Providers’ Clinical Support System – Opioid Therapies (PCSSO)

- Grant funded by SAMHSA
- Coalition of professional organizations
- Overarching goal: To offer evidence-based trainings on the safe and effective prescribing of opioid medications in the treatment of pain and/or opioid addiction.
- AAP = 2 Webinars per grant year (6 total)
- www.pcso.org

CME

CME credit is available for this Webinar upon completion of an evaluation.

More information will be provided near the end of this presentation.

Educational Objectives

At the conclusion of this activity participants should be able to:
- Review types of pain experienced by children with chronic medical conditions.
- Discuss non-opioid options for pharmacologic analgesia in children with chronic pain.
- Describe reasonable goals of therapy and appropriate ongoing control measures for children on chronic opioid.

Polling Question

How would you currently characterize yourself when providing pain management in children with chronic medical conditions?

A. Confident: here to pick up a few pointers
B. Competent: able to manage many patients much of the time
C. Uncertain: sometimes know how to start, not sure where to go next
D. Largely at a loss: help!
E. N/A: I do not see patients

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**CME: Off-Label/Investigational Use**

Many agents and techniques are widely used in children; Many such agents and techniques are NOT approved for such use.

Much (most?) of current pediatric pain practice is still officially off-label/investigational.

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**Initial Definitions: What is Pain?**

- Pain is a subjective experience
  - “…an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.” IASP - 1994
- Acute pain is 2° to noxious stimulus
  - Usually nociceptive
- Chronic pain is persistent pain
  - Widely accepted pediatric definition > 3 months
  - Nociceptive, neuropathic, functional, mixed

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**More Definitions: Type of Pain?**

- *Somatic pain (superficial, deep)*
  - Somatic A-δ, c-d, γ fibers
- *Visceral pain*
  - Autonomic c-s, c fibers
- Neuropathic pain
  - Dysfunctional transmission, +/- sympathetic (CRPS)
- Functional pain
  - "not explained by structural or biochemical abnormalities.”

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**Nociceptive Pain Management**

Acute/chronic nociceptive pain (somatic, visceral)
- Cyclooxygenase inhibitors: acetaminophen, NSAIDs
- Ketamine: NMDA antagonist; dissociative analgesia
- Clonidine: α-2 agonist; sedation/anxiolysis/analgesia
- Opioids: mainstay of therapy for moderate-severe pain
  - [Adjunctive modalities - YES]
  - [Regional anesthesia - YES]

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**Neuropathic Pain Management**

Generally chronic
- Anti-neuropathic anti-depressants: tricyclic, SNRI
- Anti-neuropathic anti-convulsants: GBN, PGN, CBZ (TGN)
- Anti-dysrhythmics: lidocaine, mexiletine
- Corticosteroid: usually depo by injection
  - [Adjunctive modalities - YES]
  - [Regional anesthesia - YES]

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**Functional Pain Management**

Generally chronic, almost by definition
- Anti-neuropathic anti-depressants?
- Anti-neuropathic anti-convulsants?
- Rehabilitation services: occupational / physical therapy
- Formal mental health care: therapy / medication
  - [Adjunctive modalities - YES]
  - [Regional anesthesia - NO]
W.H.O. Analgesic Ladder

First published 1986
Several revisions (1990)
Protocol for cancer pain
Increasing global health issue
Widely accepted paradigm
Any pharmacologic analgesia

http://www.who.int/cancer/palliative/painladder/en/

W.H.O. Analgesic Ladder

- Maximize non-opioids
- Adjuvant therapy as effective
- Incremental opioid, if used
- Escalate as effective
- Freedom from cancer pain

Assessment: Analog Scales


Assessment: Summation Scales

- Various objective assessment summation scales are available, generating pain scores hopefully corresponding to what the patient would report
- FLACC (face, legs, activity, cry, consolability)

Assessment: Chronic Pain

Functional ability more important/helpful than pain score!

