest that chemoradiotherapy for intrapelvic recurrence of rectal cancer for the purpose of pain relief appears to be more effective than radiotherapy alone.

Itoh, A. "Percutaneous coronary intervention in unstable angina." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 5(2003): 210-5 UI 12808949.

Jensen, T. S., and R. Baron. "Translation of symptoms and signs into mechanisms in neuropathic pain." *Pain*. 102, no. 1-2(2003): 1-8 UI 12620591.

Joines, J. D., et al. "A spatial analysis of county-level variation in hospitalization rates for low back problems in North Carolina." *Social Science & Medicine*. 56, no. 12(2003): 2541-53 UI 12742616.

Hospitalization rates for low back problems vary widely. In previous non-spatial analyses, population-level socioeconomic and health resource characteristics have explained little of the variation in rates. This study examines geographic variation in hospitalization rates for low back problems while controlling for spatial dependence in the data. County-level surgical and medical hospitalization rates were calculated using North Carolina hospital (USA) discharge data from 1990-92. Non-spatial and spatial regression models were estimated using socioeconomic and health resource predictors. Both surgical and medical rates varied significantly among the 100 counties. Non-spatial models explained 62% of variation in log-transformed surgical rates and 66% of variation in log-transformed medical rates; however, residuals showed significant spatial dependence. Spatial lag models were therefore applied. Using simple contiguity spatial weights, surgery rates increased with higher percent urban population, primary care physician density, and discharge rate for other causes, and decreased with higher percent college graduates, percent disabled, occupied hospital bed density, and unoccupied hospital bed density. There was a nonlinear relationship between surgery rates and percent employed in heavy lifting/transportation industries. Medical rates increased with higher other-cause

discharge rate and with MRI/CT scanner availability, and decreased with higher percent urban population, percent nonwhite population, percent in heavy lifting/transportation industries, and unoccupied hospital bed density. The results show that population-level socioeconomic and health resource characteristics are important determinants of variation in low back hospitalization rates. Independent of these variables, a separate spatial process produces geographic clustering of high-rate counties. Spatial effects are important and should be considered in small area analyses.

Joshi, G. P. "Chronogesic (DURECT)." *Idrugs*. 6, no. 4(2003): 368-71 UI 12789608.

Katoh, O., S. Negoro, and Y. Aoyagi. "Elective PTCA for angina pectoris." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 4(2003): 501-5 UI 12735023.

Kishida, H., and T. Suzuki. "Medical treatment in patients with angina pectoris." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 5(2003): 93-7 UI 12808931.

Klein, S. M., et al. "The difficulties of ambulatory interscalene and intra-articular infusions for rotator cuff surgery: a preliminary report." *Canadian Journal of Anaesthesia*. 50, no. 3(2003): 265-9 UI 12620950.

PURPOSE: Rotator cuff repair may result in severe postoperative pain. We compared a continuous intra-articular infusion to a continuous interscalene block with ropivacaine for patients undergoing outpatient rotator cuff repair. METHODS: Seventeen patients were randomized to one of two groups: 1) interscalene block with 0.5% ropivacaine (40 mL) followed by a postoperative intra-articular infusion or; 2) interscalene block with 0.5% ropivacaine (40 mL) followed by a postoperative continuous interscalene infusion. Infusions were 0.2% ropivacaine at 10 mL x hr(-1) for both groups. Infusions were maintained for 48 hr. Patients were discharged on the day of surgery. Verbal analogue pain scores (VAS) and postoperative oxycodone consumption were measured for 48 hr. RESULTS: Eight patients (47%; four in each group) had side effects or logistical problems complicating care. The mean VAS scores at rest and with movement in the postanesthesia care unit and at 12 hr, 24 hr, and 48 hr were not different ($P > 0.1$). Inadequate analgesia was reported in 50-75% of all study patients. Time until first oxycodone use was similar between groups 829 min +/- 432 (interscalene) and 999 min +/- 823 (intra-articular; $P = 0.6$). Total oxycodone consumption was also similar 49 mg +/- 48 and 59 mg +/- 51 ($P = 0.7$), respectively. CONCLUSIONS: This study demonstrates the difficulties of ambulatory interscalene and intra-articular infusion for rotator cuff surgery. The high VAS scores and need for additional medical care suggest that intra-articular administration may not be reasonable for this magnitude of surgery. Further refinement of the perineural local anesthetic infusion is necessary to consistently provide analgesia after ambulatory rotator cuff surgery.

Kobierski, L. A., et al. "A single intravenous injection of KRN5500 (antibiotic spicamycin) produces long-term decreases in multiple sensory hypersensitivities in neuropathic pain." *Anesthesia & Analgesia*. 97, no. 1(2003): 174-82, table of contents UI 12818962.

Neuropathic pain is a significant clinical problem. Currently, there are no drugs that produce complete amelioration of this type of pain. We have previously shown that KRN5500, a derivative of the antibiotic spicamycin, produces a prolonged (7-day), and significant reduction in neuropathic pain, but not nociceptive pain. Herein,

we provide further evidence for the efficacy of this drug in inhibiting pain after IV injection in a spared nerve injury model of neuropathic pain. A single IV dose of the drug produces an increase in pain thresholds to punctuate mechanical stimuli and to cold stimuli over a period of 7 days, whereas IV injection of the vehicle is without any effect. No change in pain threshold was observed in the contralateral foot. In addition, a significant antiallodynic effect to mechanical stimuli was observed at 1, 2, 4, and 6 wk. The drug may be a potential candidate for cancer-related neuropathic pain as well as a marker for discovery of effective analgesics for neuropathic pain. IMPLICATIONS: We examined the effect of a novel drug (KRN5500) on nerve damage pain. After the successful effects of this drug in a single human, we have shown that the drug infused as a single application at different doses in a rat model of nerve damage pain produces pain relief in this model for many weeks.

Kochhar, R., et al. "Opioids in cancer pain: common dosing errors." *Oncology (Huntington)*. 17, no. 4(2003): 571-5; discussion 575-6, 579 UI 12735147.

