CHRONIC/PERSISTENT POST-DELIVERY PAIN

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Disclosures

- **Off label use:**
  - Fentanyl, Sufentanil IT
  - Clonidine IT
  - Fentanyl epidural
  - NSAIDs in pregnancy, in wound infusions
  - Gabapentin for postop CS analgesia
  - Almost anything in pregnant women?...

- **Spouse stock ownership:** Amgen, Abbvie, Abbott
“All pain is per se and especially in excess, destructive and ultimately fatal in its nature and effects.”

~James Young Simpson
James Young Simpson

1st obstetric anesthetic, Jan 19, 1847
Outline—persistent pain post CS

- Introduction
- Scope/magnitude of the problem
- Risk factors
- Prevention/therapy
Pain (IASP)

- “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”

Persistent/chronic Pain (IASP)

- “lasting longer than 2 (or 3) months, or beyond the expected healing time”
- Other causes excluded, not pre-existing…
Persistent post-surgical pain

- Common reason for pain clinic visits
  - 20% of patients (Crombie et al. Pain 1998; 76: 167-71)
- Limb amputation (60-80%)
- Thoracotomy (45-65%)
- Breast surgery (45-65%)
- Hysterectomy (5-32%)
- Inguinal hernia (10-30%)
- CABG (30%)
- Cesarean (?)
- Vaginal delivery (??)

Scope of problem

- 130 millions births, 20 million cesareans worldwide annually
- “1-18%” incidence of persistent pain
  (Vaginal delivery 1-10%)

= 200,000 - 3.6 million women
RMS (dosing epidural cath for CS):

“Are your legs heavy?”

Patient:

“I don’t know, I can’t lift them.”
Pain After Cesarean

- Somatic component
  - incision
  - localized
  - iliohypogastric and ilioinguinal nerve distribution
- Visceral
  - diffuse
  - no clear nerve distribution
- Uterine contraction
- Primary v reop, multiple pregnancies, labor, surgical technique…
The “Friedman” curve for post-CS pain

Booth J et al. SOAP 2016 abstract BP-06
Houle et al. Pain 2017;2147-54
Postal questionnaire to 244 pts post CS (220 resp)
- All pts for 1 year (2001-2002)
- Mean F/U 10 months (6-17.6)

Abdominal scar pain
- 18% @ 3 months
- 12% at time of questionnaire

Daily pain
- 5%

Incidence higher after GA than regional
- 23 % v 10%

Risk factors
- GA
- Other pain syndrome/symptoms
- Acute PO pain
- Prospective, longitudinal study 2004-5
- New York and North Carolina
  - 837 VD, 391 CS
- Pts interviewed within 36 hours of CS or VD
  - Phone F/U @ 8 weeks
    - Persistent pain (severity, impact on ADL, frequency...)
    - Depression (Edinburgh Postnatal Depression Scale)
- Further F/U @ 6 and 12 months

Pain 2008; 140:87-94
"PAD" Study

ACUTE PAIN (24-48 h)

Fig. 2. Distribution of numerical rating score (NRS) of average pain for the first 24 h after vaginal and cesarean delivery.
PAD Study—8 weeks

- Persistent pain at 8 weeks
  - VD 9.2% (5.5, 12.6)
  - CS 10% (7.7, 12.3)
  - ~ 50% “daily”

- Post-partum depression in 11.2%
  - VD 11.4%
  - CS 10.5%

- 1 point on acute pain NRS ➔ 8.3% increase in Edinburgh Depression score

Severe acute post-partum pain
- 2.5 x ↑ persistent pain
- 3.0 x ↑ depression
- 500,000 cases/yr persistent pain???
Resolution of Pain after Childbirth

Patients with pain at 2 months contacted at 6 and 12 months PO

- MPQ, activities of daily living, need for medication, neuropathic, depression (EPPDI)
### Table 2. Pain Characteristics 6 Months after Delivery

