Pain management

- What are some of the things that make pain so difficult to treat?

Pain Assessment and Management

- Diane Dietzen, MD, FACP
Objectives

- Identify the steps of analgesic management
- Calculate the conversion between different opioids
- Explain the use of adjuvant analgesic agents and management of adverse effects of opioid use
What are **YOUR** goals for this session?

What are some specific issues in pain assessment and management that **YOU** would like us to address?

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**Our patient  Ms. N- from our talk this AM**

Ms. N. is a 74-year-old female, who comes to see you in your primary care office after her recent discharge from the hospital. She has a history of end-stage renal disease on chronic hemodialysis, as well as recently diagnosed lung cancer, which is be inoperable, as she has lymphadenopathy and liver metastases.

She was hospitalized for shortness of breath, volume overload, and chronic back and lower extremity pain. She arrives at your office in a wheelchair, unable to walk secondary to the pain, accompanied by her daughter, with whom she lives.
Case Discussion

- What do you suggest to help alleviate Mrs. N’s pain?
- What more do we need to know?

Pain Management in palliative care

- Is it different than pain management in other settings?
- Should it be?
Who has pain?
What is pain?

Pain is an unpleasant sensory and emotional experience

- Many types and sites of care
- In NH setting: 30% reported daily pain
- 26% of these patients received no analgesia
- Only 26% of them received strong opioids

- Outpatients: 67% outpatients with metastatic CA were in pain
- 42% of those not given adequate analgesic therapy
- also we cause pain - procedures

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Physiology of Pain Perception

- Transduction
- Transmission
- Modulation
- Perception
- Interpretation
- Behavior

Adapted with permission from WebMD Scientific American® Medicine.
Ways to Classify

- Neuropathic VS Nociceptive
- Acute pain-identified event, resolves days–weeks, usually nociceptive VS.
- Chronic pain-cause often not easily identified, multifactorial, indeterminate duration, nociceptive and / or neuropathic

Another method

- 2 types of chronic pain
  - Cancer-related pain
  - Non-cancer pain
Nociceptive pain

- Direct stimulation of intact nociceptor
- Transmission along normal nerves
  - somatic or visceral
    - somatic
      - easy to describe, localize
    - visceral
      - difficult to describe, localize
- Tissue injury apparent
  - Management
    - opioids
    - adjuvant/coanalgesics

Neuropathic Pain

- Origin:
  - Nerve damage
- Palliates/potentiates:
  - Set off by unusual stimuli, light touch, wind on skin, shaving (trigeminal neuralgia)
- Quality:
  - Electric, burning, tingling, pins & needles, shooting (system isn’t working right)
- Radiation:
  - Nerve-related pattern
- Management
  - Opioids alone will not manage this pain
  - adjuvant/coanalgesics often required
Nociceptive vs Neuropathic Pain

**Nociceptive Pain**
- Caused by activity in neural pathways in response to potentially tissue-damaging stimuli
- Postoperative pain
- Mechanical low back pain
- Sickle cell crisis
- Sports/exercise injuries

**Mixed Type**
- Caused by a combination of both primary injury and secondary effects
- Arthritis
- Postherpetic neuralgia
- Neuropathic low back pain
- Distal polyneuropathy (eg, diabetic, HIV)

**Neuropathic Pain**
- Initiated or caused by primary lesion or dysfunction in the nervous system
- CRPS*
- Trigeminal neuralgia
- Central post-stroke pain

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**Pain assessment: Pain intensity scales**

- Simple Descriptive Pain Intensity Scale
- 0-10 or 0-3 Numeric Pain Intensity Scale
- Visual Analog Scale
- Faces Scale

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*Complex regional pain syndrome*
The **FLACC scale** is a measurement used to assess pain for children between the ages of 2 months–7 years or individuals that are unable to communicate their pain. The scale is scored between a range of 0–10 with 0 representing no pain. The scale has 5 criteria which are each assigned a score of 0, 1 or 2.

