When Acute Pain Becomes Chronic

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Disclosures

- Nothing to Disclose related to the topics discussed in this lecture
Learning Objectives

- Review pain classifications
- Briefly review pain physiology and anatomy
- Describe the phenomenon of the transition from acute to chronic pain
- Review risk factors and predictors
- Discuss some clinical strategies that may reduce conversion of acute postoperative to chronic pain

Pain Management

“We must acknowledge, to ourselves and to our nonhospice/palliative care colleagues, that providing optimal pain care is difficult. . . . the trap . . . is to minimize how hard pain management truly is . . . .”

Pain Classifications

- Pain has been, and is classified:
  - Temporal: acute, subacute, chronic
  - Frequency: intermittent and consistent . . .
  - Etiology: cancer and noncancer
  - Location: headache, low back pain . . .
  - Functional or initiating: inflammation, post nerve injury etc . . .
  - Mechanism: peripheral neuropathic pain, small fiber neuropathy, etc . . .

- Proper diagnosis critical for treatment
Acute Pain

- Generally sudden onset
  - Usually obvious identifiable cause
    - Injury/disease/iatrogenic (e.g., surgery)
    - Short duration 3-6 months
    - Intensity generally variable and indicative of severity of underlying condition or situation
  - Characteristic symptoms
    - Redness, swelling, throbbing
  - Characteristic behaviors
    - Rubbing, moaning, crying, etc

Acute Pain

- Pain is not Benign
  - Pulmonary
    - TV - RR
    - Pneumonia
  - Immune System
    - Delays Healing
  - Cardiovascular
    - Hypertension
    - Tachycardia
  - Genitourinary
    - H₂O & Na Retention
  - Gastrointestinal
    - Ileus, Constipation
  - Neurologic
    - Delirium
  - Musculoskeletal
    - Muscle spasms
  - Psychological
    - Depression
    - Anxiety
Chronic Pain

- Persistent (>3-6 months)
- Frequently a thorough evaluation will elucidate cause
- Prolonged functional impairment
  - Physical
  - Psychological
- Characteristic behavior may or may not be associated
  - Insomnia, anorexia, irritability, and depression
- More difficult to manage than acute pain

Pain Treatment and Definitions

- Mechanism-based treatment elusive
  - Comprehensive mechanism based pain taxonomy, definitions, and physiology elusive
- Treatment algorithm elusive
- Selective drugs affect multiple pain types
  - “Broad spectrum approaches”
  - “Broad spectrum analgesics”
Pain Models: Biomedical

- Probably oversimplified
- Incomplete
- Explains pain through etiology
- May lead to unrealistic expectations
  - Both clinician and patient
- Pain is usually nociceptive or neuropathic


Pain Models: Biopsychosocial

- More complex
- Recognizes pathophysiology and psychological combined role
- Cultural background
- Social interactions
  - Workplace
  - Home
  - Health system

Clinical Relevance of Pain Models

<table>
<thead>
<tr>
<th>Biomedical Model</th>
<th>Biopsychosocial Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most appropriate for acute pain</td>
<td>More useful for chronic pain</td>
</tr>
<tr>
<td>Emphasizes peripheral nociception</td>
<td>Central mechanisms involved</td>
</tr>
<tr>
<td>Focuses on physical disease mechanisms</td>
<td>Focuses on illness behavior, including cognition and emotional response</td>
</tr>
<tr>
<td>“Reductionistic” approach</td>
<td>Multidimensional systems approach</td>
</tr>
<tr>
<td>Medical management approach</td>
<td>Self-management strategies important</td>
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</tbody>
</table>


Types of Pain

- Nociceptive pain
  - Activation of high-threshold peripheral neurons by noxious stimuli (e.g., mechanical, chemical, thermal)
  - Fades once peripheral source is removed
- Neuropathic pain
  - Arises after CNS sensory transmitting nerve injury to nerves
  - Combined sensory loss and paradoxical hypersensitivity
  - If nerve injury occurs during surgery, a neuropathic pain component may persist
- Descriptive terminology:
  - “The meaning and connotation of these different terms may vary widely” (Turk & Okifuji, 2001)

Pain Physiology
Pain Physiology and Anatomy

■ Peripheral sensitization
  — Tissue damage ⇔ Increased nociceptor sensitivity
    • Nociceptor firing sensitivity increased
    • Nociceptor spontaneous activity
    • Lowered thresholds
    • Heightened responsiveness
    • Responsiveness depends on receptor history

Pain Physiology and Anatomy (cont’d)

