Goals

• Epidemiology
• Pain assessment
  – Cognitively intact
  – Demented
• Treatment strategies
  – WHO ladder
  – Topical
  – Outpatient
  – Inpatient
  – Neuropathic
• Adverse effects
Epidemiology

• Twofold increase in painful conditions (Crook et al., 1984)

• Community dwelling (Breidung R, 1996)
  – 88% occasionally
  – 52% daily
  – 26% → Dreadful or agonizing

• Long-term care (Achterberg WP et al., 2009)
  – 50% daily
  – 50% → Moderate to severe

• Hospitalized (Rainfray et al., 2003)
  – 47.5-63.6%
Postoperative Pain

- ~16 million surgeries per year (35%)
- Postop pain underestimated (Gagliese et al., 2000; Gagliese et al., 2003; Macintyre, 2001)
  - Anticipate less pain
  - Less willing to spontaneously express
  - Assessment difficult in cognitively impaired
- Comparable degree of pain (Lynch et al., 1997)
Pain Perception with Aging

- Increased pain threshold
  - Underreporting of mild pain symptoms
  - Acute medical conditions less likely to present with pain including peritonitis and "silent" MI

- Increased vulnerability to severe or persistent pain
  - Reduced plasticity of nociceptive system
  - Prolonged dysfunction following tissue injury, inflammation, nerve injury

Consequences of Unrelieved Pain

- Direct suffering
- Decreased physical function
- Decreased socialization
- Depression
- Sleep disturbances
- Polypharmacy
- Increased health utilization costs
- Increased postop pulmonary and cardiac morbidity
- Increased length of hospitalization

Sub-Optimal Pain Management

• **Barriers to optimal management** (Herr et al., 2004)
  – Multiple medical comorbidities
  – Fear among providers of causing delirium
  – Concern about addiction/tolerance
  – Ageism
  – Financial

• **Cognitively impaired prescribed and administered less analgesics** (Horgas et al., 1998)

• **Misperceptions** (Miller et al., 2000)
  – Nothing can be done
  – Do not feel pain
Pain Assessment

- Patient **ALWAYS** best source
- What is the best unidimensional tool to assess pain in the clinical setting?
  
A. 6 — Pain as bad as it could be
    5 — Extreme pain
    4 — Severe pain
    3 — Moderate pain
    2 — Mild pain
    1 — Slight pain
    0 — No pain

B. No Pain ——————————————————— Very Severe Pain

C. Pain faces

D. Numerical (1-10) scale

E. None of the above
Pain Assessment

• Patient **ALWAYS** best source
• What is the best unidimensional tool to assess pain in the clinical setting?

A. 6 — Pain as bad as it could be
   5 — Extreme pain
   4 — Severe pain
   3 — Moderate pain
   2 — Mild pain
   1 — Slight pain
   0 — No pain

B. No Pain ——————————————————————————— Very Severe Pain

C. Pain faces
D. Numerical (1-10) scale
E. None of the above
Pain Assessment: Dementia

• 1:5 elders age 80 or older - Will increase to 13 million by 2050
• Usually do best with verbal descriptors
• Multiple assessment tools and explanations
• Nonverbal elders with advanced dementia → Observational scales
Observational Scales

- Three behavioral scales completed following periods of rest and activity in cognitively intact and impaired (MMSE <24) subjects
- Subjects then assessed regarding pain
- Use of observer-rated instruments improved classification of demented subjects into the correct self-reported level of pain intensity by 42.5%

From: Lukas et al. 2013.
Pain Assessment - Dementia

- Pain Assessment in Advanced Dementia (PAINAD) scale
  - Five domains generated through literature review and expert consultation (Smith M, 2005)
  - Overall pain score
  - Sensitive to detect changes in pain (Warden et al., 2003)
<table>
<thead>
<tr>
<th>PAINAD (Warden et al., 2003)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Negative Vocalization</td>
</tr>
<tr>
<td>Consolability</td>
</tr>
</tbody>
</table>
Pain Management Strategies

