

Wound Analgesia in Trauma Patients

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Pain has a protective function in nature, warning of damage, and promoting careful treatment of the affected area. However, trauma pain can be destructive too: by heightening the cellular stress response, the autonomic, somatic and endocrine reflexes are diminished, resulting in protein breakdown, platelet aggregation, nausea, ileus and a suppressed immune system (1,2). Low oxygen tension and poor perfusion can slow down the deposition of collagen in tissue undergoing repair (3), both of which can be influenced by pain: restricted breathing due to pain can lead to low-grade hypoxia, and severe pain can cause vasoconstriction, both of which ultimately impair trauma wound healing.

1. Goodwin SA. A review of preemptive analgesia. *J Perianesth Nurs* 1998; 13(2): 109-14.
2. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. *Br J Anaesth* 1997; 78(5): 606-17.
3. Jonsson K, Jensen JA, Goodson WH, Scheuenstuhl H, West J, Hopf HW, Hunt TK. Tissue oxygenation, anemia, and perfusion in relation to wound healing in surgical patients. *Ann Surg* 1991; 214(5): 605-13.

Physical and psychosocial functioning following motor vehicle trauma

Chronic pain and PTSD are known to hold substantial comorbidity following traumatic injury. Although pharmacological agents have been examined in the treatment of pain and PTSD individually, little is known regarding the relationship of medication use with functioning in patients with comorbid conditions. Clapp et al (1) examined the relationships of pain, PTSD, and medication use across physical and psychosocial functioning in patients with chronic pain following motor vehicle injury (N=234). Separate analyses were conducted for opioids, SSRIs, and sedative/anxiolytics, respectively. Several relevant effects were noted: (1) Pain evidenced strong associations with reduced functioning across both physical and psychosocial domains, (2) Opioid use held interactive relationships with PTSD across both functioning domains. Specifically, opioids were associated with greater physical impairment in patients without comorbid PTSD. Opioids also were related to greater psychosocial impairment in patients without PTSD while PTSD was associated with greater impairment in patients not using opioids, (3) Opioid use evidenced a marginal interaction with pain on psychosocial functioning. Opioids were associated with greater psychosocial impairment among patients with high-pain, and high-pain was associated with greater impairment among opioid users, (4) SSRIs held a marginal interaction with PTSD such that PTSD was related to poorer psychosocial functioning only among individuals not using an SSRI, and (5) Anxiolytic use evidenced a marginal interaction with PTSD on physical functioning although no between-group

differences were noted. These data suggest that PTSD symptomology may be an important consideration in determining treatment modality for patients experiencing pain subsequent to traumatic injury.

1. Clapp JD, Masci J, Bennett SA, Beck JG. Physical and psychosocial functioning following motor vehicle trauma: Relationships with chronic pain, posttraumatic stress, and medication use. *Eur J Pain*, 2009 Aug 10 (in press).

The relationship between posttraumatic stress disorder and trauma cognitions

Several models of PTSD suggest that dysfunctional beliefs play an important role in the maintenance of PTSD. Bennett et al. (1) examined whether thought control strategies intermediated in the relationship between PTSD and dysfunctional cognitions. It was hypothesized that PTSD would be positively associated with dysfunctional cognitions and that negative thought control strategies (worry and self-punishment) would partially account for this relationship. These maladaptive strategies were predicted to be associated with increased levels of PTSD and more trauma-related beliefs. Additionally, it was predicted that positive thought control strategies (social control and reappraisal) would be associated with decreased levels of PTSD and fewer trauma-related beliefs. Finally, because the literature supports distraction as both an adaptive and a maladaptive thought control strategy, no a priori hypothesis was made. Results support worry and self-punishment as maladaptive intervening variables in the association between PTSD and

dysfunctional cognitions, resulting in greater levels of PTSD and trauma cognitions. Social control and distraction emerged as adaptive strategies, resulting in lower levels of PTSD and trauma cognitions, while reappraisal showed no relationship with PTSD severity. Although the results are cross-sectional, continued focus on the effects of thought control strategies as meditational maintenance variables over time appears warranted.

1. Bennett SA, Beck JG, Clapp JD. Understanding the relationship between posttraumatic stress disorder and trauma cognitions: The impact of thought control strategies. *Behav Res Ther* 2009 Dec;47(12):1018-23.

Infections and treatment of wounds in survivors of the 2004 Tsunami in Thailand

On 26 December 2004, a tsunami devastated the west coast of Thailand and caused 8457 injuries and 5395 deaths. Data were collected from 26 December 2004 to 31 January 2005 at four public hospitals to describe the character and treatment of wounds of 523 persons who were injured during tsunami and sought medical treatment. Wounds were contaminated with mud, sand, debris and sea water and had an infection rate of 66.5% (674/1013). Most wounds (45%) had poly-microbial infection with gram-negative rods such as *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus* and *Pseudomonas* species. The risk of wound infection increased with size of the wound and

presence of an open fracture. Infections occurred more frequently on the lower than upper trunk of the body. Early treatment with antibiotics was protective against wound infection. Many patients asked to have their wounds sutured so that they could return to their village to look for their families and to repair damage. This report suggests that wounds should be aggressively debrided and suturing postponed if possible. Patients should be given broad spectrum antibiotics to assist with wound healing (1).

1. Doung-ngern P, Vatanaprasan T, Chungpaibulpatana J, Sitamanoch W, Netwong T, Sukhumkumpee S, O'Reilly M, Henderson A, Jiraphongsa C. Infections and treatment of wounds in survivors of the 2004 Tsunami in Thailand. *Int Wound J.* 2009 Oct;6(5):347-54.

Field hospital analgesia

Acute pain is every health care worker's responsibility, a key area of clinical management and one of Surgeon General's four focus points for improving quality of life after battlefield injury. The evolving practice of acute pain management requires an informed multidisciplinary and multimodal therapeutic approach to minimise each individual patient's experience of pain. Whilst subject matter experts progress the policies, protocols and capabilities associated with pain management, it remains the duty of every clinician, nurse, health care support worker and all Professions Allied to medicine (PAMs) to keep updated and maintain capability in this key area of clinical management (1).