<table>
<thead>
<tr>
<th>Categories</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face</td>
<td>No particular expression or sound</td>
<td>Occasional grimace or crying,        </td>
<td>Frequent to constant crying,        </td>
</tr>
<tr>
<td></td>
<td></td>
<td>breath, writhing,</td>
<td>clenching jaw</td>
</tr>
<tr>
<td>Legs</td>
<td>Normal position or relaxed</td>
<td>Uncooperative, restless,</td>
<td>Kicking or legs drawn up</td>
</tr>
<tr>
<td></td>
<td></td>
<td>kicking, moving</td>
<td></td>
</tr>
<tr>
<td>Activity</td>
<td>Sitting quietly, normal position, moves easily</td>
<td>Reclining, shifting back and forth,</td>
<td>Arching, rigid, or jerking</td>
</tr>
<tr>
<td></td>
<td></td>
<td>sitting, rocking</td>
<td></td>
</tr>
<tr>
<td>Cry</td>
<td>No cry (no tears or audible)</td>
<td>Moans or whimpers, occasional complaints</td>
<td>Crying steadily, screams or wails, frequent crying</td>
</tr>
<tr>
<td>Consolability</td>
<td>Content, relaxed</td>
<td>Resists being consoled or comforted,</td>
<td>Difficult to console or comfort</td>
</tr>
<tr>
<td></td>
<td></td>
<td>restless or irritable,</td>
<td></td>
</tr>
</tbody>
</table>

*Note: Each of the five categories Face (F), Legs (L), Activity (A), Cry (C), and Consolability (O) is scored from 0-2, which results in a total score between 0 and 10.*


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**We do not do this well**

<table>
<thead>
<tr>
<th>Patients’ assessment correlated with those of:</th>
<th>0-2 Little or no pain</th>
<th>3-6 Moderate pain</th>
<th>7-10 Severe pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nurse</td>
<td>82%</td>
<td>51%</td>
<td>7%</td>
</tr>
<tr>
<td>House Officer</td>
<td>66%</td>
<td>26%</td>
<td>21%</td>
</tr>
<tr>
<td>Onc Fellow</td>
<td>70%</td>
<td>29%</td>
<td>27%</td>
</tr>
<tr>
<td>Caregiver</td>
<td>79%</td>
<td>37%</td>
<td>13%</td>
</tr>
</tbody>
</table>

Pain assessment: one method

- N - Number of pains?
- O - Origin/causes?
- P - Palliates, potentiates?
- Q - Quality?
- R - Radiation?
- S - Severity, suffering?
- T - Timing, trend?
- U - how is the pain affecting “YOU”? 

Circumstances In Which Incident Pain Often Occurs- ask about these

- Bone metastases
- Neuropathic pain
- Skin ulcer: dressing change, debridement
- Disimpaction
- Catheterization
- Procedures
Medication(s) Taken

- Dose
- Route
- Frequency
- Duration
- Efficacy
- Adverse effects
Domains of Chronic Pain

**Quality of Life**
- Physical functioning
- Ability to perform activities of daily living
- Work
- Recreation

**Psychological Morbidity**
- Depression
- Anxiety, anger
- Sleep disturbances
- Loss of self-esteem

**Social Consequences**
- Marital/family relations
- Intimacy/sexual activity
- Social isolation

**Socioeconomic Consequences**
- Healthcare costs
- Disability
- Lost workdays

**Other symptoms**
- **Symptom**
- **Pain**
- Fatigue/Asthenia
- Constipation
- Dyspnea
- Nausea
- Vomiting
- Delirium
- Depression/suffering

ESAS and other tools to assess

- **Prevalence**
  - Pain: 80 - 90+%%
  - Fatigue/Asthenia: 75 - 90%
  - Constipation: 70%
  - Dyspnea: 60%
  - Nausea: 50 - 60%
  - Vomiting: 30%
  - Delirium: 30 - 90%
  - Depression/suffering: 40 - 60%
Keep in Mind……

- Pain is always subjective
- Past experiences can influence a patient's perception of pain
- MYTH: Lack of physical symptoms (↑HR, ↑RR, obvious discomfort) indicate a psychogenic pain
- The patient's self-report of pain is the most reliable indicator of pain
- Do not delay treatment for evaluation

Principles of Assessment

- Assess and reassess
- Use methods appropriate to cognitive status and context
- Assess intensity, relief, mood, and side effects
- Use verbal report whenever possible
- Document in a visible place
- Expect accountability
- Include the family
What are the effects of pain?

- **Physiologic:**
  - Increased catabolic demands: poor wound healing, weakness, muscle breakdown
  - Decreased limb movement: increased risk of DVT/PE
  - Respiratory effects: shallow breathing, tachypnea, cough suppression increasing risk of pneumonia and atelectasis
  - Increased sodium and water retention (renal)
  - Decreased gastrointestinal mobility
  - Tachycardia and elevated blood pressure
  - Decrease natural killer cell counts
  - Effects on other lymphocytes not yet defined.

