Ending the Pain is a Good Start: Inter-professional Insights into Pain Management

2014 Geriatric Update
Meharry Consortium Geriatric Education Center
Ending the Pain is a Good Start: Inter-professional Insights into Pain Management

**Moderator: Mohamad Sidani, MD, MS**
Interim Chair, Department of Family and Community Medicine
Meharry Medical College; MCGEC Faculty

**Daniel Lonergan, MD**
Clinical Director, Vanderbilt Interventional Pain Center at Cool Springs
Assistant Professor of Anesthesiology, Vanderbilt University Medical Center

**Rebecca Warr, MSN, RN, CNE**
Assistant Professor, Ida V. Moffett School of Nursing, Samford University

**Timothy Atkinson, PharmD**
Clinical Pharmacy Specialist, Pain Management
Dept. of Veterans Affairs, Tennessee Valley Healthcare System
Objectives

- Discuss the value of an inter-professional approach to pain management in older adults
- Describe the components of pain assessment in the Alzheimer’s patient
- Differentiate among the various chemical classes of opioids
- Summarize recent guideline updates pertaining to pain management in geriatrics
- Discuss physiologic changes in drug metabolism with aging
No Disclosures

- Mohamad Sidani, MD, MS
- Daniel Lonergan, MD
- Rebecca Warr, MSN, RN, CNE
- Timothy Atkinson, PharmD
“Ending the Pain is a Good Start”
Insights into Pain Management

Dan Lonergan, MD
Assistant Professor
Vanderbilt Medical Center
Division of Pain Medicine
“Ending the Pain is a Good Start”

I have no disclosures or conflict of interest.
“Ending the Pain is a Good Start”

- When is “ending the pain” a reasonable goal?

- How many chronic pain conditions have straightforward medical or surgical solutions, especially in the elderly population?
“Ending the Pain is a Good Start”

• Many pain syndromes are chronic, complicated conditions that can be extremely frustrating for both patients and their medical providers
• Such situations will likely require interdisciplinary management
• There are a variety of tools that can be used to address persistent pain
The Pain Tool Belt

a brief look inside . . .
Medications

Geriatric patients are often more sensitive to the beneficial effects as well as negative side effects of medications.
Medications

Non-steroidal anti-inflammatory drugs (NSAIDS)
Medications

Anticonvulsants

- Gabapentin 300 mg Capsules
- Topamax 100 mg
- Lyrica 50 mg 30 Capsules
- Carbamazepine Tablets USP 200 mg
- Trileptal
Medications

Antidepressants

Tricyclic Antidepressants (TCAs)

Selective Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)
Medications

“Muscle Relaxers”

Soma

Benzodiazepines (Valium, Ativan, Clonazepam)
Medications

Narcotics -- Opioids

- Tramadol
- Hydrocodone
- Oxycodone
- Morphine
- Hydromorphone
- Fentanyl
- Methadone
- Buprenorphine

Long-term benefits in non-cancer pain??
Risk for addiction?
How to decide if these are right for a patient . . .

Analgesia
Activities of Daily Living
Adverse Side Effects
Aberrant Drug-taking behaviors (Abuse, diversion) (Passik et al)

Define your goals first!
Then determine appropriate therapy
Some patients have adverse long-term effects to opioid medications and may occasionally do better overall after discontinuing them.

“Opioid-induced hyperalgesia”
Endorphin suppression
Hormonal imbalances
Lower extremity edema
Sedation
Mental cloudiness

Deciding which patients to detox can be a very difficult task, especially in the elderly population.
Medications

Topical Compounded Creams

A great consideration for the geriatric population.

