Update on Pediatric Pain

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Society for Pediatric Anesthesia
Refresher Course    March, 2011

Disclosures: Dr. Berde and Children’s Hospital Boston have received research support and a licensure agreement with Wex Pharmaceuticals and have a collaboration agreement with Proteus, SA; both are for development of prolonged-duration local anesthetics. In the event of future commercial development, Dr. Berde, his colleagues, and Children’s Hospital Boston could all receive royalties.
Aims of the Lecture

• To summarize recent advances, trends, and outcome studies for pediatric acute pain management
• To highlight some trends in pediatric chronic pain management
• Emphasis on recent studies
• To identify current challenges in pediatric acute and chronic pain management, and areas for future research
Acknowledgements

• My colleague Dr. Navil Sethna kindly provided a number of the slides on recent advances and outcomes in postoperative pain management.
## Pain in hospital children: A prospective cross-sectional survey of pain prevalence, intensity, assessment and management in a Canadian pediatric teaching hospital

*Taylor et al., Pain Res Manage 2008*

<table>
<thead>
<tr>
<th>Pain</th>
<th>N (age)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>241 (mean 6 yrs) 24 h snap shot, medical &amp; surgical patients</td>
</tr>
<tr>
<td>Before admission</td>
<td>83%</td>
</tr>
<tr>
<td>During admission</td>
<td>77%</td>
</tr>
<tr>
<td>Moderate or severe at interview</td>
<td>23%</td>
</tr>
<tr>
<td>Moderate/severe in previous 24h</td>
<td>64%</td>
</tr>
<tr>
<td>Analgesics during interview</td>
<td>Single or intermittent; 90% helpful</td>
</tr>
<tr>
<td>Analgesia prior 24h</td>
<td>Single or intermittent 58%</td>
</tr>
<tr>
<td>Assessment in 24h</td>
<td>27%</td>
</tr>
</tbody>
</table>
Conclusions

• Approximately 50% of inpatients were experiencing moderate or severe pain on an average day.
  • No change from last survey in 16 years earlier
    – Abbott et al., Pain 1992

• Pain was infrequently assessed, treated with a single or intermittent analgesics.

• APS involvement: more likely to have pain assessment & regular analgesics.

• Pain is common, under-recognized and under-treated.
What is Clinically Meaningful Pain Control?

- Patient’s self-report of pain at rest?
- Return to normal activity?
Pain at Rest and During Cough

VAS (mmHg)

Days After Surgery

Pain During Cough
Pain at Rest
Synaptic connections & integration of circuits are immature in newborns. The secondary hyperalgesia is slower to mature after injury. Less endogenous control: Many more neurons are activated by a given stimulus. Potentially more intense pain experience.

More diffuse & less spatially focused pain experience.
Do newborns have sufficient brain maturation to experience pain in a conscious manner?

- Inferences from immediate and longer-term behavioral studies.
- Brain imaging studies
- Electrophysiologic studies
• N = 18, age 25 - 45 wks GA
• Venipuncture produces a cortical response, increased CBF, HbT in contralateral somatosensory cortex, increases with GA & occurred even in premature infant
• von Frey hair produced WR of foot; spinal segmental response
Recent Studies on Pediatric Analgesic Pharmacology

- Acetaminophen, via multiple routes
- NSAIDs and COX-2s
- Opioids
- Opioid Side-Effect Treatment
- Regional Anesthesia – Drugs, Routes, and Outcome Studies
Acetaminophen

• Now available IV in the US; has been available in Europe and elsewhere for several years
• More PK information in infants
• Opioid sparing well-demonstrated in older infants and children.
• There is still no positive postoperative analgesic efficacy trial in the immediate newborn period.
Negative Newborn Acetaminophen Trials

- Major Surgery
  Van der Marel et al. BJA 2007; 98:372-9

- Circumcision
NSAIDs

- Effective via multiple routes
- Good analgesia and opioid sparing in infants > 6 months and in children
- Good safety
- There is still no positive efficacy trial in newborns.
Postoperative Ketorolac in Infants RCT, DB, PC Safety & Pharmacokinetics

Lynn et al., Anesth Analg 2007

- N = 37, ages 6 -18 months
- A dose of 0.5 or 1 mg / kg every 4 or 6h
- No accumulation of S(-) analgesic & S(+) antipyretic isomers
- Safety assessment
  - No adverse effects on renal & hepatic function tests, surgical drain output, SpO2 measurements
- No difference in analgesic effect between infusion of morphine vs morphine + ketorolac
Implications of Infant Animal Studies (Ririe et al)