Many individuals with advanced malignancy continue to suffer from pain and, consequently, impaired quality of life. The clinical scenarios in advanced cancer pain are complex, and successful management may require a more sophisticated and individualized approach than suggested by the World Health Organization guidelines. In patients referred to the Harry R. Horvitz Center for Palliative Medicine in Cleveland, numerous commonly occurring errors in opioid use have been noted. This article describes these errors and offers strategies with which to improve outcomes for patients suffering with cancer pain. [References: 19]

Komatsu, R., and K. Haze. "Percutaneous coronary angioplasty for the treatment of angina pectoris: indication, selection of procedures, and initial and late results." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 5(2003): 98-104 UI 12808932.

Labus, J. S., F. J. Keefe, and M. P. Jensen. "Self-reports of pain intensity and direct observations of pain behavior: when are they correlated?" *Pain*. 102, no. 1-2(2003): 109-24 UI 12620602.

Meta-analytic techniques were utilized to investigate the relationship between self-reports of pain intensity and direct observations of pain behavior. Estimation of the overall effect size from 29 studies and 85 effect sizes yielded a moderately positive association, $z=0.26$. High variability across studies permitted a random-effects moderator analysis that determined chronicity of pain, the timing of the pain assessment, the use of global measures of pain behavior, and pain site significantly moderate the relationship between self-reports of pain intensity and direct observations of pain behavior. These findings indicate that self-reports of pain intensity and direct observations of pain behavior are more likely to be significantly related to each other when the individual being studied has acute pain ($z=0.35$), when the self-report of pain intensity data are collected soon after the observation of pain behavior ($z=0.40$), when global composite measures are used to quantify pain behavior ($z=0.37$), and when the person being observed suffers from chronic low back pain ($z=0.30$). Other factors not found to be significant moderators include: extent of observer training, relevance of the pain-inducing task, and pain behavior observation measure used. The implications of the findings for the assessment of pain are discussed.

Lawrie, I., M. Lloyd-Williams, and E. Waterhouse. "Breakthrough strong opioid analgesia prescription in patients using transdermal fentanyl admitted to a hospice." *American Journal of Hospice & Palliative Care*. 20, no. 3(2003): 229-30 UI 12785045.

Durogesic (fentanyl) patches have revolutionized pain relief, but patients still require breakthrough medication. A retrospective analysis of in-patient admission notes at a 25-bed hospice over a six-month period was carried out. Details of analgesia being used on admission for both background and breakthrough pain were obtained, and the appropriateness of the breakthrough dose for those patients using transdermal fentanyl was determined. During the study period 278 patients were admitted to the hospice and 56 (20 percent) were using transdermal fentanyl. Of these, 35 (62 percent) were prescribed strong opioid analgesia--the dose of breakthrough medication prescribed was appropriate in 11 patients (31 percent). Rescue dosing was less than recommended, in relation to prescribed transdermal fentanyl strength in 21 patients (60 percent) and greater than recommended in one patient (3 percent). In this study, short-acting strong opioid analgesia was not always prescribed for patients using transdermal fentanyl, and when they were prescribed, this was in the appropriate dose range in less than a third of patients.

Lindroth, J. E., M. C. Herren, and D. A. Falace. "The management of acute dental pain in the recovering alcoholic." *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, & Endodontics*. 95, no. 4(2003): 432-6 UI 12686926.

Although there have been many advances in our understanding of the neurophysiology of pain, the management of acute pain continues to be a challenge. When the need arises to provide adequate and effective pain management for the recovering alcoholic, the problem becomes much more complex. The clinician must provide the patient with adequate analgesia without causing a relapse. In the US, 6% to 10% of the population has attended Alcoholics Anonymous at some point, increasing the likelihood of the clinician being faced with the need to manage acute pain in a recovering alcoholic. The purpose of this article is to suggest guidelines for the management of acute dental pain in the recovering alcoholic based on current principles of acute pain management and for the treatment of pain in addicted patients. [References: 41]

Lower, J. "Using pain to assess neurologic response." *Nursing*. 33, no. 6(2003): 56-7 UI 12799591.

Mailis, A., and A. Furlan. "Sympathectomy for neuropathic pain." *Cochrane Database of Systematic Reviews*, no. 2(2003): CD002918 UI 12804444.

BACKGROUND: Neuropathic pain is defined as pain initiated or caused by a primary lesion or dysfunction in the nervous system. Some examples of this condition are phantom limb pain, post-stroke pain and complex regional pain syndrome type I (reflex sympathetic dystrophy) and type II (causalgia). Treatment options include drugs, physical treatments, surgery and psychological interventions. The concept that many neuropathic pain syndromes, particularly RSD and causalgia are "sympathetically maintained pains" has historically led to attempts to temporarily or permanently interrupt the sympathetic nervous system. Chemical sympathectomies use alcohol or phenol injections to destroy the sympathetic chain, but this effect is temporary until regeneration of the sympathetic chain occurs. Surgical ablation can be performed by open removal or electrocoagulation of the sympathetic chain, or minimally invasive procedures using stereotactic thermal or laser interruption. **OBJECTIVES:** The review aimed to assess the effects of both chemical and surgical sympathectomy for neuropathic pain. Secondary objectives were to compare the effects of sympathectomy with no treatment, placebo or conventional treatment, and to evaluate whether the technique of sympathectomy influences the outcomes of the procedure. **SEARCH STRATEGY:** We searched MEDLINE and EMBASE up to February 2003 and the latest issue of the Cochrane Library (Issue 1, 2003). We screened references in the retrieved articles, literature reviews and book chapters. We also contacted experts in the field of neuropathic

pain. SELECTION CRITERIA: Clinical trials and observational studies assessing the effects of sympathectomy (surgical or chemical) for neuropathic pain of both central or peripheral origin were included. DATA COLLECTION AND ANALYSIS: Two reviewers applied the selection criteria to titles and abstracts. Full articles of potentially eligible trials were obtained and the same reviewers applied the inclusion criteria to the studies. The methodological quality of the studies was evaluated. The studies were also evaluated for clinical relevance according to a classification developed by our group. Statistical pooling was not possible due to heterogeneity of data; instead a narrative description of each included study was performed. MAIN RESULTS: We included four studies. One randomized trial comparing radiofrequency sympathectomy with phenol sympathectomy was rated as low methodological quality and it showed that radiofrequency sympathectomy does not offer advantage over phenol techniques. However, a modified technique produced sympathectomy comparable to that produced by 6% phenol, with less incidence of post-sympathectomy neuralgia. REVIEWER'S CONCLUSIONS: The practice of surgical and chemical sympathectomy is based on poor quality evidence, uncontrolled studies and personal experience. Furthermore, complications of the procedure may be significant, in terms of both worsening the pain or producing a new pain syndrome; and abnormal forms of sweating (compensatory hyperhidrosis and pathological gustatory sweating). Therefore, more clinical trials of sympathectomy are required to establish the overall effectiveness and potential risks of this procedure. [References: 18]