Possible Ingredients: Ketamine, Diclofenac, Baclofen, Flexeril, Ketorolac, Lidocaine, Gabapentin, Clonidine, etc
Medications

Non-narcotic Skin Patches
Medications

Herbal Remedies
Physical Therapy

TENS

Aquatherapy

Traction

Myofascial Release
Psychological Counseling

- Biofeedback
- Relaxation Techniques
- Psychotherapy
- Improved Coping Mechanisms
- Stress Management
Alternative Medicine

Acupuncture
Yoga
Mindfulness
Chiropractic
Injections

Trigger Point Injections
Injections

Botox Injections

- **Splenius capitis**
  - Normally rotates and extends head
  - 50-150 U

- **Levator scapulae**
  - Normally elevates posterior angle of scapula and flexes neck to same side
  - 25-100 U

- **Trapezius**
  - Normally extends head, raises head, and rotates scapula
  - 50-100 U

- **Sternocleidomastoid**
  - 15-75 U

- **Scalene**
  - Normally elevates 1st rib (anterior, medius) and 2nd rib (posterior), and flexes and rotates neck
  - 15-50 U
Injections

Epidural Steroid Injections
Injections

Targeted Epidural Steroid Injections

Example:
Mrs. Smith has persistent low back pain that radiates down her right leg.

An MRI shows narrowing around the right L4 nerve root as it exits the spine.

A targeted epidural steroid injection ("transforaminal") deposits medication directly around the nerve that is irritated.
Nerve Ablations

Lumbar Medial Branch Radiofrequency ablation
Nerve Ablations

Lumbar Medial Branch Radiofrequency Ablation

Mrs. Smith has had low back pain for years. It is worse when the weather gets cold and wet, first thing in the morning, and with any activity. It does not radiate into the legs. An MRI shows arthritis in the facet joints of her lumbar spine. After diagnostic nerve blocks, she underwent radiofrequency ablation and enjoyed 80% pain relief in her lower back for 9 months.
Neurostimulation

Nerve & Spinal Cord Stimulators
Spinal Pain Pumps

- Receiver in pump controls the amount of medication delivered.
- External controller allows your doctor to turn the system on or off and adjust medication settings.
- Medication goes through a catheter and into the intrathecal space around the spinal cord.
To Recap . . .

There are a multitude of inter-disciplinary options to explore for managing persistent pain syndromes!
Pain and the patient with Alzheimer’s Disease

Rebecca J. Warr, MSN, CNE, RN
Assistant Professor of Nursing
Samford University
Prevalence of Pain in Older Adults

- Over 50% of older adults
- 80% in nursing home residents
- 73% - >90% community-dwelling older adults report pain
  - most frequently reported symptom
- Older adults are more likely to have chronic pain than younger people

Gibson SJ. 2006
Brown S, et al. 2011
Chronic pain leads to....

- Depression
- Sleep disturbance
- Decreased mobility
- Increased healthcare utilization
- Physical and social role dysfunction
- Severe untreated pain can lead to delirium

(Yet pain is often overlooked and undertreated)

Gibson SJ. 2006
Common Causes of Pain in Older Adults

- Musculoskeletal pain
- Circulatory problems
- Shingles and post-herpetic neuralgia
- Certain bowel diseases
- Cancer
- Diabetic peripheral neuropathy

www.partnersagainstpain.com
Gibson S. 2006
Assess a Friend

- Groups of 2 –
- No talking! Use only your powers of observation!
- 20 seconds to assess for any physical signs of pain
Assessment of Pain – Physical Signs

- Increased pulse rate greater than 88/min
- Blood pressure greater than 130/90 mm Hg
- Pupil diameter greater than 5 mm
- Cold hands or feet

Tennant F, Leavitt S. 2008
Assessment of Pain – Physical Signs

- Body position
- Insomnia
- Nausea or anorexia
- Diarrhea

Tennant F, Leavitt S. 2008
Behaviors indicating Pain

- Groaning, Grimacing, resistance to movement
- Guarding a body area
- Teeth clenching
- Rubbing body area that is producing pain

Herr K, Garand. 2001
Behaviors indicating Pain

- Agitation
- Restlessness
- Irritability
- Increased confusion
- Combativeness, especially with care activities
- Changes in appetite
- Changes in usual activity

Herr K, Garand l. 2001
Behaviors indicating Pain

- Often subtle, easy to miss
- Excess sleep
- Inability to sleep
- Rigid body posture (or increased rigidity)
- Repetitious vocalization
- Repetitive movement

Herr K, Garand. 2001
Barriers to Assessment

• Common myths
  • “pain is a natural outcome of aging”
  • “treating pain will mask a problem”
  • “if the person is confused, they don’t feel pain”
  • “treatment of pain will cause addiction”

