Transition from Acute Post Surgical Pain to Chronic Post Surgical Pain

Prof E Shipton
University of Otago, Christchurch Medical Director: Pain Management Centre, CDHB

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Chronic Pain

Acute Pain

up to 30% postoperative patients show pain scores higher than 3 on VAS

every chronic pain was once acute

Acute persistent postoperative pain in 1 of 10 surgical patients

Chronic pain after 1 of every 100 operations, irrespective of type of surgery

22.5% of 5130 patients presenting to a pain clinic in UK have previous surgery as pain cause (Crombie IK et al. Pain 1998;76:167-71)
Chronic Pain
The Somatosensory System

Frontal Cortex

Descending Paths

Descending Facilitatory

Glial Cell Activation

Peripheral Receptor Activation

Somatosensory cortex

Thalamus

Hypothalamus

Ascending Tracts

Midbrain

Medulla

Dorsal Horn

Spinal Cord

Periaqueductal Gray Matter
Enhanced Pain Management

Pronociceptive targets

Antinociceptive targets

↑ Inhibition

↓ Excitation
Neural Influences on Pain and Sensory Processing

**Facilitation**
- Substance P
- Glutamate and EAA
- Serotonin (5HT$_{2a, 3a}$)
- Nerve growth factor
- CCK

**Inhibition**
- Descending antinociceptive pathways
- Norepinephrine-serotonin (5HT$_{1a, b}$), dopamine
- Opioids
- GABA
- Cannabinoids
- Adenosine

(Phillips K. Best Pract Res Clin Rheumatol 2011;25(2):141-54)
<table>
<thead>
<tr>
<th>Types of surgery</th>
<th>Estimated incidence of chronic postoperative pain (%)</th>
</tr>
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<tbody>
<tr>
<td>Hysterectomy</td>
<td>15</td>
</tr>
<tr>
<td>Hip Surgery</td>
<td>10 – 20</td>
</tr>
<tr>
<td>Amputation</td>
<td>30 – 50</td>
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<tr>
<td>Breast surgery</td>
<td>20 – 30</td>
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<tr>
<td>Thoracotomy</td>
<td>30 – 40</td>
</tr>
<tr>
<td>Inguinal hernia repair</td>
<td>10</td>
</tr>
<tr>
<td>Coronary artery bypass</td>
<td>30 – 50</td>
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<tr>
<td>Caesarean section</td>
<td>10</td>
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</table>
Transition of Acute Postoperative Pain to Chronic Post Surgical Pain - a complex, poorly understood developmental process

- Patient-related factors
- Surgery-related factors
- Psychosocial factors
- Polymorphisms in human genes
- Socio-environmental factors

Postoperative pain (association of somatic, inflammatory, neuropathic, visceral pain)
Postoperative pain

**primary hyperalgesia**
- Local Tissue Injury
  - spontaneous firing of nociceptors
  - increased sensitivity to stimuli

**secondary hyperalgesia**
- CNS changes
  - sensitisation and pain in a wider area
  - memory at supraspinal sites

primary analgesics have minor effects on secondary hyperalgesia
Graphic depiction of brain regions receiving nociceptive input and activated in MRI studies.

BOLD signal hindpaw in awake rats - 50 °C

Neurosci Lett 2012;520(2):129-30
Physical pain

Social distress

Activate Anterior Cingulate Cortex

common neurobiological pathways
normal paw, intradermal injection of PGE$_2$ ➔ episode of acute hyperalgesia

Carrageenan injection lasts less than 4 days (grey curve) ➔ priming ➔ hyperalgesia

<table>
<thead>
<tr>
<th>Risk factors for developing persisting postsurgical pain</th>
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<tbody>
<tr>
<td>Mark all patients with Risk Factors</td>
</tr>
<tr>
<td>Preoperative risk factors</td>
</tr>
<tr>
<td>Follow up at Discharge</td>
</tr>
<tr>
<td>Female Gender, younger age</td>
</tr>
<tr>
<td>Pain prior to surgery whether acute or chronic</td>
</tr>
<tr>
<td>Preop Pain at surgical site or distant</td>
</tr>
<tr>
<td>Inefficient Diffuse Noxious Inhibitory Control</td>
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</tbody>
</table>
## Risk factors for developing persisting postsurgical pain

