From Descartes to Spock - The Brain and Pain And Beyond

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Dr. Deborah Robinson MD, CCFP
Carmel Richards, NP
In the beginning…

-Descartes, 1644
**Total Pain:**
Suffering that encompasses all of person’s physical, psychological, social, spiritual, and practical struggles

-Dame Cecily Saunders

Learning Objectives

- Pain terminology
- Pain anatomy and physiology
- Pain assessment
- Pharmacologic treatment options
  - Standard opiates, methadone, oral fentanyl
- Interventional Techniques
- Non-pharmacologic treatment options
- Case-based discussions
Disclosures, Acknowledgements

Disclosures
- I have no idea how long this talk will take!
- This will be intense!

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What is Pain?

- *Pain is a subjective experience*
- *It is NOT just a stimulus*
- *Major features of the pain experience include:*
  - Sensory discriminative features
  - Affective (emotional) response
  - Cognitive modulation
- *Acute pain is important*
- *Chronic pain is the problem*
Chronic Pain

- Chronic pain is NOT merely:
  - prolonged acute pain
  - a symptom of some other chronic disease
- Chronic pain is a disease of the nervous system:
  - CENTRAL SENSITIZATION
- Two basic categories
  - Nociceptive
  - Neuropathic
Nociceptive vs Neuropathic Pain

NOCICEPTIVE:
- Noxious Stimulus – a stimulus that is intense enough to produce pain (tissue injury)
- Nociception – the neural processing of noxious stimuli

NEUROPATHIC:
- Nerve injury pain
- Associated with allodynia and hyperalgesia
Mixed Etiology of Pain

- Neuropathic pain mechanisms
- Inflammatory pain mechanisms
- OA
- RA
- PHN
- PDN
- CIDP
- Phantom Pain (post trauma)
Allodynia and Hyperalgesia

F. Cervero and J Laird. Pain 1996;68(1):13-23,
Opioid Induced Hyperalgesia

- Opioid administration paradoxically causes diminished tolerance to pain
  - chronic opioid exposure leads to up regulation of pain processing mechanisms
  - precise molecular explanation is not clearly understood but several different mechanisms are implicated.

- Features of Opioid Induced Hyperalgesia include:
  - Increased sensitivity to pain that extends beyond the location of pre-existing pain
  - ALLODYNIA may be present
  - Abrupt onset with rapid opioid escalation/high opioid dose
  - Pain worsens with increasing opioid doses
Cancer Pain

- Cancer pain is a complex chemical, neurological & psychological process that is incompletely understood.

- Chronic cancer pain is composed of two parts:
  
  **Persistent pain**
  
  ▪ Constant or continuous pain that is experienced by the patient for more than 12 hours per day.

  **Breakthrough pain**
  
  ▪ Transitory exacerbation of pain that occurs on a background of otherwise stable pain in patients receiving chronic opioid therapy.
Breakthrough Cancer Pain

- Depending on the diagnostic criteria used to evaluate breakthrough pain approximately 50% to 95% of cancer patients experience breakthrough pain
  - Only 25% of those who do experience breakthrough pain are satisfied with their pain management.
  - Breakthrough pain is associated with multiple physical, psychological and social complications

- Features of breakthrough cancer pain include:
  - Rapid Onset, Short Duration, Severe/Intense Pain
  - Classification includes incident, spontaneous, or neuropathic pain
  - Does not include end-dose failure pain
Spontaneous BTP

**Spontaneous Pain**

- Can be either rapid or slow in onset and is either brief or prolonged in duration.
- It is often related to increased activity but the temporal characteristics can be quite variable and there is no obvious incident that triggers each episode.
Incidental BTP

**Incident Pain**

- Sudden onset with activity, either volitional (predictable) or non-volitional (often unpredictable, e.g. sneezing) and is usually brief but could be associated with a component of lingering pain.

- Common with bone pain but may also be seen with tethering of organs, nerves and tissues by tumour.
Neuropathic

- Can be either spontaneous or incidental but has specific features of lancinating “lightening flash” like symptoms lasting only a few seconds. It may have some lingering mild to moderate pain with dysesthesia.
In Contrast...

