



Osteopathic EPEC

Education for Osteopathic Physicians on End-of-Life Care

Based on The EPEC Project, created by the American Medical Association and supported by the Robert Wood Johnson Foundation. Adapted by the American Osteopathic Association for educational use.



AMERICAN OSTEOPATHIC ASSOCIATION

American Osteopathic Association
AOA: Treating our Family and Yours

Module 4

Pain Management



Module 4, Part 1

Principles of Pain Management



Objectives

- Compare, contrast nociceptive, neuropathic pain
- Know steps of analgesic management
- *Understand the inter-relationship of pain and function*



General principles . . .

- **Assessment**
- **Management**
 - pharmacologic
 - non-pharmacologic
- ***The whole person assessment recognizes the inter-relationship of structure and function***



. . . General principles

- Education - patient, family, all caregivers
- Ongoing assessment of outcomes, regular review of plan of care
- Interdisciplinary care, consultative expertise



Pain pathophysiology

- **Acute pain**
 - Identified event, resolves days-weeks
 - Usually nociceptive
- **Chronic pain**
 - Cause often not easily identified, multi-factorial
 - Indeterminate duration
 - Nociceptive and/or neuropathic



Nociceptive pain . . .

- **Direct stimulation of intact nociceptors**
- **Transmission along normal nerves**
- **Sharp, aching, throbbing**
 - **Somatic**
 - **easy to describe, localize**
 - **Visceral**
 - **difficult to describe, localize**



. . . Nociceptive pain

- **Tissue injury apparent**
- **Management**
 - **Opioids**
 - **Adjuvant / co-analgesics**



Neuropathic pain . . .

- Disordered peripheral or central nerves
- Compression, transection, infiltration, ischemia, metabolic injury
- Varied types
 - Peripheral, deafferentation, complex regional syndromes



• • • Neuropathic pain

- Pain may exceed observable injury
- Described as burning, tingling, shooting, stabbing, electrical
- Management
 - Opioids
 - Adjuvant / co-analgesics often required



Pain management

- Don't delay for investigations or disease treatment
- Unmanaged pain → multisystem pathophysiologic changes leading to pain amplification and permanent changes to the adaptive response
- Treat underlying cause (e.g., radiation for a neoplasm)



Viscerosomatic Integration

- **Anatomy and Physiology**
 - Somatic and visceral pain systems interact at the spinal cord, brainstem and hypothalamic levels
 - In the brainstem and spinal cord, reflex responses involve both the somatic and autonomic nervous systems
 - In the hypothalamus, reflex responses alter endocrine functions



Viscerosomatic Integration

- **Clinical findings**
 - Segmental facilitation of somatic muscles
 - Altered visceral motor activity - hypo or hyper function
 - Referred Pain
 - Somatic to Visceral
 - Visceral to Somatic
 - Homeostatic compensation via general adaptive response



Viscerosomatic Integration

- **Significance**
 - Somatic injury can translate to altered visceral activity
 - Pathologic visceral activity can translate to altered somatic motor function
 - Either state impacts the ability to maintain maximal homeostatic response to stressor(s)



Placebos

- **No role for placebos to assess or treat pain**



Non-pharmacologic pain management . . .

- Osteopathic Manipulative Treatment
- Neurostimulation
 - TENS, acupuncture
- Anesthesiologic - e.g. nerve blocks
- Surgical - e.g. rhizotomy, cordotomy
- Physical therapy
 - Exercise, heat, cold



. . . Non-pharmacologic pain management

- **Psychological approaches**
 - Cognitive therapies
(relaxation, imagery, hypnosis)
 - Biofeedback
 - Behavior therapy, psychotherapy
- **Complementary therapies**
 - Massage
 - Art, music, aroma therapy



WHO 3-step Ladder

1 mild

ASA

Acetaminophen

NSAIDs

± Adjuvants



2 moderate

Codeine

Hydrocodone

Oxycodone

Dihydrocodeine

Tramadol

± Adjuvants



3 severe

Morphine

Hydromorphone

Methadone

Levorphanol

Fentanyl

Oxycodone

± Adjuvants

Acetaminophen

- Step 1 analgesic, co-analgesic
- Site, mechanism of action unknown
 - Minimal anti-inflammatory effect
- Hepatic toxicity if $> 4 \text{ g} / 24 \text{ hours}$
 - Increased risk
 - Hepatic disease, heavy alcohol use



NSAIDs . . .

