Introduction to Pediatric Pain

PEDiatric PAIN MANAGEMENT

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Definitions

- Pain: “An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”
  - The International Association for the Study of Pain (IASP)
    › Multidimensional in nature
    › Always a subjective experience
Definitions

- **Allodynia**
  - Pain due to a stimulus that normally does not provoke pain
- **Hyperesthesia**
  - Increased sensitivity to stimulation
- **Hypoesthesia**
  - Decreased sensitivity to stimulation
- **Hyperalgesia**
  - Increased pain response to a normally *painful* stimulus
- **Hypoalgesia**
  - Diminished pain response to a normally *painful* stimulus
- **Paresthesia**
  - Abnormal sensation to a stimulus that is normally not unpleasant such as tingling, pricking or numbness; spontaneous or evoked
- **Dysesthesia**
  - Unpleasant sensation; spontaneous or evoked
- **Hyperpathia**
  - Exaggerated response to repeated painful stimuli; often continues after the painful stimuli is discontinued and described as radiating
Pathophysiologically Classification

- Nociceptive
  - Somatic
  - Visceral
- Neuropathic
- Functional
Nociceptive Pain

- Adaptive, transient pain in response to noxious stimuli
- Leads to activation of specific pain receptors, “nociceptors”
  - Respond to heat, cold, vibration, stretch, and chemical stimulation
  - Sensitive to noxious stimuli
- Divided into two groups based on pain location and nociceptor activation
  - Somatic Pain
  - Visceral Pain
Nociceptive Pain, Cont.

- Somatic Pain
  - Activation of nociceptors located on tissue surfaces or deep tissues
    - Skin, mucosal surfaces
    - Bone, joint, muscle, connective tissue
  - Cuts, sprains secondary to tissue disruption
  - Muscle cramps due to poor oxygenation

- Visceral Pain
  - Activation of nociceptors located on thoracic and abdominal viscera
  - Infection, distension (fluid, gas), stretch, compression, disruption (solid tumors)
Nociceptors

- Key Mechanoreceptors
  - Ruffini Ending, “bulbous corpuscle”
    - Slow-adapting, tonic receptor that produces a train of action potentials proportional to the intensity of stimulus
    - Sustained pressure
  - Meissner Corpuscle, “tactile corpuscle”
    - Rapidly-acting, encapsulated, unmyelinated nerve endings; hairless skin regions
    - Low-frequency vibrations (10-50Hz) and light, discriminatory touch
  - Pacinian Corpuscle, “lamellar corpuscle”
    - Rapidly-adapting receptors
    - High-frequency vibration (250Hz)
    - Transient, deep pressure
  - Merkel Disk
    - Slow-acting, unencapsulated nerve endings
    - Present in the basal epidermal layer
    - Light, discriminative touch

- Key Thermoreceptors (cold)
  - Krause Endings, “bulboid corpuscles”
    - Conjunctiva, lips, tongue, penis, clitoris

Image by: Boundless Biology
Nociceptive Axons

- Two primary nerve fibers types involved in nociception
  - A-delta: thinly myelinated
    - 2-40 meters per second
    - Primary neurotransmitter: glutamate
    - Sharp, cold sensations
  - C-fibers: unmyelinated fibers
    - <2 meters per second
    - Primary neurotransmitter: substance P
    - Protopathic pain, “Second pain”
    - Burning, warm sensations
Non-Nociceptive Axons

- Non-Nociceptive Nerve Fibers
  - A-alpha
    - 80-120 meters per second
    - Muscle spindle motor and skeletal muscle
    - Largest, fastest sensory nerves
    - Golgi and Ruffini receptors, muscle spindle afferents
    - Muscle tension, length, velocity, proprioception
  - A-beta
    - 40-50 meters per second
    - Touch, pressure, vibration, flutter
    - Pacinian corpuscles
  - A-gamma
    - Motor fibers to muscle spindle
  - Beta
    - Pre-ganglionic sympathetic
Rexed Laminae

- Lamina I: Marginal Nucleus of Spinal Cord
  - Receives from Lissauer’s tract
  - Pain and temperature
  - Cannot be modulated

- Lamina II: Substantia Gelatinosa
  - C fibers primarily
    - A-delta may pass through on way to NP
  - Opioids, substance P

- Laminae III and IV: Nucleus Proprius
  - A-delta fibers primarily

- Lamina V
  - Wide dynamic range (“polymodal”) neurons synaptic location
    - Receive input from all somatosensory modalities (mechanical, thermal, chemical)
    - APs fired in graded fashion as stimulus intensity rises to noxious levels
    - Exhibit “wind-up”: short-term neuronal sensitization
      - Repetitive stimulation of WDR → increase of evoked response
Neuromodulators