**Uncontrolled Baseline Pain:**
- Baseline pain is unacceptably high
- Lasts for long periods
- Does not occur spontaneously or because of activity
- Dictates need for more aggressive management of chronic pain

**End of Dose Failure:**
- Represents inadequately controlled baseline pain
- Onset is just before a scheduled or around-the-clock analgesic
- Tends to be more gradual in onset and longer in duration than incident and spontaneous pain
- The general approach to management is an increase in the baseline dose of narcotic.
Visceral Pain

- *Invasion of abdominal viscera* – organs or blood vessels which are not extensively innervated by sensory nerves

- *Sensory innervations involve vagal fibres, and more importantly spinal sympathetic nerve fibres*

- *Pain is often described as dull, constant, aching and may be difficult to localize*

- *May be poorly responsive to narcotics*
Where In The Brain is Pain?

- Insula
- Cingulate gyrus
- The Midbrain
- The Medulla
- The Pons
- **Ascending Pain Pathway**
  - Tissue/nerve damage, nociceptors
  - Inflammatory mediators (ie AA)
  - Primary and secondary sensory nerves
  - Dorsal horn inter-neurons
  - Thalamus, Cortex
  - Glutamate, SP
  - Glutamate receptors (AMPA, NMDA)

- **Descending Pain Pathway**
  - Descending controls from various parts of brain and midbrain
  - Descending inhibitory neurons
  - Dorsal horn interneurons
  - Glutamate receptors, opioid receptors
  - Endorphins, enkephalins
Cross Section of a Peripheral Nerve

- **Large Aβ fibres respond to light touch**
  - innocuous, non-painful stimuli and conduct quickly
  - When active, can actually help reduce pain
  - If injured, pain can actually be worse

- **Small Aδ fibres, provide first response to pain**
  - Myelinated therefore conduct quickly

- **Small unmyelinated C fibres second response to pain**
  - Unmyelinated, therefore conduction is slower

- **In the setting of tissue injury, both Aδ and C fibres can respond to non-painful stimuli**
A. Schematic representation of ascending pain pathways.

B. Coronal section with colour-coded regions superimposed.

**Sensory-Discriminative Features**

- S1 + S2  Somatosensory Cortex
- PCC     Posterior Cingulate Cortex
- PFC     Pre-frontal Cortex
- SMA     Supplemental Motor Area
- BG      Basal Ganglia
- HT      Hypothalamus

**Affective-Motivational Features**

- ACC     Anterior Cingulate Cortex
- AMG     Amygdala
- PB      Parabrachial Nuclei
- Insular Cortex

Adapted from C. Rhodes. The Brain In Pain. 2011 The Pain Practitioner 21(2).
Peripheral Sensitization - HYPERALGESIA

- Aka Hyperalgesia
- A reduction in the threshold and increase responsiveness in the peripheral ends of nociceptors
- Local release of chemicals at the tissue level excite nociceptors or increase their sensitivity (primary hyperalgesia)
  - Secretion of inflammatory factors such as prostaglandins
  - Tumour induced acidosis, activation of bradykinin
  - Tumour induced mechanical injury
- Pro-inflammatory agents sensitize adjacent Aδ and C nociceptors (secondary hyperalgesia)
Peripheral sensitization (modified from Woolf and Chong).

**PERIPHERAL SENSITISATION**

- Tissue damage
- Inflammation
- Sympathetic terminals

"SENSITISING SOUP"

- H+
- Histamine
- Purines
- Norepinephrine
- K+
- Cytokines
- Bradykinin
- Prostaglandins
- 5-HT
- Leukotrienes
- NGF
- Neuropeptides

High threshold nociceptor

Transduction Sensitivity

Low threshold nociceptor

Peripheral sensitization (modified from Woolf and Chong).
Central Sensitization - ALLODYNIA

- Aka “pain memories”
- Maladaptive changes to the central nervous system that are created in the setting of injury
- Involves down regulation of opioid receptors and up-regulation of NMDA receptors
- Results in a complex biochemical cascade that leads to hyper-excitability of spinal neurons
  - WIND UP – injury/lesion not needed to keep pain stimulus going
  - ALLODYNIA – pain response to non-painful stimulus
What Influences the Perception of Pain

