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.pcss-o.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:

- Understand the development and neurobiology of central and peripheral pain pathways and their impact on treatment modalities.
- Describe misconceptions associated with pediatric and adolescent pain and review solutions to counteract these myths.
- Assess pain at different ages and the impact of pain on different spheres of activity.
- Recognize differences in pain perception and medication responses.
- Identify common conditions/comorbidities associated with acute and chronic pain.

Genevieve D’Souza, MD

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Speakers

Genevieve D’Souza, MD

Brenda Golianu, MD
IASP Definition of Pain

An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.

Types of Pain- Nociceptive VS Neuropathic Pain

Pain can be broadly divided

(A) Nociceptive pain - the sensation or noxious stimulus associated with tissue-damage, and is usually protective.

(B) Inflammatory pain - hypersensitivity associated with tissue damage due to inflammatory mediators.

(C) Pathological pain - disease state caused by injury to either peripheral or central nervous system (neuropathic) or by its abnormal function (dysfunctional).

Woolf, C. J. (2010). What is this thing called pain? The Journal of Clinical Investigation, 120(11), 3742–3744. doi:10.1172/JCI45178

Types of Pain

<table>
<thead>
<tr>
<th>Nociceptive Pain</th>
<th>Neuropathic Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definition</td>
<td>Pain caused by lesion or dysfunction of the sensory nervous system, especially the somatosensory pathways.</td>
</tr>
<tr>
<td>Mechanism</td>
<td>Sensitive nerve fibers which respond to mechanical, thermal, and chemical stimuli.</td>
</tr>
<tr>
<td>Location</td>
<td>Localized pain</td>
</tr>
<tr>
<td>Quality of Symptoms</td>
<td>Ordinary, paroxysmal sensations (e.g., pain, burning, tingling)</td>
</tr>
<tr>
<td>Treatment</td>
<td>Good response</td>
</tr>
</tbody>
</table>

Mechanism-Based Classification of Pain

Central sensitization/central neurogenic mechanism/central nociceptive mechanism

Peripheral sensitization/peripheral neurogenic mechanism

Peripheral nociceptive mechanism

Sympathetically maintained pain/sympathetically dependent pain mechanism

Cognitive-affective (psychosocial) mechanism

Mechanism-Based Classification of Pain

Central Sensitization

- An enhancement in the function of neurons and circuits in nociceptive pathways
- Caused by $↑$ in membrane excitability and synaptic efficacy as well as by $↓$ inhibition
- It is a manifestation of the remarkable plasticity of the somatosensory nervous system in response to activity, inflammation, and neural injury.

Mechanism-Based Classification of Pain

Peripheral Sensitization

- Pain arising as a direct consequence of a lesion or disease affecting the somatosensory system.
- Pathophysiological & pathomechanical responses to nerve injury affect:
  - Vascular tissue
  - Connective tissue
  - Impulse-conducting tissue components of the nervous system
- Leads to the neurobiological mechanisms responsible for the $+$ and $-$ symptoms associated with musculoskeletal peripheral neuropathic pain.

Mechanism-Based Classification of Pain

Peripheral Nociceptive Mechanism

- The pain arising from bodily tissues (both somatic & visceral) follows a characteristic anatomical pattern that corresponds to the tissue-at-fault.

Mechanism-Based Classification of Pain

Sympathetically maintained pain/sympathetically dependent pain mechanism

- Ongoing pain and allodynia, which is typically out of proportion to the injury.
- The causative event can vary widely from trivial injury to major trauma, or there may be no significant trauma at all.
- Allodynia and spontaneous ongoing pain in SMP is a result of chronic maladaptive sensitization of wide dynamic range neurons in the dorsal horn of the spinal cord, that leads to release of catecholamines and is not due to heightened sympathetic tone.