- **Psychological:**
  - Negative emotions: anxiety, depression
  - Sleep deprivation
  - Existential suffering: may lead to patients seeking active end of life.

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**Physical Exam In Pain Assessment**

**Inspection / Observation**

"You can observe a lot just by watching"  
* Yogi Berra

- Overall impression... the "gestalt"?
- Facial expression: Grimacing; furrowed brow; appears anxious; flat affect
- Body position and spontaneous movement: there may be positioning to protect painful areas, limited movement due to pain
- Diaphoresis - can be caused by pain
- Areas of redness, swelling
- Atrophied muscles
- Gait Myoclonus – possibly indicating opioid-induced neurotoxicity
  - Localized tenderness to pressure or percussion

- Fullness / mass
- Induration / warmth

Further areas of focus of the physical examination are determined by the clinical presentation.  
Eg: evaluation of pleuritic chest pain would involve a detailed respiratory and chest wall examination.
### Physical Exam in Pain Assessment

#### Neurological Examination

- Important in evaluating pain, due to the possibility of spinal cord compression, and nerve root or peripheral nerve lesions.
- Sensory examination:
  - Areas of numbness / decreased sensation
  - Areas of increased sensitivity, such as allodynia or hyperalgesia
- Motor (strength) exam - caution if bony metastases (may fracture)
- Deep tendon reflexes – intensity, symmetry
  - Hyperreflexia and clonus: possible upper motor neuron lesion, such as spinal cord compression or cerebral metastases.
  - Hyporeflexia - possible lower motor neuron impairment, including lesions of the cauda equina of the spinal cord or leptomeningeal metastases.
- Sacral reflexes – diminished rectal tone and absent anal reflexes may indicate cauda equina involvement of by tumour

### Goals in Treating Pain

- May vary - should be discussed
- Competing factors - pain, function, side effects, other
- Analgesia, activities of daily living, adverse events, and aberrant behavior
- What are your goals for our patient?
Case responses

- Mrs. N. notes-
  - Dyspnea with exertion-walking from one room to the next
  - Pain described as 5/10 in her lower back, increased with activity and also 5/10 in both lower extremities, 10 this pain is described as numb and tingling
  - She’s been taking Tylenol 500 mg 4 times daily
  - With some relief but her activities remain very limited
  - She’s not tried any previous medication
  - When asked she describes she is very discouraged by her recent events, and agrees that she may be depressed

Approach To Pain Control

After assessment by skilled and knowledgeable clinician

1. Discuss with patient/family the goals of care, hopes, expectations, anticipated course of illness. This will influence consideration of investigations and interventions
2. **Investigations** – X-Ray, CT, MRI, etc - *if they will affect approach to care*
3. **Treatments** – pharmacological and non-pharmacological; interventional analgesia (e.g. Spinal)
4. **Ongoing reassessment and review** of options, goals, expectations, etc.
Non-pharmacologic Approaches to Pain

- Behavioral therapy
- Spiritual counseling
- Physical therapy
- Psychotherapy
- Splinting
- Cold packs
- Meditation
- Support groups
- Acupuncture
- Hypnosis
- Cultural healing rituals
- Heat packs
- Prayer
- Community resources
- And others...

Medications to consider for Mrs. N.

- To treat pain
- Treat dyspnea
- Treat other symptoms
- “two- fers” and combinations
When is pall care consult desirable?

What about pain management?

- Other options?

A general list of medications to consider:

- Local measures
- Acetominophen
- NSAIDS
- Tramadol
- Narcotics
- Adjuncts: antidepressants
  - anti epileptics
- other
WHO 3-step Ladder

1 mild
- ASA
- Acetaminophen
- NSAID's
- COX-2 selective
- NSAIDS
  ± Adjuvants

2 moderate
- A/Codeine
- Tramadol
- A/Hydrocodone
- A/Oxycodone
  ± Adjuvants

3 severe
- Morphine
- Oxycodone
- Hydromorphone
- Methadone
- Levorphanol
- Fentanyl
  ± Adjuvants

Drug name:
- Starting dose
- Half-life
- Dosage forms
- Side effects
- Cautions
- Cost concerns
Drug name: Acetaminophen

- Starting dose 325mg
- Half-life 2-3 hours
- Dosage forms - oral, now IV
- Side effects - few
- Cautions - next slide
- Cost concerns - none