- Targets of analgesic effects of NSAIDs, COX-2s, and possibly acetaminophen might not be fully developed in infant animals, and possibly in infant humans
- Are the negative trials for acetaminophen in newborns due to this effect, or insufficient measures, model sensitivity, selection of dose, excessive rescue analgesia, .....?
An Everyday Scenario:

• 6 week old full term baby, in the PACU following inguinal hernia repair under general anesthesia.
• The baby has received acetaminophen, ± ilioinguinal or caudal block, ± an intraoperative IV dose of an opioid.
The Problem:

- The baby is screaming continuously, not consolable with attempted feeding or cuddling.
- Heart rate 190, no signs of respiratory or hemodynamic problem, no signs of surgical complication or non-incisional sources of pain.
- You “round up the usual suspects” and find no treatable problem, other than incisional pain.
- This was a day-surgery case, and the baby is scheduled to go home.
Options:

- Give IV opioid, observe, and send the baby home.
- Give IV opioid and admit for observation.
- Give the baby an oral opioid now and for going home.
- Declare that “this is as good as we can do safely” and send home.
- Give an NSAID and reassess, and consider NSAID + acetaminophen for going home.
Problems:

• There is no consensus or common practice standard on which infants can be sent home following opioid administration.
• There are few or no positive analgesic efficacy data for acetaminophen or NSAIDs in this age group.
• What about safety data for NSAIDs in newborns and young infants?
Opinions

- I would rather take on the risks of ibuprofen compared to an opioid for home use in this setting.
- Ibuprofen has a body of safety data for very sick newborns undergoing ductus repair. By extrapolation, a few doses are probably safe for this infant.
Opioids and Opioid Side-Effects

• There is no magical new opioid on the market.

• Opioid-sparing and pre-emptive treatment of opioid-side-effects are increasing parts of acute pain management.
Opioid Side-Effects

• Micro-dose naloxone infusions are effective for both nausea and itching

• Nalbuphine has produced mixed results
  (Nakatsuka et al. Canadian J Anesth. 2006; 53: 1103-10)

• Peripherally-constrained opioid antagonists (methylnaltrexone, alvimopan) deserve further study in pediatrics.
  (Berde and Nurko, NEJM 2008; 358: 2400-01)

• Antihistamamines are largely ineffective.
Opioids: Safety

• Despite opposition from JCAHO and APSF and others, NCA has become standard of care in pediatric tertiary centers worldwide.

• Further discussion of Parent-Controlled Analgesia will be provided in the lecture.
Nurse-controlled analgesia (NCA) following major surgery in 10,000 patients in a children's hospital.

Howard et al
Pediatric Anesthesia 2010; 20:126-34

• 1996 – 2008
• median age 2.3 years, including 510 neonates
• No deaths.
• SAEs 0.4% overall; 2.5% in neonates.
• Relative risk = 9.4
• Satisfaction rated good or very good in 98%
Recent Trends and Outcome Studies with Pediatric Regional Anesthesia

- Increasing use of peripheral blockade, declining use of epidurals
- Increasing use of ultrasound-guidance
- Larger safety and effectiveness studies
- Studies of epidural combinations
Figure 1
Percentage of regional anesthesia over all anesthesia performed in children ≤4 years or older.

Figure 2
Percentage of neuraxial blocks over regional anesthesia in children ≤4 years or older.
Decline of Epidural Analgesia Use

Rochette et al, Pediatr Anesth 07
Ganesh et al., Anesth Analg 07

- CPNB is equally effective for orthopedic surgery on LE
- Local anesthetic alone reduces incidence of N/V: 14%
- Avoids potential complications of neural axis
- Fewer technical failures
- Negates the need for bladder catheterization
- Less interference with ambulation & PT
- CPNB offers prolong analgesia for outpatient/home
### TABLE 1. Statements of Evidence and Grades of Recommendation for the Outcomes Evaluated in This Review