- *Depends on who is being stimulated*
- *Depends on the psychological state of the individual at the time of the stimulus*
  - Emotions alter how pain is processed in the limbic cortex
  - Emotions alter pain unpleasantness
- *Depends on how much attention is paid to the stimulus*
  - Attention changes how pain is processed in the sensory cortex
  - Attention alters pain intensity
- *Depends on how much pain is expected or anticipated in advance of the stimulus*
Pain Assessment

- A thorough and inter-professional assessment that goes beyond the visual analogue scale is essential
  - What is the temporal nature of the pain (onset, duration, frequency)?
  - Is there a specific time when the pain occurs and what is the temporal relationship to long acting narcotic dose?
  - Is there pain with voluntary or involuntary movement?
  - What is the severity of the pain?
  - How does the pain impact quality of life/function?
  - How many doses of analgesic taken?
  - Are doses being missed and why?
Pain Assessment

- Visual Analogue Scales
Pain Assessment - Kids
Edmonton Classification System for Cancer Pain (ECS-CP)

Patient Name: ____________________________ HN: ____________________

1. Mechanism of Pain
   No - No pain syndrome
   Nc - Any nociceptive combination of visceral and/or bone or soft tissue pain
   Ne - Neuropathic pain syndrome with or without any combination of nociceptive pain
   Nx - Insufficient information to classify

2. Incident Pain
   Io - No incident pain
   II - Incident pain present
   IX - Insufficient information to classify

3. Psychological Distress
   Po - No psychological distress
   Pp - Psychological distress present
   Px - Insufficient information to classify

4. Addictive Behavior
   Ao - No addictive behavior
   Aa - Addictive behavior present
   Ax - Insufficient information to classify

5. Cognitive Function
   Co - No impairment. Patient able to provide accurate present and past pain history unimpaired
   CI - Partial impairment. Sufficient impairment to affect patient’s ability to provide accurate present and/or past pain history
   Cu - Total impairment. Patient unresponsive, delirious or demented to the stage of being unable to provide any present

Treatment Options

- Aspirin and other NSAIDS
- Morphine and other standard opioids
- Transcutaneous electrical stimulation
- Deep brain stimulation
- Placebo, Hypnosis
- Acupuncture, ice, heat, counter irritant creams
- Adjuvants and other Therapies for Neuropathic Pain
  - TCAs, neuroleptics, ketamine, methadone
- Interventional techniques
  - Intraspinal, peripheral and sympathetic nerve blocks, neurolysis
- Breakthrough Pain Management consideration
Other Treatment Options

- Chemotherapy
- Radiation
- Surgery
- Physiotherapy
- Complementary Therapies
- Limitation of activities
Medications Used According to Their Site of Action

Descending Inhibitor Pathways (NE/5HT, opioid receptors)

Brain

Peripheral Sensitization

- Na+
  - carbamazepine
  - TCA
  - topiramat
  - lidocaine

Central Sensitization

- Ca++
  - gabapentin
  - pregabalin
  - lamotrigine

- NMDA
  - ketamine
  - dextromethorphan
  - methadone
  - memantine
  - cannabinoids

Spinal cord

Capsaicin (Substance P)

NSAIDS (COX)

Levodopa

Deep Brain Stimulation

- Brain stimulation of the **PAG** evokes the release of endorphins
- This initiates descending inhibition and "pain" control
Opiate Analgesia

- Systemic opiates provide relief of pain by binding to receptors in the same region that endorphins bind.

- However, side effects occur because opiate receptors are found elsewhere in the body.