Acetaminophen – Adverse effects

- Doses greater than 4g per 24 hours are not recommended as they may cause hepatotoxicity.
- Hepatic disease or heavy alcohol use increases this risk further.
- On the outpatient basis, patients may not realize their Lortab, Percocet, etc., has acetaminophen included (it is called “apap” on the prescription bottle) and they may then take additional separate acetaminophen, increasing risk of accidental overdose and hepatotoxicity.
NSAIDs

- NSAIDs are effective step 1 analgesics
- They may also be useful coanalgesics
- They are effective for bone and inflammatory pain.
- They work in part by inhibiting cyclo-oxygenase (COX), the enzyme that converts arachidonic acid to prostaglandins.
- All NSAIDs inhibit COX but vary in COX-2 selectivity.
- Ketorolac (Toradol) is available in an intravenous formulation.

Drug class NSAID

- Starting dose-varies
- Half-life- varies
- Dosage forms- oral and IV
- Side effects familiar
- Cautions- bleeding, RI, CHF
- Cost concerns few
Drug name: Tramadol

- Weak μ opioid receptor agonist, and weak inhibitor of epinephrine and serotonin uptake
- Starting dose 50 mg tid
- Half-life 6 hours
- Dosage forms- oral IR and ER forms
- Side effects- constipation, nausea
- Cautions metabolites, liver and renal disease
- Drug interactions SSRI
- can be addictive
- Cost concerns some

What can we offer Ms. N. of above?

What else should we offer?
It is not necessary to traverse each step sequentially; a patient with severe pain may need to have opioids right away.

Opiates: How do you choose an initial opioid?
Opioid Analgesics

- Opioids used conventionally for moderate pain (Step 2):
  - codeine, hydrocodone, oxycodone.
  - typically combined with non-opioid (e.g. Tylenol #3, Percocet) which limits dose titration.

- Opioids used conventionally for severe pain (Step 3):
  - morphine, hydromorphone, fentanyl, oxycodone.
  - levorphanol, methadone, oxymorphone

Drug name: Morphine

- Starting dose- 2.5-5 mg p.o. 0.5-2 mg IV/sq
- Half-life- dependent on form – oral 2-4 hours
- Dosage forms- multiple
- Side effects: histamine release
- Cautions-opiate class cautions
- Also caution in renal failure and liver disease
- Cost concerns-only with long-acting forms
- Many patient have associations that will need to be addressed
Drug name: Oxycodone

- Starting dose 2.5-5 mg p.o. q.4
- Half-life-dependent on preparation oral SA 2-4 hours
- Dosage forms- oral
- Long acting and short acting
- Side effects class effects of opiates
- Cautions liver disease
- Cost concerns-more expensive than morphine

Drug name: Hydromorphone

- Starting dose 2 mg po, 0.2 Iv
- Half-life 2-4 hours po
- Dosage forms po/Iv, no SR form
- Side effects class
- Cautions- potency
- Cost concerns few
Drug name: Fentanyl

- Starting dose
- Half-life based on route: for patch 12-20 hours
- Dosage forms: patch, oral transmucosal, IV
- Side effects: class, skin reaction
- Cautions: patch awareness, fat for absorption, sweat, fever
- Cost concerns: some

Transdermal Fentanyl

- Advantages
  - Non-enteral administration
  - Change q72h
  - Steady blood levels
- Disadvantages
  - Local skin problems
  - Delayed onset and offset
  - Cumbersome to titrate (only q72h)
  - 20% of people need it changed q48h
Metabolism and clearance concerns for all opiates

- Conjugated by liver
- 90–95% excreted in urine for all
- Dehydration, renal failure, severe hepatic failure
  - ↓ dosing interval (space out doses) or ↓ dosage

Selecting a Starting Dose

No prior opioid and younger, healthier: Begin one of the strong opioids at a dose equivalent to 5 - 10 mg of MSO4 IV/SC every four hours.

Smaller dose in older, with other illnesses

Base dosing intervals on “time to peak” and duration
- Usual IV dosing interval: q2-3hprn
- Usual oral dosing interval: q3-4hprn
- Fentanyl - quicker peak/duration
Principles of Opioid Analgesic Use in Acute and Cancer Pain

- Individualize route, dosage, and schedule
- Administer analgesics regularly (not PRN) if pain is present most of day
- Become familiar with dose / time course of several strong opioids
- Give infants / children adequate opioid dose
- Follow patients closely, particularly when beginning or changing analgesic regimens
Opioids - Principles of Dosing

Individualize dose by gradual escalation until development of adequate analgesia or intolerable and unmanageable side effects.

