Palliative Care Practices

Hospitalists and other physicians

ECM Hospital, Florence, AL

IV. Pain Management

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Objectives …

- Describe the concept of Total Pain
- Understand the pathophysiology of physical pain and sensitization to chronic pain
- Know the steps of analgesic management
- Know alternative routes of delivery
- Understand the principles of equianalgesic opioid dosing

…Objectives

- Know the use of adjuvant agents
- Understand the adverse effects of analgesics
- List barriers to pain management and understand the concepts of addiction, tolerance, dependence

Principles of Symptom Mgmt

- Directed H & P
  - Look for treatable causes
  - **Severe Distress is an Emergency !!**
- Work w/ interdisciplinary team
  - symptoms are exacerbated by psychological, social, and spiritual stressors
- Communicate effectively
- Follow up: what did/did not work

PAIN Symptoms

- **Do NOT withhold Rx waiting to identify cause !**
- Mr. Carcinoma – pain in back/hips
  - He decided to take chemoRx but now 6 mo later he found boney mets causing pain = 7-8 /10 most days

Consequences of Under Treated Pain

- Untreated pain can cause a patient's emotional and ***spiritual*** death long before the actual end of life – and result in **permanent nerve hypersensitivity**.
- Depression & Agitation/anxiety
- Sleep problems & Anorexia
- Decreased socialization/conditioning

Pain pathophysiology

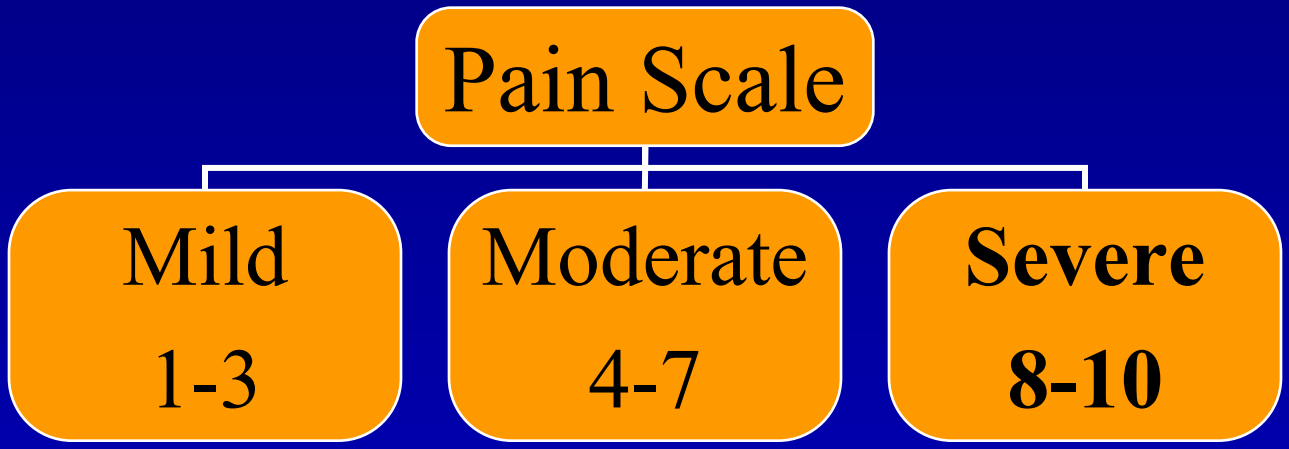
- Acute pain
  - identified event, resolves days–weeks
  - usually nociceptive
- Chronic pain
  - cause often not easily identified, multifactorial
  - indeterminate duration
  - Increased sensitization to all stimuli
    - Hyperalgesia – exaggerated response to noxious stim.
    - Hyperesthesia – exaggerated response to touch
    - Allodynia –non-nociceptive stim. perceived as painful
  - nociceptive and / or neuropathic