Brainstem - Respiratory Depression

Gut - Constipation...
## Opioid Receptors in Pain

<table>
<thead>
<tr>
<th></th>
<th>μ</th>
<th>δ</th>
<th>κ</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Endogenous opioid</strong></td>
<td>β-Endorphin</td>
<td>Enkephalin</td>
<td>Dynorphin</td>
</tr>
<tr>
<td><strong>Agonists</strong></td>
<td>Morphine, Codeine, Oxycodone, Hydromorphone, Fentanyl, <strong>Methadone</strong></td>
<td><strong>Methadone</strong>, Hydromorphone</td>
<td>Pentazocine, Oxycodone(?) Morphine (?)</td>
</tr>
<tr>
<td><strong>Mechanism of action</strong></td>
<td>Protein G, Potassium channel opening</td>
<td>Protein G, Potassium channel opening</td>
<td>Protein G, Calcium channel closing</td>
</tr>
<tr>
<td><strong>Clinical effect</strong></td>
<td>Supraspinal analgesia, euphoria, anxiolysis, nausea, constipation, cough suppression, sedation, respiratory depression, physical dependance</td>
<td>Same effects as μ but less pronounced (spinal analgesia, respiratory depression)</td>
<td>Spinal analgesia, aversion, sedation Diuresis, respiratory depression</td>
</tr>
</tbody>
</table>

***Sigma Opioid receptors don’t play a role in analgesia but may contribute to dysphoria, delirium, hallucinations, tachycardia and hypertension***

Adapted from: AH Dickinson, 1997.
<table>
<thead>
<tr>
<th>Opioid</th>
<th>Terminal Half-Life (hours)</th>
<th>Oral (transdermal) Bioavailability %</th>
<th>Active Metabolites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>2 – 4</td>
<td>10 – 50</td>
<td>M6G, M3G</td>
</tr>
<tr>
<td>Meperidine</td>
<td>3 – 4</td>
<td>30 – 60</td>
<td>Normeperidine</td>
</tr>
<tr>
<td>Methadone</td>
<td>6 – 150</td>
<td>60 – 90</td>
<td>None known</td>
</tr>
<tr>
<td>Fentanyl Transdermal</td>
<td>17</td>
<td>92 – 95</td>
<td>Norfentanyl</td>
</tr>
<tr>
<td>Codeine</td>
<td>3 – 4</td>
<td>60 – 90</td>
<td>Morphine</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>2 – 6</td>
<td>40 – 80</td>
<td>Oxymorphone</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>2 – 4</td>
<td>35 – 80</td>
<td>H3G?, H6G</td>
</tr>
</tbody>
</table>
Placebo vs Hypnosis

**Placebo**
- The more pain you have, the more likely you will respond to placebo
- *Placebo analgesia can be blocked by naloxone...stimulates endorphins*

**Hypnosis**
- If pain is cognitive, then manipulating cognition should work
- This is not blocked by naloxone
- 80% of people are hypnotizable
Neuropathic Pain Treatment

- Stabbing sensation
- Electric shock-like sensation
- Pins and needles sensation
- Numb sensation
- Throbbing sensation
- Shooting sensation
- Burning sensation
CPS Guidelines - Neuropathic Pain

1st Line: TCA, Gabapentin or Pregabalin

2nd Line: SNRI, Topical lidocaine

3rd Line: Tramadol or CR opioid analgesic

4th Line: Methadone, Ketamine, Cannabinoids, lamotrigine, topiramate, valproic acid

Moulin et al., Pain Res Manage 2007

OBJECTIVE: Neuropathic pain is difficult to diagnose and difficult to treat with certainty. So the aim of the study was to evaluate comparative clinical efficacy of pregabalin with amitriptyline and gabapentin in neuropathic cancer pain.

METHODS: A total of 120 patients with cancer having severe neuropathic cancer pain were enrolled in the study .......

RESULTS: Our results suggested that all antineuropathic drugs are effective in relieving cancer-related neuropathic pain.

CONCLUSION: There was statistically and clinically significant morphine sparing effect of pregabalin in relieving neuropathic cancer pain and neuropathic symptoms as compared to other antineuropathic drugs.

OBJECTIVES: We assessed the efficacy and tolerability of combined nortriptyline and gabapentin compared with each drug given alone.

METHODS: In this double-blind, double-dummy, crossover trial, patients with diabetic polyneuropathy or postherpetic neuralgia, .......

RESULTS: The most common adverse event was dry mouth, which was significantly less frequent in patients on gabapentin than on nortriptyline (p<0.0001) or combination treatment (p<0.0001). No serious adverse events were recorded for any patients during the trial.