Malan, T. P., Jr., et al. "CB2 cannabinoid receptor agonists: pain relief without psychoactive effects?" *Current Opinion in Pharmacology*. 3, no. 1(2003): 62-7 UI 12550743.

Cannabinoid receptor agonists significantly diminish pain responses in animal models; however, they exhibit only modest analgesic effects in humans. The relative lack of efficacy in man may be because of the dose limitations imposed by psychoactive side effects. Cannabinoid agonists that selectively target CB(2) (peripheral) cannabinoid receptors should be free of psychoactive effects, perhaps allowing for more effective dosing. CB(2) receptor activation inhibits acute, inflammatory and neuropathic pain responses in animal models. In preclinical studies, CB(2) receptor agonists do not produce central nervous system effects. Therefore, they show promise for the treatment of acute and chronic pain without psychoactive effects. [References: 43]

Maneuf, Y. P., et al. "Cellular and molecular action of the putative GABA-mimetic, gabapentin." *Cellular & Molecular Life Sciences*. 60, no. 4(2003): 742-50 UI 12785720.

Gabapentin was originally designed as an anti-convulsant gamma-aminobutyric acid (GABA) mimetic capable of crossing the blood-brain barrier. In the present review we show that although gabapentin is not a GABA mimetic, it has great utility as an add-on therapy for epilepsy and as a first-line treatment for neuropathic pain. We summarise the studies that have been performed which demonstrate that gabapentin appears to interact with a novel binding site expressed at high density within the central nervous system (CNS), namely the alpha2delta voltage-dependent calcium channel subunit. The review continues by examining the effects of gabapentin on calcium channel function and neurotransmitter release before, in the latter part of the review, summarising the more recently discovered actions of gabapentin in relation to intracellular signalling. [References: 93]

Mann, E. "Managing pain." *Bmj*. 326, no. 7402(2003): 1320-1 UI 12805176.

McCaffery, M. "Switching from i.v. to p.o." *AJN, American Journal of Nursing*. 103, no. 5(2003): 62-3 UI 12759604.

McKellar, J. D., M. E. Clark, and J. Shriner. "The cognitive specificity of associative responses in patients with chronic pain." *British Journal of Clinical Psychology*. 42, no. Pt 1(2003): 27-39 UI 12675977.

OBJECTIVE: Previous studies have found evidence of an associative response bias for patients with chronic pain. This body of research is not clear, however, on whether this bias is specific to patients with chronic pain, or whether the bias is specific to pain stimuli or illness/disability stimuli. DESIGN: This is a cross-sectional study involving the comparison of selected groups (chronic pain, acute pain, and medical-staff controls). METHOD: This study included 80 male participants with chronic pain, 50 male participants with acute pain, and 49 male participants who served as medical staff controls. All participants completed the Beck Depression Inventory, the State-Trait Anxiety Inventory, a pain intensity VAS, and the single-word associate homographic response task. RESULTS: Evidence was found for the specificity of pain responses to homographic pain stimuli as the chronic pain group produced more of these responses than the two comparison groups. CONCLUSIONS: These findings were seen as providing evidence for an associative response bias. This bias appears specific to pain-related stimuli and reflects the cumulative effects of pain over a period of time.

Mizoguchi, H., et al. "Buprenorphine blocks epsilon- and micro-opioid receptor-mediated antinociception in the mouse." *Journal of Pharmacology & Experimental Therapeutics*. 306, no. 1(2003): 394-400 UI 12721333.

Antagonistic properties of buprenorphine for epsilon- and micro-opioid receptors were characterized in beta-endorphin- and [d-Ala²,N-Me-Phe⁴,Gly⁵-ol]-enkephalin (DAMGO)-induced antinociception, respectively, with the tail-flick test in male ICR mice. epsilon-Opioid receptor agonist beta-endorphin (0.1-1 micro g), micro-opioid receptor agonist DAMGO (0.5-20 ng), or buprenorphine (0.1-20 micro g) administered i.c.v. dose dependently produced antinociception. The antinociception induced by 10 micro g of buprenorphine given i.c.v. was completely blocked by the pretreatment with beta-funaltrexamine (beta-FNA) (0.3 micro g i.c.v.), indicating that the buprenorphine-induced antinociception is mediated by the stimulation of the micro-opioid receptor. The antinociceptive effects induced by beta-endorphin (1 micro g i.c.v.) and DAMGO (16 ng i.c.v.) were dose dependently blocked by pretreatment with smaller doses of buprenorphine (0.001-1 micro g i.c.v.), but not by a higher dose of buprenorphine (10 micro g i.c.v.). beta-FNA at a dose (0.3 micro g i.c.v.) that strongly attenuated DAMGO-induced antinociception had no effect on the antinociception produced by beta-endorphin (1 micro g i.c.v.). However, pretreatment with buprenorphine (0.1-10 micro g) in mice pretreated with this same dose of beta-FNA was effective in blocking beta-endorphin-induced antinociception. beta-FNA was 226-fold more effective at antagonizing the antinociception induced by DAMGO (16 ng i.c.v.) than by beta-endorphin (1 micro g i.c.v.). The antinociception induced by delta-opioid receptor agonist [d-Ala²]deltorphin II (10 micro g i.c.v.) or kappa1-opioid receptor agonist trans-3,4-dichloro-N-methyl-N-(2- and 2 over black square); [1 and 2 over black square]-pyrrolidinyl]cyclohexyl]benzeneacetamide methanesulfonate salt [(-)-U50,488H] (75 micro g i.c.v.) was not affected by pretreatment with buprenorphine (0.1-1.0 micro g i.c.v.). It is concluded that buprenorphine, at small doses, blocks epsilon-opioid receptor-mediated beta-endorphin-induced antinociception and micro-opioid receptor-mediated DAMGO-induced antinociception, and at high doses produces a micro-opioid receptor-mediated antinociception.