• Important to include pharmacologic and nonpharmacologic treatments

• Physicians most commonly prescribe
  – Medications
  – Physical therapy
  – Exercise

• Elders prefer home remedies, massage, topical agents, physical modalities (heat/cold), and informal cognitive strategies (social gatherings, prayer, humor)

WHO Analgesic Ladder

“Step Up” Approach

Severe Pain
Morphine
Hydromorphone
Fentanyl
Oxycodone
Methadone
± Adjuvants

Moderate Pain
Codeine
Tramadol
± Adjuvants

Mild Pain
Acetaminophen
NSAIDs
± Adjuvants
Outpatient Pain-Topical Analgesia

Mr. K is a 92 y/o man with PMH significant for HTN, mild cognitive impairment, and chronic kidney disease (GFR 35) who presents urgently to your clinic with worsening of his right knee OA after going shopping with his son. He reports walking more than baseline. There is bony enlargement and crepitus of the right knee. No warmth, effusion, or erythema. Mr. K requests “cream” for his knee as he does not want to take additional pills. What would you suggest?
Topical NSAIDs

- Effective and efficient means to reduce systemic exposure - Systemic bioavailability 5-15% of that seen with oral use (Flores et al., 2012)
- Primary side effect mild, local skin inflammation
- Since 2007, diclofenac sodium 1% gel, diclofenac 1.5% in 45.5% dimethyl sulfoxide solution, and 1.3% topical patch approved in US
- Half life is 9-12 hours with local drug accumulation
- Guidelines suggest reasonable first line therapy for localized OA (Altman R, 2010)
Diclofenac - The Evidence

• 19 double-blind RCTs in >3,000 patients found (Zacher et al., 2008)
  – Reduced pain and inflammation compared to placebo
  – Comparable to other ibuprofen and naproxen
  – Improved mobility

• Pooled data from three 12-week, double-blind trials evaluating diclofenac in patients aged 25-64 versus ≥65 years (Baraf et al., 2011)
  – Significant improvement in pain and physical function scales among subjects ≥65 years
  – Similar efficacy in older and younger subjects
Diclofenac- The Evidence

• Pooled analysis of 7 Phase III clinical trials focused on patients ≥75 years with OA of the knee or hand (Roth and Fuller, 2012)
  – Higher incidence of dry skin (36.2%)
  – No increase GI or renal side effects

• Post hoc analysis in two groups of patients (≥35 and ≥65 years) using for 12 weeks (Peniston et al., 2012)
  – No difference side effects based on age
  – No increase in side effects in subjects with HTN, CAD, or DM
Topical Capsaicin

- Interacts with neurotransmitter substance P in sensory C nerve fibers and with the vanilloid receptor TRPV1 which triggers thermal and inflammatory pain
- Repeated application leads to desensitization and inactivation of the neurons
- Can be effective option for OA, RA, soft tissue pain, and neuralgia
Capsaicin- The Evidence

- Systematic review comparing capsaicin to placebo found 50% reduction of musculoskeletal pain in treatment group.
- Similar pain relief results in crossover trial comparing capsaicin and placebo.
- ~54% subjects experienced side effects with capsaicin compared to 15% with placebo.

Mrs. P is a 84 y/o lady with PMH significant for HTN, GERD, and chronic kidney disease (GFR 20) who presents to your clinic to establish care. She has significant osteoarthritis affecting multiple joints. She is taking ibuprofen 800 mg TID with moderate relief. What changes, if any, would you suggest to her analgesic regimen?
Acetaminophen

- First line analgesic agent in elderly
- Centrally acting prostaglandin inhibitor
- 650 versus 1000 mg per dose--- Do not exceed 4 g/24 hrs
- Scheduled dosing
  - Decreased opioid requirement
  - Increased pain control
  - Increased socialization among elders with dementia
Acetaminophen Regulations