1. Connor DJ, Ralph JK, Aldington DJ. Field hospital analgesia. J R Army Med Corps, 2009 Mar; 155(1):49-56

The evolution of pain management in the critically ill trauma patient

The evolution of military medical care to manage polytrauma, critically ill-wounded warriors from the greater war on terrorism has been accompanied by significant changes in the diagnosis, management, and modulation of acute and chronic trauma-related pain. A paradigm shift in pain management includes early treatment of pain at the point of injury and throughout the continuum of care with a combination of standard and novel therapeutic interventions. These concepts are important for all critical care providers because they translate to most critically ill patients, including those resulting from natural disasters. Previous authors have reported a high incidence of moderate to severe pain and poor analgesia in intensive care units associated with sleep disturbances, tachycardia, pulmonary complications, increased stress response with thromboembolic incidents, and immunosuppression, increased intensive care unit and hospital stays, and needless suffering. Although opioids have traditionally been the cornerstone of acute pain management, they have potential negative effects ranging from sedation, confusion, respiratory depression, nausea, ileus, constipation, tolerance, opioid-induced hyperalgesia as well as potential for immunosuppression. Alternatively, multimodal therapy is increasingly recognized as a critical pain

management approach, especially when combined with early nutrition and ambulation, designed to improve functional recovery and decrease chronic pain conditions. Multimodal therapy encompasses a wide range of procedures and medications, including regional analgesia with continuous epidural or peripheral nerve block infusions, judicious opioids, acetaminophen, anti-inflammatory agents, anticonvulsants, ketamine, clonidine, mexiletine, antidepressants, and anxiolytics as options to treat or modulate pain at various sites of action. With a more aggressive acute pain management strategy, the military has decreased acute and chronic pain conditions, which may have application in the civilian sector as well (1).

1. Malchow RJ, Black IH. The evolution of pain management in the critically ill trauma patient: Emerging concepts from the global war on terrorism. Crit Care Med 2008 Jul; 36(7 Suppl):S346-57.

What is the ideal pre-hospital analgesic?

Structured electronic questionnaire distributed to selected individuals in UK and on operations. 122 UK Defence Medical Services and US Medical Corps doctors, nurses and combat medical technicians involved in the early management of severe trauma on deployment. 54 (44%) agreed and 63 (52%) disagreed that intramuscular morphine had the ideal analgesic properties for the military pre-hospital environment. Over half of those with operational experience reported multiple instances of intramuscular morphine

providing inadequate analgesia. 86 (70%) desired a more potent analgesic than morphine in the first hour following injury. 101 (83%) identified simplicity and reliability of use by a soldier as of high importance. 99 (81%) identified rapid onset of action of high importance. With regard to an acceptable route of drug self-administration, 88 (72%) supported a nasal spray; 78 (64%) supported a sustained release buccal tablet (adhesive to the gum); 61 (50%) supported a disposable inhaler of volatile gas (although 91% had no experience of the currently available drug in this formulation); and 55 (45%) supported a skin patch. Intramuscular morphine does not meet the needs of the majority of clinical stakeholders. Alternative routes of self-administration are acceptable, but support for available commercial solutions is clouded by incomplete awareness. Anaesthetists and emergency physicians desire a multimodal approach to battlefield analgesia within the evacuation chain (1).

1. Smith JE, Russell R, Mahoney PF, Hodgetts TJ. What is the ideal pre-hospital analgesic?--a questionnaire study. J R Army Med Corps. 2009 Mar;155(1):44-6.

Continuous infusion of local anesthetic into the surgical wound for pain relief : Is it good also for trauma wound analgesia?

Gómez Ríos et al. (1) assessed the quality of postoperative analgesia provided by intravenous administration of paracetamol and ketorolac plus morphine in bolus doses with or without continuous infusion of local

anesthetic into the surgical wound after abdominal hysterectomy. Patient satisfaction was included among the outcomes assessed. Prospective pilot study in ASA 1-2 patients randomized to 2 groups: women in the subcutaneous catheter group received intravenous analgesics plus a continuous infusion (2 mL/h) of 0.25% bupivacaine whereas women in the control group received only the intravenous analgesics. The outcome measures were pain intensity assessed on a verbal numerical scale at rest and with movement, morphine requirements in the first 48 hours after surgery, and complications related to the drugs used or the technique. Twenty-six patients were enrolled; 10 were randomized to the catheter group and 16 to the control group. Statistically significant between-group differences in pain both at rest and with movement were found while the women were in the postoperative recovery unit. Postoperative pain with movement was also significantly different at 24 hours ($P<.004$) and 48 hours ($P<.02$). Similarly, mean (SD) morphine requirements in the recovery unit were significantly greater in the control group, at 8 (2.27) mg, compared with 3.20 (1.79) mg in the catheter group ($P<.002$). Walking began earlier in the catheter group. No differences were found in the incidences of complications. Postoperative pain is effectively relieved by continuous infusion of local anesthetic into the surgical wound after abdominal hysterectomy. This technique provides good analgesia with less morphine consumption and scarce adverse effects. Patient satisfaction and the sense of receiving quality pain management are high.

1. Gómez Ríos MA, Vázquez Barreiro L, Nieto Serradilla L, Diz Gómez JC, López Alvarez S. Efficacy of a continuous infusion of local anesthetic into the

surgical wound for pain relief after abdominal hysterectomy. Rev Esp Anesthesiol Reanim. 2009 Aug-Sep;56(7):417-24.

Intraperitoneal application of bupivacaine : Is it good also for trauma analgesia?