■ Peripheral sensitization
  — Algogenic peptides couple with receptors
    • Bradykinin, substance P, prostaglandins
    • G-protein-coupled subtype
    • Triggers phosphorylation
      — TXR sodium channels
      — Calcium Channels
  — Increased neuronal barrage to CNS
    • Resultant functional changes in CNS and spinal cord
Peripheral Sensitization


Pain Perception

- Things necessary for nociceptors to relay pain to the CNS
  - A brain
  - Transduction
  - Action potential generation
  - Transmission
  - Signal transmission to the thalamus
  - Signal transmission to the cerebral cortex
- Each event controlled separately and potential treatment targets

Aδ fibers
C fibers
Aβ fibers

Pain Physiology and Anatomy

- Descending modulation of persistent pain
  - Links periaqueductal gray (PAG), rostral ventromedial medulla (RVM), and spinal cord
  - Rostral ventromedial medulla
    - “Enhanced modulation clearly includes shifts in the balance between inhibitory and facilitatory components” (Dubner, 2002)
      - Peripheral sensitization potentially results in imbalance
      - Neural tissue injury can upset balance

Normal Pain Pathways

Key:
- RVM = rostroventral medulla
- PAG = periaqueductal grey
- C = cingulate cortex
- F = frontal cortex
- SS = somatosensory cortex
- A = amygdala
- H = hypothalamus
- Ascending pathway
- Descending pathway

Pain Physiology and Anatomy

“..the biggest hurdle is that the exact mechanisms for pain have not been definitively established for any condition. ... the unproven assumption that important mechanistic similarities connect the many different types of neuropathic pain.”

Rowbotham, 2005

Transition From Acute to Chronic Pain

- Neuroplasticity (Voscopoulos, 2010)
  - Compensatory mechanism that allows the brain to compensate for injury adjust activity accordingly in response to new situations or to changes in environment
  - Involves either reversible inflammatory changes or physical remodeling of neuronal cytoarchitecture
  - ↓ inhibition of pain modulation
  - Ultimately leads to central sensitization (neuronal hypersensitivity)

Modulation vs Modification

- **Modulation**
  - Reversible changes in primary sensory and central excitability

- **Modification**
  - Long-lasting changes in the expression of:
    - Transmitters
    - Receptors
    - Ion channels
  - More likely the link from acute → chronic pain


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Postoperative Chronic Pain as a Model
Chronic Postoperative Pain

- Poorly understood, poorly characterized
  - Complex and no clear distinction from acute to chronic
  - Neuropathic? Inflammatory? Ongoing nociception?
  - At least in part neuropathic resulting from neuroplastic changes

- Postprocedural pain (IASP, 1994): “a persistent pain state that is apparent more than 2 months after operation and cannot be explained by other causes”

Chronic Postoperative Pain (cont’d)

- First reference in 1998
  - 40% of 5,130 chronic pain patients in 10 UK pain clinics posttrauma or surgery
  - Not limited to major surgery
    - Frequent problem identified postherniorrhaphy
  - Overall, the incidence of chronic pain after major surgery is estimated to lie in the range of 20% to 50%
  - Relatively minor operations such as inguinal hernia repair or a C-section seem ~10%

Incidence of Chronic Postoperative Pain

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Incidence of Chronic Pain (%)</th>
<th>Estimated % Severe (≥5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amputation</td>
<td>30-85</td>
<td>5-10</td>
</tr>
<tr>
<td>Thoracotomy</td>
<td>5-65</td>
<td>10</td>
</tr>
<tr>
<td>Mastectomy</td>
<td>11-57</td>
<td>5-10</td>
</tr>
<tr>
<td>Inguinal hernia</td>
<td>5-63</td>
<td>2-4</td>
</tr>
<tr>
<td>CABG</td>
<td>30-50</td>
<td>5-10</td>
</tr>
<tr>
<td>C-Section</td>
<td>6-55</td>
<td>4</td>
</tr>
<tr>
<td>Cholecystectomy (open)</td>
<td>3-50</td>
<td>?</td>
</tr>
<tr>
<td>Vasectomy</td>
<td>0-37</td>
<td>?</td>
</tr>
<tr>
<td>Dental surgery</td>
<td>5-13</td>
<td>?</td>
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Chronic Postoperative Pain

Predisposing factors include:
- Psychosocial status (eg, anxiety)
- Pre-existing pain/recurrence/high pain sensitivity
- Genetics
- Gender (female)
- Age??
- Coping skills
- Co-existing disease/type of disease
- Adjuvant therapy (eg, radiation, chemotherapy)

