CHRONIC PAIN
INTRODUCTION FOR
SURGERY RESIDENTS

Dr. Neilesh Soneji
Anesthesiologist and Pain Physician
TWH-UHN Dept of Anesthesiology and Pain Management
Women’s College Hospital
Assistant Professor - University of Toronto
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Objectives

• Define pain - IASP guidelines
• Pathophysiology chronic pain – differences from acute pain
• Define common terms: allodynia, hyperalgesia and dysesthesia
• Define and differentiate nociceptive and neuropathic pain
• Chronic pain assessment
• Review common screening tools pain and differentiate (BPI, DN4, quantitative sensory testing)
• Evidence-based guidelines treatment nociceptive pain and neuropathic pain
PAIN

an unpleasant experience

sensory

emotional

associated with actual or potential tissue damage or described in terms of such damage

The International Association for the Study of Pain

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.
Pain is the fifth vital sign
What if pain did not exist?

- Essential for protection from injury and recognition of the presence of injury

- Congenital/Acquired insensitivity to pain:
  - Hereditary Sensory and Autonomic Neuropathy (HSAN I – IV)
  - Diabetic neuropathy
  - Reduced life expectancy - repeated injuries, infections

- Absence of pain may be adaptive (i.e. soldier injured)
Chronic Pain

• Pain > 2 months (some definitions: > 6 months)

• Persisting beyond a reasonable amount of time for an injury to heal

• Persistent pain no discernible protective or reparative role

• Pain may become the disease or pathology
Burden of Chronic Pain

Figure 2. Incidence of pain in the USA compared with other major conditions. *Percentage of the US population who have reported a problem with each condition. Reprinted with permission from [American Pain Foundation 2011].
Chronic post surgical pain (CPSP)

- Post surgical procedure
- ≥ 2 months in duration
- Exclusion of other causes (malignancy, infection)
- Pain from pre-existing problem excluded
### CPSP: Epidemiology

#### Persistent postsurgical pain: risk factors and prevention

*Henrik Kehlet, Troels S Jensen, Clifford J Woolf*

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Estimated incidence of chronic pain</th>
<th>Estimated chronic severe (disabling) pain (&gt;5 out of score of 10)</th>
<th>US surgical volumes (1000s)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amputation²</td>
<td>30–50%</td>
<td>5–10%</td>
<td>159 (lower limb only)</td>
</tr>
<tr>
<td>Breast surgery (lumpectomy and mastectomy)³</td>
<td>20–30%</td>
<td>5–10%</td>
<td>479</td>
</tr>
<tr>
<td>Thoracotomy⁴⁻⁷</td>
<td>30–40%</td>
<td>10%</td>
<td>Unknown</td>
</tr>
<tr>
<td>Inguinal hernia repair⁸⁻¹⁰</td>
<td>10%</td>
<td>2–4%</td>
<td>609</td>
</tr>
<tr>
<td>Coronary artery bypass surgery¹¹⁻¹³</td>
<td>30–50%</td>
<td>5–10%</td>
<td>598</td>
</tr>
<tr>
<td>Caesarean section¹⁴</td>
<td>10%</td>
<td>4%</td>
<td>220</td>
</tr>
</tbody>
</table>

*Gall bladder surgery not included, since preoperative diagnosis of pain specifically from gall bladder is difficult and persistent postoperative pain could therefore be related to other intra-abdominal disorders. †National Center For Health Statistics, Ambulatory and Inpatients Procedures, USA, 1996.

**Table 1: Estimated incidence of chronic postoperative pain and disability after selected surgical procedures**
Figure 46-3

Physiology of Pain Perception

Pain perception point

Nociceptors (receptors)

A-delta fibers (fast transmission of sharp, localized pain)

Spinal ganglia

Lateral spinothalamic tract

Dorsal horn (pain signal modified)

C fibers (slow transmission of dull, burning chronic pain)
TABLE 1
The Main Characteristics of Primary Sensory Afferents Innervating Human Skin

<table>
<thead>
<tr>
<th>Fiber group</th>
<th>Receptor type</th>
<th>Modality</th>
<th>Axonal diameter (μm, appr. mean values)</th>
<th>Conduction velocity (ms⁻¹, appr. mean values)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-beta</td>
<td>Low-threshold mechanoreceptors</td>
<td>Discriminative touch</td>
<td>10</td>
<td>60</td>
</tr>
<tr>
<td>A-delta</td>
<td>Nociceptors</td>
<td>Pain</td>
<td>2.5</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Cool receptors</td>
<td>Temperature</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low-threshold mechanoreceptors</td>
<td>?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Nociceptors</td>
<td>Pain</td>
<td>1</td>
<td>&lt;2</td>
</tr>
<tr>
<td></td>
<td>Warm and cool receptors</td>
<td>Temperature</td>
<td>1</td>
<td>&lt;2</td>
</tr>
<tr>
<td></td>
<td>Itch receptors</td>
<td>Itch</td>
<td>1</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td>Low-threshold mechanoreceptors (CT)</td>
<td>Emotional touch</td>
<td>1</td>
<td>&lt;2</td>
</tr>
</tbody>
</table>

¹ Described in humans by Adriaensen, Gybels, Handwerker, and Van Hees, 1983. Their finding has not been confirmed, and the functional role of the receptors is unknown.