Intraperitoneal administration of a local anaesthetic in combination with an opioid, for the relief of postoperative pain, has already been reported. Hernández-Palazón et al. (1) assessed the analgesic effect of the intraperitoneal administration of bupivacaine and morphine in patients undergoing laparoscopic cholecystectomy. At the end of laparoscopic cholecystectomy, in a double-blind, randomized manner, one of the following injections was given intraperitoneally. There were 30 patients in each group: Group 1, physiological saline 30 mL; Group 2, bupivacaine 0.25% 30 mL; Group 3, bupivacaine 0.25% 30 mL plus morphine 2 mg. In addition, Group 2 received 2 mg intravenous (i.v.) morphine in 2 mL saline, and Groups 1 and 3, 2 mL saline intravenously. Patients' postoperative pain was evaluated using a visual analogue scale and a verbal rating score. The postoperative analgesic requirement was assessed by the total dose of metamizol administered by an i.v. patient-controlled analgesia (PCA) device. Pain, vital signs, supplemental analgesic consumption and side-effects were recorded for all patients for 24 h. There were no differences between the three groups regarding pain scores (at rest and coughing) during the study except in the first 2 h, when scores were lower for patients receiving intraperitoneal bupivacaine plus i.v.

morphine ($P < 0.05$). Supplemental consumption of metamizol was significantly lower ($P < 0.05$) in Group 3 than in Group 1 during the first 6 h after surgery. However, the cumulative doses of metamizol were also lower in Group 2 than in Groups 1 and 3 over the entire study (2025 ± 1044 mg vs. 4925 ± 1238 and 4125 ± 1276 mg; $P < 0.05$). In patients undergoing laparoscopic cholecystectomy, the intraperitoneal administration of morphine plus bupivacaine 0.25% reduced the analgesic requirements during the first 6 postoperative hours compared with the control group. However, the combination of intraperitoneal bupivacaine 0.25% and i.v. morphine was more effective for treatment of pain after laparoscopic cholecystectomy.

1. Hernández-Palazón J, Tortosa JA, Nuño de la Rosa V, Giménez-Viudes J, Ramírez G, Robles R. Intraperitoneal application of bupivacaine plus morphine for pain relief after laparoscopic cholecystectomy. *Eur J Anaesthesiol.* 2003 Nov;20(11):891-6.

The efficacy of two doses of intraperitoneal bupivacaine for pain relief after operative laparoscopy: Is it good also for trauma patients?

Malhotra et al. (1) evaluated the effect of two doses of intraperitoneal bupivacaine administration for pain relief after operative gynecological laparoscopy in a prospective randomized study. The study group comprised 52 women undergoing gynecological laparoscopic surgery. A dose of either 0.125% bupivacaine 10 ml (50 mg) or 0.25% bupivacaine (100 mg) was instilled intraperitoneally at the end of the procedure. Pain scores were

recorded in the postoperative period on a scale of 0-10 at 2, 4, 6 and 8 h intervals after the surgery. Any other side effect and the time and dose of analgesia required were noted. The results were compared in the two groups. One hundred milligrams of bupivacaine provided pain relief for a longer duration (8 h), as compared to 50 mg of the drug (4-6 h). This difference was statistically significant. Analgesic requirement was also less in the 100 mg group. One hundred milligrams of intraperitoneal bupivacaine is much better than 50 mg in relieving pain after laparoscopic surgery.

1. Malhotra N, Chanana C, Roy KK, Kumar S, Rewari V, Sharma JB. To compare the efficacy of two doses of intraperitoneal bupivacaine for pain relief after operative laparoscopy in gynecology. *Gynecol Obstet* 2007 Oct;276(4):323-6.

The safety of adding bupivacaine to the subcutaneous infiltration solution used for donor site harvest: Is it safe also for trauma wounds?

Pain is a major problem for patients with burns. Donor sites are a significant source of this pain. Fischer et al. (1) hypothesized that bupivacaine infiltration of the donor site before skin harvest would prove to be a safe technique as determined by the measurement of blood levels of bupivacaine at various time intervals after infiltration. Fourteen patients were enrolled and studied.

Average age was 14.3 +/- 3.1 years, weight was 43.1 +/- 9.1 kg, and donor site size was 6.3 +/- 2.0% TBSA. Mean dose of bupivacaine infused was 1.86 +/- 0.21 mg/kg. Maximum mean bupivacaine blood level was 0.39 +/- 0.09 microg/ml. The highest level measured in any one patient was 1.2 microg/ml;

4.0 microg/ml is considered to be the safe upper limit in children. Time to maximum blood level was 8.9 +/- 1.7 hours after infusion. Twelve of the 14 patients had measurable blood levels of bupivacaine at 24 hours after infusion. The maximum bupivacaine level was found to correlate significantly with both the mg/kg of bupivacaine infused ($r = .60$, $P = .04$) and the donor site size ($r = 0.81$, $P = 0.002$). Bupivacaine at a dose of slightly less than 1.9 mg/kg added to donor site infiltration solution is safe, as demonstrated by low blood levels and the absence of clinical signs of toxicity.

1. Fischer CG, Lloyd S, Kopcha R, Warden GD, McCall JE. The safety of adding bupivacaine to the subcutaneous infiltration solution used for donor site harvest. *J Burn Care Rehabil.* 2003 Nov-Dec;24(6):361-4.

Lipid emulsion improves recovery from bupivacaine-induced cardiac arrest, but not from ropivacaine- or mepivacaine-induced cardiac arrest

Cardiac toxicity significantly correlates with the lipophilicity of local anesthetics (LAs). Recently, the infusion of lipid emulsions has been shown to be a promising approach to treat LA-induced cardiac arrest. As the postulated mechanism of action, the so-called "lipid sink" effect may depend on the lipophilicity of LAs. Zausig et al. (1) investigated whether lipid effects differ with regard to the administered LAs. In the isolated rat heart, cardiac arrest was induced by administration of equipotent doses of bupivacaine,

ropivacaine, and mepivacaine, respectively, followed by cardiac perfusion with or without lipid emulsion ($0.25 \text{ mL} \times \text{kg}^{-1} \times \text{min}^{-1}$). Subsequently, the times from the start of perfusion to return of first heart activity and to recovery of heart rate and rate-pressure product (to 90% of baseline values) were assessed. In all groups, lipid infusion had no effects on the time to the return of any cardiac activity. However, recovery times of heart rate and rate-pressure product (to 90% of baseline values) were significantly shorter with the administration of lipids in bupivacaine-induced cardiac toxicity, but not in ropivacaine- or mepivacaine-induced cardiac toxicity. These data show that the effects of lipid infusion on LA-induced cardiac arrest are strongly dependent on the administered LAs itself. It was concluded that lipophilicity of LAs has a marked impact on the efficacy of lipid infusions to treat cardiac arrest induced by these drugs.

1. Zausig YA, Zink W, Keil M, Sinner B, Barwing J, Wiese CH, Graf BM. Lipid emulsion improves recovery from bupivacaine-induced cardiac arrest, but not from ropivacaine- or mepivacaine-induced cardiac arrest. *Anesth Analg*. 2009 Oct;109(4):1323-6.