Moskowitz, M. H. "Pharmacotherapy of neuropathic low back pain." *Current Pain & Headache Reports*. 7, no. 3(2003): 178-87 UI 12720597.

Neuropathic low back pain is examined from a structural standpoint, distinguishing processes that start from chronic inflammation and mechanical compromise and cross into the realm of neuropathy with primary neurogenic pathophysiology. The disease of chronic pain is discussed, examining peripheral and central changes in neuroanatomy, neurophysiology, and neuromolecular dynamics. The limitations of inadequate random controlled trials regarding long-term pharmacologic interventions are contrasted with excellent work in the basic science of chronic pain. Complex rational pharmacologic strategies for structural pathology, central pain processes, sites of medication action, and differing routes of administration are delineated. [References: 35]

Nash, M. R. "Three core hypnotic phenomena studied with both scientific precision and clinical savvy." *International Journal of Clinical & Experimental Hypnosis*. 51, no. 1(2003): 86-90 UI 12825921.

Three especially interesting and important studies on hypnosis have appeared in the scientific and medical literatures over the past few months. They are in the finest tradition of the field. Each study examines a phenomenon that is at once core to scientific hypnosis but also of keen interest to clinicians: conversion disorder, amnesia, and pain. It is testimony to the vigor of the field that these 3 phenomena endure as topics of discourse within and across disciplines. Further, the 3 studies make use of sophisticated designs and methodologies to render findings more (not less) relevant to clinical work. These 3 studies are wonderful examples of the field at its best: eschewing the partisan, embracing discourse, and in so doing mapping the domain of hypnosis with imagination and passion.

Nishida, H., H. Kurosawa, and M. Endo. "Indications and results of emergency coronary artery bypass grafting in unstable angina." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 4(2003): 612-7 UI 12735040.

Nonogi, H. "Pathophysiology and management for unstable angina based on the responsiveness to drug treatment." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 5(2003): 172-7 UI 12808943.

Ochi, M. "Surgical indication for unstable angina." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 5(2003): 216-21 UI 12808950.

Ohtani, T., A. Hirayama, and K. Kodama. "Clinical value of biochemical markers in patients with unstable angina." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 5(2003): 200-5 UI 12808947.

Paqueron, X., D. Conklin, and J. C. Eisenach. "Plasticity in action of intrathecal clonidine to mechanical but not thermal nociception after peripheral nerve injury." *Anesthesiology*. 99, no. 1(2003): 199-204 UI 12826860.

BACKGROUND: Intrathecal clonidine reduces tactile allodynia in animal models of neuropathic pain, and this effect is blocked by atropine. However, the role of tonic spinal cholinergic activity and its interaction with alpha2-adrenergic systems in normal and neuropathic conditions and to different sensory methods has not been systematically examined. The authors examined cholinergic receptor involvement in thermal and mechanical sensitivity in normal and neuropathic animals and its interaction with intrathecal clonidine. METHODS: Normal rats and rats that received L5/L6 spinal nerve ligation were tested with acute radiant heat, paw pressure, and punctate mechanical stimulation before and after the intrathecal administration of saline, the muscarinic receptor antagonist, atropine, or a toxin to destroy cholinergic

neurons, and then after intrathecal clonidine. RESULTS: Atropine, the cholinergic neuronal toxin, and saline did not alter baseline withdrawal thresholds. In nerve-injured rats, neither saline nor atropine altered antinociception from clonidine to a thermal stimulus, but atropine reduced the effect of clonidine to von Frey filament withdrawal threshold (34 +/- 5.6 vs. 14 +/- 5.8 g [mean +/- SEM], saline vs. atropine; P < 0.05) and to withdrawal threshold to paw pressure after clonidine (174 +/- 18 g vs. 137 +/- 16 g, saline vs. atropine; P < 0.05). CONCLUSIONS: These data suggest that after nerve injury, mechanical but not thermal antinociception from intrathecal clonidine relies on a muscarinic interaction, because only mechanical antinociception was antagonized by atropine. These results do not favor a regulation of nociceptive transmission by a tonic release of acetylcholine in nerve-injured rats.

Pfizer, J., and D. G. Moyes. "Pain scores" in the early postoperative period." *Anaesthesia & Intensive Care*. 31, no. 2(2003): 233 UI 12712794.

Rabinstein, A. A., and L. M. Shulman. "Acupuncture in clinical neurology." *Neurologist*. 9, no. 3(2003): 137-48 UI 12808410.

BACKGROUND: A majority of people in the United States use alternative or complementary therapy at some point in their lives, and acupuncture is among the most frequently used modalities. Many United States medical schools offer courses in alternative medicine, and a growing number of insurers offer coverage for alternative therapies. This paper critically reviews our current knowledge about the safety and efficacy of acupuncture for neurologic conditions. REVIEW SUMMARY: Acupuncture is a safe procedure when performed by trained professionals. Complications from acupuncture are rare and mainly related to negligence of sterile technique. Studies of the therapeutic value of acupuncture are fraught with challenging methodologic problems, including the choice of a placebo, a suitable control treatment, and the technique of stimulation applied. Clinical trials of the use of acupuncture for pain syndromes (headache, neck, and back pain), stroke rehabilitation, Parkinson's disease, multiple sclerosis, and substance abuse are reviewed. CONCLUSIONS: Based on the current literature, no definitive recommendation can be made regarding the efficacy of acupuncture for common pain syndromes including headache, and neck and back pain. Better quality clinical trials fail to demonstrate efficacy for the use of acupuncture as part of a rehabilitation program following stroke or as a treatment for drug addiction. Acupuncture may have a role in the treatment of sleep disturbance associated with Parkinson's disease but was not efficacious for the primary symptoms of either Parkinson's disease or multiple sclerosis. In light of increasing public interest and use of alternative therapies, this review may be helpful in promoting more discussion between patients and physicians about the use of acupuncture. [References: 120]

Reddy, M., et al. "Practical treatment of wound pain and trauma: a patient-centered approach. An overview." *Ostomy Wound Management*. 49, no. 4 Suppl(2003): 2-15 UI 12856288.