² Emotional touch being underpinned by CT afferents is a working hypothesis (Vallbo, Olausson, Wessberg, and Norsell, 1993; Olausson et al., 2002).
Representation in Cortex
Pain Processing – 4 Stages

- **Transduction** – Activation of nociceptors by tissue damage and resulting influx of cell mediators

- **Transmission** – Relay of signals from the site of injury to the brain

- **Modulation** – Mainly descending pain pathways. Can be sensitization or dampening of pain signals

- **Perception** – conscious awareness of pain
REPEAT TISSUE DAMAGE

Sustained Release of noxious substances

increase in the excitability of the afferent nerves by molecules that decrease the excitation threshold (Substance P & CGRP)
<table>
<thead>
<tr>
<th>Neurotransmitter</th>
<th>Receptor</th>
<th>Effect on Nociception</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substance P</td>
<td>NK-1</td>
<td>Excitatory</td>
</tr>
<tr>
<td>Calcitonin</td>
<td></td>
<td>Excitatory</td>
</tr>
<tr>
<td>Glutamate</td>
<td>NMDA</td>
<td>Excitatory</td>
</tr>
<tr>
<td>Aspartate</td>
<td>NMDA</td>
<td>Excitatory</td>
</tr>
<tr>
<td>ATP</td>
<td>P1, P2</td>
<td>Excitatory</td>
</tr>
<tr>
<td>Somatoatatin</td>
<td></td>
<td>Inhibitory</td>
</tr>
<tr>
<td>Ach</td>
<td>M1</td>
<td>Inhibitory</td>
</tr>
<tr>
<td>Enkephalin</td>
<td>μ, δ, κ</td>
<td>Inhibitory</td>
</tr>
<tr>
<td>B- Endorphin</td>
<td>μ, δ, κ</td>
<td>Inhibitory</td>
</tr>
<tr>
<td>Noradrenaline</td>
<td>A2</td>
<td>Inhibitory</td>
</tr>
<tr>
<td>Adenosine</td>
<td>A1</td>
<td>Inhibitory</td>
</tr>
<tr>
<td>Serotonin</td>
<td>5-HT</td>
<td>Inhibitory</td>
</tr>
<tr>
<td>GABA</td>
<td>A,B</td>
<td>Inhibitory</td>
</tr>
<tr>
<td>Glycine</td>
<td></td>
<td>Inhibitory</td>
</tr>
</tbody>
</table>
Neurochemical level

- Neurochemical mediators increase level of membrane excitability

- Substance P, CGRP, CCK, glutamate, aspartate

- Induced gene expression, increase in number and excitability of receptors

- Increased NMDA activity is pivotal in the development of chronic pain syndromes
Peripheral Sensitization

- Peripheral sensitization occurs at the level of the nociceptor
- Nociceptors and their neurons may display sensitization
- Decrease in the threshold to the same stimulus intensity
- Decrease in response latency
- Spontaneous firing to no stimuli
- Practically speaking, this results in an enhanced response to noxious stimulation or a newly acquired responsiveness to a wider range of stimuli (non-noxious)
Central Sensitization

- **Wind-up:** Prolonged depolarization second order neurons. WDR neurons increase frequency of discharge with same repetitive stimuli even after afferent C fiber input has stopped.

- **Receptor field expansion:** Dorsal horn neurons increase their receptive fields such that adjacent neurons become responsive to stimuli (whether noxious or not) to which they were previously unresponsive.

- **Multiple Other Mechanisms**
  - neuro-inflammatory processes
Pain Imaging - Functional MRI
Case: Mrs. B. Pain

45 y/o female 9 month history of severe leg pain
- MRI shows multilevel DDD, broad based disc herniation at L4/5 and L5/S1, moderate-severe spinal stenosis
- Referred for surgical intervention

• What do you want to know on pain history?
Pain History: Pain characteristics

- Onset
- Palliative and Provoking factors
- Quality (nociceptive/neuropathic/mixed)
- Radiation
- Severity
- Timing (duration)

Assessment tools:
- NRS
- Brief Pain Inventory
- Body Pain Diagram
- DN4
Figure.
Categorizing Chronic Pain

- **Nociceptive (Inflammatory)**
  - Somatic
  - Visceral

- **Mixed**
  - Central
  - Peripheral
  - Other

- **Neuropathic**

- **Superficial**
- **Deep**

References:
Types of Pain IASP definitions

- **Nociceptive Pain**
  - Pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors
  - i.e. A-delta (myelinated) and C-fibers (unmyelinated)

- **Neuropathic Pain:**
  - Pain initiated or caused by a primary lesion in the CNS/PNS
  - Lesion can be microscopic or gross

- **Nociplastic Pain:**
  - Pain from altered nociception
  - Despite no clear evidence of actual or threatened tissue damage
# Differentiating Neuropathic vs. Nociceptive Pain