• FDA has taken action to prevent unintentional overdose by limiting acetaminophen dose in combination drug products
  – 1/14/2014 - FDA recommends health care professionals discontinue prescribing and dispensing prescription combination drug products with >325 mg of acetaminophen
  – 3/26/2014 - All manufacturers of prescription combination drug products with >325 mg of acetaminophen have discontinued marketing

• Studies do not show improved effect with higher doses in combination drugs

• May still prescribe 2 tablets (650 mg dose) if appropriate for patient
Oral NSAIDs

• Inhibit cyclo-oxygenase and reduce prostaglandin synthesis
• 2x increased risk GI bleeding (~30% risk GI adverse event)
• Renal toxicity
• If use, employ caution
  – Limit to conditions requiring anti-inflammatory effect
  – Time limited
  – Adequate hydration
  – Gastro protective agent
Mrs. P

- Ibuprofen discontinued
- Acetaminophen 650 mg TID initiated
- After one week, Mrs. P calls to report that her pain is fairly well controlled at rest but increased to 6/10 with activities such as walking or cleaning her house. Which of the following would be the best addition to her regimen?
  1. Acetaminophen/Oxycodone
  2. Codeine
  3. Tramadol
Tramadol

• Binds μ-opiate receptors in CNS resulting in inhibition of ascending pain pathway---Inhibits uptake of norepinephrine and serotonin
• Potency 1/4-1/3 morphine
• Recommend starting dose of 25 mg Q6H PRN with usual dose 50 mg Q6H PRN
• Side effects include nausea (24-30%), constipation (24-30%), dizziness (26-30%), sedation, and delirium (1-5%)
• Avoid abrupt discontinuation and use caution if patient on SSRI
Tramadol for Osteoarthritis

- Cochrane analysis eleven RCTs
- 12% decrease in pain from baseline
- Less pain than placebo
- 2.27 times risk of developing minor adverse events and 2.6 times risk of developing major adverse events compared to placebo

From: Cepeda et al., 2009.
Combination Medications

- Commonly prescribed include
  - Acetaminophen/oxycodone
  - Acetaminophen/hydrocodone
  - Acetaminophen/codeine
  - Aspirin/oxycodone
- Avoid in elders
  - Scheduled acetaminophen first line
  - May receive higher dose of opioid than needed
Weak Opioids

- Class includes Codeine, Tramadol, Dihydrocodeine
- Codeine commonly prescribed
- Binds opioid receptors in the CNS causing inhibition of ascending pain pathways and general CNS depression
- Increased constipation compared to stronger opioids
- Commonly causes confusion
Mr. N is an 86 y/o man with moderate dementia and HTN admitted to the hospital with cough and change in mental status. He is diagnosed with PNA and started on antibiotics. Skin exam is significant for a 2x3 cm stage III sacral pressure ulcer. Despite scheduled acetaminophen, his pain is 8/10 with dressing changes.
Breakthrough Pain

• Any acute transient pain that flares over baseline (Driver LC, 2007; Bennett et al., 2005; Payne R., 2007)
  – Incident- predictable or unpredictable
  – Idiopathic
  – End of dose

• Predictable incident pain should be treated with a short-acting opioid given 30 minutes prior to trigger activity

• Idiopathic and spontaneous incident pain is difficult to treat because unpredictable---Consider lipophilic fentanyl
Opioid Analgesics

- Conjugated in liver
- 90-95% renally excreted
- Steady state achieved after 4-5 half-lives or 24 hours
- Duration of effect of “immediate release” formulations (except methadone)
  - 3-5 hours PO or PR
  - 1-2 hours parenteral
- No longer using meperidine and propoxyphene
Morphine

• Advantages
  – Versatility of administration
  – Extensive experience

• Disadvantages
  – Poor oral bioavailability
  – Active metabolite (merphine-6-glucuronide)
  – T1/2 for elimination 4.5 hours in elders (2.9 hours in younger individuals)