- No therapeutic ceiling effect.

“Around the clock dosing” for continuous or frequently recurring pain.

As needed (“prn”) dosing for dose finding and for “rescue doses”.

Upward Titration

- Mild pain (1-3)
  - titrate by 25%

- Moderate (4-6)
  - titrate by 50%

- Severe (7-10)
  - titrate 100%

- Titrate the rescue dose when you titrate the regular scheduled dose
Ongoing assessment

- Increase analgesics until pain relieved or adverse effects unacceptable
- Be prepared for sudden changes in pain
- Titration of doses should be based on pain intensity and frequency

Combination Drugs

- Advantages:
  - Aspirin or acetaminophen may act as co-analgesic
  - Lower level regulatory control
- Disadvantages:
  - Available in short-acting formulations only
  - ‘Combo wall’
What we offer Ms. N. of above?

- And what else?

Breakthrough/ Incident pain

Transitory exacerbations of severe pain over a baseline of moderate to mild pain
Reported by 2/3 of cancer patients with controlled baseline pain
Often due to: incident pain or end-of-dose failure (important to distinguish)
Breakthrough dosing

- Use immediate-release opioids
  - 10% of 24 hr dose (range 5-20)
  - offer after Cmax reached
    - PO / PR  \( \approx q 1\text{-}2\text{ h} \)
    - SC, IM  \( \approx q 30\text{min} \)
    - IV  \( \approx q 10\text{-}15\text{min} \)
- Do not use extended-release opioids
- Try to avoid mixing opioids

Having a steady level of enough opioid to treat the peaks of incident pain...

...would result in excessive dosing for the periods between incidents
Using Opioids for Breakthrough Pain

- Patient must feel in control, empowered
- Use aggressive dose and interval

Patient Taking Short-Acting Opioids:
- 50 - 100% of the q4h dose, given q1h prn

Patient Taking Long-Acting Opioids:
- 10 - 20% of total daily dose given, q1h prn with short-acting opioid preparation

What can we offer Ms. N. of above?
Pain poorly responsive to opioids

- If dose escalation results in adverse effects
  - alternative
    - route of administration- IV, SQ, PCA
    - opioid (‘opioid rotation’)

- Adjuvants
  - Re examine pain classification
  - NMDA anatagonist

Principles: Use of Opioid Rotation

- Use when one opioid ineffective or for adverse effects
Changing opioids

- Cross-tolerance (mu agonists)
  - start with 75% of published equianalgesic dose
    - more if pain, less if adverse effects
- Methadone
  - start with 10-25% of published equianalgesic dose

General principles of dosing

- Never start a long acting without a prn trial
- Consider all long acting and prn medications taken in the last 24 hrs, the current pain rating and the amt of comfort in the past 24 hours
- IV opioid medications tend to be 3-5 x more potent than po medications
- Allow pt or family input into route or schedule when formulating POC.
- Do the math !!!!!
- Are you looking for a larger number or a smaller number
- Double check calculations with a second source
- Use a conversion tool that works for you
- Globalrph.com
Equianalgesic doses of opioid analgesics

PO / PR (mg) Analgesic SC / IV / IM (mg)
30 Hydrocodone -
30 Morphine 10
15-20 Oxycodone -
7.5 Hydromorphone 1.5
- Fentanyl 0.10
225 Meperidine 75

Steps

Calculate 24 hour dose of current agent
Choose agent to switch to
Decide on dose increase for inadequate control
Decide on dose decrease for cross tolerance (usually 25%)
DO The math and verify the math
Divide new med into appropriate pills and dosing intervals
Some math

- To highlight, Mrs. N has been taking hydromorphone 2 mg p.o. q.4 p.r.n.
- She’s been taking 4 doses a day most days, with an added dose on dialysis days for pain related to transportation
- She also continues to take round-the-clock Tylenol
- She asks if she could be changed to a long-acting agent
Barriers to Effective Opioid Therapy

- **Patient Barriers**
  - Save for “when it’s really bad”
  - Fear of addiction
  - Stigma of morphine
  - Side effects
  - Reluctant to report pain

- **Physician Barriers**
  - Fear of addiction
  - Knowledge deficits
  - Regulatory oversight
  - Analgesia low priority compared to cure

Opioid adverse effects

**Common**
- Constipation
- Dry mouth
- *Nausea / vomiting*
- Sedation
- Sweats

**Uncommon**
- Bad dreams/hallucinations
- Dysphoria / delirium
- Myoclonus / seizures
- Pruritus / urticaria
- Respiratory depression
- Urinary retention