- **Stimulatory**
  - Bradykinin (Plasma)
  - Prostaglandins (Damaged cells)
  - Substance P (Primary nerve afferents)
  - Glutamate
    - AMPA, NMDA, metabotropic, kainate receptors
  - Aspartate
    - Questionable involvement
  - Histamine (Mast cells, eosinophils)
  - Calcitonin Gene Related Peptide
    - Trigeminovascular system
  - Leukotrienes (Damaged cells)
  - Brain-Derived Neurotrophic Factor
  - Growth Factor

- **Inhibitory**
  - GABA
  - Serotonin (Platelets)
  - Glycine
  - Norepinephrine
  - Endogenous Opioids
    - Dynorphin
    - Enkephalins
    - Endorphins
Brief Summary of Basic Pain Pathway

Neuroreceptors & free nerve endings → peripheral nerves → dorsal horn of spinal cord → spinothalamic tract → thalamus

- Spinothalamic Tract
  - Anterior ST tract: crude touch, firm pressure
  - Lateral/Posterior spinothalamic tract: pain and temperature

- Thalamus
  - Lateral thalamus: formed by ventrobasal complex
    - Input from wide dynamic range and nociceptive-specific neurons
    - Sensory and discriminatory aspects of pain
    - Projects to somatosensory cortex
  - Medial thalamus: consists of posterior and centrolateral nuclei
    - Projects to limbic structures
      - Amygdala (emotions), hippocampus (memories), hypothalamus (neuroendocrine corticotropin response), basal ganglia, cingulate gyrus
    - Affective component of pain
      - Autonomic reflex responses
      - States of arousal
      - Emotional aspects of pain
Four Stages of Pain Processing

- Transduction
  - Harmful stimulus activates nociceptors (mechanical, thermal, heat)
  - Noxious stimulus $\rightarrow$ electrical impulse
  - Damaged tissues release histamine, substance P, prostaglandins, bradykinin, serotonin

- Transmission
- Modulation
- Perception
Four Stages of Pain Processing

- Transduction
- Transmission
  - Electrical stimulus is propagated along neurons from peripheral to central NS
  - A-delta and c-fibers transmit impulses from stimuli to dorsal horn of spinal cord via spinothalamic tract to the brainstem, thalamus, hypothalamus, and cortex
- Modulation
- Perception
Four Stages of Pain Processing

- Transduction
- Transmission
- Modulation
  - Between thalamus & brainstem and the interneurons of the dorsal horn of SC
  - Involves humoral and neural events, endogenous opioid system, NMDA
  - Segmental inhibition: Melzack & Wall’s “Gate Theory of Pain Control”
  - Descending inhibitory pathways
    - Periaqueductal gray & rostral medulla
    - Serotonin and norepinephrine
- Perception
Four Stages of Pain Processing

- Transduction
- Transmission
- Modulation
- Perception
  - Patient feels pain
  - Mediated by cerebral cortex
  - Most variable of above components; relies heavily on a combination of sensory, physiological, cognitive, affective, behavioral, and emotional factors
Gate Theory of Pain Control

- Melzack & Wall (1965): non-nociceptive stimuli can shut gate for noxious stimuli
  - Activation of large, myelinated fibers → stimulation of low-threshold mechanoreceptors → inhibitory nerves in spinal cord → inhibition of synaptic transmission
  - Rubbing a bumped arm

- Spinal cord stimulators, TENs units
  - A-alpha and A-beta stimulation → pain inhibition
Pathophysiological Classification

- Nociceptive
  - Somatic
  - Visceral
- Neuropathic
- Functional
Neuropathic Pain

- Pain caused by a lesion or disease of the somatosensory nervous system
- Caused by any process that results in nerve damage
  - Metabolic, traumatic, infectious, ischemic, toxic, immune-mediated
  - Involves abnormal processing of pain signals by CNS
- Classifications
  - Peripheral: Any location distal to spinal cord
  - Central: Lesion or disease affecting the brain and/or spinal cord
    - Spinal cord central pain syndromes more commonly neuralgic
    - Central pain originating in cortex results in evoked and steady pain
- Pediatric pain etiologies differ from those most common in adults
  - Nerve injury, entrapment, tumors (external compression or infiltration), HIV (infection or therapy), phantom limb pain, cancer treatment (radiation or chemo), spinal cord injury, neuropathic pain syndromes, inflammatory neuropathies (Guillain-Barre syndrome)
Neuropathic Pain, Cont.