Polling Question

How often in your current practice are you the provider primarily responsible for pain management in children with chronic medical conditions?

A. Consistently: rarely defer to other providers
B. Often: more frequently than other providers are
C. Occasionally: less frequently than other providers are
D. Rarely: few such patients, or defer to other providers

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Acetaminophen

- "The pain reliever doctors recommend most…"
  - Central cyclooxygenase inhibitor
  - No anti-inflammatory effects
  - No GI, renal, hematologic complications
  - Hepatic toxicity with overdose

- Dosing
  - 20 mg/kg PO, then 15 mg/kg PO: max 1000 mg q4-6h
  - 40 mg/kg PR, then 20 mg/kg PR: max 1300 mg q4-6h
  - No benefit, possible toxicity > 4 g/24 h
  - Reduces opioid need, particularly scheduled

NSAIDS

- Varying potencies
  - Peripheral cyclooxygenase inhibitors
  - Prostaglandin inhibitors, anti-inflammatory effects
  - Gastric, renal, hematologic complications
  - Bleeding ulcer, papillary necrosis, renal insufficiency

- Dosing
  - Ibuprofen: 10 mg/kg PO: max 800 mg q6-8h
  - Ibuprofen: no benefit, possible toxicity > ~3 g/24 h
  - Reduce opioid need, particularly scheduled

COX-2 Inhibitors

- NSAIDs with relatively selective inhibition of cyclooxygenase-2 (pain, inflammation)
- Relative sparing of cyclooxygenase-1 (gastric mucosa)
- Marketed as preferred chronic NSAIDs
- NOT so much safer as originally thought!

EBM: NSAIDS > Acetaminophen

  - Children 6-17 y with acute musculoskeletal injury
  - Acetaminophen v. Ibuprofen v. Codeine PO
  - Ibuprofen superior at 60 minutes

EBM: Synergism

  - Children 6-36 m with fever
  - Acetaminophen v. Ibuprofen v. Combination PO
  - Combination superior at every outcome

COX-2 Inhibitors

- Celecoxib: 100, 200, 400 mg: sulfa moiety
  - 100-200 mg PO q6-8h (400 mg PO bid in FAP)
- [Rofecoxib: withdrawn 09/30/04]
  - Voluntary withdrawal by Merck given increased CV risk
- [Valdecoxib]: withdrawn 04/07/05
  - Withdrawal by Pfizer at FDA request
- Meloxicam, Nabumetone
  - COX-2 preferential, not selective
Anti-Neuropathic Analgesics

Anti-neuropathic anti-depressants
- Amitriptyline 0.25-3+ mg/kg/day qhs
- Nortriptyline 0.25-3+ mg/kg/day qhs
- Duloxetine 0.3-2 mg/kg/day qAM

Anti-neuropathic anti-convulsants
- Gabapentin 5-15+ mg/kg/day div-tid
- Pregabalin 1-3 mg/kg/day div-tid
- Carbamazepine 10-30+ mg/kg/day div-qid (TGN)

Antidysrhythmics, including topical steroid, usually depo by injection

Opioids

- “Among the remedies which it has pleased Almighty God to give to man to relieve his suffering, none is so universal and so efficacious as opium.” Sydenham, 1680
- “God’s own medicine,” Osler, often
- Mu, kappa (analgesia), sigma (dysphoria), delta (limbic) receptors

More Definitions

- Tolerance, tachyphylaxis
  - Increasing dose for same effect
  - Not unique to opioids
- Dependence
  - Discontinuation precipitates withdrawal
  - Not unique to opioids
- Addiction
  - Psychopathological drug-seeking (DSM diagnosis)
  - Thought to be rare with appropriate Rx

Even More Definitions

- Controlled Substance
  - Title II of the Comprehensive Drug Abuse Prevention and Control Act - 10/27/70
  - Schedules I-V
- Narcotic
  - Legal definition varying by state
  - Conveys no pharmacologic information
- Opioid/opiate
  - Opioid receptor activity
  - Several chemical classes