<table>
<thead>
<tr>
<th>Pain Characteristic</th>
<th>Vaginal Delivery (n = 11)</th>
<th>Cesarean Delivery (n = 6)</th>
<th>Overall (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pain severity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average for last week</td>
<td>3.7 ± 2.3</td>
<td>2.0 ± 1.3</td>
<td>3.1 ± 2.1</td>
</tr>
<tr>
<td>Worst in last week</td>
<td>4.5 ± 2.7*</td>
<td>1.8 ± 1.0</td>
<td>3.5 ± 2.6</td>
</tr>
<tr>
<td>Now</td>
<td>1.3 ± 2.2</td>
<td>1.0 ± 1.3</td>
<td>1.2 ± 1.9</td>
</tr>
<tr>
<td><strong>Pain interference or problem with</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standing &gt; 30 min</td>
<td>73%</td>
<td>17%</td>
<td>53%</td>
</tr>
<tr>
<td>Sitting &gt; 30 min</td>
<td>64%</td>
<td>17%</td>
<td>47%</td>
</tr>
<tr>
<td>Carrying heavy bags</td>
<td>45%</td>
<td>50%</td>
<td>47%</td>
</tr>
<tr>
<td>Athletics / sports</td>
<td>64%</td>
<td>17%</td>
<td>47%</td>
</tr>
<tr>
<td>Getting up from a chair</td>
<td>45%</td>
<td>33%</td>
<td>41%</td>
</tr>
<tr>
<td>Going up / down stairs</td>
<td>55%</td>
<td>17%</td>
<td>41%</td>
</tr>
<tr>
<td>Walking</td>
<td>36%</td>
<td>17%</td>
<td>29%</td>
</tr>
<tr>
<td>Mood</td>
<td>36%</td>
<td>17%</td>
<td>29%</td>
</tr>
<tr>
<td>Sleep</td>
<td>45%</td>
<td>0%</td>
<td>29%</td>
</tr>
<tr>
<td>Working</td>
<td>45%</td>
<td>0%</td>
<td>29%</td>
</tr>
<tr>
<td>Relations with others</td>
<td>27%</td>
<td>0%</td>
<td>18%</td>
</tr>
<tr>
<td>Ability to concentrate</td>
<td>18%</td>
<td>0%</td>
<td>12%</td>
</tr>
<tr>
<td>Driving</td>
<td>9%</td>
<td>0%</td>
<td>6%</td>
</tr>
<tr>
<td>No. of items/patient</td>
<td>5 [1, 125, 10]</td>
<td>2 [0, 3]</td>
<td>[1, 7, 25]</td>
</tr>
<tr>
<td><strong>Pain frequency</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constantly</td>
<td>9%</td>
<td>17%</td>
<td>12%</td>
</tr>
<tr>
<td>Daily</td>
<td>18%</td>
<td>17%</td>
<td>18%</td>
</tr>
<tr>
<td>Several times / week</td>
<td>36%</td>
<td>17%</td>
<td>29%</td>
</tr>
<tr>
<td>Once a week</td>
<td>36%</td>
<td>17%</td>
<td>29%</td>
</tr>
<tr>
<td>Less than once a week</td>
<td>0%</td>
<td>33%</td>
<td>33%</td>
</tr>
<tr>
<td>Taking medication for pain</td>
<td>73%</td>
<td>0%</td>
<td>47%</td>
</tr>
<tr>
<td><strong>Location of pain</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pelvis</td>
<td>55%</td>
<td>50%</td>
<td>53%</td>
</tr>
<tr>
<td>Area of incision</td>
<td>27%</td>
<td>83%</td>
<td>47%</td>
</tr>
<tr>
<td>Back</td>
<td>55%</td>
<td>33%</td>
<td>47%</td>
</tr>
<tr>
<td>Abdomen</td>
<td>27%</td>
<td>17%</td>
<td>24%</td>
</tr>
<tr>
<td>Buttocks</td>
<td>18%</td>
<td>0%</td>
<td>12%</td>
</tr>
<tr>
<td>Legs</td>
<td>18%</td>
<td>0%</td>
<td>12%</td>
</tr>
<tr>
<td>Headache</td>
<td>18%</td>
<td>0%</td>
<td>12%</td>
</tr>
</tbody>
</table>