<table>
<thead>
<tr>
<th>Neuropathic Pain (diabetic neuropathy, lumbar radiculopathy/sciatica, post-herpetic neuralgia)</th>
<th>Nociceptive Pain (burn, broken limb, osteoarthritis)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Listen</strong></td>
<td><strong>Locate</strong></td>
</tr>
<tr>
<td>Common Descriptors:</td>
<td>• The painful region may not necessarily be the same as the site of injury</td>
</tr>
<tr>
<td>• Burning</td>
<td>• Pain occurs in the neurological territory of the affected structure (nerve, root, spinal cord, brain in the case of stroke= hemi-body pain)</td>
</tr>
<tr>
<td>• Tingling</td>
<td></td>
</tr>
<tr>
<td>• Shooting</td>
<td></td>
</tr>
<tr>
<td>• Numbness</td>
<td></td>
</tr>
<tr>
<td>• Electric shocks</td>
<td></td>
</tr>
</tbody>
</table>

Common Descriptors:• Burning• Tingling• Shooting• Numbness• Electric shocks

Painful region is typically localized at the site of injury

Physical manipulation causes pain sensations at site of injury

Common Descriptors:• Aching• Throbbing• Stiffness
How do patients describe pain?

- 35F
- Wrist fracture with surgical pinning
- Developed signs/symptoms of Complex Regional Pain Syndrome
- “It feels like mosquitoes are landing on my arm all the time”
How do patients describe pain?

- 40M
- Colon cancer
- Treated with chemotherapy
- “It feels like I’m walking on rocks whenever I take a step.”
Neuropathic Pain Etiology

- **Central:**
  - Post-stroke (i.e., hemi-body pain), multiple sclerosis, spinal cord injury

- **Peripheral:**
  - Diabetic neuropathy, chemotherapy-induced neuropathy, sciatica/lumbar radiculopathy, post-surgical or post-traumatic neuralgia (nerves are cut but often heal in the “on” position when there is central and peripheral sensitization)

- **Mixed:**
  - Post-herpetic neuralgia
Pain Terminology

• **Allodynia**: Pain from stimulus which does not normally cause pain (i.e. light touch)

• **Hyperalgesia**: Increased pain response from normally painful stimulus (i.e. pinprick)

• **Dysesthesia**: Unpleasant abnormal sensation, spontaneous or evoked (i.e. tingling and numbness)
Overlapping Aspects of Chronic Pain

- Psychological
- Social
- Biological
Functional Domains

Activities
- ADLs
- SeADLs
- Self care
- Household duties
- Community engagement
- Productivity

Leisure

Sleep
- Lower sleep efficacy
- Fragmentation of sleep
- Increased wake time
- Cyclical effect on pain
The Psychiatric Component

Mental disorders among persons with chronic back or neck pain: Results from the world mental health surveys

Koen Demyttenaere a,*, Ronny Bruffaerts a, Sing Lee b, José Posada-Villa c
Vivianne Kovess d, Matthias C. Angermeyer e, Daphna Levinson f
Giovanni de Girolamo g, Hideyuki Nakane h, Zeina Mneimneh i, Carmen Lara j
Ron de Graaf k, Kate Margaret Scott l, Oye Gureje m, Dan J. Stein n
Josep Maria Haro o, Evelyn J. Bromet p, Ronald C. Kessler q, Jordi Alonso r
Michael Von Korff s

- Depression: 2.3
- Dysthymia: 2.8
- GAD: 2.7
- PHQ-2
- GAD-2
# The Psychiatric Component

## Patient Health Questionnaire-2: Screening Instrument for Depression

<table>
<thead>
<tr>
<th>OVER THE PAST TWO WEEKS, HOW OFTEN HAVE YOU BEEN BOTHERED BY ANY OF THE FOLLOWING PROBLEMS?</th>
<th>NOT AT ALL</th>
<th>SEVERAL DAYS</th>
<th>MORE THAN ONE-HALF THE DAYS</th>
<th>NEARLY EVERY DAY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

## GAD-2

<table>
<thead>
<tr>
<th>Over the last 2 weeks, how often have you been bothered by the following problems? (Use “✔” to indicate your answer)</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Feeling nervous, anxious, or on edge</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Not being able to stop or control worrying</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
Catastrophization

1. I worry all the time about whether the pain will end.
2. I feel I can’t go on.
3. It’s terrible and I think it’s never going to get any better.
4. It’s awful and I feel that it overwhelms me.
5. I feel I can’t stand it anymore.
6. I become afraid that the pain will get worse.
7. I keep thinking of other painful events.
8. I anxiously want the pain to go away.
9. I can’t seem to keep it out of my mind.
10. I keep thinking about how much it hurts.
11. I keep thinking about how badly I want the pain to stop.
12. There’s nothing I can do to reduce the intensity of the pain.
13. I wonder whether something serious may happen.
Chronic Pain Assessment - Psychosocial History

