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

Psychological Vicious Circle
- Anger, anxiety, fear, distress etc.
- Impoverished mood
- Depression
- Increased perception of pain

Physical Vicious Circle
- Activity avoidance
- Pain with decreasing activity
- Further activity avoidance
- Further deconditioning
- Progressive deconditioning
- Pain
Acute Pain
Acute Pain

- Generally sudden onset
  - Certainly recent onset
  - Usually has an obvious identifiable cause
    - Injury/disease/iatrogenic (eg, 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 (eg, 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

Let’s Not Forget the Brain...
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 → Chronic Pain

- Painful stimulus
- Acute pain
- Short-term poor sleep (reversible if pain is managed)
- Chronic pain
- Altered quality of life
- Long-term poor sleep
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”

Chronic Postoperative Pain

- First reference in 1998\(^1\)
  - 40% of 5,130 chronic pain patients in 10 UK pain clinics post-trauma or surgery
  - Not limited to major surgery
    - Frequent problem identified post-herniorrhaphy
  - Overall, the incidence of chronic pain after major surgery is estimated to lie in the range of 20%-50\(^2\)
  - Relatively minor operations such as inguinal hernia repair or a C-section seem ~10\(^2\)

## 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\(^1\)
  - Amputees with severe phantom pain often have more intense pre-amputation pain\(^1\)
  - Similar association with intensity of chronic pain after:
    - Breast surgery\(^2\)
    - Thoracotomy\(^3\)
    - Inguinal herniorrhaphy\(^4\)

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Pre-existing Pain

Vicious Cycle of Uncontrolled Pain

- Pain
- Avoidance Behaviors
- Decreased Mobility
- Diminished Self-Efficacy
- Social Limitations
- Altered Functional Status
Genetics

- High individual level of sensitivity to nociceptive stimuli and 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 “damaged” 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

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

Sometimes the arrows can also go anti-clockwise as well. For example - time off work can lead to negative thinking fear of the future - can lead to stress, fear etc.
CRPS

Mechanism of RSD

A. Original injury initiates a pain impulse carried by sensory nerves to the central nervous system.

B. The pain impulse in turn triggers an impulse in the sympathetic nervous system which returns to the original site of injury.

C. The sympathetic impulse triggers the inflammatory response causing the vessels to spasm leading to swelling and increased pain.

D. The pain triggers another response, establishing a cycle of pain and swelling.

Resulting condition with burning extremity pain, red mottling of the skin
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?