Learning Objectives

- Critically review risks and safety of analgesic undertreatment versus over-treatment in pediatric patients receiving palliative care
- Evaluate assumptions about opioid use in children
- Discuss how multiple agents, interventions, rehabilitation, psychological and integrative ("non-pharmacologic") therapies act synergistically for more effective pediatric pain control with fewer side effects than a single analgesic or modality
5-year old Marius: Procedural Pain Management


Don't have enough staff for pediatric pain control...?

Funny, how there is always enough staff to restrain a child.

Pediatric Analgesia in 1985 “Papoose Boards”
Pediatric Pain - Status Quo

- Under treatment of pain in children
- Parents expect pain to be relieved
- Parents’ greatest distress: failing to protect their child from pain
- Assumption: everything possible is done

Parents expect pain to be relieved


Parents’ greatest distress: failing to protect their child from pain


Assumption: everything possible is done

Anand's neonatal surgery studies

USA: adults receive more than two - three times as many analgesic doses as children (with identical diagnoses)


Compared to adults, pediatric patients receive fewer and/or incorrectly dosed analgesics in daily routine


The younger children are, the less likely they receive appropriate analgesia


Pediatric Pain - Status Quo

- Pain in children's hospitals is common, under recognized and under treated

- Canada: 3,822 pediatric inpatients (32 units):
  - 33% moderate to severe pain
  - 88% acute, 12% chronic pain

- USA
  - 20% of all children surveyed experienced moderate, 30% severe pain in previous 24 hours
  - 12% reported having pain routinely before admission
  - None of the 15 children with ≥ 1 severe pain score documented received consultation from Pain & Palliative Care

Inappropriate Analgesia: Why Bother...?

- Children with persistent pain suffer more physical symptoms in adult life, more anxiety and more depression
  - Medical Research Council and 1958 National Child Development Study

- Inadequate analgesia for initial procedures in children diminishes effect of adequate analgesia in subsequent procedures

- Higher morphine doses = less PTSD in months after major trauma

- Up to 25% of adults have fear of needles with most fears developing in childhood: avoidance of health care (including non-adherence with vaccination schedules)

- NICU: increased morbidity & mortality

- Up to 25% adults fear needles with most fears developing in childhood: avoidance of health care (including non-adherence with vaccination schedules)

Outcomes Improved with PPC Involvement

- Parents of children with cancer report less distress from pain, dyspnea and anxiety at EOL

- Children who received PPC/Oncology more likely to have fun (70% versus 45%) and to experience events that added meaning to life (89% versus 63%)

- Families who received PPC/Oncology report improved communication

- Children receiving PPC experience shorter hospitalizations and fewer emergency department visits
Myths and Barriers to Using Opioids

Case Scenario:

- You are taking care of a child with severe acute somatic nociceptive pain (e.g. cancer, sickle-cell crisis, major burn etc.). It crosses your mind to administer a strong opioid such as morphine or fentanyl.
- What would be the most common concerns you might hear from your colleagues or parents arguing against opioid use in this child?

Common Opioid Assumptions

- **Addiction** - "chronic relapsing condition characterized by persistent, compulsive dependence on a behavior or substance despite adverse consequences"
  - Tolerance ≠ addiction
  - Pseudo-addiction
- **Over Sedation / Respiratory Depression**
- **Ileus / Constipation**
- **Medication “Too strong”**
- **Masking symptoms**
  - Abdominal Pain
  - Opioids after major cranial surgery in children do NOT result in altered mental status nor respiratory depression
  - As always... Think first (e.g. compartment syndrome?)... analgesia second...

Safety of Analgesics

“Dr. Cox, I am worried about drug safety... ...would it be okay not using analgesia for children in acute pain?”

Says:
**Opioid Safety & Long-Term Outcome**

- Studies in neonatal rats suggest potential adverse effects of opioids (changes in behavior and brain functioning).
- NEOPAIN multicenter trial: Detailed secondary analysis: Although morphine associated with hypotension among ventilated preterm neonates, it does NOT increase the risk of severe IVH, any IVH, or death.

**Long-Term Outcome**

- Higher cumulative fentanyl dose in preterm infants correlated with higher incidence of cerebellar injury, lower cerebellar diameter: No correlation was detected between cumulative fentanyl dose and development at 2 years of age.
- Higher cumulative fentanyl dose in preterm infants correlated with higher incidence of cerebellar injury, lower cerebellar diameter: No correlation was detected between cumulative fentanyl dose and development at 2 years of age.
- Continuous morphine infusion of 10 mcg/kg/h during the neonatal period does not harm general functioning and may even have a positive influence on executive functions at 8 to 9 years.