- Step 1 analgesic, co-analgesic
- Inhibit cyclo-oxygenase (COX)
 - Vary in COX-2 selectivity
- All have analgesic ceiling effects
 - Effective for bone, inflammatory pain
 - Individual variation, serial trials



• • • NSAIDs

- **Highest incidence of adverse events**
- **Gastropathy**
 - **Gastric cytoprotection**
 - **COX-2 selective inhibitors**



NSAID adverse effects

- **Renal insufficiency**
 - Maintain adequate hydration
 - COX-2 selection inhibitors
- **Inhibition of platelet aggregation**
 - Assess for coagulopathy



Opioid pharmacology . . .

- **Conjugated in liver**
- **Excreted via kidney (90%-95%)**
- **First-order kinetics**



Opioid pharmacology . . .

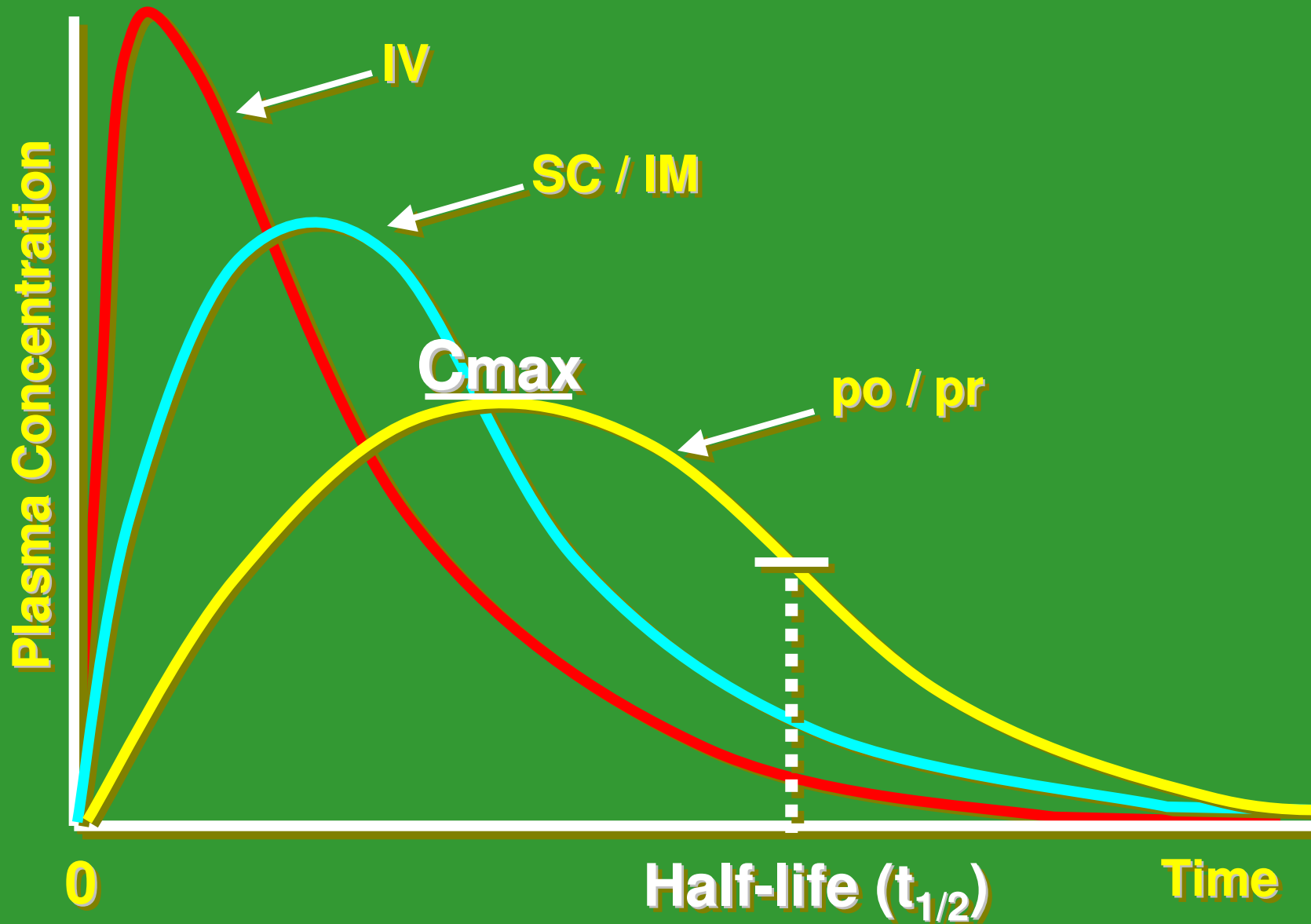
- **C_{max} after**
 - po \approx 1 h
 - SC, IM \approx 30 min
 - IV \approx 6 min
- **Half-life at steady state**
 - po / pr / SC / IM / IV \approx 3-4 h