Psychological
- Personal / family history
- Previous physical, sexual, and/or emotional abuse
- Current life stressors
- Family / cultural factors
- Catastrophizing

Social
- Family configuration
- Level of education
- Type of work
- Income
- Isolation
- Secondary benefits of pain (conscious or unconscious)

Disability
Chronic Pain Assessment Pearls

• Past treatments:
  • consultations (physiatrist, chronic pain specialist)
  • surgery
  • physical modalities – physio/chiro/massage/acupuncture,
  • psychological – CBT
  • pharmacological
“It may surprise you to hear that, actually, morphine is the best medicine.”
Chronic Pain Assessment Pearls: Medication History

- **Opioid Use Hx**
  - Dose, duration, dose escalation
  - Tolerance, dependence, addiction

- **Aberrant Medication Use:**
  - Early refills (not receiving enough medication to treat pain or inappropriate use), lost rx, hoarding, taking more than prescribed, requests for dose increase, giving drugs to others, selling drugs, use for effects other than analgesia (i.e. sleep difficulties)

- **Substance Use History:**
  - First use, regular use, pattern of use, amount, route, length of use, last use, current use
  - which substances – alcohol, BZD, barbiturates, THC, cocaine, amphetamines, ecstasy, hallucinogens, opioids, solvents, tobacco, caffeine
  - Harmful effects of substance use – family, friends, employment, housing, education, finances, legal
  - Harmful substance use related behaviour – source, IV, needle sharing, sexual activity, crime, driving

- **Prior medications tried**
  - Reason for failure (dose, side effects)

- **Collateral History:**
  - Family MD, other consultants, pharmacist, family members, etc.
YELLOW FLAGS: RISK OF CHRONIC DISABILITY

- A belief that back pain is harmful or potentially severely disabling
- Fear-avoidance behaviour (avoiding a movement or activity due to misplaced anticipation of pain) and reduced activity.
- Tendency to low mood and withdrawal from social interaction
- Expectation of passive treatment(s) rather than a belief that active participation will help.
- Poor job satisfaction and hx of time-off
- Overprotective family or lack of support
Red Flags

- Age <20 or >55 years
- Recent history of trauma
- Constant progressive pain - this includes pain that is not associated with movement and not relieved by lying down
- Thoracic pain
- Past history of malignancy
- Recurrent or prolonged use of corticosteroids
- Immunosuppression/HIV
- Substance misuse
- Being systemically unwell
- Unexplained weight loss
- Neurological symptoms such as weakness of the limbs
- Structural deformity of the spine.
Pain Assessment Tools

• Various tests/tools used to assess pain

• Validated

• Useful for monitoring effect of treatments and interventions

• Used in both acute and chronic pain
BPI - Brief Pain Inventory

- Measures pain intensity
- Examines interference of pain on life
- Pain relief, quality, perception of pain

- Patient fills this in at EACH visit
- Useful for following trends (not as useful in isolation)
- Normal variation in VAS (visual analogue scale) of 2 points
Brief Pain Inventory

Date / / 
Name: 

1) Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today? 
   Yes  No

2) On the diagram shade in the areas where you feel pain. Put an X on the area that hurts the most.

Right  Left  Right

3) Please rate your pain by circling the one number that best describes your pain at its worst in the past 24 hours.
   0 1 2 3 4 5 6 7 8 9 10
   No pain
   pain as bad as you can imagine

4) Please rate your pain by circling the one number that best describes your pain at its least in the past 24 hours.
   0 1 2 3 4 5 6 7 8 9 10
   No pain
   pain as bad as you can imagine

5) Please rate your pain by circling the one number that best describes your pain on the average.
   0 1 2 3 4 5 6 7 8 9 10
   No pain
   pain as bad as you can imagine

6) Please rate your pain by circling the one number that tells how much pain you have right now.
   0 1 2 3 4 5 6 7 8 9 10
   No pain
   pain as bad as you can imagine

7) What treatments or medications are you receiving for your pain?

8) In the Past 24 hours, how much relief have pain treatments or medications provided? Please circle the one percentage that most shows how much relief you have received.
   0% 10 20 30 40 50 60 70 80 90 100%
   Complete relief

9) Circle the one number that describes how, during the past 24 hours, pain has interfered with your:
   A. General activity
   B. Mood
   C. Walking ability
   D. Normal work (includes both work outside the home and housework)
   E. Relations with other people
   F. Sleep
   G. Enjoyment of life
DN4 Questionnaire

- Simple diagnostic tool for neuropathic pain
- Developed in France and validated since 2005

- Physician fills this out with the patient
- 10 simple questions, score 0 for no and 1 for yes
- \( > 4/10 \) is diagnostic for neuropathic pain
<table>
<thead>
<tr>
<th>Does the pain have one of the following characteristics?</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Burning</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>2 Painful cold</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>3 Electric shocks</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td><strong>Is the pain associated with one of the following symptoms in the same area?</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Tingling</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>5. Pins and Needles</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>6. Numbness</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>7. Itching</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td><strong>Is the pain located in an area where the physical examination may reveal one or more of the following characteristics?</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Hypoesthesia to touch</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>9. Hypoesthesia to prick</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td><strong>In the painful area can the pain be caused or increased by 10 Brushing?</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Chronic Pain Assessment Pearls: Physical Exam