**Does analgesia improve outcome?**

- Yes, in animal model (Suellen Walker, PhD, London).
Declaration of Montreal (2010)

- Access to pain management is a fundamental human right
- Human right violation not to treat

So, how do we treat the individual pain patient in front of us?

Hmhh... Spoiler Alert: Crystal-clear answer on 3rd last slide!

No needless pain.

That’s why we’re called

Multimodal Analgesia

No Needless Pain, The Children’s Comfort Promise
https://vimeo.com/20329079
How Do We Manage Acute Pain in Children?

- Dosing at regular intervals (“By the Clock”)
- Adapting treatment to the individual child (“With the Child”)
- Using the appropriate route of administration (“By the appropriate route)
- Using a two-step strategy (“By the Analgesic Ladder”)

WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses (2012)

WHO Principle 1: Dosing at Regular Intervals

- PRN (pro re data =”as needed”)
- PRN = Patient Receives Nothing
- When pain is constantly present, analgesics should be administered, while monitoring side-effects, at regular intervals
- “By the clock” and NOT as an “as needed” (or pro re nata “PRN”) basis

- Regular scheduling ensures a steady blood level, reducing the peaks and troughs of PRN (“as needed”) dosing
- PRN (as needed) only:
  - May take several hours & higher opioid doses to relieve pain
  - Results in cycle of undermedication and pain, alternating with periods of overmedication and drug toxicity

### Scheduling Analgesia

“It Is After 10, Give My Daughter The Pain Shot…” (Shirley MacLaine: Terms Of Endearment, 1983)

[YouTube Video](https://www.youtube.com/watch?v=Plqzeub9B-W)

### WHO Principle 2: Adapting Treatment to the Individual Child

- Treatment should be tailored to the individual child and opioid analgesics should be titrated on an individual basis
- At analgesic dosing: no sedation expected
- The effective dose is what relieves the pain
- Different children may respond differently to same dose
- Effective dose must be adjusted to child's needs
- Dose of strong opioids: only the sky is the limit

### Pain Scales

- Assess response frequently
- Pain Scales
- Look for opioid-induced side effects and toxicity

### Regular (!) Pain Assessment

- One-dimensional self-report scores
- Multi-dimensional rating scores

**JePS/CAMU Scales**

<table>
<thead>
<tr>
<th>Scale</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>FACES</td>
<td>0 = happy, 10 = sad</td>
</tr>
<tr>
<td>Numerical</td>
<td>0 = no pain, 10 = worst pain</td>
</tr>
<tr>
<td>Verbal</td>
<td>0 = no pain, 10 = worst pain</td>
</tr>
<tr>
<td>Facial</td>
<td>0 = no pain, 10 = worst pain</td>
</tr>
<tr>
<td>Multi-dimensional</td>
<td>0 = no pain, 10 = worst pain</td>
</tr>
</tbody>
</table>

Our new easy faces scale...

A. (These are our new faces)

B. (These are our new faces)

C. (These are our new faces)

D. (These are our new faces)

E. (These are our new faces)

F. (These are our new faces)

G. (These are our new faces)

H. (These are our new faces)

I. (These are our new faces)

J. (These are our new faces)

K. (These are our new faces)

L. (These are our new faces)

M. (These are our new faces)

N. (These are our new faces)

O. (These are our new faces)

P. (These are our new faces)

Q. (These are our new faces)

R. (These are our new faces)

S. (These are our new faces)

T. (These are our new faces)

U. (These are our new faces)

V. (These are our new faces)

W. (These are our new faces)

X. (These are our new faces)

Y. (These are our new faces)

Z. (These are our new faces)
What are we measuring...

(1) Nociceptive Pain: arises from the activation of peripheral nerve endings (nociceptors) that respond to noxious stimulation
- Somatic (for example, muscles, joints)
- Chronic somatic pain typically well localized & often results from degenerative processes (such as arthritis)
- Visceral (internal organs)

(2) Neuropathic Pain: resulting from injury to, or dysfunction of, the somatosensory system.
- Central pain: caused by a lesion or disease of the central somatosensory nervous system

(3) Psycho-social-spiritual-emotional Pain / Total Pain
- Pain beyond expected time of healing

(4) Chronic Pain

Pain in children with impaired communication

- Non-communicating Children's Pain Checklist - Revised (NCCPC-R); postoperative Version (NCCPC-PV)
- Pediatric Pain Profile (PPP)
- r-FLACC

WHO Principle 3: Route of Administration
WHO Principle 4: Using a Two-Step Strategy

**WHO Step 1**

Mild Pain

- **Ibuprofen**
- and/or **Acetaminophen (Paracetamol)**

Other NSAIDs? Cox-2 Inhibitor?