Pain pathophysiology

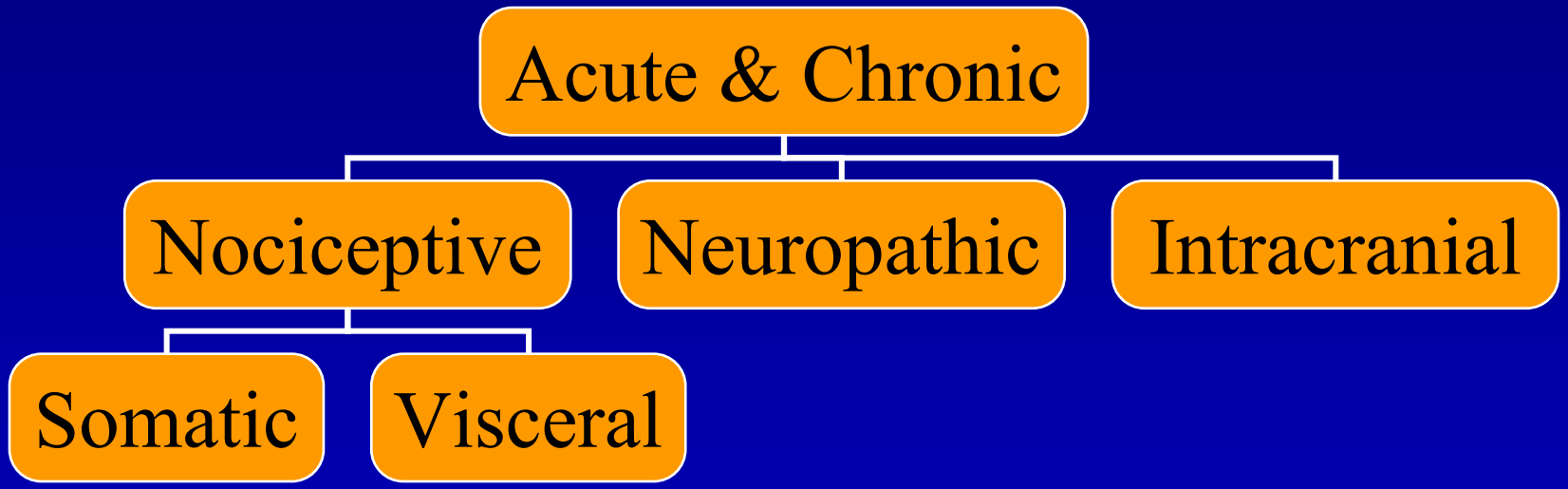
- Constant pain has diurnal/circadian pattern
  - Worse during night
- Incidental pain
  - Severe aggravation w/ movement
  - Short duration (seconds – minutes)
- Breakthrough pain

- Tx: try to avoid sedation threshold

Assessing Pain



Types of Pain



Nociceptive pain . . .

- Direct stimulation of intact nociceptors*
  [*group of cells that acts as a receptor for painful stimuli]
- Transmission along normal nerves
- sharp, aching, throbbing
  - somatic
    - easy to describe, localize
  - visceral
    - difficult to describe, localize

Neuropathic pain . . .

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

. . . Neuropathic pain

- Pain may exceed observable injury
  - E.g. diabetic neuropathy
- Described as burning, tingling, shooting, stabbing, electrical
- Management
  - opioids
  - adjuvant / co-analgesics often required

Principles of **Chronic** Pain Rx

- By mouth
- By the clock – not prn
- By the WHO ladder
- Individualize Rx & Monitor response
- Use Adjuvant drugs
- *For 'constant pain', need to Rx 'constantly'*
  - 10-30% pts have uncontrolled pain due to s/e
- Anticipate nausea & constipation w/ opioids

WHO Analgesic Ladder Rx

Start @ #1, push to maximum, then #2,etc.