Chronic wound pain is distressing and influences the patient's ability to function. One of the failures of modern medicine is the inadequate assessment and treatment of pain. The clinician's approach to chronic wound pain combines the "preparing the wound bed" paradigm with chronic wound pain models. A holistic approach must include the diagnosis and treatment of the underlying cause, identification and correction of patient-centered concerns, and the three major components of local wound care (debridement, bacterial balance/prolonged inflammation, and moisture balance). The Krasner pain model defines chronic (persistent), noncyclic acute, and cyclic acute wound pain. Chronic persistent wound pain without an event or trigger often relates to the cause of the wound that needs to be corrected to relieve the pain. Noncyclic acute pain is often experienced with a surgical procedure such as

sharp debridement. Cyclical acute pain may occur repeatedly with removal or application of new local wound dressings. Securing a thorough pain history focusing on pain patterns will help healthcare professionals develop specific pain relief initiatives. Pain is a component of quality of life. Patient-centered concerns need to address pain control measures until the cause of the pain can be corrected. Controlling pain, however, may not always improve quality of life scores. Each of the components of local wound care also may be responsible for the production of pain; strategies need to be implemented to ensure adequate patient comfort. [References: 77]

Riemann, J. F. "Diagnostic laparoscopy." *Endoscopy*. 35, no. 1(2003): 43-7 UI 12510225.

Diagnostic laparoscopy is increasingly being used to aid decision-making in the treatment of serious diseases. The majority of papers on the topic published during the last year have been concerned with preoperative assessment of malignant diseases of the gastrointestinal tract, and have shown that laparoscopy alone--or, even better, in combination with laparoscopic ultrasonography--is able to identify metastatic disease and therefore to reduce significantly the risk of unnecessary laparotomies. New techniques such as the application of fluorescent dyes may improve these results even further. Surgeons are increasingly using diagnostic laparoscopy in patients with acute abdomen and abdominal trauma--a minimally invasive strategy that should also be supported by gastroenterologists. Close cooperation between surgeons and gastroenterologists can also be promoted by using laparoscopy in critically ill patients in intensive-care units when a decision needs to be taken on whether or not laparotomy should be performed. The technique of diagnostic laparoscopy is returning to widespread use after a period of decline. [References: 38]

Saade, N. E., et al. "A thymulin analogue peptide with powerful inhibitory effects on pain of neurogenic origin." *Neuroscience*. 119, no. 1(2003): 155-65 UI 12763077.

The effects of a synthetic peptide analog of thymulin (PAT) were tested on nociceptive behavior in two animal models for peripheral mononeuropathy and in another two models for capsaicin-induced hyperalgesia. Treatment with PAT (0.25-25 microg/rat, i.p.) produced significant reduction of the mechanical allodynia and heat hyperalgesia in rats subjected to either chronic constriction injury (CCI) or spared nerve injury (SNI) models for mononeuropathy. Cold allodynia was moderately reduced in the CCI model. The inhibition of neuropathic manifestations peaked at 1-2 h post-treatment and disappeared in 3-4 h. Daily treatment with PAT, however, produced progressive attenuation of all neuropathic manifestations in the SNI model. On the other hand, pretreatment with similar doses of PAT produced dose-dependent reduction of the hyperalgesia induced by intraplantar injection of capsaicin (10 microg in 50 microl). The highest dose of PAT (50 microg) produced significant reduction of abdominal aversive behavior induced by i.p injection of capsaicin (20 microg in 100 microl). Compared with the effects of treatment with morphine or meloxicam (injected at single doses known to produce analgesia), PAT exerted equal or stronger inhibitory effects on neuropathic manifestations. The reported results suggest a possible direct action of PAT on afferent nerve fibers but its mechanisms remain to be determined.

Sah, D. W., M. H. Ossipo, and F. Porreca. "Neurotrophic factors as novel therapeutics for neuropathic pain." *Nature Reviews. Drug Discovery*. 2, no. 6(2003): 460-72 UI 12776221.

Neuropathic pain is a chronic condition that is caused by injury to the nervous system. Unlike acute pain, which is protective, neuropathic pain persists and serves no useful purpose, and severely affects quality of life. However, present therapies

have modest efficacy in most patients, are palliative rather than curative, and their side effects represent significant limitations. Tremendous progress has been made over the past decade in our understanding of the biology of pain sensory neurons. The recent discovery that neurotrophic factors play an important role in neuropathic pain indicates that these pathways could serve as novel intervention points for therapy. Moreover, neurotrophic factors have the potential to address the underlying pathophysiology of neuropathic pain, thereby halting or reversing the disease process. [References: 216]

Sawanobori, T., and K. Kugiyama. "Antianginal drugs." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 4(2003): 654-9 UI 12735046.

Sekhri, N., and A. D. Timmis. "Rapid access chest pain clinics: are they clinically effective?" *Hospital Medicine (London)*. 64, no. 6(2003): 324-5 UI 12833821.

Severgnini, A., et al. "The role of the pain therapist in the approach to chronic headache." *Neurological Sciences*. 24, no. Suppl 2(2003): S115-7 UI 12811607.

Chronic daily headache (CDH) represents, for the anesthesiologists, a big match in the management of a pain which is simultaneously central and periferic, of a pain wich is psychical and disabling. This is a pain conducting the patient to overuse analgesic medicaments even making worse "allodynia" and the organic integrity. That's why a multidisciplinary approach to this kind of chronic benign pathology permits to improve prognosis and quality of life.

Shang, A. B., and T. J. Gan. "Optimising postoperative pain management in the ambulatory patient." *Drugs*. 63, no. 9(2003): 855-67 UI 12678572.