. . . Opioid pharmacology

- **Steady state after 4-5 half-lives**
 - **Steady state after 1 day (24 hours)**
- **Duration of effect of “immediate-release” formulations (except methadone)**
 - **3-5 hours po / pr**
 - **Shorter with parenteral bolus**





Routine oral dosing immediate-release preparations

- Codeine, hydrocodone, morphine, hydromorphone, oxycodone
 - Dose q 4 h
 - Adjust dose daily
 - mild / moderate pain ↑ 25%-50%
 - severe / uncontrolled pain ↑ 50%-100%
 - Adjust more quickly for severe uncontrolled pain



Management of Anxiety

- **Counseling, supportive therapy**
- **Benzodiaepines**
 - **Short vs long half-life**
 - **diazepam**



Routine oral dosing extended-release preparations

- Improve compliance, adherence
- Dose q 8, 12, or 24 h (product specific)
 - Don't crush or chew tablets
 - May flush time-release granules down feeding tubes
- Adjust dose q 2-4 days (once steady state reached)



Routine oral dosing long-half-life opioids

- Dose interval for methadone is variable (q 6 h or q 8 h usually adequate)
- Adjust methadone dose q 4-7 days



Breakthrough dosing

- Use immediate-release opioids
 - 5%-15% of 24-h dose
 - Offer after C_{max} reached
 - po / pr ≈ q 1 h
 - SC, IM ≈ q 30 min
 - IV ≈ q 10-15 min
- Do NOT use extended-release opioids



Clearance concerns

- **Conjugated by liver**
- **90%-95% excreted in urine**
- **Dehydration, renal failure, severe hepatic failure**
 - ⑩ ↓ dosing interval, ↓ dosage size
 - **If oliguria or anuria**
 - **STOP routine dosing of morphine**
 - **use ONLY prn**



Not recommended . . .

- **Meperidine**
 - **Poor oral absorption**
 - **Normeperidine is a toxic metabolite**
 - longer half-life (6 hours), no analgesia
 - psychotomimetic adverse effects, myoclonus, seizures
 - if dosing q 3 h for analgesia, normeperidine builds up
 - accumulates with renal failure



Not recommended . . .

- **Propoxyphene**
 - **No better than placebo**
 - low efficacy at commercially available doses
 - **Toxic metabolite at high doses**



• • • Not recommended

- **Mixed agonist-antagonists**
 - **Pentazocine, butorphanol, nalbuphine, dezocine**
 - compete with agonists → withdrawal
 - analgesic ceiling effect
 - high risk of psychotomimetic adverse effects with pentazocine, butorphanol



Addiction . . .

- Psychological dependence
- Compulsive use
- Loss of control over drugs
- Loss of interest in pleasurable activities



Addiction . . .