Use of lipid emulsion to reverse local anesthetic-induced toxicity

Corman and Skledar (1) evaluated the use of lipid emulsion for reversal of local anesthetic-induced toxicity. Literature was accessed through PubMed and OVID (1966-May 2007) using the search terms lipid emulsion and local

anesthetic. Reference lists were consulted to identify additional publications. All articles published in English were evaluated for inclusion. Publications describing the use of lipid emulsion for reversal of local anesthetic in either humans or animals were included. It has been suggested that lipid emulsion (Intralipid) may reverse local anesthetic toxicity by extracting lipophilic local anesthetics from aqueous plasma or tissues or by counteracting local anesthetic inhibition of myocardial fatty acid oxygenation. Studies in rats and dogs have shown that lipid emulsion is effective in resuscitating animals who are asystolic after the administration of intravenous bupivacaine. Three case reports support the use of lipid emulsion to reverse systemic toxicity, including seizures, electrocardiogram abnormalities, and cardiac arrest, resulting from the administration of levobupivacaine, ropivacaine, bupivacaine, or mepivacaine. The regimens used in these cases consisted of bolus doses of 1.2-2 mL/kg followed by continuous infusions of 0.25-0.5 mL/kg/min. All of the patients recovered fully with no neurologic sequelae. Literature describing animal studies and human case reports suggests that lipid emulsion is effective in the reversal of local anesthetic toxicity. The potential risks of administering the relatively high doses of this agent are uncertain, and the optimal dose has not been established. In light of these uncertainties, it is appropriate to administer lipid emulsion only after advanced cardiac life support has failed and prior to cardiopulmonary bypass.

1. Corman SL, Skledar SJ. Use of lipid emulsion to reverse local anesthetic-induced toxicity. *Ann Pharmacother.* 2007 Nov;41(11):1873-7.

Epinephrine impairs lipid resuscitation from bupivacaine overdose: a threshold effect

Lipid emulsion infusion reverses local anesthetic-induced cardiac toxicity, but the effect of adding epinephrine has not been studied. Hiller et al. (1) compared escalating doses of epinephrine on recovery with lipid infusion in a rat model of bupivacaine overdose. Rats anesthetized with isoflurane received an IV bolus of 20 mg/kg bupivacaine, producing asystole (zero time) in all animals. Ventilation (100% oxygen) and chest compressions were started immediately, and at 3 min the rats received one of six IV treatments (n = 5 for all groups): 5 ml/kg saline followed by infusion for 2 min at 1.0 ml x kg x min, and a second 5 ml/kg bolus at 5 min; or the same bolus and infusion treatment using 30% lipid emulsion plus a single injection of epinephrine at one of five doses: 0 (lipid control), 1, 2.5, 10, or 25 mcg/kg. An electrocardiogram and arterial pressure were monitored continuously, and arterial blood gas was measured at 7.5 and 15 min. Epinephrine improved initial return of spontaneous circulation (rate-pressure product > 30% baseline) but only 3 of 5 rats at 10 mcg/kg and 1 of 5 rats at 25 mcg/kg sustained return of spontaneous circulation by 15 min. Lipid alone resulted in slower but more sustained recovery. Epinephrine doses above a threshold near 10 mcg/kg increased lactate, worsened acidosis, and resulted in poor recovery at 15 min, as compared with lipid controls. There was tight correlation of epinephrine dose to serum lactate at 15 min. Epinephrine over a threshold dose near 10 mcg/kg impairs lipid resuscitation from bupivacaine overdose, possibly by inducing hyperlactatemia.

1. Hiller DB, Gregorio GD, Ripper R, Kelly K, Massad M, Edelman L, Edelman G, Feinstein DL, Weinberg GL. Epinephrine impairs lipid resuscitation from bupivacaine overdose: a threshold effect. *Anesthesiology*. 2009 Sep;111(3):498-505.

Lipid emulsion is superior to vasopressin in a rodent model of resuscitation from toxin-induced cardiac arrest

Lipid emulsion infusion is an emerging antidotal therapy for toxin-induced cardiac arrest. Di Gregorio et al. (1) compared the efficacy of resuscitation from bupivacaine-induced asystole using lipid emulsion infusion vs. vasopressin, alone and with epinephrine in a prospective, randomized, animal study of adult, male Sprague-Dawley rats. Instrumented rats were given an intravenous bolus of 20 mg/kg bupivacaine to induce asystole (zero time). Rats (n = 6 for all groups) were ventilated with 100% oxygen, given chest compressions, and randomized to receive 30% lipid emulsion (L, 5 mL/kg bolus then 1.0 mL/kg/min infusion) and vasopressin 0.4 U/kg bolus alone (V) or combined with epinephrine, 30 microg/kg (V + E); boluses (L, V, or V + E) were repeated at 2.5 and 5 minutes for a rate-pressure product (RPP) less than 20% baseline. The arterial blood pressure and electrocardiogram were measured continuously for 10 minutes when blood

was drawn for arterial blood gas analysis, lactate content, and central venous oxygen saturation (ScvpO₂). Hemodynamic parameters of the L group at 10 minutes (30,615 +/- 4782 mm Hg/min; 151 +/- 19.1 mm Hg; 197 +/- 8.6 min; RPP, systolic blood pressure and heart rate, respectively) exceeded those of the V group (5395 +/- 1310 mm Hg/min; 85.8 +/- 12 mm Hg; 61 +/- 10.8 min) and the V + E group (11,183 +/- 1857 mm Hg/min; 75.5 +/- 12.9 min, RPP and heart rate, respectively; systolic blood pressure was not different). Metrics indicated better tissue perfusion in the L group (7.24 +/- 0.02; 83% +/- 3.5%; 2.2 +/- 0.36 mmol/L; pH, ScvpO₂, lactate, respectively) than V (7.13 +/- 0.02; 29.9% +/- 4.4%; 7.5 +/- 0.6 mmol/L) and V + E groups (7.07 +/- 0.03; 26.2% +/- 8.9%; 7.7 +/- 1 mmol/L). Wet-to-dry lung ratios in V (8.3 +/- 0.6) and V + E (8.7 +/- 0.2) were greater than that in the L group (6.2 +/- 0.5) (mean +/- sem; p < 0.05 for all shown results). Lipid emulsion in this rat model provides superior hemodynamic and metabolic recovery from bupivacaine-induced cardiac arrest than do vasopressors. Systolic pressure was not a useful metric in the vasopressor groups. Vasopressin was associated with adverse outcomes.