<table>
<thead>
<tr>
<th>Evaluated Outcomes</th>
<th>Statements of Evidence</th>
<th>Grade of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral nerve blockade</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Reduces block performance time</em></td>
<td>No evidence found.</td>
<td>N/A</td>
</tr>
<tr>
<td><em>Hastens block onset</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultrasound guidance reduces onset of sensory block for upper extremity PNBs.</td>
<td>Ib</td>
<td>B</td>
</tr>
<tr>
<td>Improves block success</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultrasound guidance does not improve block success rates in upper extremity PNBs when compared with nerve stimulation guidance.</td>
<td>Ib</td>
<td>B</td>
</tr>
<tr>
<td>Ultrasound guidance improves the intraoperative block success for PNBs at the trunk.</td>
<td>Ib</td>
<td>A</td>
</tr>
<tr>
<td>Improves block quality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultrasound guidance prolongs analgesia for upper and lower extremity blocks.</td>
<td>Ib</td>
<td>A</td>
</tr>
<tr>
<td>Ultrasound-guided blocks at the anterior trunk improve early postoperative pain relief for inguinal and umbilical procedures.</td>
<td>Ib</td>
<td>B</td>
</tr>
<tr>
<td>Reduces local anesthetic dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultrasound guidance reduces the volume of local anesthetic required for successful perioperative analgesia in PNBs.</td>
<td>Ib</td>
<td>A</td>
</tr>
<tr>
<td>Ultrasound guidance achieves sufficient intraoperative analgesia using minimal volumes (0.1 mL/kg) of local anesthetic for blocks of the nerves in the anterior trunk.</td>
<td>Ib</td>
<td>B</td>
</tr>
</tbody>
</table>
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<th>Statements of Evidence</th>
<th>Grade of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuraxial anesthesia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clear visibility of landmarks</td>
<td>Ultrasound enables sufficient visibility of the dura mater and ligamentum flavum in neonates, infants and children.</td>
<td>Ib</td>
</tr>
<tr>
<td>Good prediction of depth to LOR</td>
<td>Preprocedural ultrasound imaging offers a moderate prediction of the depth to LOR.</td>
<td>III</td>
</tr>
<tr>
<td>Visibility of needle puncture or LOR</td>
<td>Ultrasound offers visibility of a needle within the epidural space in neonates.</td>
<td>III</td>
</tr>
<tr>
<td>Visibility of catheter (directly or indirectly)</td>
<td>Ultrasound guidance can directly detect catheters during advancement in some young infants.</td>
<td>III</td>
</tr>
<tr>
<td></td>
<td>Ultrasound guidance can confirm epidural catheter placement via surrogacy during injection of fluid.</td>
<td>III</td>
</tr>
<tr>
<td>Reduces bone contact</td>
<td>Bone contact can be reduced in most cases in infants and children using real-time ultrasound guidance.</td>
<td>Ib</td>
</tr>
</tbody>
</table>
Efficacy of Addition of Fentanyl to Epidural Bupivacaine on Postoperative Analgesia after Thoracotomy for Lung Resection in Infants

Arjunan Ganesh, M.B.B.S.,* N. Scott Adzick, M.D.,† Travis Foster, Ph.D.,‡ Giovanni Cucchiaro, M.D.*

Table 1. Demographic and Intraoperative Data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group BF, n = 16</th>
<th>Group B, n = 16</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, days</td>
<td>67 ± 26</td>
<td>66 ± 52</td>
<td>0.48</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>7/9</td>
<td>9/7</td>
<td>0.48</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>5.1 ± 1</td>
<td>4.8 ± 1.3</td>
<td>0.22</td>
</tr>
<tr>
<td>Location of the tip of the epidural catheter, range</td>
<td>T5–T9</td>
<td>T6–T10</td>
<td>0.2</td>
</tr>
<tr>
<td>Duration of surgery, min</td>
<td>105 ± 57</td>
<td>109 ± 36</td>
<td>0.43</td>
</tr>
<tr>
<td>Procedure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower lobectomy</td>
<td>12</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Upper lobectomy</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Middle lobectomy</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Removal of bronchopulmonary sequestration</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Level of incision</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fifth intercostal space</td>
<td>15</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>Sixth intercostal space</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Group B = 0.1% bupivacaine; group BF = 0.1% bupivacaine and 2 μg/ml fentanyl.
<table>
<thead>
<tr>
<th>Study Parameter</th>
<th>BF</th>
<th>B</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain score (CRIES)*/24h</td>
<td>1.5 ± 2</td>
<td>2.9 ± 2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Behavioral scores</td>
<td>1 ± 0.7</td>
<td>1.9 ± 1.3</td>
<td>0.01</td>
</tr>
<tr>
<td>Time first analgesic</td>
<td>516 ± 524</td>
<td>126 ± 89</td>
<td>0.005</td>
</tr>
<tr>
<td>Nalbuphine mcg/kg/24h</td>
<td>121 ± 91</td>
<td>218 ± 77</td>
<td>0.001</td>
</tr>
<tr>
<td>Ketorolac (mg)</td>
<td>0.7 ± 0.7</td>
<td>1 ± 0.7</td>
<td>0.08</td>
</tr>
<tr>
<td>Bupivacaine mg/kg/24h</td>
<td>61 ± 4</td>
<td>60 ± 3</td>
<td>0.35</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Assisted ventilation</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Naloxone requirement</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Time to discharge (days)</td>
<td>Median 2</td>
<td>Median 2</td>
<td>0.43</td>
</tr>
</tbody>
</table>