*P = 0.009 compared with cesarean delivery by Fisher’s exact test. †P = 0.047 compared with cesarean delivery by Student † test.*
Predicting pain and depression?
Helsinki, Finland
600 patients
- 300 CS/300 VD
- Mail questionnaire @1 year PP
- 438 returned (229CS/209VD)
Pain lasted longer after CS
- 18% (CS) and 10% (VD) pain at 1 year
Associated with increased pain post delivery
Chronic/persistent pain after surgery COMMON
  • pain 2-3 months post surgery
CS/vaginal delivery?
  • 6-18% post CS
  • 4-10% post vaginal delivery
Low(ish) percentage but high numbers
Persistent Pain After Cesarean Delivery and Vaginal Delivery: A Prospective Cohort Study

J. Petter Kainu, MD, Erja Halmesmäki, MD, PhD, Kari T. Korttila, MD, PhD, and P. Johanna Sarvela MD, PhD

Table 2. Duration of Pain After Delivery

<table>
<thead>
<tr>
<th>Duration</th>
<th>Cesarean Delivery (N = 377)</th>
<th>Vaginal Delivery (N = 711)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 3 wk</td>
<td>147 (39%)</td>
<td>397 (56%)</td>
</tr>
<tr>
<td>3 wk to 2 mo</td>
<td>112 (30%)</td>
<td>177 (25%)</td>
</tr>
<tr>
<td>2–5 mo</td>
<td>17 (5%)</td>
<td>29 (4%)</td>
</tr>
<tr>
<td>Over 5 mo</td>
<td>10 (3%)</td>
<td>11 (2%)</td>
</tr>
<tr>
<td>Pain at 1 y</td>
<td>85 (23%)</td>
<td>58 (8%)</td>
</tr>
<tr>
<td>No response</td>
<td>6 (2%)</td>
<td>39 (5%)</td>
</tr>
</tbody>
</table>

\( P < .001 \) overall duration of pain; cesarean delivery vs vaginal delivery.

\( P < .001 \).
Figure 2. A. Visual analog pain scale (VAS) 0–10 cm at 1 y in the vaginal delivery group in those women reporting persistent pain at 1 y after delivery. N = 58/711. B. VAS 0–10 cm at 1 y in the cesarean delivery group in those women reporting persistent pain at 1 y after delivery. N = 84/377.
2007-2008: 426 women enrolled 24 hours post CS (prospective)
- ~ 40% of all pts enrolled, few exclusions
- Multi-modal postop analgesia
- Telephone @ 2 and 12 months
Risk factors

- Mail versus phone (reporting bias)
- Prior pain syndrome
  - *Chronic pelvic pain, other (central sensitization, primary hyperalgesia)*
- “Pain” personality/somatization
- Severe post-partum pain
  - *Causal?*
  - *Will better treatment help??????*
- Repeat CS? Or 1st CS?? Reason for CS?
- Pfannenstiel incision, uterine exteriorization, uterine closure


Surgical factors-incision?

The “Goldilocks” (three bears) principle?
690 CDs, (100 in Seattle, 590 in Sao Paulo)
So why is the incidence of chronic/persistent pain so low after cesarean delivery??
Spinal nerve ligation in rats.

Assessed withdrawal threshold.

Postpartum OR administered oxytocin increased withdrawal threshold.