Opioids: Chemical Classification

- Morphine congeners
  - Agonists except as below
  - Agonists / antagonists
  - Antagonists
- Phenylpiperidines
  - Meperidine
  - Fentanyl & congeners
- Methadone
  - Methadone
  - (Propoxyphene – withdrawn in US 11/19/10)

http://kff.org/other/state-indicator/retail-rx-drugs-per-capita/#
- TN Retail Drugs Per Capita: 18.7 (3rd Highest in US)
- 2015 Data
131.2 million prescriptions for acetaminophen-hydrocodone were filled in the US in 2011

- IMS Health - 2011 Data

### Opioid Overdose Mortality

- Since the mid-1990s, opioids have consistently been the most common cause of unintentional fatal overdose in the US.


### Polling Question

What is your current pattern of opioid prescription?

- A. Both short and long acting opioid: comfortable with both
- B. Primarily long acting opioid: prefer to avoid short acting agent
- C. Primarily short acting opioid: prefer to avoid long acting
- D. Usually do not prescribe opioid of any kind: defer to other providers

### Lower Potency Oral Opioids

- Codeine: 1 mg/kg: pruritus, emesis, pharmacogenomics
- Hydrocodone: 0.2 mg/kg
- Oxycodone: 0.1 mg/kg
- All available in liquid form
- Generally q3-4h: +/- acetaminophen

### Codeine-Associated Mortality

- In 2009 we reported the fatal case of a toddler who had received codeine after adenotonsillectomy for obstructive sleep apnea. We now report 3 additional fatal or life-threatening cases from North America. These cases demonstrate that analgesia with codeine may not be safe in young children.


### CYP2D2 Opioid Metabolism

- Opioids metabolized by CYP2D6 include codeine, tramadol, hydrocodone, and oxycodone. Ultrarapid metabolizers and some extensive metabolizers of CYP2D6 relatively produce more active opioid metabolites resulting in life-threatening adverse effects. The adverse outcomes can be avoided by CYP2D6 genetic testing before prescribing these opioids or by using alternative analgesics.

Polling Question
How often in your current practice do you prescribe codeine?

A. As analgesic and/or cough suppressant: do not avoid it
B. Only as analgesic: prefer other cough suppressants
C. Only as cough suppressant: prefer other analgesics
D. Usually do not prescribe for any indication: prefer other agents

Meperidine: Just Say No
- Not only are there limited reasons for using meperidine, there are acceptable alternatives for every known indication. Limiting meperidine’s use via a restriction policy and/or removal from the institution formulary can help limit the use of this potentially toxic agent in the pediatric patient.

Morphine
- Intermittent IV:
  0.05-0.1 mg/kg: max initial 5-10 mg q3h
  Onset 5-10 min; t-1/2 α ~3h
  Histamine: pruritus, urticaria, nausea, bronchospasm
- IV PCA; reduces overall opioid requirement:
  0.02 mg/kg/h: max initial 1 mg/h basal, if used
  0.02 mg/kg pm: max initial 1 mg: = basal
  Demand q8-10min for patient-controlled
  Demand q15-60min for parent- or nurse-controlled

Hydromorphone
- Intermittent IV:
  0.01-0.02 mg/kg: max initial 1-2 mg q3h
  Onset 5-10 min; t-1/2 α ~3h
  Less histamine: useful if intolerant of morphine; burns
- IV PCA; reduces overall opioid requirement:
  0.004 mg/kg/h: max initial 0.2 mg/h basal, if used
  0.004 mg/kg pm: max initial 0.2 mg: = basal
  Demand q8-10min for patient-controlled
  Demand q15-60min for parent- or nurse-controlled

Fentanyl
- Intermittent IV:
  0.5-1 mcg/kg (max initial 50-100 mcg) q1h
  Onset 1-2 min; t-1/2 α ~30-60min
  Little histamine; context-sensitive clearance
- IV PCA; reduces overall opioid requirement:
  0.5-1 mcg/kg/h (max initial 50 mcg/h) basal, if used
  0.5-1 mcg/kg pm (max initial 50 mcg), = basal
  Demand q8-10min for patient-controlled
  Demand q15-60min for parent- or nurse-controlled