- Mechanisms of Neuropathic Pain with Injury
  - Central nervous system
    - Loss of large fiber inhibition
    - Deafferentation hyperactivity of central pain transmission neurons
    - Aberrant connections resulting from reorganization of the central nervous system
  - Peripheral nervous system
    - Ectopic impulse generation
    - Enhanced adrenergic sensitivity
    - Inflammation of the neural trunk
Pathophysiological Classification

- Nociceptive
  - Somatic
  - Visceral
- Neuropathic
- Functional
Functional Pain

- Pain and related dysfunction without clear "organic" etiology
- Particularly prominent in pediatric chronic pain population
  - Frequent persistence into adulthood
- Biological and psychosocial contribution
- Frequently concurrent diagnoses
- Many historical diagnoses for "somatic symptom disorder" [Simons]
  - Somatoform disorder
  - Somatization
  - Functional somatic syndrome
  - Bodily distress disorder
  - Central sensitization disorder
  - Amplified pain syndrome
  - Primary pain disorder
- Patient outcome differs based on diagnosis given [Hamilton]
Functional Pain

- Theories for etiology
  - Neuronal sensitization
  - Immune system sensitization
  - Endocrine dysregulation
  - Signal filter theory
    - Decreased filter activity secondary to selective attention, health anxiety, depressed mood, lack of distraction, etc.
  - Somatosensory amplification theory
  - Autonomic system dysfunction
  - Illness behavior theory
    - Fear avoidance model
  - Sensitivity theory - genetic predisposition
  - Biopsychosocial theory
Functional Pain

- Biopsychosocial theory
  - Incorporates several above theories
  - Self-perpetuating cycle with various influencers
    - Physiological
    - Cognitive
    - Affective
  - Treatment
    - CBT
    - Physical exercise
    - Pharmacological interventions
Classification Based on Duration

- **Acute**
  - In pediatrics, typically nociceptive pain secondary to inflammation, tissue injury, or infection\textsuperscript{[Greco]}
    - Most pronounced immediately following the insult with gradual improvement accompanying tissue repair
    - Responds well to neuraxial & regional anesthesia, opioids, adjunctive analgesics, and non-pharmacological management
    - Rarely progresses to chronic pain

- **Chronic**
  - Continuous or recurrent pain that persists beyond expected time of healing
    - 3 months vs. 6 months
  - May begin as acute pain and persist for long periods
  - May recur due to persistence of noxious stimuli or repeated exacerbation of injury
  - May exist in the absence of identifiable pathophysiology or medical illness
  - **Impact**
    - Physical activities and abilities
    - School attendance
    - Sleep patterns
    - Familial and social interactions
    - Psychological health (depression, anxiety, mood fluctuations, changes in affect)
  - Multifactorial; holistic treatment approach often necessary
Classification Based on Duration - Chronic Pain

Pediatric Chronic Pain

- Risk factors [Schecter]
  - Preadolescent abuse
  - Depression
  - Anxiety, catastrophizing
  - Older age
  - Female assigned sex

- Family dynamics implicated in escalation and maintenance
  - Overprotection
  - Misguided support
  - Parental dependence
The Many Components of the Pain Experience

- Noxious stimuli
- Physiological transmission of pain
- Sensory perception of pain
- Overall experience of pain

Dimensions of pain:

- Cognitive: Beliefs, attitudes, spiritual and cultural attitudes
- Affective: Emotions
- Behavioural: Changes in behaviour

[WHO]
## Quantification – Pain Scales

- Neonates and Preverbal Children

<table>
<thead>
<tr>
<th>Scale</th>
<th>Clinical setting</th>
<th>Age group</th>
<th>Indicators</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRIES scale</td>
<td>Postoperative pain</td>
<td>Neonate–6 months</td>
<td>Crying, Requires oxygen, Increased vital signs from baseline, Expression, Sleeplessness</td>
<td>0–10</td>
</tr>
<tr>
<td>COMFORT Scale</td>
<td>Postoperative and periprocedural pain</td>
<td>Term neonates and &lt; 3 years</td>
<td>6 behavioral items</td>
<td>&gt; 4 additional analgesic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Alertness, Calmness, Muscle tone, Movement, Facial tension, Respiratory response for ventilated/crying for nonventilated</td>
<td>8–40</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 physiological items</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Heart rate, Mean arterial Pressure</td>
<td></td>
</tr>
<tr>
<td>CHEOPS</td>
<td>Postoperative and periprocedural pain</td>
<td>1–7 years</td>
<td>Crying, Facial expression, Verbal expression</td>
<td>4–13</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Torso position, Touch, Leg position</td>
<td>&gt; 6 additional analgesic</td>
</tr>
<tr>
<td>FLACC</td>
<td>Postoperative and periprocedural pain</td>
<td>2 months–7 years</td>
<td>Facial expression, Leg movement, Activity</td>
<td>0–10</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cry, Consolability</td>
<td>4–6 = moderate,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>7–10 = severe</td>
</tr>
</tbody>
</table>
Quantification – Pain Scales