• Inability to communicate
  • “if they are asleep, they can’t be in pain”
  • “if they aren’t talking or are confused, they can’t feel pain”
Assessment of Pain

- Patient self-report = “the gold standard”
- What is the pain intensity?

http://www.wongbakerfaces.org/
Assessment of Pain

• **Location**: Where does it hurt?
• **Quality**: How does it feel? Sharp, shooting, burning?
• **Onset and duration**: When did the pain start? Is it constant or come and go?
• **Aggravating and relieving factors**: What makes it worse? What helps it feel better?
• **Effect of pain on function and quality of life**: Does it keep you from your regular activities?
• **Comfort-function goal**
• **Other**

Herr K, Garand L. 2001
Li, Liu, & Herr. 2007
Assessment of Ability to Respond

- Mini-mental state exam - 12 items
  - Time (5 questions)
  - Place (5 questions)
  - Name 3 objects (ball/car/man), repeat them, remember (1 per object)
  - Spell word, spell it backwards (world) (5 points)
  - Ask to name the 3 objects they were to remember (1 point for each object)
  - Identify items such as a watch, pencil (2 points)
  - Repeat phrase, “No ifs, ands, or buts” (1 point)
  - Ask to read directions “close your eyes” on a piece of paper and ask them to follow the directions (1)
  - Write a complete sentence (1)
  - Copy a design of a geometric figure (1)
  - Ask if right or left handed, ask them to take a paper into the non-dominant hand and fold it in half with both hands (3)

Voisin T, Vellas B. 2009
Identification of Pain in the Alzheimer’s patient

- Mild to Moderate stage
  - Able to give accurate ratings on a pain scale
- Moderate to Severe
  - Pain overlooked and untreated
Pain Assessment Tools

- Numeric Rating Scale
- Visual Analogue Scale
- Pain Assessment in Advanced Dementia tool
- Discomfort Behavior Scale
- FLACC Behavioral Pain Assessment
Visual Analog Scale

Visual Analog Scale (VAS)

0 1 2 3 4 5 6 7 8 9 10

no pain

worst possible pain

http://www.ttuhs.edu/provost/clinic/forms/ACForm3.02.A.pdf
Pain Assessment in Advanced Dementia tool

<table>
<thead>
<tr>
<th>Items</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative vocalization</td>
<td>None</td>
<td>Occasional moan or groan. Low level speech with a negative or disapproving quality.</td>
<td>Repeated troubled calling out. Loud moaning or groaning. Crying.</td>
<td></td>
</tr>
<tr>
<td>Consolability</td>
<td>No need to console</td>
<td>Distracted or reassured by voice or touch.</td>
<td>Unable to console. distract or reassure.</td>
<td></td>
</tr>
</tbody>
</table>

* Five-item observational tool (see the description of each item below).

** Total scores range from 0 to 10 (based on a scale of 0 to 2 for five items), with a higher score indicating more severe pain (0: no pain to 10: severe pain).**