Mechanism-Based Classification of Pain

Cognitive-affective mechanism

- Psychological factors play a significant role in various aspects of chronic pain experience among patients:
  - Causative
  - Receptive
  - Perceptive
  - Cognitive
  - Reproductive
  - Behavioral
- While cognitive factors include patients’ knowledge and maladaptive understanding of pain and ‘pain behavior’, affective factors involve emotions and feelings associated with the ‘pain experience.’
Mechanisms of Central Sensitization


Developmental Implications of Pain

Infants exposed to a painful stimulus (circumcision) exhibit an exaggerated pain response to future painful events (immunization) 6 months later.

This effect can be modulated with application of EMLA cream, or penile block.


Developmental Implications of Pain

What happens if the pain impulse happens before 32 weeks?

C fiber to dorsal horn connections lead to prolonged excitation following a single stimulus, repetitive stimulation leads to temporal summation and wind-up and lowered thresholds to subsequent stimuli, via increased density of NMDA receptors in spinal cord.

These changes result not only in ↑ transmission, but also modulation and long term potentiation.

Opioid receptor uncoupling may also play a role in regulating pain mechanisms.

Developmental Implications of Pain

Nociceptive pathways are functional after birth, and pain produces significant physiologic and behavioral responses in both preterm and term neonates.

Clinical evidence for adverse impacts on neurodevelopmental outcome and subsequent pain response is increasing.

Evaluating the impact of early life pain and/or analgesia requires consideration of intercurrent illness and stress, particularly in preterm-born neonates requiring prolonged intensive care treatment.

In addition, genetic and environmental factors, and social and family factors can modulate subsequent behavioral responses.


Developmental Implications of Pain

Persistent alterations in sensory function have been shown in a range of preclinical models of early pain and injury, and allow evaluation of underlying mechanisms and potential preventive interventions.

Adequate management of pain is a goal of care at all ages.

Specific evaluation of efficacy and effects in early life is required because responses in the developing nervous system may differ from those seen at older ages.

Developmental Implications of Pain

Nociceptors

• These are specialized sensory receptors responsible for the detection of noxious (unpleasant) stimuli, transforming the stimuli into electrical signals, which are then conducted to the central nervous system.
• They are the free nerve endings of primary afferent Aδ and C fibers.
• Distributed throughout the body (skin, viscera, muscles, joints, meninges) they can be stimulated by mechanical, thermal or chemical stimuli.
• Primary afferent Aβ fibers carry non-noxious stimuli

Pain Receptors

<table>
<thead>
<tr>
<th>Aβ fibers</th>
<th>Aδ fibers</th>
<th>C fibers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter</td>
<td>Large</td>
<td>Smallest-μm</td>
</tr>
<tr>
<td>Myelination</td>
<td>Highly</td>
<td>Thinly</td>
</tr>
<tr>
<td>Conductive velocity</td>
<td>&gt; 40 ms-1</td>
<td>5-15 ms-1</td>
</tr>
<tr>
<td>Receptor activation</td>
<td>Low</td>
<td>High and low</td>
</tr>
<tr>
<td>Sensation on stimulation</td>
<td>Light touch, non-noxious</td>
<td>Rapid, sharp, localized pain</td>
</tr>
</tbody>
</table>

Nociceptors

Wide Dynamic Range Neurons

• WDR neurons located in lamina V
• Receive Aβ, Aδ and C fiber input
• Respond to both benign and painful stimuli in a graded (dynamic) fashion
• Responsible for referred pain due to organ convergence from skin/muscle and various visceral organs – such as angina in the left neck and arm

Pain Pathways


Impact of Pain

- In 2011, at least 100 million adult Americans have common chronic pain conditions, a conservative estimate because it does not include acute pain or children.
- Pain is a significant public health problem that costs society at least $560-635 billion annually, an amount equal to about $2,000 for everyone living in the U.S.
- This includes the total incremental cost of health care due to pain from ranging between $261 to $300 billion and $297-$336 billion due to lost productivity (based on days of work missed, hours of work lost, and lower wages).

Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education and Research (Institute of Medicine Report)

Impact of Pain

- Most people in chronic pain have multiple sites of pain.
- For US adults reporting pain, causes include: severe headache or migraine (16.1%), low back pain (28.1%), neck pain (15.1%), knee pain (19.5%), shoulder pain (9.0%), finger pain (7.6%), and hip pain (7.1%).