Reversal of Peripheral Nerve Injury-induced Hypersensitivity in the Postpartum Period

Role of Spinal Oxytocin

Silvia Gutierrez, Ph.D.,* Baogang Liu, M.D.,† Ken-ichiro Hayashida, D.V.M., Ph.D.,‡ Timothy T. Houle, Ph.D.,§ James C. Eisenach, M.D.†

Anesthesiology 2013; 118: 152-159
Phase 1 Safety Assessment of Intrathecal Oxytocin

James C. Eisenach, M.D., Chuanyao Tong, M.D., Regina Curry, R.N.

(Anesthesiology 2015; 122:407-13)

- 5, 15, 50, 150 mcg
- 5 subjects per dose

What We Already Know about This Topic

- There have been few advances in new drugs producing spinal analgesia
- There are oxytocin receptors in the dorsal horn of the spinal cord indicating oxytocin may be a potential spinal analgesic

What This Article Tells Us That Is New

- Subarachnoid injections of oxytocin did not produce any major adverse events or complications
- In a limited protocol for testing analgesia, no analgesic effects were apparent
IF... acute perioperative pain predicts chronic pain, would decreasing postop pain help???
Preoperative scar hyperalgesia is associated with post-operative pain in women undergoing a repeat Caesarean delivery

C.M. Ortner1, M. Granot2, P. Richebé1, M. Cardoso3, L. Bollag1, R. Landau1

1 Department of Anesthesiology and Pain Medicine, University of Washington, Seattle, WA, USA
2 Faculty of Social Welfare and Health Studies, University of Haifa, Israel
3 Department of Anesthesiology, Maternity Hospital Santa Joana, São Paulo, Brazil

Preoperative Scar Hyperalgesia and Post-Operative Pain

Figure 1 Post-operative pain was tested on a 10-point visual analogue pain scale (VAS) (0 = no pain, 10 = worst pain imaginable) at rest (R), while sitting (S) and for uterine cramping pain (U) at 12, 24 and 48 h following Caesarean delivery. With the exception of VAS-R24, pain scores were always higher in women with scar hyperalgesia. SHA = women with pre-operative scar hyperalgesia (index > 0). No SHA = women with no pre-operative scar hyperalgesia. *p < 0.05, **p < 0.01.

Table 2 Preoperative tests and post-operative pain outcomes according to SHA.

<table>
<thead>
<tr>
<th></th>
<th>No SHA (n = 96)</th>
<th>SHA (n = 67)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative mT5 (0–100)</td>
<td>0 (0–8)</td>
<td>9 (0.25; 19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VAS-S48</td>
<td>2.45 (2.39)</td>
<td>3.54 (2.67)</td>
<td>0.004</td>
</tr>
<tr>
<td>WHA at 48 h (n, %)</td>
<td>42 (44%)</td>
<td>56 (84%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WHA at 48 h (INDEX)</td>
<td>0 (0; 0.53)</td>
<td>0.72 (0.7; 1.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intravenous morphine equivalent (mg)</td>
<td>17 (11)</td>
<td>19 (16)</td>
<td>0.34</td>
</tr>
</tbody>
</table>

Data are presented as mean and standard deviation or median and quartiles [Q1, Q3]. p-value is calculated using Student’s t-test for parametric or Wilcoxon rank sum test for non-parametric data. SHA, scar hyperalgnesia; mT5, mechanical temporal summation (0–100 scale); VAS-S48, visual analogue pain scale while sitting at 48 h (0 = no pain, 10 = worst pain imaginable); WHA, wound hyperalgnesia.
“On a scale of 0-100…how anxious are you?”