Horgas A. 2012
## Discomfort Behavior Scale

### Discomfort Behavior Scale Scoring Grid

<table>
<thead>
<tr>
<th>MDS 2.0 Item</th>
<th>MDS Item Score</th>
<th>DBS Item Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>E1c. Repetitive verbalizations</td>
<td>X 3 =</td>
<td></td>
</tr>
<tr>
<td>E1k. Insomnia/change in usual sleep pattern</td>
<td>X 3 =</td>
<td></td>
</tr>
<tr>
<td>E1l. Sad, pained, worried facial expressions</td>
<td>X 3 =</td>
<td></td>
</tr>
<tr>
<td>E1m. Crying, tearfulness</td>
<td>X 3 =</td>
<td></td>
</tr>
<tr>
<td>E1n. Repetitive physical movements</td>
<td>X 3 =</td>
<td></td>
</tr>
<tr>
<td>E1o. Withdrawal from activities of interest</td>
<td>X 3 =</td>
<td></td>
</tr>
<tr>
<td>E1p. Reduced social interaction</td>
<td>X 3 =</td>
<td></td>
</tr>
<tr>
<td>E4a(A). Wandering - Frequency</td>
<td>X 2 =</td>
<td></td>
</tr>
<tr>
<td>E4a(B). Wandering - Alterability</td>
<td>X 6 =</td>
<td></td>
</tr>
<tr>
<td>E4b(A). Verbally abusive behavioral symptoms - Frequency</td>
<td>X 2 =</td>
<td></td>
</tr>
<tr>
<td>E4b(B). Verbally abusive behavioral symptoms - Alterability</td>
<td>X 6 =</td>
<td></td>
</tr>
<tr>
<td>E4c(A). Physically abusive behavioral symptoms — Frequency</td>
<td>X 2 =</td>
<td></td>
</tr>
<tr>
<td>E4c(B). Physically abusive behavioral symptoms — Alterability</td>
<td>X 6 =</td>
<td></td>
</tr>
<tr>
<td>E4d(A). Socially inappropriate/disruptive behavioral symptoms - Frequency</td>
<td>X 2 =</td>
<td></td>
</tr>
<tr>
<td>E4d(B). Socially inappropriate/disruptive behavioral symptoms - Alterability</td>
<td>X 6 =</td>
<td></td>
</tr>
<tr>
<td>E4e(A). Resists care - Frequency</td>
<td>X 2 =</td>
<td></td>
</tr>
<tr>
<td>E4e(B). Resists care - Alterability</td>
<td>X 6 =</td>
<td>Sum = DBS Score</td>
</tr>
</tbody>
</table>

© University of Wisconsin Board of Regents, 2008
Permission granted to copy and distribute for use in quality improvement efforts.

## FLACC Behavioral Pain Assessment Scale

<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 smile</td>
<td>Occasional grimace or frown; withdrawn, disinterested</td>
<td>Frequent to constant frown, clenched jaw, quivering chin</td>
</tr>
<tr>
<td>Legs</td>
<td>Normal position or relaxed</td>
<td>Uneasy, restless, tense</td>
<td>Kicking or legs drawn up</td>
</tr>
<tr>
<td>Activity</td>
<td>Lying quietly, normal position, moves easily</td>
<td>Squirming, shifting back and forth, tense</td>
<td>Arched, rigid, or jerking</td>
</tr>
<tr>
<td>Cry</td>
<td>No cry (awake or asleep)</td>
<td>Moans or whimper, occasional complaint</td>
<td>Crying steadily, screams or sobs; frequent complaints</td>
</tr>
<tr>
<td>Consolability</td>
<td>Content, relaxed</td>
<td>Reassured by occasional touching, hugging, or being talked to; distractable</td>
<td>Difficult to console or comfort</td>
</tr>
</tbody>
</table>

### How to Use the FLACC

**In patients who are awake:** observe for 1 to 5 minutes or longer. Observe legs and body uncovered. Reposition patient or observe activity. Assess body for tenseness and tone. Initiate consoling interventions if needed.

**In patients who are asleep:** observe for 5 minutes or longer. Observe body and legs uncovered. If possible, reposition the patient. Touch the body and assess for tenseness and tone.

---

No Visible Signs?

- Following lumbar puncture:
  - 40% cognitively intact report headache
  - 2% dementia patients report headache
- Altered autonomic responses present in Alzheimer's disease patients
- Pain may be more distressing for Alzheimer’s disease patients

Blennow K, et al 1993
Treatment of Pain

- 33-40+% of dementia patients are untreated
- Does the person without behavioral signs of pain actually experience pain?
- If a condition is known to be painful, treat even without their ability to demonstrate behavioral signs

Plooij, van der Spek and Scherder, 2012
Pautex s, Michon A, Guedira M, et al. 2006
Cole L, et al. 2006
Thank You

Questions?
References

• Herr K, Garand I. Assessment and measurement of pain in older adults. Clinics in Geriatric Medicine. 2001: 17(3); 457-478
• Herr K. Numeric Rating Scale. 2009
• Horgas A. Assessing Pain in Older adults with dementia. 2012: Try This: Best Practices in Nursing Care to Older Adults with dementia
• SP – Facts on Pain in Older Persons – www.iasp-pain.org


[www.wongbakerfaces.org/](http://www.wongbakerfaces.org/)


[www.wongbakerfaces.org/](http://www.wongbakerfaces.org/)