Over 60% of surgery is now performed in an ambulatory setting. Despite improved analgesics and sophisticated drug delivery systems, surveys indicate that over 80% of patients experience moderate to severe pain postoperatively. Inadequate postoperative pain relief can prolong recovery, precipitate or increase the duration of hospital stay, increase healthcare costs, and reduce patient satisfaction. Effective postoperative pain management involves a multimodal approach and the use of various drugs with different mechanisms of action. Local anaesthetics are widely administered in the ambulatory setting using techniques such as local injection, field block, regional nerve block or neuraxial block. Continuous wound infusion pumps may have great potential in an ambulatory setting. Regional anaesthesia (involving anaesthetising regional areas of the body, including single extremities, multiple extremities, the torso, and the face or jaw) allows surgery to be performed in a specific location, usually an extremity, without the use of general anaesthesia, and potentially with little or no sedation. Opioids remain an important component of any analgesic regimen in treating moderate to severe acute postoperative pain. However, the incorporation of non-opioids, local anaesthetics and regional techniques will enhance current postoperative analgesic regimens. The development of new modalities of treatment, such as patient controlled analgesia, and newer drugs, such as cyclo-oxygenase-2 inhibitors, provide additional choices for the practitioner. While there are different routes of administration for analgesics (e.g. oral, parenteral, intramuscular, transmucosal, transdermal and sublingual), oral delivery of medications has remained the mainstay for postoperative pain control. The oral route is effective, the simplest to use and typically the least expensive. The intravenous route has the advantages of a rapid onset of action and easier titratability, and so is recommended for the treatment of acute pain. Non-pharmacological methods for the management of postoperative pain include acupuncture, electromagnetic millimetre waves, hypnosis and the use of music during surgery. However, further research of these techniques is warranted to elucidate their effectiveness in this indication. Pain is a multifactorial experience, not

just a sensation. Emotion, perception and past experience all affect an individual's response to noxious stimuli. Improved postoperative pain control through innovation and creativity may improve compliance, ease of delivery, reduce length of hospital stay and improve patient satisfaction. Patient education, early diagnosis of symptoms and aggressive treatment of pain using an integrative approach, combining pharmacotherapy as well as complementary technique, should serve us well in dealing with this complex problem. [References: 67]

Shin, S. W., and J. C. Eisenach. "Intrathecal morphine reduces the visceromotor response to acute uterine cervical distension in an estrogen-independent manner." *Anesthesiology*. 98, no. 6(2003): 1467-71; discussion 6A UI 12766659.

BACKGROUND: Acute uterine cervical distension (UCD) forms the basis for obstetric and some gynecologic pain. Systemic morphine inhibits the visceromotor response to UCD in rats by an action in the central nervous system, but the effect of morphine is blocked by exposure to estrogen. The purpose of the present study was to determine whether this estrogen blockade of the action of morphine reflects a spinal mechanism. METHODS: Virgin Sprague-Dawley rats received estrogen or placebo treatment for 1 week after ovariectomy. Rats were then anesthetized, and the electromyographic response in the rectus abdominis muscle to UCD was recorded in the absence and presence of cumulative dosing with intrathecal morphine. RESULTS: Estrogen treatment did not alter the stimulus-response relationship between UCD and reflex muscle contraction. Intrathecal morphine reduced the visceromotor reflex response to UCD in a dose-dependent manner that was unaffected by estrogen treatment. CONCLUSIONS: These data suggest that intrathecal morphine is effective in reducing the visceromotor response to UCD and that the reduction in efficacy of systemic morphine in this model is unlikely to reflect a reduction of the efficacy of morphine at the spinal level. These data agree with clinical studies that indicate that systemic morphine, in doses that reduce acute postoperative pain, have minimal to no effect in women in labor, yet intrathecal injection of opioids provides rapid, complete analgesia.

Sibbald, R. G., D. G. Armstrong, and H. L. Orsted. "Pain in diabetic foot ulcers." *Ostomy Wound Management*. 49, no. 4 Suppl(2003): 24-9 UI 12856290.

People with diabetes who have foot ulcers require adequate vasculature, infection control, and pressure offloading to heal. Pain is uncommon in diabetic foot disorders, but it may herald the onset of limb-threatening complications such as deep infection, Charcot change, or critical ischemia. Although neuropathy is most commonly painless, a minority of patients experience disturbing burning, stinging, stabbing, or shooting sensations. Using the "preparing the wound bed" model, the cause of pain in the person with diabetic foot problems can be diagnosed systematically and important therapeutic measures can be instituted in an attempt to prevent potential complications, including amputation. [References: 38]

Stephenson, N. L., and J. A. Dalton. "Using reflexology for pain management. A review." *Journal of Holistic Nursing*. 21, no. 2(2003): 179-91 UI 12794960.

More than two thirds of Americans with chronic pain are now using complementary and alternative therapies. One complementary and alternative therapy, reflexology, has a long history and has been found useful on a case-by-case basis. This article provides a review of the literature on the use of reflexology as a therapy in pain management. Although reflexology is widely used, systematic research is needed to examine its effectiveness. To date, however, only a few studies have focused on reflexology's use in pain management. Because reflexology is a noninvasive, nonpharmacological therapy, nurses are in a position to do research on and make decisions about its clinical effectiveness. [References: 47]

Suzuki, M., and T. Isshiki. "Treatment and prognosis of stable effort angina." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 5(2003): 251-5 UI 12808955.

Tait, D. "Through the pain." *Nursing Standard*. 17, no. 39(2003): 22-3 UI 12836432.

Takayama, M. "Acute coronary syndrome." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 5(2003): 303-11 UI 12808962.

Tallia, A. F., and D. A. Cardone. "Diagnostic and therapeutic injection of the shoulder region." *American Family Physician*. 67, no. 6(2003): 1271-8 UI 12674455.

