Objectives

1. Identify physiologic and behavioral responses to pain, as well as reliable instruments to measure pain.
2. Discuss nonpharmacologic and pharmacologic strategies for pain management.

Prospective study in NICU showed minimal procedural analgesia despite perception of pain by providers

NICU: 3-4 handling interventions/hour, and 5-24 painful procedures/day

Pain: Historical Perspectives

- Universally feared, yet ignored in newborn care until recently
  - lack of research and understanding
  - preverbal patient
  - safety concerns
  - Myths and ignorance minimized importance of neonatal pain relief

Pain: Historical Perspectives

- Currently
  - Newborn Pain Assessment and Management: Guidelines for Practice, 2012. Walden & Gibbins. NANN

CPS/AAP and NANN

- Ethical responsibilities
- Repeated exposure to painful exposures has known consequences
  - Altered pain sensitivity
  - Neuroanatomic and behavioral change
  - Growing concern about emotional, behavioral, and learning disabilities
  - "Double hit" phenomenon
Myth: Neonates don’t feel pain

Physiology: CNS Transmission
- Sensory neurons (nociceptors)
- Afferent nerve pathways
  - carry impulses from nociceptors to spinal cord, then to cerebral cortex
  - triggers cortical awareness
- Efferent Nerve pathways
  - send impulses back to motor and biochemical neurons
  - autonomic awareness with reflexive withdrawal

Fetal Neurophysiology
- Sensory neurons (nociceptors)
  - 7th week: found around mouth and face
  - 20th week: cover entire body
- Fetus has more sensory nerve endings than adult, closer to skin surface
**Fetal neurophysiology**

- Afferent nerve pathways
  - 12th week: begin to develop from periphery to spinal cord
  - 24-26th week: pathway from cord to brain completed
- Efferent nerve pathways
  - Develop more slowly, continue postnatally

**CNS Maturation: Neuromodulators**

- Neuromodulators (norepinephrine, serotonin) control pain signals
  - Reduce or block continued transmission of painful stimuli
  - Genetic variations
  - Ability to modulate (inhibit pain) undeveloped until 36-40 wks

**Pain may be prolonged**

- Lack of neuromodulators results in prolonged and increased pain responses
- Symptoms may be immediate or delayed

**Children with past pain experience**

- Preterms (28-32 wks) exposed to multiple painful/noxious stimuli compared with children without past pain experiences
  - different pain responses
  - less reactive to bumps/bruises
  
    
    Grunau, Whitfield, & Petrie (1994)

  - Increased somatization shown in 4-5 year olds who were former LBW
    
    Grunau, Whitfield, Petrie & Fryer, 1994

**Myths:**

**NB's don't remember pain**

**NB pain is only temporary**

**Pain perception and response**

- Learning about pain occurs with first pain experience, and has profound impact on subsequent pain perception and responses

**Altered long-term pain response**

- Chemical irritant applied to paw
  - Increased number and responsiveness of nerves in spinal cord on affected side
    
    Anand, 1999

- NB rats subjected to multiple needle sticks
  - Lower pain thresholds at 3 weeks
  - As adults, demonstrated more anxiety and defensive withdrawal behaviors
    
    Ruda, 2000
Tissue injury triggers inflammatory response and hypersensitivity.

- Sensitivity persists and extends into surrounding healthy tissue.

- Proliferation of nerve endings in injured area worsens pain experience.

- Hyperinnervation can cause pain and hypersensitivity long after wound healing.

- Even touch can be transmitted as pain.

**Touch may be painful**

- Nerve fibers that transmit pain and touch messages are located in close proximity in the dorsal horn of spinal cord.

- Touch impulses may “jump” over to the pain pathway, so touch may be perceived as pain.

- Observed in animal models when pain pathway was frequently activated.

**Preterm neural plasticity**

- Capability of brain to be formed/molded.

- Every experience has potential to alter normal brain development.

- Brain grows redundant connections among neurons from fetal period onward.

- Connections that are used are stabilized; those that are not used are “pruned.”

**Neural plasticity and permanence?**

Overstimulation of one neural pathway (“bad touch” or pain pathway) can lead to understimulation and underdevelopment of other pathways (“good touch” pathway).
**NB pain is not just temporary**

At follow-up, preterms show many differences from term counterparts, suggesting alternative brain development.