• **Inspection and Palpation:**
  - Look for signs of CRPS – temperature and colour changes, hair/nail, diaphoresis
  - Identify areas of allodynia/hyperesthesia/hypoesthesia
  - Correlation nerve root or peripheral nerve

• **Neurological deficits:** reflexes, sensation, strength

• **Special Tests:** straight leg raise for sciatica

• **Generalized pain:** may be a marker of fibromyalgia, myofascial pain syndrome or central sensitization
Radiological/ Laboratory tests

- **X-ray**: initial investigation- tumor, fracture, OA, disc height, spondylolisthesis
- **CT Scan**: complex bony involvement, OA, fracture
- **MRI**: soft tissue pathology, spinal cord, radiculopathy, malignancy
- **Bone scan**: useful for osteomyelitis, primary or metastatic bone tumor, occult fracture, spondyloarthropathy.
- **EMG/NCS**: neuropathic pain, radiculopathy
- **Bloodwork**: biomarkers for connective tissue disorders, ESR, CRP, CBC as appropriate
Case Continued – Ms. B Pain

• 45 y/o female for planned L3 – S1 decompression and fusion
• Pain leg 8-9/10 constant, sharp, stabbing,
• Oxycontin 30 mg TID, Oxycodone 10mg 5 tabs/day
• Cymbalta 60 mg OD

• Limited ADLs
• Anxiety
• Employed as office manager
• Work related back strain and has been off work for four months waiting surgery
• Married
• No history alcohol use, non-smoker
Case Continued – Ms. B Pain

- Receives intended surgery
- Returns for follow up visit 3 months post surgery
- Severe low back and leg pain (right sided)
- Off work, describes significant anxiety and depressive symptoms
- Meds:
  - Oxycontin increased 30 mg TID ➔ 40mg TID
  - Oxycodone increased ➔ 10mg tabs 10 per day
  - Cymbalta 60 mg OD
Treatment Chronic Pain

• Pillars of Pain Management
  • Pharmacological
  • Procedural
  • Psychological
  • Physical (PT and physical modalities)

• Multidisciplinary
  • Chronic pain service
  • Nursing
  • OT
  • PT
  • Psychologist
  • Social worker
Nociceptive Pain Treatment

- Has been applied for non-cancer pain as well
- Caution against opioid dose escalation for non-cancer pain
Opioids in Chronic Non-Cancer Pain

• The 2017 Canadian Guidelines for Opioids for Chronic Non-Cancer Pain
  • Published by the National Opioid Use Guideline Group (NOUGG)

• Limited evidence for long term opioid use in non cancer pain
  • Common side effects: constipation, nauseas, pruritus, urinary retention
  • Tolerance
  • Dependence
  • Addiction and aberrant use
  • Endocrine - hypogonadism
Strong recommendations from Canadian Opioid Guidelines

• Recommend non opioid pharmacotherapy and non-pharmacological therapy

• Recommend against use in patients with active substance use disorder

• Recommend dose of < or = 90mg morphine equivalent

• Multidisciplinary program to facilitate tapering in patients on higher dose of opioids
Opioid Risk Tool

• Brief screening method to predict which individuals may develop aberrant behaviors when prescribed opioids for chronic pain

• Assesses and scores the following risk factors associated in scientific literature with substance abuse:
  • personal and family history of substance abuse
  • age
  • history of preadolescent sexual abuse
  • psychological disorders
<table>
<thead>
<tr>
<th>Item</th>
<th>Mark each box that applies</th>
<th>Item score if female</th>
<th>Item score if male</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Family History of Substance Abuse:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>[ ]</td>
<td>1</td>
<td>3</td>
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<tr>
<td>Illegal Drugs</td>
<td>[ ]</td>
<td>2</td>
<td>3</td>
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<tr>
<td>Prescription Drugs</td>
<td>[ ]</td>
<td>4</td>
<td>4</td>
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<tr>
<td><strong>2. Personal History of Substance Abuse:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>[ ]</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Illegal Drugs</td>
<td>[ ]</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Prescription Drugs</td>
<td>[ ]</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td><strong>3. Age (mark box if 16-45)</strong></td>
<td></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>4. History of Preadolescent Sexual Abuse</strong></td>
<td></td>
<td>3</td>
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<tr>
<td><strong>5. Psychological Disease</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Attention Deficit Disorder, Obsessive-Compulsive Disorder, or Bipolar, Schizophrenia</td>
<td>[ ]</td>
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<td>2</td>
</tr>
<tr>
<td>Depression</td>
<td>[ ]</td>
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<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Total Score Risk Category:</strong> Low Risk: 0 to 3</td>
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<td></td>
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<tr>
<td>Moderate Risk: 4 to 7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High Risk: 8 and above</td>
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<td></td>
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</tbody>
</table>
Opioid Contract

Since other treatments have not worked to control your pain, the physicians of General Internal Medicine (GIM) have decided to give you long-term opioids to help manage your pain better and improve your social and work activities. This is a serious decision. You must adhere to several conditions in order to continue with this type of treatment.