• Reasonable starting dose in opioid-naïve elder is 1 mg IV morphine Q4H
Hydromorphone and Oxycodone

• Hydromorphone
  – PO, IV, IM and SC
  – Reasonable initial dose is 0.25 mg IV Q6H
  – 1 mg of IV hydromorphone = 5-10 mg IV morphine

• Oxycodone
  – Generally preferred oral opioid
  – Capsules/tablets, liquids, and concentrates
  – T1/2 increased renal and liver failure
  – Reasonable initial dose 2.5 mg Q4-6H
  – Frequent treatment for predictable breakthrough pain
Tapentadol

- Acts on *mu* opioid receptor and blocks norepinephrine uptake
- Immediate and extended release formulations
  - 50-100 Q4-H PRN
  - 50 mg BID
- Primary safety concern is respiratory depression
  - Avoid if underlying pulmonary issue
  - Caution in elders
- Concurrent use of extended release and ETOH can be fatal
- Less GI side effects than oxycodone at low doses

From: Erlich and Bodine, 2012.
Tapentadol- The Evidence

• 849 subjects randomly assigned to tapentadol or oxycodone
• No age dependent effect on pain relief
• Among subjects ≥65 years
  – Lower instance constipation (19.0 vs 35.6%)
  – Lower instance vomiting (30.4 vs 51.1%)
  – Non-significant higher risk of somnolence, headache, dry mouth, and fatigue
Fentanyl Patch

• Usually for chronic, stable pain
• Avoid in opioid naïve patients- 12.5 mcg patch = 25 mg morphine per 24 hours
• Beware increased delivery rate if low albumin, febrile, or lack of adipose tissues
• Peak effect 24 hours after application---Must bridge with other analgesic
• Effect lingers after removal
Methadone

• Advantages
  – High oral bioavailability with rapid onset of action
  – Infrequent dosing schedule
  – Inexpensive

• Disadvantages
  – High potential for accumulation leading to delayed toxicity
  – Variable pharmacokinetics
  – Highest drug-drug interaction potential
  – Associated with dose related prolongation of the QT interval and torsade de pointes
  – 2% analgesic prescriptions but involved in 30% deaths
Patient-Controlled Analgesia (PCA)

- Often used first 24 to 48 hours postop
- Morphine most frequently used opioid
- PCA versus IM morphine
  - Less postoperative confusion (2.3 vs. 18%)
  - No severe pulmonary complications (0 vs. 10%)
  - Improved pain relief
  - Improved patient satisfaction

From: Egbert et al., 1990.
PCA Dosing

• Continuous background infusion contraindicated
  – Increased respiratory depression and sedation
  – Does not reduce overall opioid requirements

• Relationship between patient age and postoperative PCA morphine requirements
  – Estimated requirement in first 24 hours postop = 100 – Age
  – Start with low bolus doses of 1 or 1.5 mg morphine Q5-7 minutes

From: Egbert et al., 1993; Frank et al., 1995; Schug et al., 1993.
PCA Usage Guidelines

PCA usage guidelines

– Avoid in elders with lack of mental capacity to understand and use effectively
– Risk factors respiratory depression
– Age itself is NOT a risk factor for respiratory depression

From: Mann et al., 2003.
Opioid Conversion

http://www.hopweb.org/hop/hop.cfm?cfd=33124981&cftoken=37872068

iphone app “Opioids”
Neuropathic Pain

Mr. M is an 89 y/o gentleman with PMH significant for depression and OA who presents to your clinic with ongoing pain across the right flank after a recent bout of shingles. He tells you that the pain is 7/10 and burning in nature. The scheduled acetaminophen he takes for his OA has not been helpful in alleviating the burning flank pain.
Neuropathic Pain

• Arises from abnormal nervous system pathology and can occur without any ongoing tissue damage or inflammation

• Common causes include compression myelopathy, post CVA pain, peripheral neuropathy, and postherpetic neuralgia