- Pain Scales
  - Child
    - Wong-Baker FACES®
    - Faces Pain Scale Revised (FPS-R)
  - Adolescent
    - NRS
    - VAS
    - Brief Pain Inventory
## Quantification of Pain

### FLACC

<table>
<thead>
<tr>
<th>Category</th>
<th>Scoring</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Face</td>
<td>No particular expression or smile</td>
</tr>
<tr>
<td></td>
<td>Occasional grimace or frown, withdrawn, disinterested</td>
</tr>
<tr>
<td></td>
<td>Frequent to constant quivering chin, clenched jaw</td>
</tr>
<tr>
<td>Legs</td>
<td>Normal position or relaxed</td>
</tr>
<tr>
<td></td>
<td>Uneasy, restless, tense</td>
</tr>
<tr>
<td></td>
<td>Kicking or legs drawn up</td>
</tr>
<tr>
<td>Activity</td>
<td>Lying quietly, normal position moves easily</td>
</tr>
<tr>
<td></td>
<td>Squirming, shifting back and forth, tense</td>
</tr>
<tr>
<td></td>
<td>Arched, rigid, or jerking</td>
</tr>
<tr>
<td>Cry</td>
<td>No cry (awake or asleep)</td>
</tr>
<tr>
<td></td>
<td>Moans or whimpers; occasional complaint</td>
</tr>
<tr>
<td></td>
<td>Crying steadily, screams or sobs, frequent complaints</td>
</tr>
<tr>
<td>Consolability</td>
<td>Content, relaxed</td>
</tr>
<tr>
<td></td>
<td>Reassured by occasional touching, hugging or being talked to, distractible</td>
</tr>
<tr>
<td></td>
<td>Difficult to console or comfort</td>
</tr>
</tbody>
</table>
Quantification of Pain

- Wong-Baker FACES®

![Wong-Baker FACES® Pain Rating Scale](image)
Quantification of Pain

- FACES Pain Scale Revised
Quantification of Pain

- Visual Analog Scale (VAS)
  - Score 1-100
    - 35mm = score of 35
Quantification of Pain

- Numerical Rating Scale (NRS)
Quantification of Pain

- Verbal Rating Scale (VRS)
  - Most commonly reported as:
    - No pain
    - Mild pain
    - Moderate pain
    - Severe pain
- Most reliable in patients with profound dementia
Quantification of Pain

- Brief Pain Inventory (BPI)

1) Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?

   1. Yes 2. No

2) On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.

3) Please rate your pain by circling the one number that best describes your pain as its WORST in the past 24 hours.

   0 1 2 3 4 5 6 7 8 9 10

   No Pain

   Pain as bad as you can imagine

4) Please rate your pain by circling the one number that best describes your pain as its LEAST in the past 24 hours.

   0 1 2 3 4 5 6 7 8 9 10

   No Pain

   Pain as bad as you can imagine

5) Please rate your pain by circling the one number that best describes your pain on the AVERAGE.

   0 1 2 3 4 5 6 7 8 9 10

   No Pain

   Pain as bad as you can imagine

6) Please rate your pain by circling the one number that tells how much pain you have RIGHT NOW.

   0 1 2 3 4 5 6 7 8 9 10

   No Pain

   Pain as bad as you can imagine

7) What treatments or medications are you receiving for your pain?

8) In the past 24 hours, how much RELIEF have pain treatments or medications provided? Please circle the one percentage that most shows how much relief you have received.