*Anaphylaxis / Bronchospasm is only true opioid allergy*
Constipation …

- Common to all opioids due to opioid effects on CNS, spinal cord, myenteric plexus of gut
- Easier to prevent than treat
- Methods:
  - Diet usually insufficient, bulk forming agents not recommended
  - Softeners
    - Docusate
    - Cathartics
    - Senna
    - Biscadoly (Dulcolax)
  - Osmotic Laxatives
    - Magnesium/aluminum salts
    - Lactulose
    - Sorbitol

Opioid-Induced Nausea and Vomiting

Stimulation of Medullary chemoreceptor trigger zone.
- Peak soon after administration
  - metoclopramide, neuroleptics

Enhanced vestibular sensitivity
- vertigo or prominent movement induced nausea
  - scopolamine, meclizine

Increased gastric antral tone
- early satiety, bloating, postprandial vomiting
  - Metoclopramide

Other antiemetics also be effective
- Alternative opioid if refractory
Opioid Side Effects -
Sedation and Cognitive Impairment

Common with initiation of therapy or dose escalation.
Tolerance usually develops in days-weeks.

Management of Persistent Opioid Induced
Sedation and Cognitive Impairment

D/C non-essential centrally acting medications.
Evaluate and treat other potential causes.
If analgesia satisfactory, decrease dose by 25%.
If analgesia inadequate or symptoms persist despite dose reduction:
- trial of psychostimulant (if sedation) or neuroleptic (if delirium).
- switch to an alternative opioid.
- trial of other invasive/non-invasive approach to decrease systemic opioid requirements.
Respiratory depression

- Opioid effects differ for patients treated for pain
  - somnolence, loss of consciousness precedes respiratory depression
- Management
  - identify, treat contributing causes
  - if unstable vital signs, naloxone 0.1-0.2 mg IV q 1-2 min

**Spectrum of Opioid-Induced Neurotoxicity**

- Neurotoxicity (OIN): delirium, myoclonus, seizures

Opioid tolerance
- Mild myoclonus (eg. with sleeping)
- Severe myoclonus
- Seizures, Death

Delirium → Hyperalgesia
- Opioids Increased → Agitation
- Misinterpreted as Pain
- Opioids Increased
- Misinterpreted as Disease-Related Pain
OIN: Treatment

- Switch opioid (rotation) or reduce opioid dose; often much lower than expected doses of alternate opioid required... often use prn initially
- Hydration
- Benzodiazepines for neuromuscular excitation

What side effects do we anticipate in Ms. N. of above?
When dose-limiting side effects occur with opioid pharmacotherapy...

More aggressive treatment of adverse effect(s)

Opioid-sparing strategies
- Analgesic adjuvants
- Alternate route (e.g. intraspinal)
- Anaesthetic/Neurolytic procedures
- PM&R approaches
- Cognitive therapy
- Complementary therapies
  - e.g., acupuncture, massage, music therapy

Opioid rotation

Modified WHO Analgesic Ladder

Proposed 4th Step

The WHO Ladder

Deer, et al., 1999
Adjuvant analgesics

- Medications that supplement primary analgesics
  - may themselves be primary analgesics
  - may not be analgesic class medications
  - use at any step of WHO ladder

Co Analgesics Commonly Used For Pain

- NSAIDS
- Acetaminophen
- Antidepressants
- Anticonvulsants
- Corticosteroids
- Neuroleptics
- Antihistamines
- Cannabinoids
- Alpha agonists
- Benzodiazepines
- Antispasmodics
- Muscle relaxants
- Topicals
- Systemic local anesthetics- ketamine
- Methadone
Lidocaine Patch 5%

- Lidocaine 5% in pliable patch
- Up to 3 patches applied once daily directly over painful site
  - 12 h on, 12 h off (FDA-approved label)
- Efficacy demonstrated in 3 randomized controlled trials on postherpetic neuralgia
- Drug interactions and systemic side effects unlikely
  - Most common side effect: application-site sensitivity
- Clinically insignificant serum lidocaine levels
- Mechanical barrier decreases allodynia

Topical vs Transdermal Drug Delivery Systems

Topical (lidocaine patch 5%)
- Peripheral tissue activity
- Applied directly over painful site
- Insignificant serum levels
- Systemic side effects unlikely

Transdermal (fentanyl patch)
- Systemic activity
- Applied away from painful site
- Serum levels necessary
- Systemic side effects
Drug name: Methadone