1. Di Gregorio G, Schwartz D, Ripper R, Kelly K, Feinstein DL, Minshall RD, Massad M, Ori C, Weinberg GL. Lipid emulsion is superior to vasopressin in a rodent model of resuscitation from toxin-induced cardiac arrest. Crit Care Med. 2009 Mar;37(3):993-9.

Serum bupivacaine concentrations during continuous extrapleural infusion

Dauphin et al. (1) examined the rate of increase in serum bupivacaine concentration during continuous extrapleural infusion. After thoracotomy for lobectomy under general anaesthesia, nine patients had an extrapleural catheter inserted, before chest closure, in a costovertebral gutter constructed surgically by lifting the parietal pleural. Bupivacaine 0.5% with epinephrine 1:200,000 was injected through the catheter as 0.3 ml.kg⁻¹ bolus followed by 0.1 ml.kg⁻¹.hr⁻¹ for five days. Serum bupivacaine (free and total), albumin, alpha-1 acid glycoprotein concentrations were measured 15 min after injection and at 24 hr intervals for five days. Bupivacaine concentrations were determined by column liquid chromatography using solid phase extraction. Serum alpha-1 acid glycoprotein concentration was determined by nephelometry on QM 300 protein analyzer. Serum albumin concentration was determined by bromocresol green dye binding procedure on Hitachi 717 Autoanalyzer. A continuous elevation in total serum bupivacaine was observed, with an average value of 0.75 microgram.ml⁻¹ on day 1 to 2.77 micrograms.ml⁻¹ on day 4 (P < 0.05). There was no increase in postoperative free serum bupivacaine concentration; average value of 177 pcg.ml⁻¹ on day 1 and 249 pcg.ml⁻¹ on day 4 (P = 0.92). Postoperative serum alpha-1 acid glycoprotein concentration showed a steady rise with an average value of 0.94 microgram.ml⁻¹ on day 1 and 1.47 micrograms.ml⁻¹ on day 4 (P < 0.05). No change was observed in post-operative serum albumin with an average value of 31.4 g.l⁻¹ on day 1 and 31.3 g.l⁻¹ on day 4. Continuous extrapleural infusion of bupivacaine over five days after thoracotomy is associated with a

steady increase in total serum bupivacaine concentration and no elevation in free serum bupivacaine concentration.

1. Dauphin A, Gupta RN, Young JE, Morton WD. Serum bupivacaine concentrations during continuous extrapleural infusion. *Can J Anaesth.* 1997 Apr;44(4):367-70.

Postthoracotomy pain management

The following techniques appear efficacious in controlling postthoracotomy pain and reducing the amount of systemic opioids consumed (1) : continuous intercostal blockade, paravertebral blockade, and epidural opioids and/or anesthetics. The combination of thoracic epidural opioid and local anesthetic is very effective at relieving postthoracotomy pain, however, considerable experience is required for insertion of the thoracic epidural catheter and postoperative respiratory monitoring. Intercostal and paravertebral catheters can be inserted intraoperatively under direct visualization, to reduce complications of insertion. One-time intraoperative intercostal blockade may effectively reduce postoperative pain in the first day, but is not a practical long-term method for postthoracotomy pain. The effectiveness of interpleural analgesia, even with proper technique, appears inferior to epidural and other regional techniques. Contraindications include low platelet count (< 100,000), abnormal coagulation profile, medicinal anticoagulation (aspirin and nonsteroidal anti-inflammatories are not contraindications), bony spinal abnormalities, or neurological disorders. The T5/6 interspace is the preferred level, but T10 can work well with an increased dose of bupivacaine. Upon completion of the muscle sparing, minimal-access thoracotomy, close the

wound and perform a percutaneous intercostal nerve block (two ribs above and three below the incision). Then use patient-controlled epidural analgesia, with a basal infusion of bupivacaine and hydromorphone. To supplement inadequate or nonfunctioning epidurals, intravenous patient-controlled opioids are added. When choosing an approach to postthoracotomy pain management, the thoracic surgeon and anesthesiologist must consider the following: (1) the physician's experience, familiarity and personal complication rate with specific techniques; (2) the desired extent of local and systemic pain control; (3) the presence of contraindications to specific analgesic techniques and medications; and (4) availability of appropriate facilities for patient assessment and monitoring postthoracotomy. Refinements in surgical technique including limited or muscle-sparing thoracotomy, video-assisted thoracoscopic surgery (VATS) and robotic surgery may lessen the magnitude of postthoracotomy pain.

1. Savage C, McQuitty C, Wang D, Zwischenberger JB. Postthoracotomy pain management. *Chest Surg Clin N Am.* 2002 May;12(2):251-63.

Use of prehospital dressings in soft tissue trauma: is there any conformity or plan?

Acute soft tissue wounds are commonly seen in the prehospital setting. It was hypothesised that there is a lack of consistency in early management of trauma wounds, particularly in the dressings used. In January 2007 a

questionnaire-based study was undertaken to evaluate the early management of such injuries (1) . All 13 UK ambulance services were contacted, as well as 2 voluntary ambulance services. The questionnaire considered the implementation of a wound treatment policy and staff training, immediate wound management including haemostasis, cleansing, analgesia, dressings and the use of antibiotics. The response rate was 100%. Only 27% of services had a wound treatment policy in place, but all services implemented staff training. All services regularly achieved haemostasis of wounds using a combination of pressure and elevation. Regular cleansing was performed by 47% of services and those that did so used normal saline or water. All ambulance services administered analgesics. The most commonly used analgesics were Entonox and intravenous morphine. Other analgesics administered were paracetamol and ibuprofen. No local anaesthesia was used. Dressings were applied regularly by all services; 13 different types of dressings were in regular use. This study confirmed that there is currently no standard protocol for early acute wound management in the prehospital care setting. The key areas for improvement are cleansing, simplification of dressings and the introduction of standardised protocols and teaching.