1. Non-opioid + adjuvant
2. Mild opioid + non-opioid + adjuvant
3. Strong opioid + non-opioid + adjuvant

* Purpose of Step 2 is to go to step 3 !
* **Frail elders = start low & go slow !**

WHO 3-step Ladder

3 severe

- Morphine
- Hydromorphone
- Methadone
- Levorphanol
- Fentanyl
- Oxycodone
- ± *Adjuvants*

2 moderate

- A/Codeine
- A/Hydrocodone
- A/Oxycodone
- A/Dihydrocodeine
- Tramadol
- ± *Adjuvants*

1 mild

- ASA
- Acetaminophen
- NSAIDs
- ± *Adjuvants*

Chronic PAIN types – Rx Guide*

1. Somatic/tissue & bone
   - Opioids; Bone often needs NSAID or steroid
2. Neuropathic
   - opioid + anticonvulsant +/or TCA
3. Visceral
   - Opioid + anticholinergic

Principles of Analgesics Use in the Tx of Acute Pain and Cancer Pain. Am.Pain Soc., 1999.

Fine PG. Chronic pain management in older adults. J Pain & Symp.Management. 2009 .

Morrison LJ. Pall.care and pain mgmt. Med.Clinics North Am. 2006

Analgesics

Non-opioids

- Acetaminophen (max. 4gm/day but 3gm/day seniors)

Adjuvants

- NSAIDS; Steroids; benzo's; neuroleptics;
- antidepressants; anti-convulsants

Opioids [3 classes] [* synthetic]

1) morphine, codeine, Dilaudid*, hydrocodone, oxycodone*, tramadol [Ultram]
2) Fentanyl*, meperidine* [Demerol]
3) Methadone*, propoxyphene* [Darvon]

Hospice & PC Formulary USA 2nd Ed. 2008

NSAIDs . . .

- Step 1 analgesic, co-analgesic
- If one class ineffective, change to dif. class (5)
  - E.g. ibuprofen [Motrin] to diclofenac [Voltaren]
- Inhibit cyclo-oxygenase (COX 1 & 2) [PG's]
  - vary in COX-2 selectivity
- All have analgesic ceiling effects
  - effective for bone, inflammatory pain
  - individual variation, serial trials

NSAID adverse effects

- Renal insufficiency & edema
  - maintain adequate hydration
  - COX-2 selection inhibitors
- Inhibition of platelet aggregation
  - assess for coagulopathy - GI Bleed
- Confusion/delirium in elders