- Starting dose 5 mg
- Half-life 30-60 min to onset, 2 hr to peak but half life very variable mean 20-35h
- Dosage forms po, IV/sc
- Side effects class
- Cautions- interactions, QT monitor
- Cost concerns none and a

Properties of Methadone

- Well absorbed from all routes of administration
  - oral
  - rectal
  - subcutaneous
  - IV
  - Sublingual
- Rapid onset of analgesia effect (30 - 60 min.)
- No significant cognitive impairment.
- No euphoria.
- Safe in renal and liver failure.
Methadone

- Acute pain: methadone \(\approx\) morphine (1:1)
- Chronic pain: ratio depends upon previous opioid dose (methadone:morphine)
  - < 90 mg (1:5)
  - 91-299 mg (1:10)
  - >300 mg (1:12 or 20)
- Torsade de Pointes in high parenteral doses

Bruera & Sweeney, 2002; Kranz et al., 2002

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Methadone Benefits vs Burdens

**Benefits**
- Very effective for visceral and neuropathic pain
- (NMDA Antagonist)
- Also effective for neuropathy and hyperalgesia
- No active metabolites
- No accumulation in renal insufficiency

**Burdens**
- High Variability between patients
- Takes approximately 4-7 days of continuous dosing to convert to steady state
- Half-life 15-40 hours
- Dose should not be titrated before 4 days
- Pts started at too high dose, may get relief initially but the actual overdose may occur several days later

Presented by Hope Hospice, part of the HopeHealth family of services. HopeHealthCo.org
Drug name: Gabapentin

- Starting dose 100 qd
- Half-life 5-7 hours
- Dosage forms po
- Side effects drowsiness
- Cautions renal disease
- Cost concerns few

Gabapentin in Neuropathic Pain Disorders

- FDA approved for postherpetic neuralgia
- Anticonvulsant: uncertain mechanism
- Limited intestinal absorption
- Usually well tolerated; serious adverse effects rare
  - dizziness and sedation can occur
- No significant drug interactions
- Peak time: 2 to 3 h; elimination half-life: 5 to 7 h
- Usual dosage range for neuropathic pain up to 3,600 mg/d (tid–qid)*

*Not approved by FDA for this use.
Gabapentin (Neurontin)

- Preferred Anticonvulsant for neuropathic pain
  - 100 mg PO TID, titrate
  - increase dose q 1–3 d
  - usual effective dose 900–1800 mg / day; max may be > 3600 mg / day
  - minimal adverse effects
    - drowsiness, ataxia tolerance develops within days
  - starting dose in frail elderly can be as low as 100 mg Qhs for 3 d

Drug name: Pregabalin

- Starting dose 75 mg twice daily, or 50 t.i.d.
- Max 300-450 mg daily
- Half-life
- Dosage forms
- Side effects
- Cautions
- Cost concerns
- Indicated for neuropathic pain in diabetes
- Should be tapered over one week when discontinued her
Antidepressants in Neuropathic Pain Disorders*

- Multiple mechanisms of action
- Randomized controlled trials and meta-analyses demonstrate benefit of tricyclic antidepressants (especially amitriptyline, nortriptyline, desipramine) for postherpetic neuralgia and diabetic neuropathy
- Onset of analgesia variable
  - analgesic effects independent of antidepressant activity
- Improvements in insomnia, anxiety, depression
- Desipramine and nortriptyline have fewer adverse effects

*Not approved by FDA for this use.

Drug name: TCA
there are several for Nortryptiline

- Starting dose 10-25 at HS
- Half-life
- Dosage forms oral
- Side effects agitation, sedation, arrythmia, anticholinergic
- depression
- Cautions liver disease
- Cost concerns none
Tricyclic antidepressants ...

- **Amitriptyline**
  - 10–25 mg PO nightly, titrate (escalate q 4–7 d)
  - analgesia in days to weeks

- **Desipramine**
  - 10–25 mg PO q hs, titrate
  - tricyclic of choice in seriously ill

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Tricyclic Antidepressants: Adverse Effects

- Commonly reported AEs (generally anticholinergic):
  - blurred vision
  - cognitive changes
  - constipation
  - dry mouth
  - orthostatic hypotension
  - sedation
  - sexual dysfunction
  - tachycardia
  - urinary retention

Fewest AEs
- Desipramine
- Nortriptyline
- Imipramine
- Doxepin
- Amitriptyline

Most AEs

AEs = adverse effects
Other antidepressants

- SSRI commonly used for other symptoms
- Not a lot of data for pain
- SNRI Savella
- SSNRI Cymbalta
- more data for these

Drug type- steroid

- Starting dose varies
- Half-life varies
- Dosage forms oral IV, suppository
- Side effects - hyperglycemia, delerium
- Cautions - likely short-term benefit
- Cost concerns few
Corticosteroids

- Dexamethasone
  - long half-life (>36 hrs), dose once/day
  - minimal mineralocorticoid effect
  - doses of 2–20 + mg / day
- Adverse effects
  - steroid psychosis
  - proximal myopathy
  - other long-term adverse effects

Bone pain ...