* Crying, Requires oxygen for saturation < 95%, Increased vital signs, Expression, Sleepless.
A Comparison of Epidural Bupivacaine-Fentanyl & Bupivacaine-Clonidine in Children Undergoing the Nuss Procedure (RCT)
Cucchiaro et al., Anesth Analg 2006

<table>
<thead>
<tr>
<th></th>
<th>Bupivacaine + clonidine (BC)</th>
<th>Bupivacaine + fentanyl (BF)</th>
<th>Bupivacaine + fentanyl + clonidine (BFC)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bolus</strong></td>
<td>0.3 mL/kg bupivacaine</td>
<td>0.3 mL/kg bupivacaine</td>
<td>0.3 mL/kg bupivacaine</td>
</tr>
<tr>
<td></td>
<td>0.25% (maximum, 10 mL) + 2 μg/kg clonidine</td>
<td>0.25% (maximum, 10 mL) + 2 μg/kg fentanyl</td>
<td>0.25% (maximum, 10 mL) + 1 μg/kg fentanyl + 1 μg/kg clonidine</td>
</tr>
<tr>
<td><strong>Infusion medication</strong></td>
<td>1 mg/mL bupivacaine</td>
<td>1 mg/mL bupivacaine</td>
<td>1 mg/mL bupivacaine</td>
</tr>
<tr>
<td></td>
<td>1.2 μg/mL clonidine</td>
<td>5 μg/mL fentanyl</td>
<td>2.5 μg/mL fentanyl</td>
</tr>
<tr>
<td><strong>Infusion rate</strong></td>
<td>0.25 mL · kg⁻¹ · h⁻¹ (maximum, 10 mL/h)</td>
<td>0.25 mL · kg⁻¹ · h⁻¹ (maximum, 10 mL/h)</td>
<td>0.25 mL · kg⁻¹ · h⁻¹ (maximum, 10 mL/h)</td>
</tr>
<tr>
<td><strong>PCEA</strong></td>
<td>1 mg/mL bupivacaine</td>
<td>1 mg/mL bupivacaine</td>
<td>1 mg/mL bupivacaine</td>
</tr>
<tr>
<td></td>
<td>1.2 μg/mL clonidine</td>
<td>5 μg/mL fentanyl</td>
<td>2.5 μg/mL fentanyl</td>
</tr>
</tbody>
</table>

List of medications and different modalities of administration during the intraoperative* and † postoperative period in the three study groups. The patient-controlled epidural analgesia (PCEA) settings were the same in the three groups: demand 0.05 mL/kg (maximum, 2 mL), basal infusion 0.25 mL · kg⁻¹ · h⁻¹ (maximum, 10 mL/h), lockout time 20 min, maximum dose/hour 0.4 mL · kg⁻¹ · h⁻¹ (maximum, 14 mL).
Authors’ Conclusion: Clonidine has similar safety & efficacy profile as fentanyl when combined with bupivacaine with less side effects

My Interpretation: Optimal selection of additives (e.g. fentanyl, hydromorphone, clonidine) depends on: type of surgery, location of catheter tip, individual responses, pre-existing pain, .....
Pediatric Postoperative Abdominal Wall Blockade: Recent RCTs

- **Inguinal surgery**: Ilioinguinal gives better analgesia than TAP block, using ultrasound for both.
  
  Fredrickson et al  Pediatric Anesthesia 2010; 20:1022-27

- **Appendectomy**: TAP block with ropivacaine vs. saline placebo: lower pain scores, less morphine use over next 24 hours.
  