**Avoid in DM2 and CHF – and in elders !

* Hospice & Palliative Care Formulary USA, 2nd edition. 2008

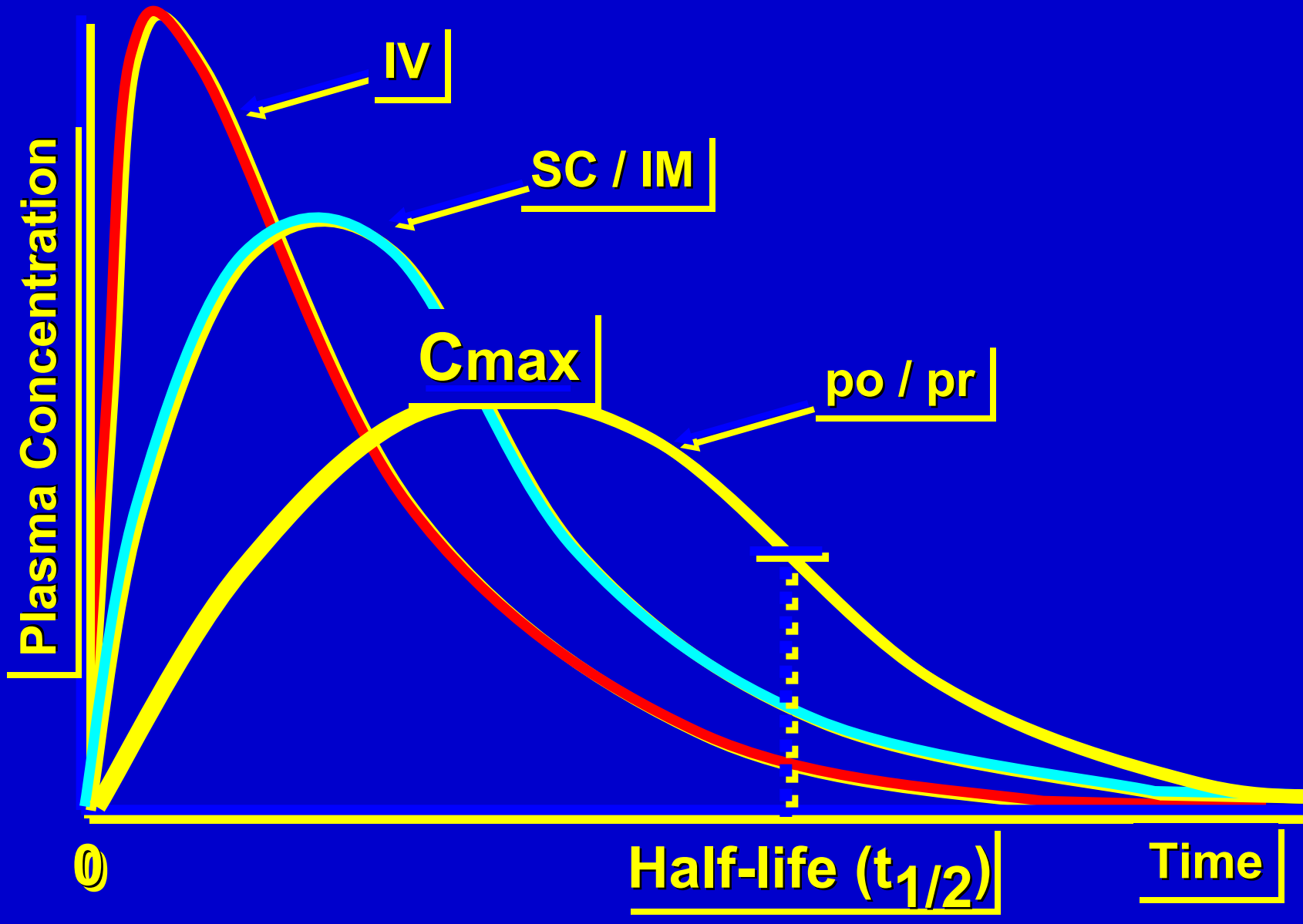
Opioids

- Preferred – Morphine = gold standard
  - No upper limit dosage e.g. 50mg/hr IV/SC !!
  - Starting doses +/- 3-5mg po, 2mg subQ q3h
- Discouraged: Demerol
- Equianalgesic doses* (for morphine 10mg po)
  - Morphine 10mg po = 3mg IV/SC
  - Oxycodone 6mg
  - Hydrocodone 10mg
  - Dilaudid 2mg po = 0.5mg IV/SC

[*Prescriber's Letter, Sept.2004. AAHPM Equianalgesic Table for Adults. 2003]

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


IV
SC / IM
Cmax
po / pr
Plasma Concentration
0
Half-life ($t_{1/2}$)
Time

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

Routine oral dosing
extended-release preparations

- Improve compliance, adherence
- No better analgesia or reduced S/E

  + 5 times more expensive in USA !
- Dose q 8, 12, or 24 h (product specific)

  –don't crush or chew tablets

  –may flush time-release granules down FT
- Adjust dose q 2–4 days (once steady state reached)

Breakthrough dosing

- 90% controlled w/ oral/SC opioids
- If >3 BT doses/day, increase base rate
- Use immediate-release opioids only
  - 10% of 24 hr dose q1h
    - If IV/subQ, can give ¼ of 10%, q15min prn
  - offer after Cmax reached
    - po / pr ≈ q 1 h
    - SC, IM ≈ q 20-30 min
    - IV ≈ q 10–15 min
- Do NOT use extended-release opioids

Opioids - Why not Demerol??