- Continued use of drugs in spite of harm
- A rare outcome of pain management
 - Particularly, if no history of substance abuse
- “Pseudoaddiction” = case of a patient receiving inadequate or too infrequent dosing of pain meds



... Addiction

- **Consider**
 - Substance use (true addiction)
 - Pseudoaddiction (undertreatment of pain)
 - Behavioral / family / psychological disorder
 - Drug diversion



Tolerance

- Reduced effectiveness to a given dose over time
- Not clinically significant with chronic dosing
- If dose is increasing, suspect disease progression



Physical dependence

- A process of neuroadaptation
- Abrupt withdrawal may → abstinence syndrome
- If dose reduction required, reduce by 50% q 2-3 days
 - Avoid antagonists



Substance users

- Can have pain too
- Treat with compassion
- Protocols, contracting
- Consultation with pain or addiction specialists



Pain poorly responsive to opioids

- If dose escalation → adverse effects
 - More sophisticated therapy to counteract adverse effect
 - Alternative
 - route of administration
 - opioid (“opioid rotation”)
 - Co-analgesic
 - Use a non-pharmacologic approach *including the power of OMT and touch*



Ongoing assessment

- Increase analgesics until pain relieved or adverse effects unacceptable
- Be prepared for sudden changes in pain
- *Assess for Functional effects on ADLs and IADLs*
 - Driving is safe if pain controlled, dose stable, no adverse effects



Principles of Pain Management Summary



Module 4, Part 2

Equianalgesic Dosing



Objectives

- Know alternative routes for delivery of opioid analgesics
- Demonstrate ability to convert between opioids while maintaining analgesia



Alternative routes of administration

- Enteral feeding tubes
- Transmucosal
- Rectal
- Transdermal
- Parenteral
- Intraspinal



Transdermal patch

- **Fentanyl**
 - Peak effect after application \approx 24 hours
 - Patch lasts 48-72 hours
 - Ensure adherence to skin



Parenteral

- **SC, IV, IM**
 - **Bolus dosing q 3-4 h**
 - **Continuous infusion**
 - **easier to administer**
 - **more even pain control**



Intraspinal

- Epidural
- Intrathecal
- Morphine, hydromorphone, fentanyl
- Consultation



Bolus effect

- **Swings in plasma concentration**
 - Drowsiness ½ -1 hour after ingestion
 - Pain before next dose due
- **Must move to**
 - Extended-release preparation
 - Continuous SC, IV infusion



Changing routes of administration

- **Equianalgesic table**
 - Guide to initial dose selection
- **Significant first-pass metabolism of po / pr doses**
 - Codeine, hydromorphone, morphine
 - po / pr to SC, IV, IM
 - 2-3 \approx 1



Equianalgesic doses of opioid analgesics

po / pr (mg)	Analgesic	SC / IV / IM (mg)
100	Codeine	60
15	Hydrocodone	-
4	Hydromorphone	1.5
15	Morphine	5
10	Oxycodone	-



Changing opioids . . .

- Equianalgesic table
- Transdermal fentanyl
 - 25- μ g patch \approx 45-135 (likely 50-60) mg morphine / 24 h



... Changing opioids

- **Cross-tolerance**
 - Start with 50%-75% of published equianalgesic dose
 - more if pain, less if adverse effects
- **Methadone**
 - Start with 10%-25% of published equianalgesic dose



Case 1

- Mrs D, 45 years old
- Breast cancer, metastases to bone
- Comfortable on morphine at 6 mg / h SC
- Convert to oral medications before discharge



Case 2

- Mr T, 73 years old, lung cancer, malignant pleural effusion, chronic chest pain
- Thoracentesis, pleurodesis
- Meperidine, 75 mg IM q 6 h
- Convert to oral morphine (without correcting for cross-tolerance)



Case 3

- **Ms M, 41 years old, ovarian cancer, ascites**
 - 2 x acetaminophen / hydrocodone (500 / 5 mg) q 4 h
 - 1 x acetaminophen / oxycodone (325 / 5 mg) q 6 h
- **Pain controlled, worried about acetaminophen toxicity**
- **Convert to hydromorphone (without correcting for cross-tolerance)**



**E
P
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C**

Equianalgesic Dosing Summary



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Module 4, Part 3

Adjuvants, Adverse Effects, Barriers



Objectives

- Know use of adjuvant analgesic agents
- Know adverse effects of analgesics, their management
- List barriers to pain management



Adjuvant analgesics

- Medications that supplement primary analgesics
 - May themselves be primary analgesics
 - Use at any step of WHO ladder



Burning, tingling, neuropathic pain

- Tricyclic antidepressants
- Gabapentin (anticonvulsant)
- SSRIs usually not so useful



Tricyclic antidepressants for burning pain . . .