“On a scale of 0-100…how much pain do you anticipate…”

“On a scale of 0-5, … how much pain medication do you expect to use…”

192 subjects (37 ≥ 80th %ile)
### Predicting Acute Pain after Cesarean Delivery Using Three Simple Questions

Peter H. Pan, M.S.E.E., M.D.,* Ashley M. Tonidandel, M.D.,† Carol A. Aschenbrenner, M.A.,‡ Timothy T. Houle, Ph.D.,§ Lynne C. Harris, B.S.N.,‖ James C. Elsenach, M.D.#

<table>
<thead>
<tr>
<th></th>
<th>Entire Population (n = 192)</th>
<th>Evoked Pain Score ≤ 80th Percentile (n = 155)</th>
<th>Evoked Pain Score &gt; 80th Percentile (n = 37)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some high school</td>
<td>12 (6.3)</td>
<td>7 (4.5)</td>
<td>5 (13.5)</td>
<td>0.01</td>
</tr>
<tr>
<td>High school graduate</td>
<td>34 (17.6)</td>
<td>23 (14.8)</td>
<td>11 (29.7)</td>
<td></td>
</tr>
<tr>
<td>Some college</td>
<td>47 (24.5)</td>
<td>38 (24.5)</td>
<td>9 (24.3)</td>
<td></td>
</tr>
<tr>
<td>College graduate</td>
<td>99 (51.6)</td>
<td>87 (56.2)</td>
<td>12 (32.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Married</td>
<td>140 (72.9)</td>
<td>121 (78.1)</td>
<td>19 (51.4)</td>
<td></td>
</tr>
<tr>
<td>Divorced</td>
<td>7 (3.6)</td>
<td>4 (2.6)</td>
<td>3 (8.1)</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>42 (21.9)</td>
<td>29 (18.7)</td>
<td>13 (35.1)</td>
<td></td>
</tr>
<tr>
<td>Separated</td>
<td>3 (1.6)</td>
<td>1 (6)</td>
<td>2 (5.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Cumulative morphine equivalents, mg</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 h postsurgery</td>
<td>12 (0–98)</td>
<td>9 (0–67)</td>
<td>30 (1–98)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>48 h postsurgery</td>
<td>26 (0–148)</td>
<td>20 (0–142)</td>
<td>65 (12–148)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
Predicting Acute Pain after Cesarean Delivery Using Three Simple Questions

Peter H. Pan, M.S.E.E., M.D.,* Ashley M. Tonidandel, M.D.,† Carol A. Ascherbrenner, M.A.,‡ Timothy T. Houle, Ph.D.,§ Lynne C. Harris, B.S.N.,‖ James C. Eisenach, M.D.#

Fig. 3. Receiver operator characteristic curves of both derivation (n = 192) and validation (n = 131) cohorts.
Predicting postoperative pain?

- Assess pain with lidocaine injection pre-spinal
- Correlate with post-CS pain
Severe pain during local infiltration for spinal anaesthesia predicts post-caesarean pain

Table 1 Demographic data, pain outcomes, and analgesic requests during first 24 h after caesarean delivery.

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Weight</th>
<th>Primary delivery</th>
<th>Repeat delivery</th>
<th>Average Peak pain</th>
<th>Average mobilisation</th>
<th>Peak pain mobilisation</th>
<th>Average cram</th>
<th>Peak cram</th>
<th>Number</th>
<th>N = ( )</th>
<th>N = 1</th>
<th>N ≥ 2</th>
</tr>
</thead>
</table>

Table 4 Preoperative ILA as a test to predict post-caesarean pain during 1st 24 h.

<table>
<thead>
<tr>
<th>Total N = 229</th>
<th>Average pain at rest &lt;70 (N = 214)</th>
<th>Average pain at rest ≥70 (N = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ILA &lt;70 (N = 197)</td>
<td>196</td>
<td>1</td>
</tr>
<tr>
<td>ILA ≥70 (N = 32)</td>
<td>18</td>
<td>14</td>
</tr>
</tbody>
</table>

ILAs, injection of local anaesthetic.

Sensitivity of ILA ≥70: 91.6% and specificity: 93.3%. Positive predictive value 85.6%, negative predictive value 43.8%.

Data presented as mean ± SD (confidence interval). Kruskal-Wallis test was performed for comparisons between groups.