<table>
<thead>
<tr>
<th>Preoperative psychological risk factors</th>
<th>Long-term fear, and pain Catastrophising (Sommer et al, 2010)</th>
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<tbody>
<tr>
<td>Preoperative anxiety, fear and depression</td>
<td>Low income, low self-rated health and lack of education</td>
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<tr>
<td></td>
<td>Cross-sectional studies support a positive relationship between history of traumatic or stressful life events and chronic pain</td>
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<td></td>
<td>Workers Compensation</td>
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</tbody>
</table>
## Risk factors for developing persisting postsurgical pain

<table>
<thead>
<tr>
<th>Preoperative social risk factors</th>
<th>Solicitous responding from significant others</th>
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<tbody>
<tr>
<td></td>
<td>Lack of social support</td>
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</table>
Risk factors for CPSP
Preoperative Genetic risk factors

Rodent Genetic studies association between genes and chronic pain after surgery

Polymorphisms in:

- **5-HTTLPR** (serotonin transporter) → burning mouth, IBS, fibromyalgia
- **IL1RN I** (encoding IL-1 receptor antagonist) + **MC1R** (encoding melanocortin-1 receptor) → vulvodynia
- **IL23R** (encodes receptor for IL-23) → Crohns
- **GCH1** (encodes GTP cyclohydrolase that catalyses cofactor for catecholamine, serotonin, NO) → radiculopathy after discectomy
- **COMT** (encoding COMT that inactivates dopamine, adrenaline, noradrenaline) → chronic pain entities
- **CACNA1, SCNIA** → Migraines
| Intra-operative risk factors | Site – greatest with intentional or unintentional nerve damage (e.g. thoracotomy, sternotomy, mastectomy, major limb amputation)  
IV fluid excess  
Extent of surgery (e.g. more invasive surgery) and duration  
Incision type (open vs minimally invasive)  
Nerve damage |
## Risk factors for developing persisting postsurgical pain

<table>
<thead>
<tr>
<th>Postoperative risk factors</th>
<th>Early unrelieved pain (days to weeks after surgery)</th>
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<tbody>
<tr>
<td>Exclude red flags (infection, bleeding, compartment syndrome)</td>
<td>Severe pain</td>
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<tr>
<td></td>
<td>Most analgesics consumed (7 days)</td>
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<td>Re-operations in same area</td>
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<td></td>
<td>Surgery in a previously injured area</td>
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<tr>
<td></td>
<td>Radiation and Chemotherapy</td>
</tr>
<tr>
<td>Postoperative risk factors</td>
<td>Pain catastrophising, Fear of movement associated with more pain and disability</td>
</tr>
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<td>---------------------------</td>
<td>----------------------------------------------------------------------------------</td>
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<tr>
<td></td>
<td>Pain hypervigilance</td>
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<td></td>
<td>Emotional numbing</td>
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<td>Low expectation of return to work</td>
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<td>Late return to work</td>
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</table>
Optimal Treatment of Acute Postoperative Pain

- accelerates recovery and rehabilitation
- achieves patient satisfaction
- reduces risk of persisting chronic pain syndromes
<table>
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<th>Prevention and Management of Risk Factors</th>
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<tbody>
<tr>
<td><strong>Preoperative prevention and management</strong></td>
</tr>
<tr>
<td>(Shipton EA. Trends Anaesth Critical Care, 2014; 4:67-70)</td>
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<tr>
<td><strong>Individualized education</strong></td>
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<tr>
<td><strong>Information</strong></td>
</tr>
<tr>
<td><strong>Address attitudes and concerns</strong></td>
</tr>
<tr>
<td><strong>Identify procedures causing severe pain</strong></td>
</tr>
<tr>
<td><strong>Identify patients with modifiable risk factors</strong></td>
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<tr>
<td><strong>Provide preoperative psychological interventions</strong></td>
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</table>
Prevention of Acute Persistent Pain

Minimise tissue trauma and nerve damage during surgery

Use standardised pain evaluation and treatment protocols

Use multimodal analgesic techniques
Use least painful surgical approach with acceptable exposure (keyhole surgery, microsurgical approach)

**Intraoperative Prevention**

- Use multimodal opioid sparing pharmacological analgesia in addition to afferent neural blockade
- Avoid nerve and tissue damage
- Use local anaesthesia at incision sites
Continue analgesia well into the postoperative period.

Bedside neurological examination if NP is suspected.

Measure pain levels.

Use enhanced Recovery Program.

Multimodal treatment for as long as surgical stimulus (inflammatory response) continues after the operation.