Conditions:
1. I will not use illegal substances, street drugs or abuse alcohol while taking controlled medications. I will not take opioids prescribed for other people.
2. I will not be involved in the sale, illegal possession, diversion, or transport of controlled substances like narcotics, sleeping pills, or nerve pills.
3. I agree to obtain drug screening tests, including blood alcohol levels, when my physician requests it.
4. I agree to obtain all prescriptions for opioids from one physician only at the GIM East Clinic and to take medications as prescribed by my doctor.
5. I agree to use only one pharmacy, _, for filling prescriptions for opioids.
6. I agree to follow up every three months with my physician regarding pain control and to keep all scheduled clinic appointments regarding my chronic pain.
7. I agree to the hospital computer system containing information about the contract so that other doctors in the hospital are informed.
8. I agree to allow my physicians in GIM to communicate with other physicians and any pharmacists regarding pain management as deemed necessary.
9. I certify that I am not pregnant. I certify that I will use appropriate measures to prevent pregnancy during the course of my treatment with opioids.
10. I agree to contact GIM at 414-805-6850 within 24 hours if an unavoidable emergency occurs requiring a prescription for opioids, an ER visit, or an inpatient admission.
11. I understand that NO allowances will be made for lost prescriptions, drugs, or any problems I may have with transportation or dates of pick up.
12. I understand the possible adverse effects and dependencies associated with opioids as outlined on the Adverse Effects Sheet.
13. I agree to have _, as a designated person to pick up my narcotic prescription in case I am unable. He/she will present a photo ID and my green clinic card to verify name and permission for pick up.
14. I agree to call 7 days in advance for all refills and to schedule an appointment for pick up.
15. I understand this mode of treatment will be stopped if any of the following occurs:
   a) I give away, sell, or misuse the drugs or use other peoples’ drugs or illegal substances
   b) I am noncompliant with any of the terms of this agreement
   c) I disrespect or harass clinic personnel
   d) I do not follow up regularly or as requested by my physician.
16. Exceptions to the above include:

I have read this agreement, understand it, and have had all questions answered satisfactorily. I consent to the use of opioids under the terms outlined in this agreement.

GIM Physician ____________________________ / Date / Witness ____________________________
Signature ____________________________ Date ________________ Nurse ____________________________
Two "yes" responses indicate that the respondent should be investigated further. The questionnaire asks the following questions:

1. Have you ever felt you needed to **Cut down** on your drinking?
2. Have people **Annoyed** you by criticizing your drinking?
3. Have you ever felt **Guilty** about drinking?
4. Have you ever felt you needed a drink first thing in the morning (**Eye-opener**) to steady your nerves or to get rid of a hangover?
Neuropathic Pain Treatment

CONSENSUS STATEMENT

Pharmacological management of chronic neuropathic pain: Revised consensus statement from the Canadian Pain Society

DE Moulin MD, A Boulanger MD, AJ Clark MD, H Clarke MD PhD, T Dao DMD PhD, GA Finley MD, A Furlan MD PhD, I Gilron MD MSc, A Gordon MD, PK Morley-Forster MD, BJ Sessle MDS PhD, P Squire MD, J Stinson RN PhD, P Taenzer PhD, A Velly DDS PhD, MA Ware MD, EL Weinberg MD, OD Williamson MBBS


La prise en charge pharmacologique de la douleur neuropathique chronique : une déclaration de consensus révisée de la canadienne de la douleur
Figure 1) Algorithm for the pharmacological management of neuropathic pain. *Topical lidocaine (second line for postherpetic neuralgia), methadone, lamotrigine, lacosamide, tapentadol, botulinum toxin; †Limited randomized controlled trial evidence to support add-on combination therapy. TCA Tricyclic antidepressants; SNRI Serotonin noradrenaline reuptake inhibitors.
Gabapentin

- NNT and NNH (Finnerup et al Lancet 2015)
- NNT = 6.3 (CI 5.0 – 8.3)
- NNH = 25.6 (CI 15.3 – 78.6)
- Dosage start 100 – 300mg QHS
- Target dose 1200mg – 3600mg divided TID gradually reached over several weeks
- No dose response gradient identified
- Onset analgesic activity delayed after therapeutic dose achieved
Pregabalin

- NNT and NNH (Finnerup et al Lancet 2015)
- NNT = 7.7 (98% CI 6.5 – 9.4)
- NNH = 13.9 (95% CI 11.6 – 17.4)
- Starting dose 25mg QHS with gradual titration to 300 – 600mg per day
- 150mg per day can be effective
- Dose response gradient
- Maximum benefit occurs approx 2 weeks after target dose of 300 – 600mg per day
Gabapentinoids – Side Effects

• Cochrane Review 2014 Gabapentin
  • Dizziness 19%
  • Somnolence 14%
  • Gait disturbance 9%
  • Peripheral edema 7%
  • Serious adverse events 3%
  • Withdrawal due to adverse event 11%
  • Over half of patients did not have worthwhile pain relief

• Other
  • Cognitive impairment (elderly)
  • Increased risk suicidal ideation (all AED)
FDA Requires Warnings About Suicidality Risk With AEDs

- December 2008 — The FDA will require the manufacturers to add a warning to their labeling indicating that AEDs increases risk for suicidal thoughts and behaviors.