Guideline Update:
Pharmacologic Pain Management
In Older Adults

Timothy J. Atkinson, PharmD
Clinical Pharmacy Specialist, Pain Management
VA Tennessee Valley Healthcare System
General Principles of Pharmacologic Management of Pain in Older Adults

#1 Physiologic changes of aging increase sensitivity to drugs
- Lower doses
- Titrate to response

#2 Incidence of Side Effects with drug therapy is higher in older adults
- Analgesics can still be safe & effective
- Consider comorbidities
- Concomitantly prescribed medications

<table>
<thead>
<tr>
<th>PHYSIOLOGICAL CHANGES WITH AGING</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
</tr>
<tr>
<td>Body fat ↑</td>
</tr>
<tr>
<td>Muscle mass ↓</td>
</tr>
<tr>
<td>Total body water ↓</td>
</tr>
<tr>
<td>Musculoskeletal system</td>
</tr>
<tr>
<td>Arthritis ↑</td>
</tr>
<tr>
<td>Myalgias ↑</td>
</tr>
<tr>
<td>Cardiovascular system</td>
</tr>
<tr>
<td>Heart weight ↑</td>
</tr>
<tr>
<td>Ejection fraction ↓</td>
</tr>
<tr>
<td>Cardiac output ↓</td>
</tr>
<tr>
<td>Response to β-adrenergic stimuli ↓</td>
</tr>
<tr>
<td>Arterial wall thickness ↑</td>
</tr>
<tr>
<td>Elastin ↓</td>
</tr>
<tr>
<td>Endothelial nitric oxide synthetase activity ↓</td>
</tr>
<tr>
<td>Arterial distensibility ↓</td>
</tr>
<tr>
<td>Vascular inflammation and thrombotic events ↑</td>
</tr>
<tr>
<td>Respiratory system</td>
</tr>
<tr>
<td>Chest wall rigidity ↑</td>
</tr>
<tr>
<td>Functional residual capacity (FRC) ↑</td>
</tr>
<tr>
<td>Elastic recoil ↓</td>
</tr>
<tr>
<td>Ventilation/ Perfusion mismatch ↑</td>
</tr>
<tr>
<td>Gastrointestinal system</td>
</tr>
<tr>
<td>Transit time ↑</td>
</tr>
<tr>
<td>Amount of lymphoid tissue ↓</td>
</tr>
<tr>
<td>Vitamin D receptors ↓</td>
</tr>
<tr>
<td>Hepatic system</td>
</tr>
<tr>
<td>Liver cells ↓ (CYP 450)</td>
</tr>
<tr>
<td>Blood flow to the liver ↓</td>
</tr>
<tr>
<td>Renal system</td>
</tr>
<tr>
<td>Blood flow ↓</td>
</tr>
<tr>
<td>eGFR ↓</td>
</tr>
<tr>
<td>Accuracy of calculating GFR ↓</td>
</tr>
</tbody>
</table>

**Key Points**

- 49% hospitalizations for Med-related Adverse Effects
  - occur in elderly
- Common Reasons:
  - Polypharmacy
  - Drug-disease interactions
- Decline in multiple physiologic systems
  - More sensitive to meds

General Principles of Pharmacologic Management of Pain in Older Adults

#3 Use least invasive route of administration
  • Oral is preferred for convenience

#4 Only one drug should be initiated at a time
  • Low dose
  • Slow titration

#5 Allow sufficiently long intervals between introducing drugs
  • Allow the assessment of effect

Guideline Clinical Pearls

Tricyclic Antidepressants (TCA) contraindicated or extreme caution:

- Urinary retention
- Postural hypotension
- Sedation
- Increased fall risk
- Glaucoma
- Cardiac arrhythmias

- Newer Serotonin Norepinephrine Reuptake Inhibitors (SNRI s) preferred

Which of the following are tricyclics (TCAs)?