Postoperative Prevention
transdermal, buccal, intra-articular, intravesical routes

Transdermal drug delivery limited by stratum corneum

Toxicity of local anaesthetics and opioids

Iontophoresis, electroporation, microporation, phonophoresis

Lipid-based nanocarriers (liposomes, lipid-core micelles, and lipid nanocapsules)

Vesicular systems (ethosomes, transfersomes and niosomes)
Liposome for Drug Delivery

Lipid Soluble Drug in bi-layer
Lipid bi-layer
Drug crystallized in aqueous fluid

Liposome for Drug Delivery

(Shipton EA. Anesthesiol Res Pract 2012;2012:546409)
use rational analgesic drug combinations (NSAIDs, cyclooxygenase-2 inhibitors, paracetamol, gabapentanoids, ketamine, clonidine and local and regional anaesthetic techniques)

use gabapentin and pregabalin in surgery with high risks of neuropathic pain

supplement with opioid analgesics as needed

direct pain relief toward periphery (surgical wound and surrounding tissues)

Reduce opioid-related side effects

early mobilisation, recovery of bowel function); rapid return to ADL
Surgeons and Anaesthetists under Chair of Henrik Kehlet

PROSPECT Group

www. postoppain.org

lap cholecystectomy, primary total hip arthroplasty, abdominal hysterectomy, colonic resection, herniorrhapsy, thoracotomy and total knee arthroplasty

Integrate procedure-specific analgesic regimen into enhanced recovery care program with early oral feeding, mobilisation, and adjustments in other principles of surgical care (drains, catheters, tubes, and monitoring)
Obtain patient preoperative information

Preoperative carbohydrate

No preoperative bowel clearance

Avoidance of fluid excess - use of goal directed therapy

Pharmacological ↓ stress

Optimise organ dysfunction

No routine use of drains

No routine use of nasogastric tubes

Early oral feeding

Epidural analgesia or non-opioid multimodal analgesia

Early mobilisation

Objective pain assessment

No preoperative bowel clearance

Daily care maps

Discharge criteria
Take Home Points- Transition Acute Post Surgical Pain to Chronic Post Surgical Pain – complex

- Mark patients with risk factors for acute persistent pain
- Psychological factors (catastrophising, emotional numbing)
- Avoid intraoperative nerve damage
- Use least painful surgical approach with acceptable exposure
- Use low dose multimodal pharmacological analgesia in addition to afferent neural blockade

- Central sensitisation induced by surgery and maintained by peripheral input
- Measure pain – ‘the fifth vital sign’
- Optimal treatment of acute postoperative pain
- Continue effective perioperative analgesic regimens well into postoperative period
- Pain Genes that confer risk of CPSP
- Follow up patients with Risk factors on discharge
Discharge from hospital

Pain decreases

Step 1
Paracetamol
± NSAIDs
± Tramadol
± Opioids

Step 2
Paracetamol
± NSAIDs
± Tramadol

Step 3
Paracetamol
± NSAIDs

Limited period – for example up to seven days for opioids and then review

Huxtable et al 2011
Take Home Points - Transition Acute Post Surgical Pain to Chronic Post Surgical Pain

- Migraine, Fibromyalgia, Endometriosis, Irritable Bowel Syndrome
- Psychological factors (catastrophising, anxiety)
- Repeated Surgery
- Reverse pain ladder used to guide the weaning process
- Opioid Risk Tool
- Patient information - Do not take more medication than you have been prescribed. Take a little less each day

- If you are sleepy do not take any more medication until you are wide awake; subsequently take a smaller dose
- Is someone else notices that you are having trouble staying awake they should take you to the ED
- See your doctor if severe pain continues
Take Home Points - Transition Acute Post Surgical Pain to Chronic Post Surgical Pain

• Limit duration of opioid treatment to expected duration of pain
• Consider onset of neuropathic pain or CRPS
• If neuropathic pain is present, a trial of an anti-neuropathic analgesic is warranted (e.g. gabapentin).
• Consider patient’s psychological vulnerability to pain (distress, depression, anxiety, catastrophising) and decreased self-efficacy
• Consider red flags such as new or undiagnosed pathology as a cause (e.g. postoperative deep infection, ischaemia or periprosthetic fractures)
• Check that the patient is taking their medication
• Make sure the patient is using additional non-pharmacological pain management effectively
• Check for other risk factors for persistent pain (pain history at other sites, opioid tolerance)