1. Jones AP, Allison K, Wright H, Porter K. Use of prehospital dressings in soft tissue trauma: is there any conformity or plan? *Emerg Med J*. 2009 Jul;26(7):532-4

Management of superficial to partial-thickness wounds

Do rates of healing, infection, and pain differ depending on whether nonmoist or moist dressings are used to manage superficial to partial-thickness wounds? (1) Investigations were identified by CINAHL, MEDLINE, Pre-MEDLINE, Cochrane Library, Current Contents, Health STAR, EMBASE, Expanded Academic Index, and Dissertation Abstracts International searches. The search terms included skin, graft, and donor. Additional searches were performed with reference lists and bibliographies of retrieved studies. The searches identified 111 studies and 1 integrative review, of which 58 studies met the inclusion and exclusion criteria. Inconsistency and variation in outcome measures and incomplete reporting of results prevented analysis of many studies. Wound healing was measured by days to complete healing (when dressings could be removed without trauma and pain) and wounds healed by day X (removal of dressings at regular intervals). Wound infection was subjectively measured based on clinical signs of infection (edema, heat, pain, or smell). Visual analog scales were used to measure pain levels. Among the broad categories of nonmoist (sterile gauze, fine mesh gauze, Xerofoam [Tyco Healthcare Group LP, Mansfield, MA]) and moist (DuoDERM hydrocolloid [ConvaTec, Princeton, NJ], Tegaderm transparent film [3M Health Care, St Paul, MN], Opsite transparent film [Smith & Nephew, London, UK]) dressings, the outcomes of healing, infection, and pain were analyzed. In 6 studies, the findings significantly favored moist dressings, compared with

nonmoist dressings, for days to complete healing (weighted mean difference [WMD] = -3.97, 95% confidence interval [CI] = -5.91, -2.02). In 9 studies, wounds healed by day X (day 7, 8, 9, 10, or 12) were analyzed. The results were varied and inconclusive because of a small number of trials and subjects. Among 10 studies, no significant difference was noted in infection rates between nonmoist and moist dressings (odds ratio [OR] = 0.41, 95% CI = 0.14, 1.18). Three studies using visual analog scales for the outcome of pain were converted into a uniform scale of 1 to 10 (10 representing most painful). The findings significantly favored moist dressings over nonmoist dressings (WMD = -1.75, 95% CI = -2.94, -0.56). Among nonmoist and specific types of moist dressings, a subset analysis was performed to examine the outcomes of healing, infection, and pain. For days to complete healing, 2 investigations significantly favored hydrocolloid dressings over nonmoist dressings (WMD = -2.19, 95% CI = -2.89, -1.49). Additionally, in 2 studies, hydrocolloid dressings were significantly favored over other moist dressings (semioclusive hydrocolloid and transparent film) for days to complete healing (WMD = -1.45, 95% CI = -2.17, -0.74). In 3 studies, the data significantly favored polyurethane semipermeable transparent film dressings over nonmoist dressings for days to complete healing (WMD = -2.82, 95% CI = -3.58, -2.07). For infection rates, 4 studies significantly favored hydrocolloid dressings over nonmoist dressings (OR = 0.21, 95% CI = 0.07, 0.65). In 4 other studies, polyurethane semipermeable transparent film dressings were significantly favored over nonmoist dressings with regard to infection rates (OR = 0.28, 95% CI = 0.09, 0.91). For the outcome of pain, varied outcome measures and insufficient data prevented analysis among specific types of

moist dressings. Moist dressings decreased the days to complete healing and pain scores when compared with nonmoist dressings. Among the broad categories of nonmoist and moist dressings, no differences were found in infection rates. The data on specific types of moist dressings revealed that days to complete healing were decreased with hydrocolloid dressings compared with nonmoist and other moist dressings. Hydrocolloid dressings also decreased infection rates compared with nonmoist dressings. Polyurethane semipermeable transparent film dressings also decreased days to complete healing and infection rates compared with nonmoist dressings. Overall, the data indicated that hydrocolloid dressings are more effective than nonmoist dressings in terms of rates of healing, infection, and pain in the management of superficial to partial-thickness wounds.

1. Beam JW. Management of superficial to partial-thickness wounds. J Athl Train. 2007 Jul-Sep;42(3):422-4

Continuous thoracic paravertebral infusion of bupivacaine for pain management in patients with multiple fractured ribs

Karmakar et al. (1) evaluated the efficacy of a continuous thoracic paravertebral infusion of bupivacaine for pain management in patients with unilateral multiple fractured ribs (MFR) in a prospective nonrandomized case series in multidisciplinary tertiary hospital. In fifteen patients with unilateral MFR was inserted a catheter into the thoracic paravertebral space. An initial injection of 0.3 mL/kg (1.5 mg/kg) bupivacaine 0.5% with 1:200,000

epinephrine was administered followed 30 min later by an infusion of bupivacaine 0.25% at 0.1 to 0.2 mL/kg/h for 4 days. The following parameters were measured during the initial assessment before thoracic paravertebral block (TPVB), 30 min after the initial injection, and during follow-up on day 1 and day 4 after commencing the infusion of bupivacaine: visual analog pain score at rest and during coughing; respiratory rate; arterial oxygen saturation (SaO₂); bedside spirometry (ie, FVC, FEV₁, FEV₁/FVC ratio, and peak expiratory flow rate [PEFR]); arterial blood gas measurements; and O₂ index (ie, PaO₂/fraction of inspired oxygen ratio). There were significant improvements in pain scores (at rest, $p = 0.002$; during coughing, $p = 0.001$), respiratory rate ($p < 0.0001$), FVC ($p = 0.007$), PEFR ($p = 0.01$), SaO₂ ($p = 0.04$), and O₂ index ($p = 0.01$) 30 min after the initial injection, which were sustained for the 4 days that the thoracic paravertebral infusion was in use ($p < 0.05$). PaCO₂ did not change significantly after the initial injection, but on day 4 it was significantly lower than the post-TPVB value ($p = 0.04$). One patient had an inadvertent epidural injection, and another developed transient ipsilateral Horner syndrome with sensory changes in the arm. No patient exhibited clinical signs of inadvertent intravascular injection or local anesthetic toxicity. Results confirmed that continuous thoracic paravertebral infusion of bupivacaine is a simple and effective method of providing continuous pain relief in patients with unilateral MFR. It also produced a sustained improvement in respiratory parameters and oxygenation.