---

**Nociceptive Pathways & Primary Sites of Action of Analgesics**

- **Thalamus**
- **Injury**

**Citius, Altius, Fortius...?**

- Ibuprofen salts: fast-acting formulations
  - Advil® Film-Coated Tablets, contains 266 mg of ibuprofen sodium (equivalent to 200 mg of standard ibuprofen)
  - Produced significantly better analgesia over 6h, fewer re-medications than standard formulations
  - 200-mg fast-acting ibuprofen (NNT 2.1; 95% confidence interval 1.9-2.4) was as effective as 400 mg standard ibuprofen (NNT 2.4; 95% CI 2.2-2.5), with faster onset of analgesia.

- More rapid absorption, faster initial pain reduction, good overall analgesia in more patients at the same dose, and probably longer-lasting analgesia, but with no higher rate of patients reporting adverse events.

- However, earlier onset preferred in other pain condition, such as chronic nociceptive or neuropathic pain? Peloso, P.M., Faster, higher, stronger: to the gold medal podium? Pain, 2014. 155(1): p. 4-5.
**WHO Principle 4: Using a Two-Step Strategy**

**WHO Step 1**
Mild Pain

- Ibuprofen
- and/or Acetaminophen (Paracetamol)
- Other NSAIDs? Cox-2 Inhibitor?

**WHO Step 2**
Moderate to Severe Pain

- Morphine
  - or fentanyl, hydromorphone, oxycodone, methadone (UK: diamorphine)

---

**Morphine Pharmacokinetics**

“A principle of pharmacokinetics teaches us that unless the drug reaches the site of action, it cannot be expected to exert its dynamic effect.

With morphine the situation is that when the drug dose not reach the PATIENT, what hope is there for pain relief?”


---

**Nociceptive Pathways & Primary Sites of Action of Analgesics**

- **Opioids**
  - Pre-synaptic nerve terminal
  - Post-synaptic nerve terminal
  - Membrane hyperpolarization

=> suppress neuronal excitability
WHO Principle 4: Using a Two-Step Strategy

**WHO Step 1**

**Mild Pain**

- Ibuprofen and/or Acetaminophen (Paracetamol)
- Other NSAIDs?
- Cox-2 Inhibitor?

**WHO Step 2**

**Moderate to Severe Pain**

- Morphine
  - or fentanyl, hydromorphone, oxycodone, methadone (UK: diamorphine)

**Intermediate Step?**

- Tramadol
- Codeine
- Hydrocodone

**Other: Non-Opioids**

- Acetaminophen / Paracetamol
- NSAIDs

**Integrative Therapies**

- Massage
- Distraction
- Deep Breathing
- Biofeedback
- Hypnosis

**Multimodal (Opioid-sparing) Analgesia**

- **Non-Opioids**
  - Acetaminophen / Paracetamol
  - NSAIDs

- **Opioids**
  - Tramadol ("weak")
  - Morphine ("strong")

**4 WHO-Principles**

- "By the clock"

Integrative Pain Management

State of the art pain management in the 21st century demands that pharmacological management must be combined with supportive and integrative, non-pharmacological therapies to manage a child’s pain.

- Physical methods (e.g. cuddle/hug, massage, comfort positioning, heat, cold, TENS)
- Cognitive behavioral techniques (e.g. guided imagery, hypnosis, abdominal breathing, distraction, biofeedback)
- Acupuncture, acupressure, aromatherapy
Integrative Pain & Symptom Management


Nociceptive Pathways & Primary Sites of Action of Analgesics

**Injury**

- Thalamus
- Periaqueductal grey (endorphins)
- Integrative (non-pharmacological) therapies
- Opioids
- Acetaminophen (Paracetamol)
- NSAIDs

**CORTEX:**
- Stress
- Anxiety
- Catastrophizing
- Depression
- Perceived injustice
- Disturbed sleep

Descending pathways that modulate transmission of nociceptive signals originate in periaqueductal grey, locus coeruleus, anterior cingulate gyrus, amygdala & hypothalamus, are relayed through brainstem nuclei in the PEG and medulla to spinal cord.

Inhibitory transmitters involved in these pathways incl. norepinephrine, 5-hydroxytryptamine, dopamine, & endogenous opioids.
Non-Opioids
• Acetaminophen / Paracetamol
• NSAIDs

Opioids
Soft: • Tramadol ("weak")
• Morphine ("strong")

4 WHO-Principles
• "By the clock"

Adjuvants
Soft: • Alpha-Agonist
• Gabapentinoids
• TCA/Antidepressants
• NMDA-Antagonists
• Na-channel blockers
• Antispasmodics
• Benzodiazepines
• Muscle relaxants
• Corticosteroids
• Bisphosphonates

Regional Anesthesia
 • Neuraxial infusion
 • Peripheral/Plexus Nerve block
 • Neurolytic block
 • Intrathecal port/pump
 • Intraventricular opioids