- Low potency – but addictive!
- Short duration
- Medical myth re pancreatitis & biliary colic
- Toxic metabolite – normeperidine
  - CNS Excitation (Serotonin) Syndrome – tremors, myoclonus, delirium, seizures

Opioids - Why not Demerol, cont'd

- Am.Pain Soc. Recommends "…meperidine should not be used >48hrs for acute pain in pts w/o renal or CNS disease, or at doses >600mg/24hrs, and should not be RX for chronic pain."
- Not recommended by any national CPG since 1990, for elders, >3days, CPS, CRI
- More hospitals removing from formulary

Also Not Recommended

- Mixed agonist-antagonists
  - Pentazocine [Talwin], butorphanol [Stadol], nalbuphine [Nubain], dezocine
    - compete with agonists → withdrawal
    - analgesic ceiling effect
    - high risk of psychotomimetic adverse effects with pentazocine, butorphanol
- Propoxyphene [Darvon] – off US formulary 2011

Addiction + . . .

- Psychological dependence
- Compulsive use: behavioral !
- Loss of control over drugs w/ continued use of drugs in spite of harm
- Loss of interest in pleasurable activities
- A rare outcome of pain management
  - particularly, if no history of substance abuse

. . . Addiction

- Consider
  - substance use (true addiction)
  - pseudoaddiction (under treatment of pain)
  - behavioral / family / psychological disorder
  - drug diversion

Tolerance

- Reduced effectiveness to a given dose over time
- 9 different mu receptors
  - opioids bind in different proportion often leading to tolerance to one opioid
  - rotating opioids helps treat tolerance
- Usually not clinically significant with chronic dosing
- If dose increasing, suspect disease progression