CONCLUSION: Combined gabapentin and nortriptyline seems to be more efficacious than either drug given alone for neuropathic pain, therefore we recommend use of this combination in patients who show a partial response to either drug given alone and seek additional pain relief.

Scrambler therapy may relieve chronic neuropathic pain more effectively than guideline-based drug management: results of a pilot, randomized, controlled trial.

OBJECTIVES: To compare guideline-based drug management with Scrambler therapy, a patient-specific electrocutaneous nerve stimulation device

METHODS: A clinical trial with patients randomized to either guideline-based pharmacological treatment or Scrambler therapy for a cycle of 10 daily sessions was performed. ....

RESULTS: Fifty-two patients were randomized. .....More relapses were seen in polyradicular pain than monoradicular pain, but retreatment and maintenance therapy gave relief. No adverse effects were observed.

CONCLUSION: In this pilot randomized trial, Scrambler therapy appeared to relieve chronic neuropathic pain better than guideline-based drug management.

Marineo G. et al., J Pain Symptom Manage. 2012 Jan;43(1):87-95
Methadone

- Binds to opioid receptors to provide analgesic effect (at high doses may negate NMDA antagonist effects)
- NMDA receptor antagonist possibly helps to reverse opioid tolerance and OIH
- Requires special license (for pain vs addiction) due to complex pharmacology
- TID dosing ideal for pain management properties
- Some research pointing to benefits as co-analgesic

J Pain Symptom Manage. 2011 and 2012
Parsons H. et al., Cancer 2010.
Ketamine

- **NMDA receptor antagonist helps to reverse opioid tolerance and OIH and also has analgesic properties**
- **PO low dose often starting at 2.5 to mg TID and titrate**
  - Burst techniques or continuous administration
- **SQ bolus/infusion protocols require hospitalization**
  - Burst technique or continuous infusion
  - CNS side effects respond to diazepam
- **Benefits and harms of adding ketamine to morphine for cancer pain are not yet established**

Cochrane Data Sys Rev 2010
J Pain Symptom Manage. 2011 Therapeutic Review: Ketamine
Lidocaine

- **Local anesthetic administered systemically for relief of neuropathic pain**
- **San Diego Hospice protocol...load 2 mg/kg IV over 15-20min**
  - If pain improves, infuse at 1-3mg/kg/hr
  - Measure blood levels 8 hours post
- **Dose dependent adverse effects in ascending order:**
  - Peri-oral numbness, metallic taste, twitching, seizure

Tremonts-Lukats et al., Anest Analg 2005
Update in Palliative Medicine. Analgs of Internal Med 2007
Sharma S. et al., JPSM 2008
Thomas J. et al. J Pall Med 2004 7(5)
Cannabis Sativa

- Research is limited in demonstrating effectiveness in treating:
  - Chemotherapy induced severe nausea and vomiting
  - Anorexia-Cachexia
  - Chronic/severe pain, particularly neuropathic pain
- Despite this, it is approved for these indications
- Available as a buccal spray Sativex®
- Oral forms include dronabinol (Marinol®) or nabilone (Cesamet)

Johnson J. et al., J Pain Symptom Manage. 2009
Interventional Techniques

- Well localized, segmental pain
- Incident pain
- Difficult visceral pain
- <6-12 month life expectancy
- For patients refractory to parental opioids
- For patients who experience intolerable side effects from systemic opioids/adjuvant therapy
Intraspinal Analgesia

- **Principle drug is opioid but can be combined with adjuvants**
- **Can be used for month via pump delivery system**
- **Can be administered in either the epidural or intrathecal space**
  - Epidural benefits: reduced risk of PDPH, side effects less intense, dura acts as a barrier to infection, greater site selection, greater toxicity safety margin
  - Intrathecal benefits: less risk of catheter obstruction, more intense, rapid and longer duration analgesia, lower volume of infusion, less risk of catheter migration
- **Efficacy (in decreasing order):**
  - Continuous somatic pain, continuous visceral pain
  - Intermittent somatic pain, intermittent visceral pain
  - Neuropathic pain
Peripheral Nerve Blocks