**Myth: If an infant isn't crying, he isn't in pain**

- Preterm or ill NB's may exhibit less robust behavioral response
- Lack of response doesn't mean “no pain”
  - Delayed, cumulative or absent
  - Energy conservation
- Physiological cues
- Behavioral cues

**Most common symptoms in infants**

- ↑ heart rate
- ↑ respiratory rate
- ↑ blood pressure
- Palmar sweating
- Crying
- Body movements
- Facial expression
Other responses to pain
- Desaturations and/or cyanosis
- Pallor or flushing
- Muscle tremors
- Hypertonicity/hypotonic
- Sleep/wake cycles changes
  - more wakeful or lethargic
- Fussy, irritable, listlessness
- Feeding difficulties

Stress response to pain
- Pain triggers "fight or flight" response
- Sympathetic nervous system activated
- Release of glucocorticoids such as cortisol, epinephrine and norepinephrine

Stress response to pain
- Sympathetic nervous system can’t cope with persistent pain
- "Protective apathy" with return to baseline physiologic parameters
- Doesn’t mean that NB is no longer in pain

Agitation as a symptom of pain
- Eliminate other causes of agitation first
  - Respiratory distress
  - Neurologic irritability
  - Noise
  - Light
  - Handling

Assessment: First step in pain relief
- Caregiver’s suspicion of pain
- If it would hurt an adult, it should be considered painful to an infant
- Assess often to keep good pain control, and to see if interventions are effective
- Pain scale that fits your population

Goals of neonatal pain management
- Reduce number of painful experiences
- Maximize infant’s ability to cope with and recover from painful experience
- Minimize intensity, duration and physiologic cost of pain experience
**Pain management**

- Synergistic effect
  - Non-pharmacologic measures always
  - Pharmacologic methods as needed

**Non-pharmacologic measures**

- Developmentally supportive care
- Cue-based care
- Supportive containment
- Reduce excessive light and sound
- Minimal handling protocols

**Supportive Containment**

- Swaddling
  - May reduce pain by providing gentle stimulation across proprioceptive, and tactile sensory systems
  - Reduced pain response seen in preterms during/after heelsticks Cignacco et al, 2007

- Facilitated tuck may significantly reduce pain response
  

**Nonnutritive Sucking (NNS)**

- Reduces pain responses in preterm/term
- May provide analgesia by stimulating ororactile and mechanoreceptors
- Rapid efficacy, but appears to stop almost immediately when sucking stops
- Rebound distress if pacifier removed
- Pain relief greater with NNS and sucrose, colostrum or breast milk

**Oral Sucrose**

- Review of 44 RCT's showed sucrose decreased pain responses during heel stick and venipuncture Stevens et al, 2010
- Best response when sucrose given to tip of tongue about 2 minutes before pain stimuli
Oral Sucrose

- Sweet taste may trigger endogenous opioid release
- No benefit if given NG
- Safety of multiple doses not established
- Cautious use for extremely preterm, critically ill, NEC or GI disorders

Does breastfeeding offer analgesia?

- In a systematic review, breastfeeding, breast milk, or glucose/sucrose reduced pain compared with placebo, positioning, or no intervention. If available, breastfeeding or breast milk should be used to alleviate procedural pain in neonates undergoing a single painful procedure.
  

Topical anesthetics

- EMLA (lidocaine and prilocaine), Ametop or Pontocaine (tetracaine/amethocaine)
- Approved for >37 weeks only
- Applied in advance of procedure
- Circumcision, PICC insertion, IV, PA stick
- Not shown to be effective with heel stick
- Repeated use should be limited

Heelsticks: More painful than venipunctures

- Three RCT (n=264) suggested venipuncture as opposed to heel puncture significantly reduces pain response.
  
  Gilbert and Franck. 2001
- Topical anesthetics appear ineffective in reducing pain response to heel sticks
- Utilize containment, sucrose or BF, etc
- Mechanical lancets preferable

Avoid “wind-up” phenomenon

- Handling prior to painful procedures can heighten nociceptive pathway activity
- Accentuate pain response
- Minimize handling prior to procedures

Avoid “wind-up” phenomenon

- After pain exposure, sensitivity is accentuated by increased excitability of nociceptive neurons in dorsal horn
- Benign stimuli may be felt as painful
- May persist well after pain experience
- Avoid routine care after procedures
**Pharmacologic Management**

- Continue nonpharmacologic measures
- Non-pharmacologic measures alone not adequate for moderate or severe pain
- Analgesics indicated, opioids if severe pain assessed or anticipated

**Nonopioids: Acetaminophen**

- NSAIDS for mild to moderate pain
- Mechanism for reducing pain is unclear
- Shown to reduce pain responses during skin excision, improve scores post-circ
- May give with opiates for additive effect, that allows lower dosages of both medications
- Metabolized by liver, avoid overdosing

**Opiate analgesia: Morphine & Fentanyl**

- Binds with receptors to alter pain perception
- Few hemodynamic side effects if well hydrated and given slowly (4-5 min)
- Use caution with hypotensive preterms
- Longer half life and delayed clearance

**Opiates & Respiratory Depression**

- Decreases RR and depth
- Gradual or abrupt
- Shallow respirations rather than slow RR
- Possibly desaturations
- Stimulate/PPV with O2 prn, give Narcan

**Pain treatment doesn’t lead to addiction**

- Infants needing long term pain control may become tolerant, need higher doses
- Prolonged therapy may lead to dependence
- Best managed by using opiate weaning protocol in conjunction with scoring tool

AAP: “Proven and safe therapies remain underused for numerous minor, yet painful procedures, that are part of routine medical and nursing care”