Data from CDC and National Center for Health Statistics

- According to the National Health and Nutrition Examination Survey (NHANES) data, 17% of US children, aged 4-18, experience frequent or severe headaches, including migraine, over the course of a year. Before puberty, boys and girls have headaches at approximately the same rate, but after 12, the rate of recurrent and severe headaches rises among girls.

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Impact of Pain

- Cross sample of sequential 100 presentations to a Pediatric Chronic Pain Clinic:
  - Abdominal pain 18%
  - Back pain 14%
  - Headache 14%
  - Fibromyalgia 12%
  - CRPS 11%
  - Other Musculoskeletal pain 11%
  - Chest and Rib pain 6%

These patients were predominantly adolescent females (73%) with frequent coexisting clinically significant anxiety (63%) and depression (64%).


Impact of Pain

- Large-scale epidemiologic studies in Netherlands have observed a 25% to 46% point prevalence of chronic pain of at least three months duration in the pediatric age group
- Headache, abdominal pain, limb pain, and back pain being the most frequent locations

Common chronic pain-related functional issues:
- Sleep problems (54%)
- Inability to pursue hobbies (53%)
- Eating problems (51%)
- School absence (49%)
- Inability to interact with friends (47%)


Impact of Pain

- Chronic “benign” pediatric pain persists for at least 1 to 2 years in 30%–45% of cases
- In a cohort of 8, 11, and 14 year olds, with chronic headache or chronic back pain, 59% of females and 35% of males reported similar pain at 21, 24, and 27 years of age
- Children and adolescents with chronic pain:
  - Utilize various healthcare services
  - Require prescription analgesic medications
- Both at a significantly greater rate than their healthy peers leading to greater healthcare costs


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Misconceptions Regarding Pain In Infancy and Childhood

<table>
<thead>
<tr>
<th>Myth</th>
<th>Reality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborns and infants are incapable of feeling pain. Children do not feel</td>
<td>By 20 weeks’ gestation, a fetus has most of the anatomic and functional</td>
</tr>
<tr>
<td>pain with the same intensity as adults because a child’s nervous system</td>
<td>requirements for pain processing. Term infants have the same level of</td>
</tr>
<tr>
<td>is immature.</td>
<td>sensitivity to pain as older infants and children. Preterm infants may actually</td>
</tr>
<tr>
<td>have greater sensitivity.</td>
<td>have greater sensitivity.</td>
</tr>
<tr>
<td>Children are not in pain if they can be distracted or if they are sleeping.</td>
<td>Children use distraction to cope with pain, but they soon become exhausted when coping with pain and fall asleep.</td>
</tr>
</tbody>
</table>

Role of Genetics in Pain Perception

- Chronic musculoskeletal pain is more common in females than males
- Women reported significantly higher ratings of worst and current pain intensity but there were no differences on the rating for least pain.

Females have...
- Greater risk of chronic pain disorders
- Greater sensitivity to noxious stimuli
- Lower thresholds, greater ability to discriminate,
- Higher pain ratings, and less tolerance of noxious stimuli than males
- Higher reporting of multiple pains in more body regions than men

- Tsang A, et al., Common chronic pain conditions in developed and developing countries: Gender and age differences and comorbidity with depression-anxiety disorders. J Pain. 2008;3:242-52
Role of Genetics in Pain Perception

- Pharmacodynamics and pharmacokinetics of analgesics change with age, changes not necessarily linear.
- Because of incomplete maturation of the hepatic enzyme system, neonates have reduced weight-normalized clearance of many drugs, but children 2-6 years of age have greater clearance than adults.
- More frequent dosing.
- Body composition: neonates have lower plasma protein concentration; they should receive lower doses of drug with high protein binding.

Role of Genetics in Pain Perception

- Females (6%) showed greater prevalence of chronic neuropathic pain compared with males (3%).
- Women are at greater risk for neuropathic pain than men.