  Carney et al  Anesth Analg 2010; 111: 998-1003
Effects of Analgesic Technique on Postoperative Outcomes

• During the lecture, we will review a series of recent studies on effects of analgesic technique on outcomes for:
  thoracotomies (neonatal and older)
  ACL repairs
  scoliosis surgery
PAIN

Chronic pain in adults after thoracotomy in childhood or youth

A. D. Kristensen¹ ²*, T. A. L. Pedersen³, V. E. Hjortdal³, T. S. Jensen² and L. Nikolajsen¹ ²

Table 1 Patient characteristics and recalled duration of post-thoracotomy pain (n=88), presented as mean (SD) or number (%)

<table>
<thead>
<tr>
<th>Age group (yr)</th>
<th>0–6 yr</th>
<th>7–12 yr</th>
<th>13–25 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
<td>22/9</td>
<td>23/13</td>
<td>12/9</td>
</tr>
<tr>
<td>Age at the time of thoracotomy (yr)</td>
<td>3.7 (2.0)</td>
<td>9.3 (1.7)</td>
<td>18.0 (4.5)</td>
</tr>
<tr>
<td>Age at the time of examination (yr)</td>
<td>32.3 (4.5)</td>
<td>39.3 (3.4)</td>
<td>49.4 (4.8)</td>
</tr>
<tr>
<td>Time since surgery (yr)</td>
<td>28.5 (4.1)</td>
<td>30.0 (2.9)</td>
<td>31.4 (3.3)</td>
</tr>
<tr>
<td>Recalled duration of post-thoracotomy pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3 months</td>
<td>10</td>
<td>21</td>
<td>13</td>
</tr>
<tr>
<td>(32.3%)</td>
<td>(58.2%)</td>
<td>(61.9%)</td>
<td></td>
</tr>
<tr>
<td>Pain more than 3 months</td>
<td>1</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>(3.2%)</td>
<td>(19.4%)</td>
<td>(28.5%)</td>
<td></td>
</tr>
<tr>
<td>3 months–1 yr</td>
<td>0</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>1–3 yr</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>3–10 yr</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>More than 10 yr, but no present pain</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pain is still present</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>No recall of duration, but pain is not present</td>
<td>20</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>(64.5%)</td>
<td>(22.2%)</td>
<td>(10.0%)</td>
<td></td>
</tr>
</tbody>
</table>
Conclusions: Groin pain in adult patients operated on for a groin hernia in childhood is uncommon.

Usually mild and occurs in relation to physical activity.

Operation before the age of 3 months does not increase the risk of chronic pain.
Pediatric Chronic Pain Management

• What kinds of patients get referred?
• What kinds of specialists should see them?
• What treatments and delivery models are clinically effective?
• How can programs be financially viable?
Cognitive-Behavioral Therapy (CBT) Benefits Many Patients with Chronic Pain.

- Evidence for efficacy from short-term treatment (based on ratings of function as well as pain) for migraine, tension-type headache, chronic abdominal pain, fibromyalgia, ....

- CBT is not “complementary” or “alternative”: it is mainstream and an integral part of any approach to chronic pain treatment.
Classical and Novel CBT Treatment Models

• “Classical” CBT: individual treatment, relaxation-based+/-biofeedback
• Emphasis on positive coping, overcoming fear of pain, avoiding catastrophizing....
• Acceptance-Commitment Therapy (ACT)
• Group treatment, including day-long group
• Web-based (Palermo et al)
• Curricula for parents.
Acceptance and Commitment Therapy (ACT) for Pediatric Chronic Pain
Wicksell et al  Pain 2009  141: 248-57

• Treatment model: similarities and differences from dialectical-behavioral therapy (DBT)
• 32 subjects, mostly girls, mostly adolescents, mean age 15 years
• Diverse diagnoses, pain ≥ 6 months
• High ratings for pain, disability, depressed mood, absence from school, …
Two Group RCT:

- Group 1: ACT – 10 once-weekly sessions with patient, 1 or 2 sessions with parent
- Group 2: “MDT” – “standard” Multi-Disciplinary Treatment: PT, CBT, and amitriptyline, titrated as tolerated up to 50 mg daily
Outcome Measures

• Pain scores
• Function/disability ratings (FDI)
• Depression scores (CES)
• Pain-related beliefs, fear of pain, fear of movement (kinesiophobia), catastrophizing
• Health-related QOL
• No direct measure of school attendance or performance
Results

- Both groups showed significantly improved scores for pain, functional disability, depressed mood, fear of pain or fear of movement, ....
- Slightly greater or more rapid improvements in the ACT group
Challenges with Providing Psychological Treatment for Pediatric Chronic Pain

• Simons et al – survey of CBT use following referral at initial Pain Clinic visit
• 35% actually completed a course of CBT
• Reasons: availability of clinicians, travel distance, cost, insurance denial, …. 
Some Opinions Regarding Pediatric Psychopharmacology - I

• Overall, antidepressant trials in children and adolescents show large placebo response magnitudes and relatively small treatment effects.