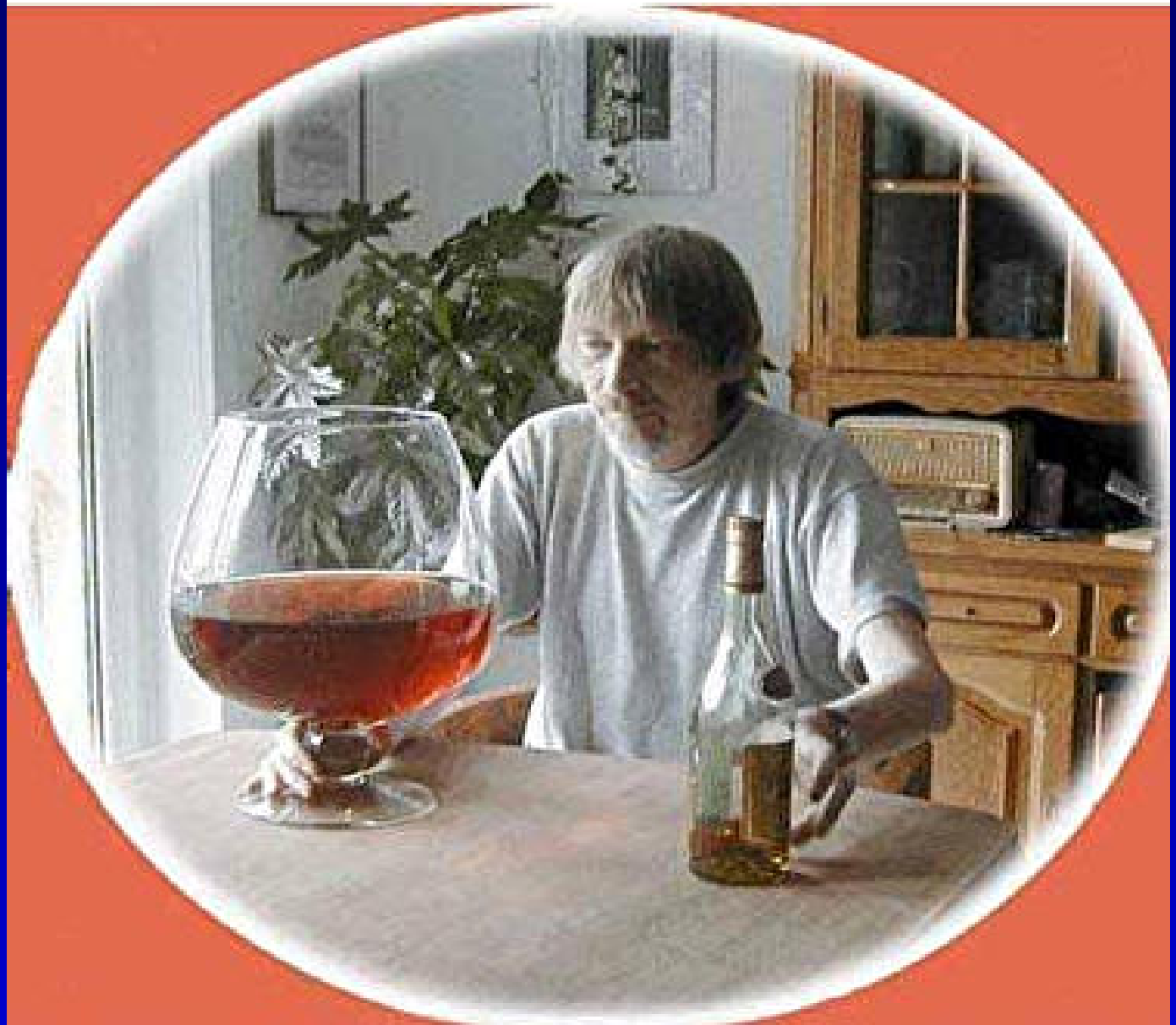
Physical dependence

- A physiologic 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
- Pain history NB – chronic pain syndrome ?
  - CAGE score 2+ = poor pain control
- Treat with compassion
- Protocols, contracting
- Consultation with pain or addiction specialists

My Doctor said "Only 1 glass of alcohol a day". I can live with that.



Pain poorly responsive to opioids

- As dose escalates → adverse effects; so…
  - more sophisticated therapy to counteract adverse effect
  - alternative
    - route of administration
    - **opioid ("opioid rotation" - <u>methadone</u>)**
  - Adjuvants
  - use a non-pharmacologic approach
  - **Look for other causes/factors**

Cancer Pain Assessment:
pain increases due to…

Cancer Related Factors:

- Tumor growth
- Infection
- Fracture
- ischemia

Patient Related Factors:

- Chemical coping
- Delirium
- Opioid tolerance
- Mood change

Methadone: why it's better

- Mu opioid agonist & NMDA [N-Methyl-d-Aspartate] receptor antagonist; inhibits reuptake serotonin, NE
- No active metabolites
- Better pain control than morphine, but more sedation
- Reduce risk of opioid induced neurotoxicity
- Low cost !!

[Bruera et al, 2000; Hospice & PC Formulary USA. 2nd Ed. 2008; Cleary JF. Methadone: the ideal long-acting opioid? AAHPM Bulletin, winter 2002.]

…Pain poorly responsive to opioids

- Lidocaine 1% IV option* [cancers]
  - 1-2mg /kg slow push over a few minutes, or, in 25ml saline over 15-30min.
  - May follow w/ continuous infusion 1-2mg/kg/hour
  - Will reduce dose of opioid needed !

*Available only on 6W or ICU/CCU

- Ketamine po/IV [separate handout]

[Thomas J, etal. IV Lidocaine relieves severe pain. J Pall Med. 2004]
[McCleane G. IV Lidocaine: an outdated or underutilized tx for Pain. J Pall Med. 2007.]

Ongoing assessment !!!

- Increase analgesics until pain relieved or adverse effects unacceptable
- Be prepared for sudden changes in pain
- BEWARE: sedation does not = analgesia !!
  - E.g. Ativan/Propofol in ICU does not relieve pain; assume pain present !
- Titrate continuous infusions based on assessment and use of AACA !
  - **Follow the <u>EOLC Order Set</u>**

Alternative routes of administration

- Enteral feeding tubes
- Transmucosal
- Rectal
- Transdermal
- Parenteral – **SubQ** , IM , IV
- Intraspinal

Transdermal patch

- Fentanyl
  - peak effect after application ≈ 24 hours
  - patch lasts 48–72 hours
  - ensure adherence to skin
  - NOT for opioid naïve !!!
  - Overrated and $$$ [$370/mo 50mcg; $750/mo 100mcg (generics ~1/2)]