Integrative Therapies
• Massage
• Distraction
• Deep Breathing
• Aromatherapy
• Hypnosis

Psychology
• CBT

Rehabilitation
• Exercise, Physical Therapy
• Sleep Hygiene
• OT

Spirituality

Cannabis
San Diego, CA

AAP Handout for parents
"Despite relaxed regulations, marijuana harms developing brain":
http://aapnews.aappublications.org/content/36/3/4.full.pdf

Updated AAP policy opposes marijuana use, citing potential harms, lack of research:
http://aapnews.aappublications.org/content/early/2015/01/26/aapnews.20150126-1

WHO-Principles
• "By the clock"
Multimodal Analgesia

- Multimodal (opioid-sparing) analgesia: Multiple agents, interventions, rehabilitation, psychological and integrative therapies act synergistically for more effective pediatric pain control with fewer side effects than single analgesic or modality.

Multimodal = Awesome!


Do you remember Marius...?

How about a Plan B?

LET Anesthesia

- Sitting upright
- Distraction
- Topical Anesthesia
- 3mL LET-gel: Lidocaine 4% - Epinephrine 0.18% - Tetracaine 0.5%


We will do everything possible to prevent and treat pain.

www.childrensMN.org/ComfortPromise
STEP 1: Topical Local Anesthetics

Flu shot @childrensmin for my 3 kids today. STEP 1: Numb the skin (over-the-counter 4% lidocaine cream, > 30 min)

STEP 2: Sucrose / Breastfeeding

STEP 2 to prevent/ease needle pain: Sugar water or breast-feeding: Not today, since my kids are older than 12 months

STEP 3: Positioning

STEP 3: NEVER ever hold a child down for vaccinations or other needle procedures (babies: swaddle or skin2skin)
STEP 4: Distraction

STEP 4: Distraction. Choice of my kids today "Fruit Ninja" & "Hair Saloon" on smartphone before & during vaccination.

Ow! I didn't feel it @childrensmn
ComfortPromise: numb the skin, sitting upright & distract
childrensMN.org/comfortpromise

IV Access Under Nitrous Gas

22 months-old. Lidocaine 4% cream in place, needed IV for radiologic procedure, history of challenging IV access in the past.
So, how do we treat the individual pain patient in front of us?

Crystal clear answer:

“It Depends”
-Socrates

Conclusions

- Withholding evidence-based analgesia to children in pain is not only unethical, but causes immediate and long-term harm
- Patients/Parents do NOT have to choose between poor pain control or over sedation
- Potential risks in safety of analgesics are real, but manageable; cannot justify denying administration of pain medications to pediatric patients
- Opioids (outside end-of-life) usually short term only - contraindicated for chronic pain
- Use multimodal (opioid-sparing) analgesia: Multiple agents, interventions, rehabilitation, psychological and integrative therapies act synergistically for more effective pediatric pain control with fewer side effects than single analgesic or modality
Further Links

- The New York Times (June 28, 2016) "Why Aren't We Managing Children's Pain?" Covering Dr. Stefan Friedrichsdorf
- Video: Kiran Stordalen and Horst Rechelbacher Pediatric Pain, Palliative and Integrative Medicine Clinic Tour
  https://vimeo.com/12664881
- Short Movie Meet the Interdisciplinary Chronic Pain Clinic Team at Children’s Minnesota LittleStars TV
  https://www.youtube.com/watch?v=13bu5fB-hPo&PF
- Video: Tour of the Kiran Stordalen and Horst Rechelbacher Pediatric Pain, Palliative and Integrative Medicine Clinic at Children’s Hospitals and Clinics of Minnesota and an overview of the three programs that are offered at Children’s under this clinic. https://vimeo.com/13157794
- Short Movie LittleStars Film Kali’s Story - Beyond the NICU: This amazing pediatric palliative care short movie (7 min) features 8-year-old Kali’s journey at Children’s Hospitals and Clinics of Minnesota from NICU to today receiving care by the Pain & Palliative & Integrative Medicine program while inpatient, in the clinic, and at home (Jan 22, 2015) http://www.littlestars.tv/short-film/beyond-the-nicu
- Twitter: @NoNeedlessPain

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Further Training

10th Annual Pediatric Pain Master Class
- Minneapolis, Minnesota, USA | June 17-23, 2017

Education in Palliative & End-of-life Care [EPEC]: Become an EPEC-Pediatrics Trainer
- Montréal, Québec, Canada | April 29-30, 2017 (Professional Development Workshop: 04/28/17)

Contact: CIPPC@ChildrensMN.org

Thank You

Children’s Minnesota
We will do everything possible to treat and prevent pain.

Children’s Comfort Promise

https://www.childrensmn.org/painpalliativeintegrativemed