1. Karmakar MK, Critchley LA, Ho AM, Gin T, Lee TW, Yim AP. Continuous thoracic paravertebral infusion of bupivacaine for pain management in patients with multiple fractured ribs. *Chest*. 2003 Feb;123(2):424-31

Wound levobupivacaine continuous infusion for postoperative analgesia in living kidney donors: case-control study

Sorbello et al. (1) evaluated the efficacy of an analgesic regimen based on levobupivacaine continuous infusion into the surgical wound of living kidney donors (LKDs). Fifty adult LKDs (mean age, 53.1 +/- 5.3 years; age range, 52-68 years) were retrospectively assigned to a no wound infusion (NWI) group (n = 25) or a wound infusion (WI) group (n = 25). At the end of surgery, patients in the WI group received 10 mg intramuscular morphine; a peridural catheter was placed 10 cm between the intercostal muscles fibers close to the lower rib extremity, and a solution of levobupivacaine, 150 mg/100 mL, was started at 5 ml/h(-1). Patients in the NWI group received intramuscular morphine, 10 mg, every 8 hours; intravenous tramadole, 100 mg, was planned as a rescue drug for incidental pain. Pain was measured using a visual analog scale (VAS) ranging from 1 (no pain) to 10 (maximum pain) in both the basal condition (VASb) and during coughing (VASc) at 1 hour after leaving the operating room and 6, 12, and 24 hours thereafter. At 1, 6, 12, and 24 hours, VASb values in the NWI vs the WI group were 5.2 vs 3.1, 6.8 vs

4.1, 5.8 vs 4.9 (all $p < .01$), and 5.4 vs 5.1, respectively, and VASc values were 8.2 vs 6.3, 8.8 vs 5.9, 7.1 vs 5.3, and 6.8 vs 5.1 (all $p < .01$). Mean VAS score was significantly higher between 1 and 6 hours in the NWI group for all VASb measurements vs VASc values. Tramadol consumption was higher in the NWI group than in the WI group. Continuous wound infusion with 5 mL/h(-1) levobupivacaine, 1.5 mg/mL(-1), resulted in a safe and effective analgesic protocol in LKDs both in the immediate postoperative period and in the first day after surgery, a result that was more effective than a morphine-tramadol regimen. No adverse effects were recorded, which confirmed the safety of the technique.

1. Sorbello M, Paratore A, Morello G, Tindaro Sidoti M, Rinzivillo D, Molino C, Di Tommaso C, Parrinello L, Veroux P, Corona D, Giuffrida G, Zerbo D, Veroux M. Wound levobupivacaine continuous infusion for postoperative analgesia in living kidney donors: case-control study. *Transplant Proc.* 2009 May;41(4):1128-31

Lidocaine patch for postoperative analgesia after radical retropubic prostatectomy

In a prospective, double-blind, placebo-controlled study (1), patients undergoing radical retropubic prostatectomy under general anesthesia were randomly assigned to receive a lidocaine patch or placebo applied on each side of the wound at the end of surgery. Data were collected for 24 h after surgery. Seventy patients completed the study (36 lidocaine group, 34

placebo group). Demographics and postoperative morphine consumption were not different between the groups. However, the lidocaine patch group reported significantly less pain on coughing (19%-33% reduction) over all time periods (treatment vs placebo $P < 0.0001$, time x treatment $P = 0.3056$) and at rest (17%-32% reduction) for up to 6 h (treatment vs placebo $P = 0.0003$, time x treatment $P = 0.0130$).

1. Habib AS, Polascik TJ, Weizer AZ, White WD, Moul JW, ElGasim MA, Gan TJ. Lidocaine patch for postoperative analgesia after radical retropubic prostatectomy. *Anesth Analg*. 2009 Jun;108(6):1950-3.

The comparison of the effects of different doses of

levobupivacaine infiltration on wound healing

The easiest method in postoperative analgesia is the infiltration of the wound with local anesthetic drugs. Although many local anesthetic drugs have been used for this type of infiltration, studies on levobupivacaine are rare. Dere et al. (1) investigated the effects of different concentrations of levobupivacaine infiltration on wound healing. Forty female Wistar-Albino rats (280-300 g) were included in the study, which were randomly separated into four groups. Rats were infiltrated with 1.25 mg/mL levobupivacaine in group L(1.25) ($n = 10$), with 2.50 mg/mL levobupivacaine in group L(2.5) ($n = 10$), with 3.75 mg/mL levobupivacaine in group L(3.75) ($n = 10$), and with normal saline in control group ($n = 10$). Breaking-strength measurements, levels of hydroxyproline, and fibrotic index were evaluated in the tissue samples taken from the rats. When the breaking-strength measurements were evaluated, it was found a

significant difference between the control and the study groups ($p < 0.05$). In the intergroup comparison the difference between groups L(1.25) and L(3.75) was statistically significant ($p < 0.05$). In all of the levobupivacaine groups the levels of hydroxyproline were higher compared to the control group. Also significant differences were observed between groups L(1.25) and L(2.5) and groups L(1.25) and L(3.75) ($p < 0.05$). The levels of tissue fibrotic index were higher in all of the levobupivacaine groups compared to the control group ($p < 0.05$) and also a difference was observed between groups L(1.25) and L(3.75) in terms of tissue fibrotic index ($p < 0.05$). Levobupivacaine used in clinical doses have a significant effect on the fastening of wound healing and this effect increases with an increase in the concentration of the levobupivacaine.

1. Dere K, Sen H, Teksoz E, Ozkan S, Dagli G, Sucullu I, Filiz AI, Ipcioglu OM, Kucukodaci Z. The comparison of the effects of different doses of levobupivacaine infiltration on wound healing. J Invest Surg. 2009 Mar-Apr;22(2):112-6

Bupivacaine and Kaltostat reduces post-operative donor site pain

A prospective double blind controlled trial was carried out to examine the differences in post-operative split skin graft donor site pain between sites dressed with three differently treated types of dressing; a dry calcium alginate dressing (Kaltostat Britcair), a saline moistened Kaltostat dressing and a bupivacaine hydrochloride (0.5%) moistened Kaltostat dressing. There was a

significant reduction in post-operative pain in the Kaltostat and bupivacaine group (group 3) at 24 and 48 h when compared to the other two groups ($p < 0.04$). There was no difference in ease of removal of dressings or the quality of wound healing on day 10 between the three groups. This study demonstrates a significant reduction in post-operative pain in bupivacaine soaked Kaltostat without reducing the beneficial effects of Kaltostat on donor site healing (1).