FYI: Relative Opioid Costs

- Morph.liq.20mg/ml 60mg/day = $2.40/day
- Morph.MSIR 15mg '' = $1.50/day
- Methad.liq.10mg/ml 30mg/day= $2.08/d
- Methad.tabs 10mg '' = $ .60/d
- Fent.patch 50mcg q3d = $5.66/d
- Duragesic 50mcg = $10.60/d
- Fentanyl buccal [Fentora 100mcg] = $20 each
- Dilaudid liq 1mg/ml 15mg/day= $4.37/d
- Dilaudid tab 2/4/8mg 16mg/day= $6.00/d
- Lorcet 10/325 qid = $1.21/d
- Morph.pump at home = $30/day pump only
- Morph.10mg/ml PLO [topical] 60mg = $5.40/day

* Avg.Retail Cost – changes !

Parenteral

- SubQ, IV, IM
  - bolus dosing q 3–4 h
  - continuous infusion
    - easier to administer
    - more even pain control

Hypodermoclysis

- For subQ meds and fluids
- Fluids for rehydration – NS, D5/NS
  - Up to 125ml/hr, +/- KCl; equal absorption
- Meds = anything that can be given IV except abx and a few others [Thorazine, AED]
  - Place #23-25 butterfly access – chest best; change only if red/draining
  - Rarely need IV; **No IM injections**

- *AAHPM Bulletin, Winter 2003*

Bolus effect

- Swings in plasma concentration
  - drowsiness ½ –1 hour after ingestion
  - pain before next dose due
- Must move to
  - extended-release preparation
  - continuous SubQ, 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 ≈ 1

Opioid Equianalgesic doses*

po / pr (mg)	Analgesic	SC / IV / IM (mg)
100	Codeine	60
15	Hydrocodone	-
4	Hydromorphone	1.5
15	Morphine	**5**
10	Oxycodone	-
150	Meperidine	40
25mcg	Fentanyl	= 50mg/day MS

Methadone – see separate formula scale.

*[*Prescriber's Letter, Sept.2004. AAHPM Equianalgesic Table for Adults. 2003]*

Case – PAIN Exercise

- Mr. Carcinoma – pain in back/hips
  - Admitted due to severe back & hip pain
    = 7-8 /10 most days
- Controlled after subQ morphine 6mg/hr
- **Convert to po morphine before discharge**

[6mg x4h =24mg x3= 72mg po q4h = 60mg q4h + 15mg q2h prn]

Adjuvant analgesics

- Medications that supplement primary analgesics
  - may themselves be primary analgesics
  - use at any step of WHO ladder

Neuropathic pain = Burning, tingling

- TriCyclic Antidepressants [TCA]
- Gabapentin (anticonvulsant)
- [Methadone – particularly effective opioid]
- Ketamine
- SSRIs usually not so useful
  - SNRIs better [venlafexine]

Tricyclic antidepressants for burning pain . . .

Nortriptyline > Amitriptyline

- 10–25 mg po q hs, titrate (escalate q 4–7 d)
  - analgesia in days to weeks
  - Fewer anticholinergic adverse effects, cardiac toxicity
  - Sedation helpful at hs
  - Bind plasma protein, displace morphine causing increased analgesia !

Neuropathic pain…

- Anticonvulsants
  - Gabapentin [Neurontin]
    - 100 mg po q8h, titrate up [3600mg max/d]
  - Carbamazepine [Tegretal]
    - 100 mg po bid, titrate
  - valproic acid [Depakote]
    - 250 mg po q hs, titrate

Adjuvant

…Gabapentin (Neurontin)
for burning pain

- Anticonvulsant
  - 100 mg po q d to Q8h, titrate
  - increase dose q 1–3 d
  - usual effective dose 900–1800 mg / d; max may be > 3600 mg / d
  - minimal adverse effects
    - nausea/drowsiness, tolerance develops within days
    - [also good for resistant cough !]

Bone pain . . .

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

Adjuvant

…Bone pain

- Management
  - **opioids**
  - NSAIDs
  - **corticosteroids**
  - bisphosphonates
  - Calcitonin [nasal]

Adjuvant

Corticosteroids . . .