- A FDA review of 199 clinical trials of 11 AEDs estimated the risk for suicidal behavior or thoughts at nearly doubled for patients receiving AEDs vs. placebo (0.43% vs. 0.24%), leading to about 1 additional case of suicidality for every 500 patients treated with AEDs instead of placebo.
Tricyclic Antidepressants

- Increase 5-HT and NE
- Dirty drug
  - multiple neurotransmitters (H1, anticholinergic)
- First line for neuropathic pain (CPS guidelines)
- Second line for depression
- Low therapeutic index
TCA

- Amitriptyline – tertiary amine (parent drug)
  - Higher number of positive studies for neuropathic pain
  - Recent Cochrane review suggested minimal benefit for neuropathic pain
  - Action on 5HT transporter 7 times more than NE
  - Inhibit some CYP 450 enzymes i.e. 2C19 and 1A2
  - Greater toxicity than secondary amines

- Nortriptyline – secondary amine (major metabolite of amitriptyline)
  - Fewer studies for neuropathic pain
  - Recent Cochrane review suggested no benefit for neuropathic pain
  - Action on NE transporter 40 times more than 5HT transporter
  - Weakly inhibit some weak CYP 450 enzymes
  - Better tolerated less side effects, less toxicity
  - Mortality from Nortriptyline in over-dosage is 5.5 per million scripts
    - (similar to SSRI)
Onset of analgesic effect 1–2 weeks, peeks at 4–6 weeks

Mean dosage for pain relief 75mg–150mg

Antidepressant dosage range 100mg–300mg

There is difference in metabolism within population
  - i.e. slow metabolizers lower dosage 50mg vs. ultrarapid metabolizer higher dosage required 150mg

Note - side effect differences above controversial

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### Table 2
**Tertiary and Secondary Amine Tricyclic Antidepressants**

<table>
<thead>
<tr>
<th>Medications</th>
<th>Initial/Max Dose</th>
<th>Comments</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tertiary Amine TCAs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline (Elavil)</td>
<td>25-75 mg/200 mg daily</td>
<td>5HT &gt; NE</td>
<td>Orthostatic hypotension, drowsiness, weight gain, anticholinergic, QT prolongation (in overdose)</td>
</tr>
<tr>
<td>Amoxapine (Asendin)</td>
<td>50 mg bid/400 mg daily</td>
<td>5HT = NE, weak DA</td>
<td></td>
</tr>
<tr>
<td>Clomipramine (Anafranil)</td>
<td>25 mg/250 mg daily</td>
<td>5HT &gt; NE</td>
<td></td>
</tr>
<tr>
<td>Doxepin (Sinequan)</td>
<td>50-75 mg/300 mg daily</td>
<td>5HT = NE; highly sedating</td>
<td></td>
</tr>
<tr>
<td>Imipramine (Tofranil)</td>
<td>50-100 mg/200 mg daily</td>
<td>5HT = NE</td>
<td></td>
</tr>
<tr>
<td><strong>Secondary Amine TCAs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desipramine (Norpramin)</td>
<td>100-200 mg/300 mg daily</td>
<td>NE &gt; 5HT; metabolite of imipramine</td>
<td>Same as above, but with more drowsiness, somnolence, and weight gain than tertiary</td>
</tr>
<tr>
<td>Maprotiline (Ludiomil)</td>
<td>25 mg tid/225 mg daily</td>
<td>NE &gt; 5HT</td>
<td></td>
</tr>
<tr>
<td>Nortriptyline (Pamelor)</td>
<td>25-50 mg/150 mg daily</td>
<td>NE &gt; 5HT; metabolite of amitriptyline</td>
<td></td>
</tr>
</tbody>
</table>

DA: dopamine; 5HT: serotonin; max: maximum; NE: norepinephrine; TCA: tricyclic antidepressant. Source: References 4, 10.
TCA

- NNT and NNH (Finnerup et al Lancet 2015)
  - NNT = 3.6 (95% CI 3.0 – 4.4)
  - NNH = 13.4 (95% CI 9.3 – 24.4)

- Low therapeutic index
  - TCA more likely than other antidepressants to cause harm due to arrhythmias
  - No dose response relationship
  - SSRI high therapeutic index
  - High withdrawal rate (some studies 20%)
TCA – side effects

1. Anticholinergic – affinity for muscarinic receptors - xerostomia, urinary retention, constipation, diplopia, memory impairment (elderly)
   • Contraindicated in glaucoma and BPH