1. Cyclobenzaprine
2. Promethazine
3. Amitriptyline
4. Venlafaxine
5. 1 & 3 above
6. All of the above
Amitriptyline

Cyclobenzaprine
General Principles of Pharmacologic Management of Pain in Older Adults

#6 Timing of medications is important

- Severe episodic pain- Short-acting, Rapid onset
- Continuous pain- Regular analgesia is most effective
  - Long-acting, Extended-release formulations

Opioid Considerations

• Poor Choices for Chronic Pain
  • Short-acting, higher peaks, higher toxicity profiles
  • Meperidine, other short acting combination products

• Improved function
  • Longitudinal study in a nursing home found ER opioids improved functional status and social engagement compared to IR opioids

• Cognitive function relatively unaffected with stable dosing
  • Caution with dose increases

• Fear of addiction
  • A review of 3 studies including over 25,000 patients on long-term opioid therapy with no history of substance abuse
    • Only 7 cases of addiction

• Risk of Falls
  • Drowsiness & Dizziness

Select Opioid Analgesic Choices

• **Extended Release Products:**
  - Buprenorphine Transdermal Patch
  - Transdermal Fentanyl Patch
  - Hydromorphone-ER
  - Morphine-ER (several products available)
  - Oxycodone-ER
  - Oxymorphone-ER

• **Synthetic Atypical**
  - Long Biological half-lives / intermediate analgesic half-lives
    - Levorphanol
    - Methadone
Which of the following does not require monitoring blood levels?

1. Carbamazepine
2. Valproate
3. Gabapentin
4. Phenytoin
5. None of the above
Guideline Clinical Pearls

Antiepileptic drugs - effective in treating neuropathic pain

- Avoid older drugs
  - Carbamazepine
  - Phenytoin
  - Valproate
- Monitor Blood levels
- Central adverse effects
- Drug-drug interactions
- Drug-disease interactions

Gabapentin & Pregabalin are preferred
- Start low & go slow

General Principles of Pharmacologic Management of Pain in Older Adults

#7 Combination therapy using drugs with complementary mechanisms of action may have synergistic effects
  • Greater pain relief
  • Fewer side effects than a single drug at higher doses

Rational Polypharmacy

Advantages

• Reduction in pain intensity
• Reduction in RX toxicity & SEs
• Improved efficacy
• Possible improvement in surgical outcome & decreased LOS?

Disadvantages

• Requires knowledge of drugs, PK data, & pharmacodynamics
• Every analgesic has its own unique adverse event profile
• May increase drug-drug interactions

What Does Pharmacologic Multimodal Therapy Imply?

- Opioid agonist
- Mixed opioid/NRI
- Opioid/non-opioid combo
- Opioid agonist/antagonist
- NSAIDs
- Acetaminophen
- Aspirin
- α₂ agonists
- Anticonvulsants
- Antidepressants

Pain Nociceptive? Inflammatory? Neuropathic?
General Principles of Pharmacologic Management of Pain in Older Adults

#8 Consider Non-pharmacologic strategies
- Physiotherapy
- Cognitive behavioral therapy
- Acupuncture

Clinical Pearl for Monitoring

Which of the following regimens will test positive for opiates on standard UDS?

1. Hydrocodone 7.5mg/ APAP 325mg 1 tab tid
2. Morphine IR 15mg bid
3. Oxycodone 5mg 1 tab qid
4. Fentanyl 50mcg/ hr q72h
5. Methadone 5mg tid
6. All of the Above
Opiate cut-off's vary by laboratory and institution. This algorithm is based on a **morphine 300 ng/ml**. Laboratory detection thresholds may range from 300 to 2000 ng/mL for morphine. Screens are calibrated for morphine only, but other phenanthrenes are included by default. The urine **opiate screen** will detect other opioids at the following concentrations where a 300ng/mL cut-off is based on morphine. These may vary by laboratory.

- Oxycodone 23000 ng/mL
- Hydrocodone 1700 ng/mL
- Hydromorphone 1700 ng/mL
- Oxymorphone 41000 ng/mL

Urine **oxycodone screen** detection threshold is **100 ng/ml**. This screen offers greater sensitivity versus the standard urine opiate screen (above) for the detection of oxycodone. The urine oxycodone screen will detect other opiates at the following concentrations:

- Hydrocodone 1562 ng/mL
- Hydromorphone 12500 ng/mL
- Oxymorphone 1562 ng/mL

### Chemical Classes of Opioids

<table>
<thead>
<tr>
<th>DI-PHENYLHEPTANES</th>
<th>BENZOMORPHANS</th>
<th>PHENYLPIPERIDINES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone</td>
<td>Methadone</td>
<td>Methadone</td>
</tr>
<tr>
<td>Rx EXAMPLES</td>
<td>methadone</td>
<td>methadone</td>
</tr>
<tr>
<td></td>
<td>codeine</td>
<td>codeine</td>
</tr>
<tr>
<td></td>
<td>propxyphene</td>
<td>propxyphene</td>
</tr>
<tr>
<td></td>
<td>hydrocodone</td>
<td>hydrocodone</td>
</tr>
<tr>
<td></td>
<td>hydromorphone</td>
<td>hydromorphone</td>
</tr>
<tr>
<td></td>
<td>levorphanol*</td>
<td>levorphanol*</td>
</tr>
<tr>
<td></td>
<td>oxycodone*</td>
<td>oxycodone*</td>
</tr>
<tr>
<td></td>
<td>oxymorphone*</td>
<td>oxymorphone*</td>
</tr>
<tr>
<td></td>
<td>buprenorphine*</td>
<td>buprenorphine*</td>
</tr>
<tr>
<td></td>
<td>nalbuphine</td>
<td>nalbuphine</td>
</tr>
<tr>
<td></td>
<td>butorphanol*</td>
<td>butorphanol*</td>
</tr>
<tr>
<td></td>
<td>naloxone*</td>
<td>naloxone*</td>
</tr>
<tr>
<td></td>
<td>heroin (diacetyl-morphine)</td>
<td>heroin (diacetyl-morphine)</td>
</tr>
</tbody>
</table>

*These agents lack the 6-OH group of morphine, possibly decreasing cross-sensitivity within the phenanthrene group.

**See separate slide for tapentadol & tramadol**

**Chemical Classes of Opioids**

- **PHENANTHRENES**
  - Morphine
  - Methadone
  - Codeine
  - Proxyphene
  - Hydrocodone
  - Hydromorphone
  - Levorphanol
  - Oxycodone
  - Oxymorphone
  - Buprenorphine
  - Nalbuphine
  - Butorphanol
  - Naloxone
  - Heroin (diacetyl-morphine)

- **BENZOMORPHANS**
  - Pentazocine
  - Diphenoxylate
  - Loperamide
  - Sufentanil
  - Remifentanil

- **PHENYLPIPERIDINES**
  - Meperidine
  - Fentanyl

**X-SENSITIVITY > PROBABLE  POSSIBLE  LOW RISK  LOW RISK**

General Principles of Pharmacologic Management of Pain in Older Adults

#9 Treatment should be monitored regularly & adjusted
  • Improve efficacy
  • Limit adverse effects

Opioid Rotation

• Switching a chronic pain patient from one opioid to another

• Reported to provide more effective analgesia
  • Interpatient variability of response
  • Incomplete cross-tolerance

• Indications for opioid rotation
  • Poorly controlled pain with inability to increase dose due to side effects
  • Adverse event or toxicity with current opioid
  • Rapid development of tolerance
  • Development of opioid hyperalgesia

# Managing Opioid Side Effects

<table>
<thead>
<tr>
<th>SIDE EFFECTS</th>
<th>TREATMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Constipation</td>
<td>• Increase fluid intake; Use of cathartics; stimulant laxatives, enemas, nonopioid analgesics</td>
</tr>
<tr>
<td>• Nausea &amp; Vomiting</td>
<td>• Switch Opioid; Use antiemetic</td>
</tr>
<tr>
<td>• Sedation</td>
<td>• Lower dose; use stimulants?</td>
</tr>
<tr>
<td>• Itching</td>
<td>• Switch opioid; antihistamines</td>
</tr>
<tr>
<td>• Edema &amp; Sweating</td>
<td>• Switch opioids</td>
</tr>
<tr>
<td>• Dizziness</td>
<td>• Anti vertiginous agent</td>
</tr>
<tr>
<td>• Confusion</td>
<td>• Titrate dose; switch opioid; add neuroleptic</td>
</tr>
<tr>
<td>• Endocrine dysfunction</td>
<td>• Endocrine monitoring; testosterone replacement</td>
</tr>
<tr>
<td>• Urinary retention</td>
<td>• Switch opioids</td>
</tr>
<tr>
<td>• Risk of falling for elderly</td>
<td>• Lower dose; use non-opioid analgesics</td>
</tr>
</tbody>
</table>