- Many uses [bone pain, nausea, appetite]
- Dexamethasone [Decadron]
  - long half-life (>36 h), dose once / day
  - Don't give later in day – insomnia inducer
  - minimal mineralocorticoid effect
  - doses of 2–20 + mg / d [wean down after 2wks]

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, nonsedating antihistamines
  - fexofenadine, 60 mg po bid, or
  - Loratadine [Claritin]
- Sedating antihistamines or doxepin if sleep desired

Constipation . . .

- Common to all opioids
- Opioid effects on CNS, spinal cord, myenteric plexus of gut
- Easier to prevent than treat
- Goal: have bm QOD – Q3days

…Constipation . . .

- Prokinetic agent
  - Metoclopramide [Reglan]
- Osmotic laxative
  - MOM, lactulose, sorbitol,
  - Miralax 17-68gm/250ml water
- Other measures

. . . Constipation

- Diet usually insufficient
- Bulk forming agents **not** recommended
  - E.g. metamucil
- Stimulant laxative
  - **senna**, bisacodyl, glycerine, casanthranol, etc
- Combine with a stool softener ?
  - Only if hard stool hard-to-pass
  - senna + docusate sodium = no benefit

Nausea / vomiting . . .

- Onset with start of opioids
  - tolerance develops within days
- Prevent or treat with dopamine-blocking antiemetics
  - Prochlorperazine [Compazine], 10 mg q 6 h
  - Haloperidol [Haldol], 1 mg q 6 h
  - Metoclopramide [Reglan], 10 mg q 6 h

. . . Nausea / vomiting

- Other anti-emetics may also be effective
- Alternative opioid if refractory

Sedation . . .

- Onset with start of opioids
  - distinguish from exhaustion due to pain !!
    - May sleep most of first day
  - tolerance develops within days
- Complex in advanced disease

. . . Sedation

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

Delirium . . .

- Presentation – hyper/hypo/mixed
  - confusion, bad dreams, hallucinations
  - Inattentiveness – fluctuating !!
  - restlessness, agitation
  - myoclonic jerks, seizures
  - depressed level of consciousness
  - respiratory depression

. . . Delirium

- Uncommon [?], 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 [Narcan], 0.1-0.2 mg IV q 1-2 min
    - Small dose – don't want to reverse all analgesia

Nonpharmacologic pain management…

- Palliative Radiotherapy – localized cancers bone
  - *Only for those >2mo prognosis*;
  - Single dose as effective as multiple usually
  - 40% have 50% pain decrease
- Neurostimulation
  - TENS, acupuncture
- Anesthesiologic
  - nerve block
- Surgical
  - cordotomy
- Physical therapy
  - exercise, heat, cold

. . . Nonpharmacologic pain management

- Psychological approaches
  - cognitive therapies (relaxation, imagery, hypnosis)
  - biofeedback
  - behavior therapy, psychotherapy
- Complementary therapies
  - massage
  - art, music, aroma therapy

Barriers . . .

- "Not important"
- Poor assessment
- Lack of knowledge
- Fear of [by pt/family/MD/RN !]
  - addiction
  - tolerance
  - adverse effects

. . . Barriers

- Regulatory oversight
- Patients unwilling to report pain
- Patients unwilling to take medicine

Pain Management Associated Problems – Mr. Charles

- NB to document doses and responses !!!
- Started on morphine 15mg q4h po (8/10)
- Reglan 10mg po q8h [anticipatory]
  - Can reduce or wean off after a week
- Added Motrin 800mg q8h
- Pain still 5/10, not sleeping; (goal=3/10)
  - **Add nortriptyline 25mg hs = slept and 3/10**

Summary & Pearls

- Severe pain is an EMERGENCY !
- Don't delay Rx while investigating !
- "Total Pain" concept of tx
- No Demerol for Chronic Pain
- Scheduled Tx – Morphine = Gold Std.
- Methadone good option
- Anticipate S/E of constipation, nausea
- Use SubQ route & NO IM's

“Growin’ old ain’t for sissies”

- Bette Davis

THANK YOU !