- Constant, worse with movement
- Metastases, compression or pathological fractures
- Prostaglandins from inflammation, metastases
- Rule out cord compression
... Bone pain

- Management
  - opioids
  - NSAIDs
  - corticosteroids
  - bisphosphonates

Management
  - radiopharmaceuticals
  - external beam radiation
  - orthopedic interventions
  - external bracing

Case Discussion

- Of these what would you suggest to help alleviate Mrs. N’s pain?
Systemic Local Anesthetics

- Indications
  - Neuropathic pain

- Toxicities
  - Dizziness, nausea, tremor, nervousness, incoordination, headaches, paresthesias

- Drugs
  - Lidocaine, mexiletine

Local Anesthetics

- Lidocaine Infusion
  - More effective in neuropathic pain but can be used for all pain syndromes. Starting dose 0.5mg-2 mg/kg per hr IV or SC. Some studies demonstrate long-lasting pain relief even after drug has been stopped. Need to decrease opioids when starting. (Ferrini,Paice, 2004)
Ketamine

- N-methyl-D-aspartate receptor antagonist (NMDA)
- Used as an anesthetic for years
- Case reports show effectiveness when traditional and invasive techniques fail
- Starting IV dose 150mg qd (0.1-0.2mg/kg) with reduction of opioid achieved or 10-15 mg q6 increasing by 10 mg dose each day
- Appears to have a synergistic effect with opioids

Miscellaneous Adjuvant Analgesics

- Pamidronate (Aredia)
- Zoledronic acid (Zometa)
- Strontium-89 (Metastron)
- Calcitonin (Calcimar) Not in cancer? arthritis
- Capsaicin (Zostrix) scheduled in neuropathic pain
- Clonidine (Catapres) all forms
- Cannabinoid (Marinol)
Non-pharmacologic ...

- Neurostimulation
  - TENS, acupuncture
- Physical therapy
  - exercise, heat, cold
- Psychological approaches
  - cognitive therapies
    (relaxation, imagery, hypnosis)
  - biofeedback
- Complementary therapies
  - Massage, Reiki
  - art, music, aroma therapy

Multiple Pathophysiology May Be Involved in Neuropathic Pain

- More than one mechanism of action likely involved
- Neuropathic pain may result from abnormal peripheral nerve function and neural processing of impulses due to abnormal neuronal receptor and mediator activity
- Combination of medications may be needed to manage pain: topicals, anticonvulsants, tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors, and opioids
- In the future, ability to determine the relationship between the pathophysiology and symptoms/signs may help target therapy
Role of Invasive Procedures

- Optimal pharmacologic management can achieve adequate pain control in 80-85% of patients
  - The need for more invasive modalities should be infrequent
  - When indicated, results may be gratifying

When is pall care consult desirable? What about pain management?
Case Discussion

- Of these what would you suggest to help alleviate Mrs. N’s pain?

- HOW do we INVOLVE THE FAMILY in her pain control and therapy??
Summary

- Patients in palliative care experience pain that is both physical and existential
- Careful assessment and appropriate use of opioids and adjuvant analgesics can improve quality of life and relieve suffering in our patient’s lives

summary

- Choose appropriate medication based on ability to manage pain syndrome and titrated for adequate pain relief not chosen for non-addicted properties
- Pain should be rated by patient using a scale that quantifies
- Treat pain continuously vs as needed. Use of “as needed medication” allows pain to escalate and requires more medication for pain control
- Use of “around the clock medication” dosing suppresses the pain, creating better quality management = decreased fear, anxiety
- Consider contracting with patients who have active addiction issues
Use Opioid Conversion Tables wisely

- Calculate 24h equivalent of old drug
- Convert to 24h equivalent of new drug or route
- Calculate new dosing interval
- Divide 24h dose by new dosing interval
- Round off this value
- Account for residual drug

Questions?