The shoulder is the site of multiple injuries and inflammatory conditions that lend themselves to diagnostic and therapeutic injection. Joint injection should be considered after other therapeutic interventions such as nonsteroidal anti-inflammatory drugs, physical therapy, and activity-modification have been tried. Indications for glenohumeral joint injection include osteoarthritis, adhesive capsulitis, and rheumatoid arthritis. For the acromioclavicular joint, injection may be used for diagnosis and treatment of osteoarthritis and distal clavicular osteolysis. Subacromial injections are useful for a range of conditions including adhesive capsulitis, subdeltoid bursitis, impingement syndrome, and rotator cuff tendinosis. Scapulothoracic injections are reserved for inflammation of the involved bursa. Persistent pain related to inflammatory conditions of the long head of the biceps responds well to injection in the region. The proper technique, choice and quantity of pharmaceuticals, and appropriate follow-up are essential for effective outcomes. [References: 25]

van Tulder, M. W., et al. "Muscle relaxants for non-specific low back pain." *Cochrane Database of Systematic Reviews*, no. 2(2003): CD004252 UI 12804507.

BACKGROUND: The use of muscle relaxants in the management of non-specific low back pain is controversial. It is not clear if they are effective, and concerns have been raised about the potential adverse effects involved. **OBJECTIVES:** The aim of this review was to determine if muscle relaxants are effective in the treatment of non-specific low back pain. **SEARCH STRATEGY:** A computer-assisted search of the Cochrane Library (Issue 2, 2002), MEDLINE (1966 up to October 2001) and EMBASE (1988 up to October 2001) was carried out. These databases were searched using the algorithm recommended by the Cochrane Back Review Group. References cited in the identified articles and other relevant literature were screened. **SELECTION CRITERIA:** Randomised and/or double-blinded controlled trials, involving patients diagnosed with non-specific low back pain, treated with muscle relaxants as monotherapy or in combination with other therapeutic modalities, were included for review. **DATA COLLECTION AND ANALYSIS:** Two reviewers independently carried out the methodological quality assessment and data extraction of the trials. The analysis comprised not only a quantitative analysis (statistical pooling) but also a qualitative analysis ("best evidence synthesis"). This involved the appraisal of the strength of evidence for various conclusions using a rating system based on the quality and outcomes of the studies included. Evidence was classified as "strong", "moderate", "limited", "conflicting" or "no" evidence. **MAIN RESULTS:** Thirty trials met the inclusion criteria. Twenty-three trials (77%) were of high quality, 24 trials (80%) were on acute low back pain. Four trials studied benzodiazepines, 11 non-benzodiazepines and two antispasticity muscle relaxants in comparison with placebo. Results showed that there is strong evidence that any of these muscle relaxants are more effective than placebo for patients with acute LBP on short-term pain relief. The pooled RR for non-benzodiazepines versus placebo after two to four days was 0.80 [95% CI; 0.71 to 0.89] for pain relief and 0.49 [95% CI; 0.25 to 0.95] for

global efficacy. Adverse events, however, with a relative risk of 1.50 [95% CI; 1.14 to 1.98] were significantly more prevalent in patients receiving muscle relaxants and especially the central nervous system adverse effects (RR 2.04; 95% CI; 1.23 to 3.37). The various muscle relaxants were found to be similar in performance. REVIEWER'S CONCLUSIONS: Muscle relaxants are effective in the management of non-specific low back pain, but the adverse effects require that they be used with caution. Trials are needed that evaluate if muscle relaxants are more effective than analgesics or non-steroidal anti-inflammatory drugs. [References: 87]

Veneroni, O., et al. "Anti-allodynic effect of NW-1029, a novel Na(+) channel blocker, in experimental animal models of inflammatory and neuropathic pain." *Pain*. 102, no. 1-2(2003): 17-25 UI 12620593.

NW-1029, a benzylamino propanamide derivative, was selected among several molecules of this chemical class on the basis of its affinity for the [(3)H]batracotoxin ligand displacement of the Na(+) channel complex and also on the basis of its voltage and use-dependent inhibitory action on the Na(+) currents of the rat DRG (dorsal root ganglia) sensory neuron. This study evaluated the analgesic activity of NW-1029 in animal models of inflammatory and neuropathic pain (formalin test in mice, complete Freund's adjuvant and chronic constriction injury in rats) as well as in acute pain test (hot-plate and tail-flick in rats). Orally administered NW-1029 dose-dependently reduced cumulative licking time in the early and late phase of the formalin test (ED(50)=10.1 mg/kg in the late phase). In the CFA model, NW-1029 reversed mechanical allodynia (von Frey test) after both i.p. and p.o. administration (ED(50)=0.57 and 0.53 mg/kg), respectively. Similarly, NW-1029 reversed mechanical allodynia in the CCI model after both i.p. and p.o. administration yielding an ED(50) of 0.89 and 0.67 mg/kg, respectively. No effects were observed in the hot-plate and tail-flick tests up to 30 mg/kg p.o. The compound orally administered (0.1-10 mg/kg) was well tolerated, without signs of neurological impairment up to high doses (ED(50)=470 and 245 mg/kg in rat and mice Rotarod test, respectively). These results indicate that NW-1029 has anti-nociceptive properties in models of inflammatory and neuropathic pain.

Weissman, D. E. "Measuring the quality of pain management." *Journal of Palliative Medicine*. 6, no. 2(2003): 185-7 UI 12854933.

Wilder-Smith, O. H., et al. "Quantitative sensory testing and human surgery: effects of analgesic management on postoperative neuroplasticity." *Anesthesiology*. 98, no. 5(2003): 1214-22 UI 12717144.

BACKGROUND: Altered central nervous system sensory processing (neuroplasticity) is a basic mechanism underlying postoperative pain that can be made visible using quantitative sensory testing. Using quantitative sensory testing, the authors investigated how perioperative analgesia affects postoperative neuroplasticity and how this relates to clinical pain measures. METHODS: Patients undergoing back surgery received placebo, fentanyl, or ketorolac (n = 15 per group) before isoflurane-nitrous oxide anesthesia. Preoperatively to 5 days postoperatively, we measured thresholds to electrical skin stimulation at the incision site, arm, and leg; pain scores; and morphine patient-controlled analgesia consumption. RESULTS: Decreased pain thresholds versus preoperatively were seen 5 days postoperatively, with decreases greater for ketorolac (-63%; P = 0.00005 vs. preoperatively) than placebo (-45%; P = 0.008 vs. preoperatively) but nonsignificant for fentanyl (-36%; P = 0.9 vs. preoperatively). Mainly nonnociceptive thresholds were increased up to 24 h postoperatively. Postoperative clinical pain measures were similar across drug groups. Postoperative pain tolerance threshold changes did not correlate with preoperative clinical pain measures but were inversely related to preoperative thresholds for placebo and ketorolac but not fentanyl. CONCLUSIONS: Without

analgesia, neuroplasticity after surgery was inhibitory the first 24 h and followed at 5 days by excitation. Fentanyl efficiently preempted this hyperalgesia, but hyperalgesia was greater with ketorolac than with placebo. Clinical pain measures neither reflected the different effects of ketorolac and fentanyl on postoperative neuroplasticity nor permitted prediction of postoperative neuroplasticity. The information obtained by perioperative quantitative sensory testing is separate from and additional to that from clinical pain measures and may enable more mechanism-based approaches to surgical analgesia management in the future.