2. Orthostatic hypotension – Alpha-1 adrenergic blockade, transient, may not be dose dependent

3. Cardiac – sinus tachycardia common, prolongation of PT, QT, QRS,
   • Used with caution in patients at risk of cardiac arrhythmias
   • Consider baseline ECG in patients over 45
   • Contraindicated – MI

4. Endocrine – weight gain due to H1 blockade, increased blood sugar (catecholamine effect), SIADH/hyponatremia

5. CNS – anticholinergic induced delirium, drowsiness, somnolence (H1 blockade), myoclonic twitches, tremors, paresthesias, extrapyramidal symptoms (rare), seizures
TCA - side effects

6. Allergy – photosensitive, rash, jaundice (rare)

7. Discontinuation withdrawal – sleep disturbance, mood fluctuation, flu-like symptoms,

8. Sexual dysfunction – anticholinergic, alpha1 blockade, 5HT reuptake inhibition, altered DA

9. Psychiatric – activation to mania up to 11.2% depressed BAD, 1-7% of unipolar depressed patients, suicidal ideation
SNRI – Duloxetine

Indications:

• MDD, GAD
• First line treatment for neuropathic pain (CPS guidelines)
• Diabetic neuropathy
• Chemotherapy induced neuropathy (JAMA 2013)
• Fibromyalgia
• Chronic low back pain (Spine 2010)
• Osteoarthritis Knee (Meta-analysis Pain Med 2015)
• Low back pain with neuropathic component (Anesthesiology 2016)

Notes:

• Spinal cord injury central neuropathic pain trial was negative
SNRI – Duloxetine Side Effects

• Drowsiness (9 – 11%)
• Insomnia (7 – 10%)
• Nausea (18 – 23%)
• Headache (13-14%)
• Weakness (approx 7 – 11%)
• Sexual dysfunction (approx 3-4%)
• Weight gain (> or = 1%)
• Suicidal ideation
• SIADH/hyponatremia
• Bleeding risk – may impair platelet aggregation resulting in increased bleeding events (particularly with ASA/NSAIDS)
• diaphoresis, dry mouth

• **Contraindicated** in hepatic impairment, severe renal impairment, glaucoma
SNRI

- NNT and NNH (Finnerup et al 2015)
  - NNT 6.4 (95% CI 5.2–8.4)
  - NNH 11.8 (95% CI 9.5–15.2)
  - Cymbalta 9 studies, 2 negative
  - Venlafaxine 4 studies, 2 negative
  - Desvenlafaxine 1 study, 1 negative

- Bonica’s Textbook of Pain
  - Cymbalta NNT for 50% pain relief
  - 60mg dose NNT = 4.3
  - 120mg dose NNT = 3.8

- Discontinuation rates (Gahimer 2007)
  - 15-20%
## Non-pharmacologic Treatment Options

<table>
<thead>
<tr>
<th>Type of treatment</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifestyle</td>
<td>Cessation of tobacco products, weight loss, nutritional counselling, posture adjustments</td>
</tr>
<tr>
<td>Physical</td>
<td>Heat, cold, massage, exercise, manipulation, physical therapy, stretching and yoga, surgical therapies (nerve blocks, trigger point injections, spinal infusion, or stimulation), transcutaneous electric nerve stimulation, intramuscular stimulation, radiofrequency lesioning</td>
</tr>
<tr>
<td>Psychological/psychiatric</td>
<td>Biofeedback, cognitive behaviour therapy, counselling, social worker support, hypnosis, relaxation</td>
</tr>
<tr>
<td>Occupational</td>
<td>Occupational therapy, work conditioning programs</td>
</tr>
<tr>
<td>Complementary/alternative</td>
<td>Acupuncture, herbal remedies, massage, mindfulness meditation, reflexology</td>
</tr>
</tbody>
</table>
Physical Therapy: Barriers

Fear Avoidance Model

- Motivation
- Deconditioning
- Kinesophobia
- Finances
Psychotherapy

• **CBT:**
  • learning skills to cope with chronic pain
  • Skill development and behavior change
  • 12 hours over 6 weeks
  • Working group with support

• **ACT:**
  • redirect focus from pain control to meaningful living
  • Clarify values
  • Move towards values

TAPMI Hub Allied Health Supports
76 Grenville Street, 3rd Floor, Toronto, Ontario M5S 1B2
Phone: 416-323-6269 Fax: 416-323-2666
E-mail: chronic.pain@wchospital.ca

Only referrals from TAPMI partner sites will be accepted
Psychotherapy

- **Self management**
  - 2.5 hours/week for 6 weeks
  - Group based
  - Pain workbook and audio CD
  - MOHLTC funded
  - [http://www.livingwellseontario.ca/](http://www.livingwellseontario.ca/)
  - [http://www.tcsmp.ca/](http://www.tcsmp.ca/)

- **MBSR**
  - 2.5 hours/week for 8 weeks
  - Group discussion
  - Home exercises
  - Meditation practice
  - UHN: TRI and TGH
Now, that's gotta hurt...
Questions?

Thank you.
Important Reading - Works Cited