- **Amitriptyline**
 - Most extensively studied
 - 10-25 mg po q hs, titrate (escalate q 4-7 d)
 - Analgesia in days to weeks



Tricyclic antidepressants for burning pain . . .

- **Amitriptyline**
 - Monitor plasma drug levels > 100 mg / 24 h for risk of toxicity
 - Anticholinergic adverse effects prominent, cardiac toxicity
 - Sedating limited usefulness in frail, elderly



. . . Tricyclic antidepressants for burning pain

- **Desipramine**
 - Minimal anticholinergic or sedating adverse effects
 - 10-25 mg po q hs, titrate
 - Tricyclic of choice in seriously ill
 - Nortriptyline is an alternative



Gabapentin for burning pain

- **Anticonvulsant**
 - 100 mg po q d to tid, titrate
 - Increase dose q 1-3 d
 - Usual effective dose 900-1800 mg / d; max may be > 3600 mg / d
 - Minimal adverse effects
 - drowsiness, tolerance develops within days



Shooting, stabbing, neuropathic pain

- **Anticonvulsants**
 - **Gabapentin**
 - 100 mg po tid, titrate
 - **Carbamazepine**
 - 100 mg po bid, titrate
 - **Valproic acid**
 - 250 mg po q hs, titrate
 - **Monitor plasma levels for risk of toxicity**



Complex neuropathic pain . . .

- Primary neuronal death
- Loss of myelin sheath
- Central sensitization
- Changes in neurotransmitters, neuroreceptors
 - Opioid receptor down-regulation
 - Increased importance of NMDA receptors, glutamate



. . . Complex neuropathic pain

- Sensory neuronal death
- Multiple other medications
- Consult pain expert early



Case 7 . . .

- John, 40-year-old accountant
- AIDS, T4 = 34
- Burning pain hands, feet
 - Initially with ddC + AZT
 - disappeared when stopped



... Case 7

- **Burning pain hands, feet**
 - **now returned x 6 months**
 - **severe**
 - **keeps awake at night**
 - **numbness in feet**
 - **trouble buttoning shirt**
- **How to manage John's pain?**



Bone pain . . .

- Constant, worse with movement
- Metastases, compression or pathologic fractures
- Prostaglandins from inflammation, metastases
- Rule out cord compression



Bone pain . . .

- **Pharmacologic Management**
 - Opioids
 - NSAIDs
 - Corticosteroids
 - Bisphosphonates
 - Calcitonin
- **Non-pharmacologic Management**
 - *Osteopathic Manipulative Treatment*
 - Physical therapy



• • • Bone pain

- **Management**
 - Radiopharmaceuticals
 - External beam radiation
 - Orthopedic intervention
 - External bracing
- **Consultation**



Case 8

- Sarah, 73-year-old attorney
- Breast cancer, metastases to bone
- Treated with Adriamycin, cyclophosphamide
 - 2 months tamoxifen
- How to manage Sarah's pain?



Pain from bowel obstruction . . .

- Constipation
- External compression
- Bowel wall stretch, inflammation
- Associated symptoms
- Definitive intervention
 - Relief of constipation
 - Surgical removal or bypass



. . . Pain from bowel obstruction

- **Management**
 - Opioids
 - Corticosteroids
 - NSAIDs
 - Anticholinergic medications
eg, scopolamine
 - Octreotide
- **Consultation**



Non-pharmacologic

- *Osteopathic Manipulative Treatment*
Attention to spinal levels T-12 to L-2
 - *And S - 2 to S - 4*
- *Attention to the whole person*
 - *Mind - body - spirit*
- **Physical therapy**
- **Complementary therapy**



Corticosteroids . . .