1. Butler PE, Eadie PA, Lawlor D, Edwards G, McHugh M. Bupivacaine and Kaltostat reduces post-operative donor site pain. *Br J Plast Surg*. 1993 Sep;46(6):523-4.

The effect of topical analgesics on ex vivo skin growth and human keratinocyte and fibroblast behavior

The application of topical analgesics to the donor site of split thickness skin grafts has been proven to be an effective method of pain management but little is known about their effects on wound reepithelialization. Harris et al. (1) compared the effect of four analgesics on human keratinocytes and fibroblasts and whole skin explants in vitro to determine whether epithelial cell behavior is affected by topical analgesics. The effect of diclofenac, bupivacaine, lidocaine, and ketorolac was studied at concentrations between 10 mM and 1 nM. The effect on epithelial growth was measured using an ex vivo skin explant model. In addition, cell proliferation, and cytotoxicity were measured in cultured primary human keratinocytes and fibroblasts. Epithelial

growth from the explant model was most inhibited by diclofenac with a significant reduction at 100 microM ($p > 0.001$). Diclofenac also exhibited the strongest inhibitory effect on cell proliferation especially in keratinocytes. Ketorolac was the most cytotoxic. Bupivacaine showed cytotoxicity in a dose-dependent manner with only the very highest concentrations having a significant inhibitory effect. Lidocaine showed no evidence of cytotoxicity at the concentrations tested in either the in vitro cell studies or the ex vivo explant model. Topical analgesics alter keratinocyte and fibroblast behavior and such inhibition may affect wound healing.

1. Harris KL, Bainbridge NJ, Jordan NR, Sharpe JR. The effect of topical analgesics on ex vivo skin growth and human keratinocyte and fibroblast behavior. *Wound Repair Regen.* 2009 May-Jun;17(3):340-6.

Four major adverse effects of severe pain

An understanding of the implications of unrelieved pain is not new, and Nimmo and Duthie (1) in 1987 highlighted the four major adverse effects of severe pain following surgery:

1. Decreased respiratory movement especially after upper laparotomy or thoractomy. A decreased functional lung capacity, difficulty in breathing deeply and in coughing all contribute to hypoxia after operation.

2. Decreased mobility because of pain on movement. Early mobilisation is more difficult and the risk of deep venous thrombosis is increased.
3. Increased sympathetic activity leads to a release of catecholamines which has adverse effects such as hypertension followed by myocardial ischaemia and decreased blood flow to some tissues.
4. Hormonal and metabolic activity resulting from surgery and made worse by pain increases protein breakdown and mobilisation of free fatty acids.

Nimmo WS, Duthie DJ. Pain relief after surgery. *Anaesth Intensive Care* 1987; 15(1): 68-71.

Analgesic infiltration at the site of bone marrow harvest significantly reduces donor morbidity

Little information has been published concerning the severity of pain experienced by bone marrow donors or the use of local analgesia following bone marrow harvesting procedures. Chern et al. (1) assessed the duration and severity of pain experienced by bone marrow donors and the effectiveness of bupivacaine as a local analgesic agent following bone marrow harvest. During a single blinded randomised study of 24 bone marrow donors, 10 ml of 0.5% bupivacaine was infiltrated either into the right or left posterior iliac crest of the donor immediately following bone marrow harvest. Donors were requested to record the level of pain experienced at the right and left harvest sites on a pain rating score sheet (0-10) at time intervals of 4, 8,

12, 24, 48 and 72 h following harvest. A significant reduction in pain was experienced at the harvest site infiltrated with bupivacaine when compared with the control site during the first 3 days post-harvest. It is recommended that bupivacaine be infiltrated routinely into the harvest sites of all bone marrow donors to reduce the pain experienced in the 3 days following harvest.

1. Chern B, McCarthy N, Hutchins C, Durrant ST. Analgesic infiltration at the site of bone marrow harvest significantly reduces donor morbidity. Bone Marrow Transplant. 1999 May;23(9):947-9.

Preoperative infiltration of bupivacaine--effects on pain relief and trauma response (cortisol and interleukin-6)

Subcutaneous infiltration of bupivacaine before skin incision can reduce postoperative pain and modulate the stress response. In a randomized study on pain relief after hysterectomy 29 patients were referred into one of three groups, receiving 30 ml of bupivacaine 0.25% with adrenaline, 30 ml of saline or no infiltration along the line of the proposed incision 10 min before start of surgery. A Visual Analogue Scale was used for repeated pain ratings.

Postoperative pain relief was provided with patient-controlled analgesia with intravenous morphine 0.04 mg/kg. Lockout time was 10 min. The immunological and endocrine stress response to trauma was reflected by blood interleukin-6 (IL-6) and cortisol concentrations measured during 72 h following skin incision. There were large individual variations in the accumulated postoperative consumption of morphine at 20 h after start of

surgery. It was significantly reduced in patients receiving infiltration of bupivacaine. They used 39 mg (9-62) median (range) of intravenous morphine whereas the patients in the saline group used 65 mg (47-120) and patients in the control group used 54 mg (36-130) ($P < 0.05$). Significant elevation of plasma IL-6 and serum cortisol levels appeared in all groups with peak values at 3 h. There were no differences between the groups. There was a correlation between cortisol and IL-6. Six of the 29 patients had a postoperative infection which was reflected in increased IL-6 levels. Preoperative subcutaneous infiltration of bupivacaine significantly reduced the postoperative consumption of intravenous morphine.

1. Eriksson-Mjöberg M, Kristiansson M, Carlström K, Eklund J, Gustafsson LL, Olund A. Preoperative infiltration of bupivacaine--effects on pain relief and trauma response (cortisol and interleukin-6). *Acta Anaesthesiol Scand*. 1997 Apr;41(4):466-72.