Patient Controlled Analgesia

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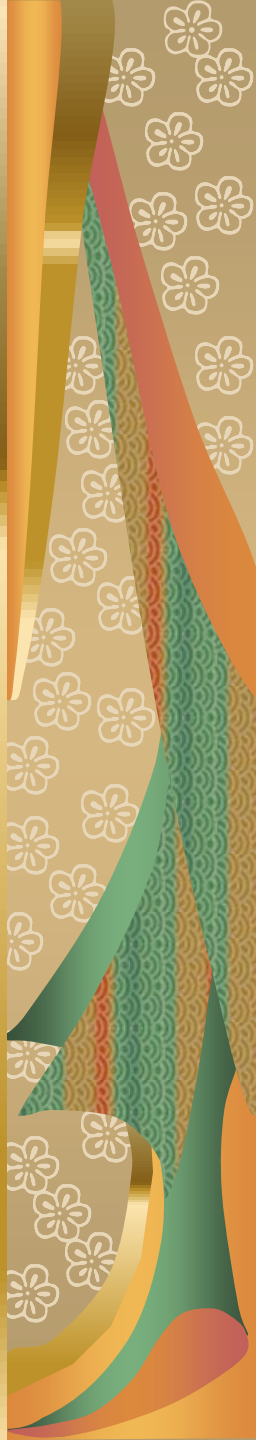
PCA - History

- 3rd Century BC – first documented opium use for analgesia from writings of Theophrastus
- Hippocrates – used opium in his regular practice
- Until 19th century cocktails of opium with henbane and mandragora were mainstay of analgesic Tx for 2000 years

PCA – History cont…

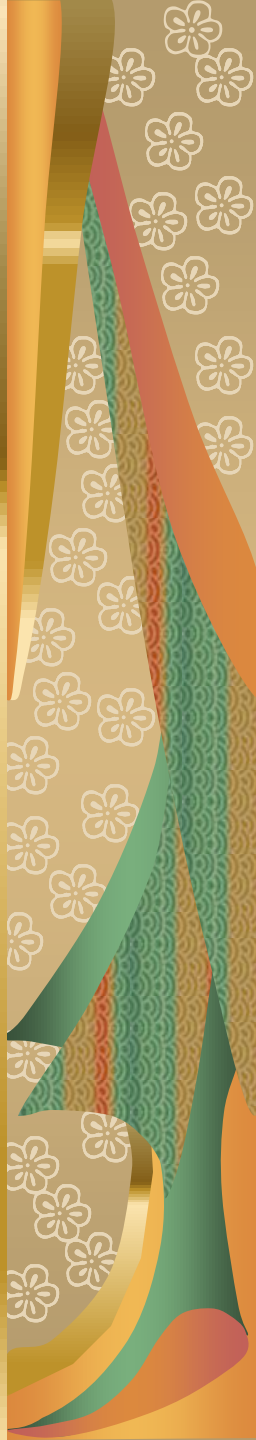
- 1806 – opium's active component, morphine was isolated. Named after Morpheus (Greek god of dreams)
- 1853 – hypodermic needle and syringe were invented - allowed for IV and IM delivery of analgesic meds
- Standard became opioid delivery via IM route either prn or RTC
- 1963 – Roe demonstrated small IV opioid doses provided more effective relief than IM regimens



PCA – History cont…

- 1968 & 1971 – Sechzer had series of experiments to evaluate analgesic response to small IV doses of opioids
  - Pt could choose to receive more analgesia as measure of pain perceived
    - Initially had bedside attendant administering meds
    - Later med delivered by machine

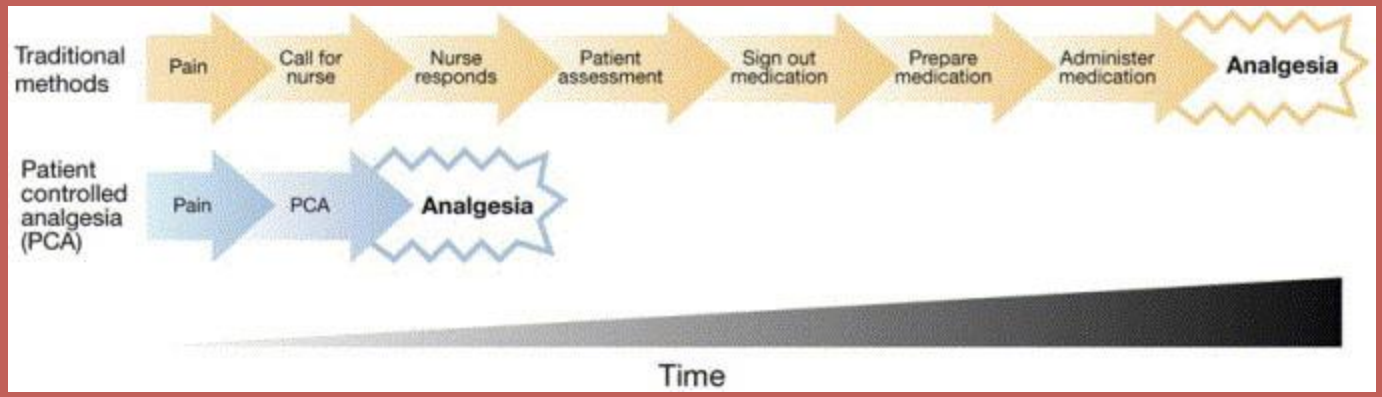
  Conclusion: Analgesic-demand system improved pain control with lower total doses of drugs.