Pediatric IV PCA
- Useful if requiring more than occasional intermittent IV opioid: easier on care staff, better analgesia, lower opioid dose
- Allows precise assessment of daily opioid requirement, pattern of use
- Basal rate – if used - and demand dose should be =concordant
Pediatric PCA Basal

- Children with HgSS hospitalized for crisis: IV PCA with basal > demand (compared to demand > basal) associated with:
  - Higher opioid use overall
  - Longer time on IV PCA
  - Longer time in hospital
  - Higher pain scores throughout


Designated-Agent Pediatric PCA

Incidence of clinically significant events in designated-agent PCA was similar to that with patient-controlled administration, although incidence of rescue events was higher


Chronic Opioid Therapy

- Longer-acting agents analogous to PCA basal:
  - Baseline analgesia, prevent withdrawal

- Shorter-acting agents analogous to PCA demand:
  - Breakthrough pain, treat withdrawal

- Titrate up or down as needed:
  - Patient still having pain? Opioid still effective?

- Logistical/legal concerns:
  - Opioid rotation? Control measures? Compliant?

Transdermal Fentanyl

- 12, 25, 50, 75, 100 mcg/h patches
  - Remove (!) and replace q72h

- 12-24 h for full onset or elimination
  - NOT FOR ACUTE USE

- Begin at ~50% of stable opioid dose
  - 25 mcg/h per 1mg/h IV morphine

Higher Potency Oral Opioids

- Morphine:
  - PO = 3 x IV dose: 0.3 mg/kg
  - 15+ mg tablets, liquids, 5+ mg PR

- Hydromorphone:
  - PO = 1-2 x IV dose: 0.02-0.04 mg/kg
  - 1-8 mg tablets, 1 mg/ml liquid, 3 mg PR

  - Generally q3h for breakthrough

Long Acting Oral Opioids

- Morphine SR:
  - PO = 3 x IV dose
  - 10+ mg tablets only

- Oxycodone SR:
  - PO = IV morphine equivalent
  - 10+ mg tablets only

- Methadone:
  - PO = ½ x IV dose = IV morphine equivalent
  - 5/10/[40] mg tablets, liquid
Methadone

Approval
- Adults ≥ 18 years: moderate to severe pain
- Adults ≥ 18 years: detoxification of opioid addiction*
- Adults ≥ 18 years: maintenance therapy of opioid addiction*
* Opioid Treatment Programs certified by Federal Substance Abuse & Mental Health Services Administration & registered by Drug Enforcement Agency
- Single PO = 1:1 with single dose IV morphine
- Daily PO = 5-30% daily PO morphine
- IV:PO methadone = 1:2

Methadone

Supplied
- Tablets: 10, 20, 40* mg
* Opioid Treatment Programs certified by Federal Substance Abuse & Mental Health Services Administration & registered by Drug Enforcement Agency
- 20 ml vials 10 mg/ml for IV administration
- Oral liquid formulations as prepared, often 1 mg/ml

Administration
- Orally (with or without food)
- IV push; IM/SC

Social stigma:
- Association with addiction treatment programs

Logistical/regulatory concerns:
- Restricted formulations/indications

QTc prolongation:
- Clinical significance unclear, monitoring controversial

Practitioner reluctance:
- Many practitioners have never prescribed

Polling Question
How often in your current practice do you prescribe methadone?
A. Consistently: provide initial and refill prescriptions
B. Often: provide refills of stable regimen initiated and titrated by other providers
C. Occasionally: only under extenuating circumstances
D. Rarely: few such patients, or defer to other providers

Physical/Mental Rehabilitation

- Occupational/physical/speech therapy
- Multi-modal mental health care
  - Often most important interventions
  - Emphasis on coping mechanisms, function
  - Redirect focus from symptomatology
  - Consider in any chronic condition

Psychiatric Co-Morbidity

Biopsychosocial Model


Multi-Modal Approach

Phenotype: Bi-Modal Distribution

“Two distinct types of families were identified.”