   0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

   No Relief

   Complete Relief

9) Circle the one number that describes how, during the past 24 hours, PAIN HAS INTERFERED with your:

   A. General Activity:

   0 1 2 3 4 5 6 7 8 9 10

   Does not interfere

   Completely interferes

   B. Mood

   0 1 2 3 4 5 6 7 8 9 10

   Does not interfere

   Completely interferes

   C. Walking Ability

   0 1 2 3 4 5 6 7 8 9 10

   Does not interfere

   Completely interferes

   D. Normal work (includes both work outside the home and household)

   0 1 2 3 4 5 6 7 8 9 10

   Does not interfere

   Completely interferes

   E. Relation with other people

   0 1 2 3 4 5 6 7 8 9 10

   Does not interfere

   Completely interferes

   F. Sleep

   0 1 2 3 4 5 6 7 8 9 10

   Does not interfere

   Completely interferes

   G. Enjoyment of life

   0 1 2 3 4 5 6 7 8 9 10

   Does not interfere

   Completely interferes
Pain Evaluation

- **PQRST**
  - Provocation/Palliation
  - Quality/Quantity
  - Region/Radiation
  - Severity Scale
  - Timing

- **SOCRATES**
  - Site – Location or maximal site of pain
  - Onset – When, sudden vs. gradual, progressive vs. regressive
  - Character – Sharp, shooting, aching, dull, cramping, gnawing
  - Radiation – Does the pain radiate anywhere
  - Associated Symptoms – Concerns which patient associates with pain
  - Time Course – Does pain occurrence follow a pattern
  - Exacerbating/Relieving Factors – Does anything change the pain
  - Severity – Developmentally appropriate quantification scale
Common Qualifiers

- Nociceptive
  - Somatic
    - Localized, aching, gnawing
  - Visceral
    - Aching, associated with nausea

- Neuropathic
  - Burning, constricting, shock-like
    - Note: Sympathetic-mediated typically noted as more severe burning, squeezing, pins-and-needles, razor blades, “walking on glass”
#### Neonatal Pain - Development

- Historically under-treated
  - Perceived inability to experience pain due to immature nervous system
  - Innocuous effects of untreated pain in children
- Peri-oral cutaneous sensory nerve terminals present at 7 weeks gestation
  - All body areas by 20 weeks
- Extension of peripheral nociceptive fibers into the dorsal spinal cord at 8-12 weeks
- Myelination of pain transmission pathways
  - Completed in spine & brain stem between 22-30 weeks
  - Thalamus by 30 weeks
  - Cortex by 37-40 weeks
- Cortical descending inhibition develops post-term
- Excitatory and inhibitory neurotransmitters and neuromodulators
  - Calcitonin gene related peptide (CGRP), substance P, and glutamate-NMDA systems present at 8-10 weeks gestation
  - Enkephalins and vasoactive intestinal peptide at 10-14 weeks
Neonatal Pain - Physiological & Behavioral Assessment

- Preterm neonatal pain evaluation
  - Assessment
    - Unidimensional
      - Single type of variable (facial activity)
      - Single dimensions of pain (changes in cry, general or specific body movements, muscle tone, color, sleep/wake states)
    - Multidimensional
      - Combine behavioral with physiological pain indicators (heart rate, heart rate variability, respiratory rate or pattern, oxygen saturation and blood pressure)
      - May include other contextual factors
    - Typically extrapolated from full-term pain behaviors
    - Neonatal pain behaviors not consistently captured by assessment based on full-term infants; preterm assessment more complex
      - Immature regulatory systems and ongoing maturation of CNS
      - Behavioral and physiological responses of smaller magnitude
      - Different pain behaviors
Neonatal Pain - Outcome

- Preterm neonates more sensitive to pain than term
  - Lower threshold to touch; repeated touch further decreases threshold
    - Spinal cord sensory neuron excitability
  - More pronounced reflex responses to touch
  - Dependent on preceding stimulation
    - Diaper change producing pain-like behaviors and physiologic responses when preceded by heel lance 30 minutes before \cite{Holsti}

- Not self-regulated in the very preterm infant
  - Undeveloped descending endogenous pain modulation

- Repeated exposure during rapid brain development and programming of the hypothalamic-pituitary-adrenal (HPA) axis
  - Neurologically immature infants most susceptible to long-term effects of pain
  - Pain processing, neurodevelopment, sleep, immune function, and behavioral effects \cite{Grunau}
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WHO GUIDELINES ON THE PHARMACOLOGICAL TREATMENT OF PERSISTING PAIN IN CHILDREN WITH MEDICAL ILLNESSES. GENEVA: WORLD HEALTH ORGANIZATION; 2012.
IMPROVED PAIN SCALE

1. IT MIGHT BE AN ITCH
2. I JUST NEED A BANDAID
3. ITS KIND OF ANNOYING
4. THIS IS CONCERNING BUT I CAN STILL WORK
5. BEES?
6. BEES!
7. I CANT STOP CRYING
8. I CANT MOVE IT HURTS SO BAD
9. MAULED BY A BEAR OR NINJAS
10. UNCONSCIOUS