Willoch, F., et al. "Analgesia by electrostimulation of the trigeminal ganglion in patients with trigeminopathic pain: a PET activation study." *Pain*. 103, no. 1-2(2003): 119-30 UI 12749966.

Electrostimulation of the trigeminal ganglion (TGES) has shown good results in treatment of trigeminopathic pain in selected patients. To map the mechanisms of TGES analgesia, we determined changes in relative regional cerebral blood flow (rCBF) in ten patients with trigeminopathic pain using positron emission tomography. The patients were scanned before stimulation (habitual pain), after short-term stimulation (1 min, stTGES) and after long-term stimulation (ltTGES). Highly significant pain alleviation was reported after ltTGES. Relative rCBF changes after stTGES, which was without significant pain relief, were attributed mainly to intrinsic TGES effects. A statistical comparison of the subtraction images of ltTGES and stTGES disclosed significant rCBF increases after ltTGES in rostral parts of anterior cingulate cortex (ACC) and neighboring orbitofrontal and medial frontal cortices. Regression analysis of rCBF changes and subjective ratings of pain revealed an inverse relationship in the ipsilateral rostral ACC, and only rCBF changes in the caudal part of the contralateral ACC were consistent with the encoding of pain. The present study provides evidence for a pain modulating role of the rostral ACC, critically important in electrostimulation-induced analgesia, and identifies the caudal ACC as a region encoding pain sensation.

Wright, K. D., and J. Shirey. "A pain management protocol for wound care." *Ostomy Wound Management*. 49, no. 5(2003): 18-20 UI 12732754.

Xu, Y., et al. "Adeno-associated viral transfer of opioid receptor gene to primary sensory neurons: a strategy to increase opioid antinociception." *Proceedings of the National Academy of Sciences of the United States of America*. 100, no. 10(2003): 6204-9 UI 12719538.

To develop a genetic approach for the treatment of pain, we introduced a recombinant adeno-associated viral (rAAV) vector containing the cDNA for the mu-opioid receptor (muOR) into primary afferent neurons in dorsal root ganglia (DRGs) of rats, which resulted in a long-lasting (>6 months) increase in muOR expression in DRG neurons. The increase greatly potentiated the antinociceptive effects of morphine in rAAV-muOR-infected rats with and without inflammation. Perforated patch recordings indicated that the efficacy and potency of opioid inhibition of voltage-dependent Ca(2+) channels were enhanced in infected neurons, which may underlie the increase in opiate efficacy. These data suggest that transfer of opioid receptor genes into DRG cells with rAAV vectors may offer a new therapeutic strategy for pain management.

Yasue, H. "Angina pectoris: symptomatology and differential diagnosis." *Nippon Rinsho - Japanese Journal of Clinical Medicine*. 61, no. Suppl 5(2003): 27-31 UI 12808922.

Zanni, G. R., and J. Y. Wick. "Low back pain: eliminating myths and elucidating realities." *Journal of the American Pharmacists Association: JAPhA*. 43, no. 3(2003): 357-62 UI 12836785.

Zaveri, N. "Peptide and nonpeptide ligands for the nociceptin/orphanin FQ receptor ORL1: research tools and potential therapeutic agents." *Life Sciences*. 73, no. 6(2003): 663-78 UI 12801588.

The 17-amino acid neuropeptide nociceptin/Orphanin FQ (N/OFQ) was recently identified as the endogenous ligand for the opioid receptor-like (ORL1) receptor, a fourth member of the classical mu, delta, and kappa opioid receptor family. Although ORL1 clearly belongs to the opioid receptor family, it does not bind classical opiates and the ORL1-N/OFQ system has pharmacological actions distinct from the opioid receptor system. This new ligand-receptor system has generated active interest in the opioid community because of its wide distribution and involvement in a myriad of neurological pathways. The past two years have witnessed tremendous advances in the design and discovery of very potent and selective peptide and nonpeptide agonist and antagonist ligands at ORL1. These discoveries have facilitated the understanding of the role of the ORL1-N/OFQ system in a variety of processes such as pain modulation, anxiety, food intake, learning, memory, neurotransmitter release, reward pathways, and tolerance development. The ORL1 receptor therefore represents a new molecular target for the design of novel agents for anxiety, analgesia, and drug addiction. Indeed, there is tremendous interest in the pharmaceutical industry in the development of nonpeptide ligands such as the potent ORL1 agonist, Ro 64-6198, as anxiolytics and the ORL1 antagonist JTC-801 as novel analgesics. This review presents an overview of the various peptide and nonpeptide ORL1 ligands with an emphasis on their potential therapeutic utility in various human disorders. [References: 114]

Zimberg, S. E. "Reducing pain and costs with innovative postoperative pain management." *Managed Care Quarterly*. 11, no. 1(2003): 34-6 UI 12790064.

Individual patient responses to some of the standard-of-care treatments for post operative pain management are unpredictable, but studies have shown undertreatment of acute post operative pain is common. There are new, innovative techniques for postoperative pain management that may improve a patients' recovery period. These techniques are also economically beneficial, and may contribute to the reduction of long-term care costs. Overall, the less time a patient is removed from normal day-to-day activity, the more satisfied they tend to be with their surgical experience. The following article addresses these and other issues surrounding the reduction of pain and cost after surgery.