Psychosocial Status\textsuperscript{1,2}

- Expectation of pain
- Fear, anxiety, depression
- Past experiences
- Social environment
- Work-related factors (eg, disability, Workers Compensation)
- Prior level of physical activity
- Neuroticism

Pre-existing Pain

- High correlation with the development of chronic neuropathic pain\textsuperscript{1}
  - Amputees with severe phantom pain often have more intense preamputation pain\textsuperscript{1}
  - Similar association with intensity of chronic pain after
    - Breast surgery\textsuperscript{2}
    - Thoracotomy\textsuperscript{3}
    - Inguinal herniorrhaphy\textsuperscript{4}

Genetics

- High level of nociceptive sensitivity
  - Inheritable susceptibility
  - Response to analgesics
    - Polymorphisms of opioid-receptor sites
  - Catecholamine-O-methyltransferase (COMT) polymorphisms
    - Altered pain sensitivity


Other Risk Factors

- Age
  - Older people less likely to transition from acute to chronic postoperative pain
  - Opposite with postherpetic neuralgia

- Gender
  - Females seem to be more likely

- Coping skills
  - Catastrophizing

- Co-existing disease/therapeutic causes
Other Effective Factors

- Anesthetic technique
- Surgical approach
  - Duration/multiple procedures
  - Nerve damage
  - Postop infection/prolonged inflammation
- Recurrence or worsening of condition


Potential Therapeutic Approaches
Acute Pain Service

- Goal to reduce and improve postoperative pain
  - Secondary goal to decrease acute → chronic
  - Team:
    - “It has responsibility for the day to day management of patients with acute pain and for providing an appropriate level of care and monitoring, adjusted to the clinical condition of the patient and the technique used.”
      (Royal College of Surgeons, 1990; Werner, 2002; Meissner, 2015)

Acute Pain Service (cont’d)

- “In the US and Western Europe, a high proportion of hospitals have an acute pain service, but the structure and responsibilities vary both within and between countries.”
  (Meissner, 2015)

- UK hospital survey (Powell 2004):
  - Described their acute pain service as
    - 17% no acute pain service
    - 52% as “struggling acute pain service”
    - 30% as “thriving acute pain service”
Potential Treatments of Postsurgical Pain

- All may reduce likelihood of chronic pain
  - Intrathecal clonidine (De Kock, 2005)
  - Intraoperative ketamine (Lavand'homme, 2005)
  - Epidural analgesia (Senturk, 2002)

Approaches

- Multimodal treatments
  - Preventing neuroplastic changes
    - Aggressively treat acute pain
    - Maintenance of activity
  - Pharmaceutical agents
  - Ice/heat
  - Topical agents
  - Physical therapy
  - Whatever works ... 😊

Case Study

- 85 year old female
  - Brought into the hospital for further evaluation
  - Presents with severe left lower quadrant abdominal pain

- What are you going to do?
Case Study (cont’d)

- History:
  - Pain has been present on and off for over 15 years
  - She has had multiple imaging and multiple endoscopies
  - She has been tried on multiple medications
  - No other serious medical or past psychiatric history

- Social history:
  - No ETOH, TOB or drug history or concerns

- What are you going to do now?

Case Study (cont’d)

- Physical examination
  - Patient states she can’t remember ever having an examination
  - Trigger point in the left lower quadrant
    - Reproduced patient’s pain “exactly”
  - Remainder of physical examination not significant

- What are you going to do now?
Case Study (cont’d)

- Treatment
  - Injection of bupivacaine and dexamethasone
  - Pain reproduced with the injection
  - Pain resolved within 5-10 minutes
  - Didn’t recur during hospitalization

Conclusion
Conclusion

“Finally, there is a tremendous gap in the literature on postsurgical pain duration, with a great need for studies to test whether we can intervene therapeutically to reduce the duration of acute and subacute pain for the 34 million Americans undergoing surgery every year.”

Wang, 2009

Conclusion (cont’d)

- The transition from acute to chronic pain occurs in discrete pathophysiological steps involving multiple signaling pathways
- The duration and intensity of the initial stimulus leads to both peripheral and central sensitization that synergistically exacerbate pain perception
- A multimodal therapeutic approach may be best suited to target the complex mechanisms leading to the transition from acute to chronic pain

Conclusion (cont’d)

“Physicians, like beer, are better when they are old.”

Thomas Fuller, 1608-1661

Questions?