*Note: The table lists common side effects of opioid use and possible treatments. Additional strategies may be necessary for individual cases.*
#10 Analgesic selection should be individualized for each patient

- Comorbidities
- Drug-drug interactions
- Drug-disease interactions

Accumulation, Metabolism, and Elimination of Opioids in ESRD

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Hepatic metabolism</th>
<th>Elimination: Renal/ Hepatic (R/H)</th>
<th>Phase of Hepatic Metabolism</th>
<th>CYP450 Hepatic Enzymes</th>
<th>Primary Metabolites</th>
<th>Minor Metabolites</th>
<th>Active Metabolites</th>
<th>Accumulation of Parent Compound in ESRD</th>
<th>Accumulation of Active Metabolite in ESRD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone</td>
<td>Yes</td>
<td>R=20-50%&lt;sup&gt;c&lt;/sup&gt; H=balance unknown</td>
<td>Phase I</td>
<td>CYP3A4, CYP2B6, CYP2C8, CYP2C19, CYP2C9, CYP2D6</td>
<td>EDDP (2-ethyl-1,5-dimethyl-3,3-diphenylpyrroline)</td>
<td>N/A</td>
<td>None</td>
<td>No&lt;sup&gt;f&lt;/sup&gt;</td>
<td>No</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Yes</td>
<td>R=75%&lt;sup&gt;c&lt;/sup&gt; 10% unchanged H=9%</td>
<td>Phase I</td>
<td>CYP3A4</td>
<td>Norfentanyl (&gt;99%)</td>
<td>Despropionylfentanyl, hydroxyfentanyl, and hydroxyl-norfentanyl (less than 1%)</td>
<td>None</td>
<td>Unknown</td>
<td>N/A</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Yes</td>
<td>R=balance unknown H=balance unknown</td>
<td>Phase II: via UGT2B7</td>
<td>N/A</td>
<td>Hydromorphone-3-glucuronide (36.8%) [H3G]</td>
<td>dihydromorphine (0.1%) and dihydroiso-morphine (1%)</td>
<td>H3G</td>
<td>Yes&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Yes: H3G&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

### Accumulation, Metabolism, and Elimination of Opioids in ESRD

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Hepatic metabolism(^A)</th>
<th>Elimination: Renal/ Hepatic (R/H)(^A)</th>
<th>Phase of Hepatic Metabolism</th>
<th>CYP450 Hepatic Enzymes (^B)</th>
<th>Primary Metabolites</th>
<th>Minor Metabolites</th>
<th>Active Metabolites</th>
<th>Accumulation of Parent Compound in ESRD</th>
<th>Accumulation of Active Metabolite in ESRD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxycodone</td>
<td>Yes</td>
<td>R=72+19%(^C) H=balance unknown</td>
<td>Phase I</td>
<td>CYP3A4 CYP2D6</td>
<td>Noroxycodone, Oxymorphon e</td>
<td>Oxycodyl, Oxymorphol, Noroxycodyl</td>
<td>Nor-oxycodone and Oxy-morphone(^G)</td>
<td>Yes</td>
<td>Yes: Nor-oxycodone Yes: Oxy-morphone(^G)</td>
</tr>
<tr>
<td>Oxy-morphone</td>
<td>Yes</td>
<td>R=&gt;40% H=balance unknown</td>
<td>Phase II: via UGT2B7</td>
<td>N/A</td>
<td>Oxymorphon e-3-glucuronide (38%)</td>
<td>Oxymorphon e-6-gluronide (1%)</td>
<td>Oxymorphon e-6-gluronide</td>
<td>Yes</td>
<td>Yes: O6G</td>
</tr>
<tr>
<td>Tapentadol</td>
<td>Yes</td>
<td>R= 99% H= ~1%</td>
<td>Phase II</td>
<td>CYP 2C9 CYP 2C19</td>
<td>Tapentadol-O-Glucuronide (55%) Tapentadol-O-Sulfate (15%)</td>
<td>N-desmethy-tapentadol (13%) Hydroxyl tapentadol (2%)</td>
<td>N/A</td>
<td>Unknown</td>
<td>No</td>
</tr>
</tbody>
</table>

---

Questions?