- Femoral or sciatic nerves for leg pain
- Brachial plexus as well
- Not usually the sole or primary pain treatment
- Long term infusions of local anesthetic or neurolysis
- Best for somatic pain and for when pain is well localized to a known nerve/plexus distribution
- Complications may include damage to surrounding structures from neurolytic agent, muscle weakness, regrowth neuritis
Sympathetic Plexus Blocks

- Great for treatment of poorly controlled visceral pain
- Collections of nerve bodies (ganglia) of the sympathetic nervous system lie near the thoraco-lumbar vertebrae through which visceral inputs travel before entering the spinal cord
  - Celiac plexus – stomach, liver, GB, pancreas, spleen kidneys and gut to transverse colon
  - Lumbar plexus – lower extremities, uterus, cervix, kidney, ureters, transverse colon
  - Hypogastric plexus – rectum, bladder, distal colon, prostate, uterus, cervix, vagina, ovaries
  - Ganglion impar – perineum, distal rectum, anus, distal urethra, vulva, distal vagina
  - Thoracic ganglia – mediastinum, esophagus, trachea, bronchi, pericardium, heart, thoracic aorta, pleura, lung
THORACIC GANGLIA

SPLANCHNIC NERVES and CELIAC PLEXUS

LUMBAR GANGLIA

LUMBAR GANGLIA

HYPOGASTRIC PLEXUS

GANGLION IMPAR
Neurolysis

- Sacral nerves for somatic perineal pain
- Chemical rhizotomy that is localized to posterior column, through which most nociceptive impulses pass
- Simple to carry out (so they say), no serious side effects
- Requires only a brief stay in hospital and does not require special equipment
- Contraindications include poorly localized or neuropathic pain, intraspinal tumor, no relief with diagnostic block, coagulopathy
- Complications may include headache, meningitis, arachnoiditis, paresis of muscle if anterior roots affected, incontinence/bladder dysfunction
Ideal Treatment of BTP

Uncontrolled BTP

Controlled BTP

Analgesic closely matches time profile of BTcP
Rapid onset of action controls BTcP
Short duration of action minimises systemic exposure
Increase ATC Opioids

- Controlled release opioids have slow onset and long duration of action\(^2\)
- May result in excess drug accumulation and increased risk of toxicity

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**Uncontrolled BTP**

- Btcp is not controlled
- ATC analgesia controls baseline pain

**Suboptimal Control of BTP**

- Slow onset of action
- Increased ATC analgesia controls some Btcp
- High systemic exposure risks adverse events

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Adapted from Bennett\(^1\), Simmonds\(^3\) and Coluzzi\(^4\)

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Use of Oral IR Opioids

- Long-standing clinical use with established efficacy and ease of administration for patient
- Onset of action is too slow and duration of action is too long (time-action profile does not follow BTP pattern)

Onset of action is too slow

Duration of action is too long

Adapted from Bennett\(^1\), Coluzzi\(^2\) and Simmonds\(^3\)

The hydrophilic nature of some IR opioids largely accounts for their suboptimal pharmacokinetics:

- do not pass rapidly across oral mucosal cells
- absorbed primarily in the gastrointestinal tract
- have extensive first-pass effect, which slows the onset of action

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“Immediate Release” Fentanyl

- **Lipophilic nature and pharmacokinetic properties** make fentanyl an appropriate treatment for BTP

- **“IR” routes of administration include**
  - IV, SubQ or transmucosally (sublingual, intranasal)

- **Bioavailability depends on route of administration**
  - Transdermal 92%
  - Intranasal 89%
  - Buccal, sublingually 50%
  - Oral 33%
Oral Transmucosal Administration

- **Advantages over subcutaneous route**
  - Better mimics BTP pattern
  - Less costly, less invasive (simple administration)
  - No worries about edema, circulation, coagulopathy

- **Advantage over oral ATC or IR opioids**
  - Better mimics BTP pattern
  - Works even if GI tract not available due to obstruction, dysphagia, odynophagia, nausea/vomiting
  - Can be used even with decreased LOC