- Migraines - Prepubertal girls and boys have equal prevalence; lifetime prevalence increases to 18% for women and 6% for men after puberty.
- TM joint disorders - no difference between boys and girls in childhood and higher prevalence in women after puberty.
- Menstrual cycle affects pain due to IBS, headaches, TMD, fibromyalgia.
- Pregnancy reduces frequency of migraines and TMD pain.

Role of Genetics in Pain Perception

- NMDA antagonism enhances opioid antinociception greater in male versus female animals.
- Opioid Agonists - high estradiol levels are associated with reduced sensitivity to opioid agonists.

In Summary

- Most common types of pain are more common in females than males.
- Women have greater pain after an invasive procedure than men.
- Women show higher levels of temporal summation of pain.
- Gonadal hormones have significant influence on pain perception and analgesic responses.

Pain Assessment in different age groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Self-Report</th>
<th>Observational</th>
<th>Physiological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant</td>
<td>---</td>
<td>Premature Infant Pain Profile; Neonatal Infant Pain Scale</td>
<td>---</td>
</tr>
<tr>
<td>Child</td>
<td>Faces Pain Scale – Revised; Wong-Baker FACES Pain Rating Scale</td>
<td>FLACC (Face Legs Activity Consolability Scale); Comfort</td>
<td></td>
</tr>
<tr>
<td>Adult</td>
<td>Numerical Rating Scale; Visual Analog Scale; Brief Pain Inventory</td>
<td>---</td>
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</tr>
</tbody>
</table>
Pain Assessment in different age groups

Glossary of Pain

Neuropathic Pain
Pain initiated or caused by a primary lesion or dysfunction in the nervous system

Allodynia
Pain due to a stimulus that does not normally provoke pain

Dysesthesia
An unpleasant abnormal sensation, which can be spontaneous or evoked

Paresthesia
An abnormal skin sensation that can include tingling, prickling or numbness

Temporal Summation
A mechanism whereby repeated stimuli elicit increasing responses in spite of unchanged stimulus intensity

Hyperalgesia
An increased response to a stimulus that is normally painful

Diffuse Noxious Inhibitory Control
Inhibition of nociceptive neurons in the spinal and trigeminal dorsal horns by noxious stimulation of widespread areas of the body distant from the neurons' receptive field

Common Presentations to a Pediatric Clinic

<table>
<thead>
<tr>
<th>Acute Pain</th>
<th>Cancer Pain</th>
<th>Chronic Nonmalignant Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure related pain</td>
<td>Tumor related pain</td>
<td>Headaches</td>
</tr>
<tr>
<td>Perioperative pain</td>
<td>Therapy related pain</td>
<td>Musculoskeletal pain or pain from Rheum conditions like JRA</td>
</tr>
<tr>
<td>Burns</td>
<td></td>
<td>Chronic abdominal pain</td>
</tr>
<tr>
<td>Trauma</td>
<td></td>
<td>Sickle cell disease, hemophilia</td>
</tr>
<tr>
<td>Acute Illness</td>
<td></td>
<td>CRPS</td>
</tr>
</tbody>
</table>
Common Presentations to a Pediatric Clinic

Q & A

- Please use the chat box to submit a question for the speakers.
- Follow-up discussion – July 8th @ 11am central
  - 877-273-4202 | Room #: 9156562
- Obtaining CME
  - After the event, you will receive a link taking you to an evaluation. Upon completion, you will be emailed your CME certification.

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 College 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 (ASPMN), International Nurses Society on Addictions (INSA), and Southeast Consortium for Substance Abuse Training (SECSAT).

For more information about PCSSO, visit: www.pcss-o.org
For questions PCSSO, email: pcss-o@aaap.org
AAP Section on Anesthesiology and Pain Medicine: www2.aap.org/sections/anesthesiology
AAP Committee on Substance Abuse: www.aap.org/en-us/about-the-aap/Committees-Councils-Sections/substanceabuse

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