*p < 0.01 (95% CI).

**p < 0.001 (95% CI).
A Randomized Controlled Trial Comparing Two Multimodal Analgesic Techniques in Patients Predicted to Have Severe Pain After Cesarean Delivery

Jessica L. Booth, MD, Lynnette C. Harris, BSN, CCRC, James C. Eisenach, MD, and Peter H. Pan, MD
Anesth Analg 2016;122:1114–9

- Used “three simple questions” to find subjects more likely (80th percentile) to have more postop pain
- 74 subjects
- Spinal anesthesia with 12 mg bupivacaine and 15-20 mcg fentanyl

- RANDOMIZED TO (both groups got ibuprofen 800 q6 and MS PCA)

300 mcg IT morphine + 1000 mg acetaminophen q 6 h
OR
150 mcg IT morphine + placebo
**A Randomized Controlled Trial Comparing Two Multimodal Analgesic Techniques in Patients Predicted to Have Severe Pain After Cesarean Delivery**

Jessica L. Booth, MD, Lynnette C. Harris, BSN, CCRC, James C. Eisenach, MD, and Peter H. Pan, MD

*Anesth Analg 2016;122:1114–9*

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### Table 2. Visual Analog Pain Score Assessment and Side Effects for the First 24 Hours After Cesarean Delivery

<table>
<thead>
<tr>
<th></th>
<th>150 mcg PF-morphine + placebo (control group, n = 30)</th>
<th>300 mcg PF-morphine + acetaminophen (intervention group, n = 30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Visual analog pain score (0–100 mm)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Movement at 24 hours, mean ± SD (mm)</td>
<td>46 ± 25</td>
<td>31 ± 17</td>
<td>0.009</td>
</tr>
<tr>
<td>Resting at 24 hours, median [IQR] (mm)</td>
<td>19 (0–33)</td>
<td>4 (0–10)</td>
<td>0.011</td>
</tr>
<tr>
<td>Average over 24 hours, mean ± SD (mm)</td>
<td>37 ± 19</td>
<td>23 ± 14</td>
<td>0.002</td>
</tr>
<tr>
<td>Worst over 24 hours, median [IQR] (mm)</td>
<td>69 (49–77)</td>
<td>62 (42–70)</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>Side effects</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of pruritus requiring treatment</td>
<td>Overall: 50%</td>
<td>Overall: 70%</td>
<td>0.11</td>
</tr>
<tr>
<td>Postanesthesia care unit: 33%</td>
<td>Postanesthesia care unit: 47%</td>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>Postpartum unit: 40%</td>
<td>Postpartum unit: 57%</td>
<td>0.17</td>
<td></td>
</tr>
<tr>
<td>Percentage of nausea requiring treatment</td>
<td>Overall: 53%</td>
<td>Overall: 60%</td>
<td>0.60</td>
</tr>
<tr>
<td>Postanesthesia care unit: 33%</td>
<td>Postanesthesia care unit: 23%</td>
<td>0.33</td>
<td></td>
</tr>
<tr>
<td>Postpartum unit: 37%</td>
<td>Postpartum unit: 50%</td>
<td>0.33</td>
<td></td>
</tr>
</tbody>
</table>
An Evaluation of the Postoperative Antihyperalgesic and Analgesic Effects of Intrathecal Clonidine Administered During Elective Cesarean Delivery

Intrathecal Administration of Morphine Decreases Persistent Pain after Cesarean Section: A Prospective Observational Study

Kumi Moriyama, Yuki Ohashi, Akira Motoyasu, Tadao Ando, Kiyoshi Moriyama*, Tomoko Yorozu

Summary

- Chronic/persistent pain after CD real, but maybe low incidence
- Pain NOT always relate to surgery
- PROBABLY associated with postop pain, personality, surgical factors, general health
- UNCLEAR if preventable
  - NO REASON NOT TO TREAT ACUTE PAIN