- **Advantage over Rectal Transmucosal**
  - Rectal route is impractical, difficulty of administration, diarrhea, constipation, fistulas

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Indications for Sublingual Fentanyl

- For the management of BTP in cancer patients:
  - Who are 18 years of age and older
  - Already receiving chronic opioid therapy
  - Tolerant to opioid therapy
  - Baseline pain well controlled
  - Ideally no more than 4 BTP episodes per day

- Patients taking for one week or longer at least:
  - 60 mg oral morphine/day
  - 25 mcg TD fentanyl
  - 30 mg oral oxycodone/day
  - 8 mg oral hydromorphone/day
Contraindications

- Non opioid-tolerant patients
- Management of postoperative pain
- Headache/migraine/dental pain
- Acute pain crisis presenting to the ER
- Severe respiratory depression/severe COPD
- Sensitivity to fentanyl products or inactive ingredients

- Patients taking buprenorphine or tramadol
- Patients with significant drug abuse potential
Abstral Dosage and administration

- To administer Abstral, one tablet is placed under the tongue at the deepest part of the sublingual cavity, where it is allowed to dissolve completely
  - Rapid disintegration, dissolution and absorption

- Chewing, sucking or swallowing could result in reduced absorption and low plasma concentrations of fentanyl

- Abstral tablets are available in six dosing strengths:
  - 100, 200, 300, 400, 600 and 800 µg

Abstral™ Product Monograph 2011
Abstral Recommended titration schedule

- The initial dose of Abstral used must be 100 µg
- Abstral dosing for a subsequent episode should be separated by at least 2 hours
- No more than four doses per day
Pain management and cognitive impairment

Case studies
Knowledge transfer
Cognitive impairment

- Elderly patients report less pain than younger patients even though may have more pain experience
- Cognitive impairment is a big barrier to assessment and management of pain
- Although self report gold standard in pain assessment is decreased because of dementia severity
- Patient with memory impairment have decreased ability to recall, interpret or articulate the pain experience
- Pain recall and ability to integrate pain experience lessens over time – patients with moderate dementia may be able relay pain in the moment if prompted
Clinical Practice Guidelines

- American Geriatric Society (AGS) – Clinical Practice Guidelines 2011 specific to aged population
- American Medical Directors Association (AMDA) - CPG’s for long term care settings
- American Society for Pain Management Nursing (ASPMN) has position statement and guidelines for pain management in the non verbal patient.
AGS Guidelines 2011 hierarchy pain assessment strategies

- **Self report**
- **Capacity to provide self report ratings diminished in demented patients** (Kunz, M et al, Pain, 2007)
- **Is feasible in patients with mild –moderate cognitive impairment and should be attempted initially** (Ni Thuathail, A, et al, Nursing Standard 2011)

- **Search for potential causes of pain**
- **Put down to natural aging process**
Hierarchy cont’d

- Observation of patient behaviours- as severity of dementia progresses rely on caregivers (professional and family), rely on non-verbal cues

- Proxy reporting of pain - family and caregivers may recognize pain but over or under estimate intensity

- Difficult to know quality of the pain experience by proxy info

- Attempt analgesic trial
John- 89 yr old male

- Dx of intramucosal carcinoma with bowel intussusception and perforation (2010) with presumed peritoneal and serosal metastatic deposits (Nov 2012)-declined investigation
- Hx: OA, Angina CAD, Dyslipidemia, BPH, Dementia

- Initial visit....most information provided by spouse Alice as patient’s memory issues and dementia evident. Patient would have difficulty providing info and would turn to wife to help him answer. With review of symptoms wife reported that John had occasional abdominal pain relieved by Tylenol ES. He was also reported as having sleeplessness at night and had recently been prescribed Serax 15mg by family practitioner. It did not have the desired effect.
- With review of sleep problem he was reported as having had bothersome cough for several weeks and to her memory perhaps sleeplessness in association with cough. He was completing a 2nd course of abx
John Cont’d

