When Acute Pain Becomes Chronic

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Disclosures

- Nothing to Disclose
Learning Objectives

- Describe the phenomenon of the transition from acute to chronic pain
- Review risk factors and predictors
- Identify clinical strategies to reduce/modify the risk of developing chronic pain

Some Key Questions

- What is the relationship between acute and chronic pain?
- Are there specific patients who are “at risk”?
- What are the circumstances of this risk?
- What (if anything) can be done to prevent this transition?
The “Vicious” Circles

Acute Pain
Acute Pain

- Generally sudden onset
  - Certainly recent onset
  - Usually has an obvious identifiable cause
    - Injury/disease/iatrogenic (e.g., surgery)
    - Short duration (< 1 month)
    - Intensity generally variable and indicative of severity of underlying condition or situation
  - Characteristic symptoms
    - Redness, swelling, throbbing
  - Characteristic behaviors
    - Rubbing, moaning, crying, etc

Chronic Pain
Chronic Pain

- Persistent (generally 3 months or longer)
- Often undetermined onset
- Often the result of some chronic disease, condition, or situation
- May have no obvious cause

Chronic Pain

- Prolonged functional impairment
  - Physical
  - Psychological
- May or may not be associated with characteristic behavior, such as insomnia, anorexia, irritability, and depression
- Often more difficult to manage than acute pain
Subacute Pain?

Acute Pain Mechanisms

- Postoperative pain similar to trauma
- Varies according to:
  - Intensity
  - Quality
  - Duration of stimulus
- Involves activation of peripheral nociceptors
Peripheral Sensitization


Pain Perception

- Five things are necessary for nociceptors to relay pain information to the CNS
  - Transduction
  - Action potential generation
  - Transmission
  - Signal transmission to the thalamus
  - Signal transmission to the cerebral cortex
- Each event controlled separately and potential targets for treatment

Pain Models

- Biomedical model
  - Probably oversimplified
  - Incomplete
  - Explains pain through etiology
  - May lead to unrealistic expectations
    - Clinician
    - Patient
  - Pain is usually nociceptive or neuropathic


Pain Models

- Biopsychosocial model
  - More complex
  - Recognizes the combined role of pathophysiology and psychological state
  - Cultural background
  - Social interactions
    - Workplace
    - Home
    - Health system

Chronic Pain


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>
</tr>
</tbody>
</table>

End Result

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

- Inflammatory pain
  - Heightened pain sensitivity in response to tissue injury and inflammation
  - Results from release of mediators that reduce pain threshold
  - Can outlast tissue injury for hours or days

Types of Pain

- **Neuropathic pain**
  - Arises after injury to nerves or sensory transmitting systems in the CNS
  - Combined sensory loss and paradoxical hypersensitivity
  - If nerve injury occurs during surgery, a neuropathic component of pain may develop and persist
Hyperalgesia

- **Primary**
  - Occurs in the periphery

- **Secondary**
  - Occurs within the CNS and precedes central sensitization
  - Thought to be a possible source of chronic postoperative pain

Inflammation

- Occurs in the face of tissue damage with release of chemical mediators
  - Result
    - Inflammatory response
    - Nociceptor sensitization and threshold reduction
    - Short-term central sensitization

Transition from Acute to Chronic Pain

- **Neuroplasticity**
  - Compensatory mechanism that allows for neurons in the brain to compensate for injury and disease and 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.
Acute Pain $\rightarrow$ Chronic Pain

Case #1

- A 44-year-old woman 3 months s/p right radical mastectomy presenting the chief complaint of continuous moderate to severe pain average of 8-9/10 in her right arm of 3 months duration
  - The patient states that the pain is interfering with sleep, performance of daily activities, and use of the affected arm
  - The patient also reports that she has been in pain to this degree or greater since the immediate post-operative period
  - Physical examination is negative for evidence of an infectious process
Postoperative Chronic Pain as a Model

Normal vs Abnormal?
Chronic Postoperative Pain

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

- The IASP defines postprocedural pain as
  "a persistent pain state that is apparent more than 2 months after operation and cannot be explained by other causes"

Incidence of Chronic Postoperative Pain

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Incidence of Chronic Pain (%)</th>
<th>Estimated % Severe (&gt;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>
</tr>
</tbody>
</table>


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, Worker's 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 pre-amputation pain\textsuperscript{1}
  - Similar association with intensity of chronic pain after:
    - Breast surgery\textsuperscript{2}
    - Thoracotomy\textsuperscript{3}
    - Inguinal herniorrhaphy\textsuperscript{4}

Pre-existing Pain

Genetics

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

Other Factors

- Age
  - Older people less likely to transition from acute to chronic postoperative pain
  - Opposite with post-herpetic neuralgia
- Gender
  - Females seem to be more likely
- Coping skills
  - Catastrophizing
- Co-existing disease/therapeutic causes

Other Factors

- Anesthetic technique
- Surgical approach
  - Duration/multiple procedures
  - Nerve damage
  - Post-op infection/prolonged inflammation
- Malignancy/recurrence of condition

## Chronic Postoperative Pain

### Characteristic features of neuropathic and inflammatory pain

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Neuropathic</th>
<th>Inflammatory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous pain in &quot;damaged&quot; area</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Heat-related hyperalgesia</td>
<td>Rarely</td>
<td>Often</td>
</tr>
<tr>
<td>Cold-related allodynia</td>
<td>Often</td>
<td>Rarely</td>
</tr>
<tr>
<td>Hyperpathia (exaggerated relative to stimulus)</td>
<td>Often</td>
<td>Never</td>
</tr>
<tr>
<td>After-sensations</td>
<td>Often</td>
<td>Rarely</td>
</tr>
<tr>
<td>Paroxysms</td>
<td>Often</td>
<td>Rarely</td>
</tr>
<tr>
<td>Throbbing</td>
<td>Rarely</td>
<td>Often</td>
</tr>
<tr>
<td>Sensory loss</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Motor deficit</td>
<td>Often</td>
<td>No</td>
</tr>
</tbody>
</table>


### Chronic Regional Pain Syndrome (CRPS/RSD) as a Model
Case #2

- 42-year-old oral surgeon with Fx (R) thumb after skiing accident
  - Pain with injury
  - Requires ORIF
  - Pain with recovery
  - Pain after bone healing
  - At 10 weeks patient presents with swelling, erythema, exquisite pain

CRPS

Persistent Pain

- Time off work, money worries, relationship concerns
- Negative thinking, fear of the future, depression/mood swings
- Weight gain/loss
- Stress/fear/anxiety/anger/frustration

Being less active
- Loss of fitness, weak muscles and joint stiffness
- Create "no go" lists of things you cannot do
- Sleep problems/tiredness/fatigue
**CRPS**

**Approaches**

- **Preventing neuroplastic changes**
  - Aggressively treat acute pain
  - Maintenance of activity

- **Multimodal treatments**
  - N-methyl-D-aspartic acid receptor antagonists
  - Cyclo-oxygenase-2 inhibitors
  - Cannabinoids?
  - Transient receptor potential cation channel VI (TRPV1) agents

Take Home

- 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

Approaches

- Communication
  - Understand the patient’s perspective
  - Emphasize realistic expectations
  - Stratify risk for acute → chronic
- Vigilance
  - Think about all possible causes of acute/subacute pain
    - Expeditious/effective/multimodal treatments
- Prevention

Questions?