• Anticonvulsants may produce adverse effects on mood and, in pooled analysis of RCTs, compared to placebo, increase the risk of suicidal thoughts and attempts.
Some Opinions Regarding Pediatric Psychopharmacology - II

• Many pediatric drug RCTs for treatment of major depressive disorder and for bipolar disorder have been negative.
• There remains a concern about positive publication bias in industry funded trials.
Numbers-Needed-to-Treat (NNTs) for Antidepressants in Children and Adolescents

- Major depressive disorder: 10
- Anxiety with OCD: 6
- Anxiety without OCD: 3

Efficacy of antidepressants in juvenile depression: meta-analysis
Chronic Opioid Therapy for Non-Life-Limiting Chronic Pain in Pediatrics

• Overall, indications appear quite limited
• Age-specific effects on tolerance and opioid-induced hyperalgesia
• Effects on cognition, mood, motivation, and endocrine function are substantial.
• Addiction and pseudo-addiction both can occur.
• Diversion of prescribed opioids is the most rapidly increasing form of drug abuse among adolescents in the U.S.
• Outcome data from our clinic will be presented at the lecture.
Exercise for Treatment of Depression and Anxiety in Children and Adolescents

• Cochrane review 2006
• 11 RCTs, 1191 participants
• Overall relatively low quality, no anxiety scores.
• Most trials examined preventive intervention, i.e. depression scores in a general population, not specific treatment of patients who met criteria for MDD.
• In some adult studies, exercise appears as effective as any SSRI.
Complex Regional Pain Syndromes (CRPS) in Children

- Recent case series and clinical outcome studies
- PT, OT and CBT as primary treatment
- Controversy regarding the role of regional anesthesia
- Increasing use of peripheral nerve catheters when regional anesthesia is used.
Treatment Models for Pediatric CRPS

- Outpatient PT, OT, CBT
- Inpatient PT, OT, CBT +/- regional
- Day-Hospital PT, OT, CBT

At the lecture, we will review outcome data for the first 2 years of our day-hospital program for pediatric CRPS
Selective Use of Regional Anesthesia for Pain due to Advanced Cancer

• Please refer to my lecture notes for the Pre-Meeting talk on this topic.
Future Directions: Acute Pain

• Wider use of regional anesthesia
• Development of novel local anesthetics with longer duration (see my disclaimer in the first slide) and with greater sensory selectivity (Binshtock et al, Kohane et al)
• Better treatment of opioid side-effects
• Efficacy trials in infants
Comparison of Neosaxitoxin Versus Bupivacaine via Port Infiltration for Postoperative Analgesia Following Laparoscopic Cholecystectomy
A Randomized, Double-Blind Trial

Alberto J. Rodriguez-Navarro, MD,*†‡ Charles B. Berde, MD, PhD,§∥ Gonzalo Wiedmaier, MD,*
Andres Mercado, MD,* Carlos Garcia, MSc,‡ Veronica Iglesias, PhD,¶ and David Zurakowski, PhD§∥

RAPM, March, 2011
137 subjects, cholecystectomy, double-blind
Superiority trial comparing Neosaxitoxin to Bupivacaine
Better pain scores at 12 and 24 hours
Global recovery score – 2 days faster for Neosaxitoxin group
Further studies in progress
Future Directions: Chronic Pain

• Efficient delivery models for CBT, PT (group, web, self-teaching, tele-health…)
• Preventive interventions (school-based, parent-education based)
• Saps et al: brief CBT in healthy children in school prevents absence due to headache & abdominal pain
Future Directions: Regulatory Affairs

- FDA Consensus Group on Pediatric Analgesic Trials
- Berde, Krane, Walco et al 2011, manuscript submitted
- What patients should be studied?
- What is an ethical primary outcome measure for analgesic trials in pediatrics?
Conclusions

• Pediatric anesthesiologists can improve the care of children following surgery by active participation in acute pain management.

• Delivery models for chronic pain treatment in children deserve further study.