- Discussed that cough and mild abd pain may be helped with low dose narcotic, spouse reluctant to increase pain control at that time
- Patient started on advair and hycodan at bedtime for persistent cough, abx changed and cough improved
- Patient was provided Lorazepam one weekend because of increased anxiety with sleeplessness
- Sleeplessness and behaviours escalated, wife exhausted
- Remeron trialled and sleep pattern worsened
- Discussed night pattern and on inquiry spouse said that John was moaning more at night. During exam with light palpation elicited that patient has tenderness across abdomen, some slight distention noted. Discussed plan to start low dose hydromorphone 0.5mg qid and as needed
John cont’d

- Remeron D/C’ed and Trazodone started
- Patient continued to report he had no pain when visited but with exam he would acknowledge pain in the moment
- With help of the visiting nurses gradually titrated to hydromorphone 3mg q12h and now on q8h dose with occasional breakthrough. Trazodone at 50mg qhs
- Analgesic trial successful in resolving sleeplessness and accompanying behaviours
AGS Hierarchy

- Self report
- Search for potential causes of pain
- Observation of behaviour
- Proxy reporting by caregivers
- Analgesic trial
Jean 89 years of age

- **Medical Dx:** End stage CHF

- **Medical Hx:** Hypothyroidism, angina, GERD, hiatus hernia, type II diabetes, diverticulosis, Raynaud phenomenon, glaucoma, osteoarthritis, osteoporosis, right retinal embolus, carotid bruits, carotid plaques with no narrowing, degenerative disc disease with a wedge fracture at T12, falls.

ROS: Panic and anxiety, history of depression in past.
Jean cont’d

- **Issues:**
  1. Delirium and calling out at night continues – start Mirtazapine 7.5 mg x 1 week and if tolerates increase to 15mg
  2. Pain management – complicated by delirium on dementia – D/C tramacet, hydromorphone 0.5 mg qid and q4h prn
  3. Epigastric pain - d/c Tramacet restart Rabeprazole
Knowledge transfer

- Innovation is about novel ideas and translating those ideas into better products, services, and ways of doing things. There are many ways of getting there, but at the heart of the innovation journey is knowledge translation. Knowledge translation is a deliberate, two-way, iterative process of using evidence to help inform decisions but what are the key ingredients for doing this successfully - what knowledge, skills and tools do we need to make knowledge translation effective?

- Difficult sometimes, there are valid reliable tools for assessment of pain in the cognitively impaired.....how to use with family and other untrained caregivers in community
Tools for assessment pain

  - Website contains current, detailed critiques of 17 tools for the assessment of pain in non-verbal older adults. The tools critiqued on this site address the elements of the 2002 AGS Pain on Persistent Pain in Older Persons’ list of pain behaviors.

- Behavioral Pain Indicators organized in a comprehensive framework in the American Geriatrics Society Guidelines for Persistent Pain in Older Adults (2002)
Pain behaviour indicators

- **Facial Expression**—slight frown, sad, frightened face
- **Verbalizations & Vocalizations**—sighing, moaning, groaning, grunting
- **Body Movements**—rigid, tense body posture, guarding, fidgeting, rocking
- **Changes in Interpersonal Interactions**—aggressive, combative, resisting care
- **Changes in the Activity Patterns or Routines**—refusing food, appetite change, changes in rest or sleep patterns
- **Mental Status Changes**—crying or tears, increased confusion, irritability, or distress
Knowledge transfer & using the research in practice

- Values and goals - let people know what is at stake – in Jean and John’s case comfort can be achieved
- Narratives and story telling – discuss cases and what works - palliative care rounds are great examples
- Celebrate small successes - the untrained caregivers Aha moment that helps them to understand behaviours
- Metaphors – scenarios that help contribute to understanding

And other unlisted strategies......

Thanks!
Summary

- **Pain is a disease of the central nervous system**
  - Sensory-discriminative, emotional and cognitive components
  - Chronic pain includes both neuropathic and nociceptive categories, of which there is LOTS of overlap

- **Assessment MUST go beyond the pain scale**
  - Do we need to worry about OIH? Tolerance?

- **Treatment Strategies**
  - Treatment of pain goes way beyond the WHO analgesic ladder
  - Treatment strategies will depend on the nature of the pain
  - The pain
Pain Cocktail?