• Common in elders due to changes in nociceptive pathways- 1 million have postherpetic neuralgia and 3 million diabetic neuropathy

Capsaicin Patch

• High-concentration 8% dermal patch (NGX-4010)
• Delivers therapeutic dose during single 60 minute application
• Randomized, double-blind trial of patients with postherpetic neuralgia (Backonja et al., 2010)
  – 30% decrease in pain score maintained over 4 week study period
  – Pain relief maintained with retreatment over 48 week study period
Gabapentin

- Binds $\alpha_2\beta$ sub unit of the presynaptic voltage gated calcium channel in spinal nociceptive neurons → Inhibition of calcium influx → Reduction in release of excitatory transmitters in the pain pathway
- Renally cleared
- Reduced pain and improved sleep compared to placebo
- Dizziness and somnolence most common side effects

Pregabalin

• Structural analogue of inhibitory neurotransmitter gamma-aminobutyric acid (GABA)
• Binds $\alpha_2\beta$ subunit of voltage gated calcium channels $\rightarrow$ Reduced release of several excitatory neurotransmitters including glutamate, nor adrenaline, and substance P
• Eliminated unaltered by the kidneys
• 150-600 mg/day in two or three divided doses significantly more effective than placebo (McKeage and Keam, 2009)
Pregabalin

- Pooled data from 11 double-blind, randomized, placebo-controlled studies
- Statistically significant pain reduction at all doses (150 mg/day, 300 mg/day, 600 mg/day)
- Adverse events
  - >10% included dizziness, somnolence, edema, dry mouth, infection
  - Side effects dose dependent
  - Increased incidence age ≥65 years

From: Semel et al., 2010.
Antidepressants

• Try to avoid tricyclics in elders given risk of side effects
  – Dry mouth, constipation, urinary retention, sedation
  – Cardiac dysrhythmias

• SNRI (duloxetine and venlafaxine)
  – Duloxetine usually first line
  – Starting dose 60 mg daily but may increase to 60 mg BID
  – Monitor liver function tests
General Management Opioid Side Effects

- European Association of Palliative Care (EAPC) recommendations
  - Dose reduction of systemic opioid
  - Symptomatic management of adverse effect
  - Opioid rotation
  - Changing the route of systemic administration

Constipation

- Most common adverse effect
- 15-41% of patients being treated for nonmalignant pain (Moore and McQuay, 2005 & Kalso et al., 2004)
- Transdermal fentanyl least constipating
- Variety of mechanisms
  - Increased ileocecral and anal sphincter tone
  - Inhibition of enteric nerve activity
  - Reduced secretions into the gut
  - Increased reabsorption of fluid
Treatment of Constipation

- **Nonpharmacologic** (Swegle and Logemann, 2006 & Pappagallo, 2001)
  - Fluid intake
  - Mobility
  - Stool at same time daily

- **Pharmacologic**
  - Start bowel regimen when you start the opioid
  - Stool softener plus a stimulant laxative
  - If not relieved, rule out obstruction. Then can add a osmotic agent, lubricant, or cathartic laxative
Nausea and Vomiting

- ~25% patients treated with opioids
- Tolerance develops 7-10 days
- Evaluate for and treat refractory constipation and impaction of stool prior to medicating
- Select treatment on individual basis
Pain and Delirium

- Meperidine and propoxyphene increased risk of delirium - No longer in use
- No other opioid analgesic specifically precipitates delirium (Fong et al., 2006 & Morrison et al., 2003)
- Low doses (<10 mg of morphine sulfate equivalents per day) or no opioid analgesics postop associated with increased risk of delirium (Morrison et al., 2003)
Summary

• Pain is common, undertreated, significant consequences in elders
• Numerical and verbal descriptor scales to assess pain—If nonverbal, end stage dementia use observational scale
• Consider topical analgesics
• Scheduled acetaminophen is first line analgesic treatment
• Start low, go slow
• Anticipate side effects