- **Many uses**
- **Dexamethasone**
 - **Long half-life (>36 h), dose once / day**
 - **Minimal mineralocorticoid effect**
 - **Doses of 2-20 + mg / d**



. . . Corticosteroids

- **Adverse effects**
 - Steroid psychosis
 - Proximal myopathy
 - Other long-term adverse effects



Case 9

- David, 67-year-old farmer
- Colon cancer, metastases to liver
- Right upper quadrant pain
 - Tender liver
 - No shifting dullness
- How to manage David's pain?



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



Opioid allergy

- Nausea / vomiting, constipation, drowsiness, confusion
 - Adverse effects, not allergic reactions
- Anaphylactic reactions are the only true allergies
 - Bronchospasm
- Urticaria, bronchospasm can be allergies; need careful assessment



Urticaria, pruritus

- Mast cell destabilization by morphine, hydromorphone
- Treat with routine long-acting, non-sedating antihistamines
 - Fexofenadine, 60 mg po bid, or higher
 - Or try diphenhydramine, loratadine, or doxepin



Constipation . . .

- Common to all opioids
- Opioid effects on CNS, spinal cord, myenteric plexus of gut
- Easier to prevent than treat



Constipation . . .

- **Prokinetic agent**
 - Metoclopramide, cisapride
- **Osmotic laxative**
 - MOM, lactulose, sorbitol
- ***Osteopathic Manipulative Treatment***
 - *Suboccipital, mid cervical and thoracolumbar junction regions*



• • • Constipation

- Diet usually insufficient
- Bulk forming agents not recommended
- Stimulant laxative
 - Senna, bisacodyl, glycerine, casanthranol, etc
- Combine with a stool softener
 - Senna + docusate sodium



Nausea / vomiting . . .

- Onset with start of opioids
 - Tolerance develops within days
- Prevent or treat with dopamine-blocking antiemetics
 - Prochlorperazine, 10 mg q 6 h
 - Haloperidol, 1 mg q 6 h
 - Metoclopramide, 10 mg q 6 h



. . . Nausea / vomiting

- Other antiemetics may also be effective
- Alternative opioid if refractory
- *Osteopathic Manipulative Treatment*
 - *Attention to Suboccipital, upper cervical and mid thoracic regions*



Sedation . . .

- Onset with start of opioids
 - Distinguish from exhaustion due to pain
 - Tolerance develops within days
- Complex in advanced disease



. . . Sedation

- If persistent, alternative opioid or route of administration
- Psychostimulants may be useful
 - Methylphenidate, 5 mg q am and q noon, titrate



Delirium . . .

- **Presentation**
 - Confusion, bad dreams, hallucinations
 - Restlessness, agitation
 - Myoclonic jerks, seizures
 - Depressed level of consciousness
 - Respiratory depression



... Delirium

- Rare, unless multiple factors contributing, if
 - Opioid dosing guidelines followed
 - Renal clearance normal



Respiratory depression . . .

- Opioid effects differ for patients treated for pain
 - Pain is a potent stimulus to breathe
 - Loss of consciousness precedes respiratory depression
 - Pharmacologic tolerance rapid



. . . Respiratory depression

- **Management**
 - **Identify, treat contributing causes**
 - reduce opioid dose
 - observe
 - **If unstable vital signs**
naloxone, 0.1-0.2 mg IV q 1-2 min



Barriers . . .

- Pain is not important
- Poor assessment of whole person
- Lack of knowledge
- Fear of
 - Addiction
 - Tolerance
 - Adverse effects



• • • Barriers

- *Failure to consider non-pharmacological approaches*
 - *OMT, Biofeedback, Physical Therapy etc*
- *Failure to consider impact on whole person, family, ADLs and IADLs*
- **Regulatory oversight**
- **Patients unwilling to report pain**
- **Patients unwilling to take medicine**



Adjuvants, Adverse Effects, Barriers **Summary**