Rational Pain Management

Understand type and severity of pain:
- Mixed pain states common
- Realistic expectations crucial

Maximize non-opioid interventions:
- Anti-nociceptive and/or anti-neuropathic agents
- Physical/mental rehabilitation services
- Adjuvant/interventional modalities

Challenge of appropriate opioid therapy:
- Initial trial of short-acting agent
- Chronic therapy generally with long-acting agent
- Logistical/legal considerations

Additional Resources: Textbooks


Q & A

- Please use the chat box to submit a question for the speakers.
- Obtaining CME
  - After the event, you will receive a link taking you to an evaluation. Upon completion, you will be emailed your CME certification.

Case Scenario

A 16 year old male presents with several months of diffuse low back pain after a motor vehicle accident. He is no longer in school secondary to pain. Occasional acetaminophen and ibuprofen have provided little relief. He does report feeling better after taking acetaminophen-hydrocodone prescribed for his mother. He is tender across his lower back diffusely without sensorimotor deficit. Conventional spine radiographs are normal; there are no alarm symptoms suggesting need for further imaging.

At this point, it would be MOST appropriate to recommend:

A. Scheduled acetaminophen and ibuprofen
B. PRN muscle relaxant
C. PRN acetaminophen-hydrocodone (or other short acting opioid)
D. Conversion to long acting opioid
E. Physical therapy
F. No additional intervention

With regard to management of chronic non-malignant back pain:

A. Scheduled acetaminophen and/or ibuprofen: Although not likely harmful at usual doses and durations, anti-inflammatory analgesics are not generally beneficial in most patients in this setting.
B. PRN muscle relaxant: Although potentially providing modest symptomatic relief in some patients, muscle relaxants are not generally beneficial in most patients in this setting.
C. PRN acetaminophen-hydrocodone (or other short acting opioid): Opioids have consistently been shown to be of little benefit in this setting.
D. Conversion to long acting opioid: Opioids have consistently been shown to be of little benefit in this setting.
E. Physical therapy: **LIKELY THE MOST APPROPRIATE INTERVENTION AT THIS POINT** Rehabilitation services have consistently been shown to be the most likely effective intervention in this setting.
F. No additional interventions: Potentially reasonable if patient/family willing, but may reinforce deconditioning.

PCSS-O Colleague Support Program and Listserv

- PCSS-O Colleague Support Program is designed to offer general information to health professionals seeking guidance in their clinical practice in prescribing opioid medications.
- PCSS-O Mentors comprise a national network of trained providers with expertise in addiction medicine/psychiatry and pain management.
- Our mentoring approach allows every mentor/mentee relationship to be unique and catered to the specific needs of both parties.
- The mentoring program is available at no cost to providers.

For more information on requesting or becoming a mentor visit: [www.pcss-o.org/colleague-support](http://www.pcss-o.org/colleague-support)

- Listserv: A resource that provides an "Expert of the Month" who will answer questions about educational content that has been presented through PCSS-O project. To join email: pcss-o@aaap.org

PCSS-O is a collaborative effort led by American Academy of Addiction Psychiatry (AAAP) in partnership with Addiction Technology Transfer Center (ATTC), American Academy of Neurology (AAN), American Academy of Pain Medicine (AAPM), American Academy of Pediatrics (AAP), American Academy of Physicians (ACP), American Dental Association (ADA), American Medical Association (AMA), American Osteopathic Academy of Addiction Medicine (AOAAM), American Psychiatric Association (APA), American Society for Pain Management Nursing (ASPAN), International Nurses Society on Addictions (INNSA), and Southeast Consortium for Substance Abuse Training (SECSAT).

For more information visit: [www.pcss-o.org](http://www.pcss-o.org)
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