Is there anything magical about PCA?

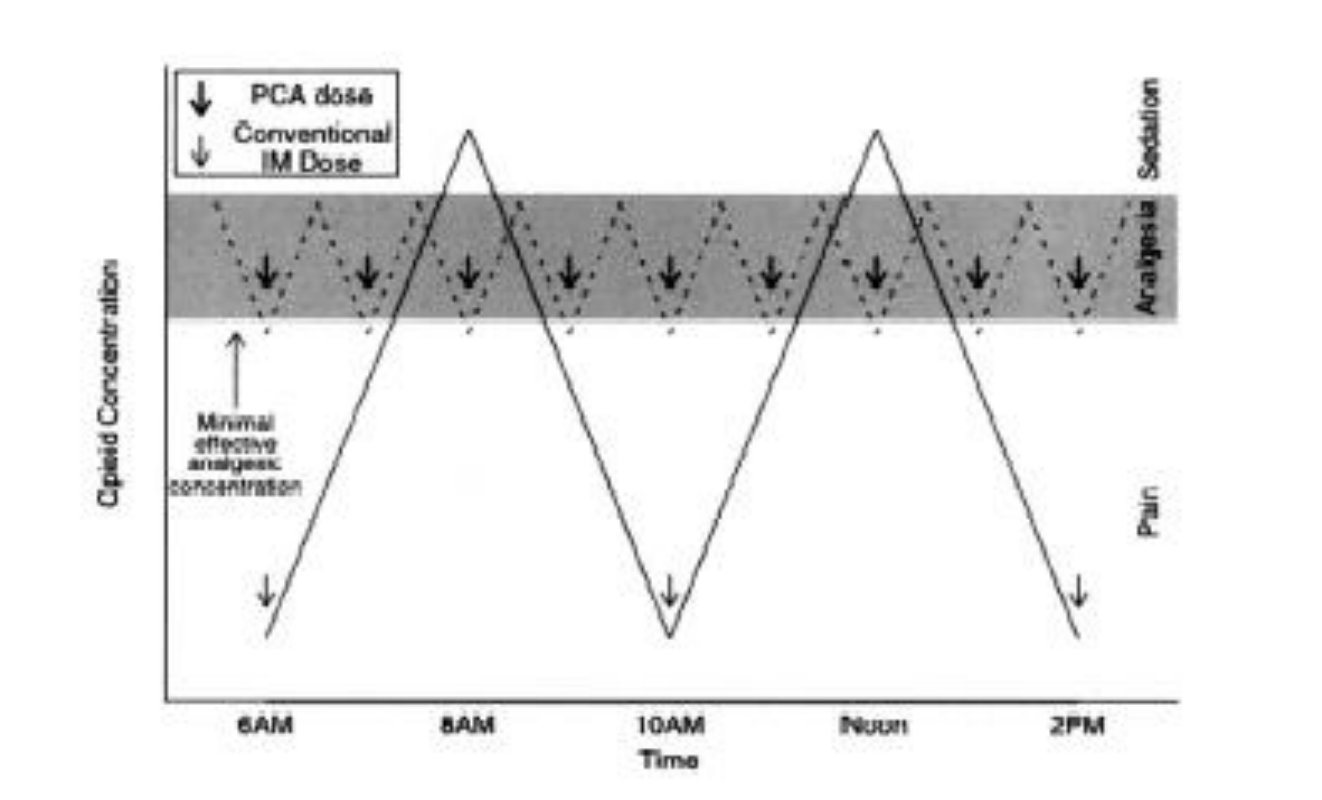
- There is no reason to believe that PCA would be superior to an RN (or bedside attendant) assessing the patient frequently and giving IV opioids as needed.
- Demands for more analgesia may be tempered by adverse effects

Traditional IM prn vs IV PCA



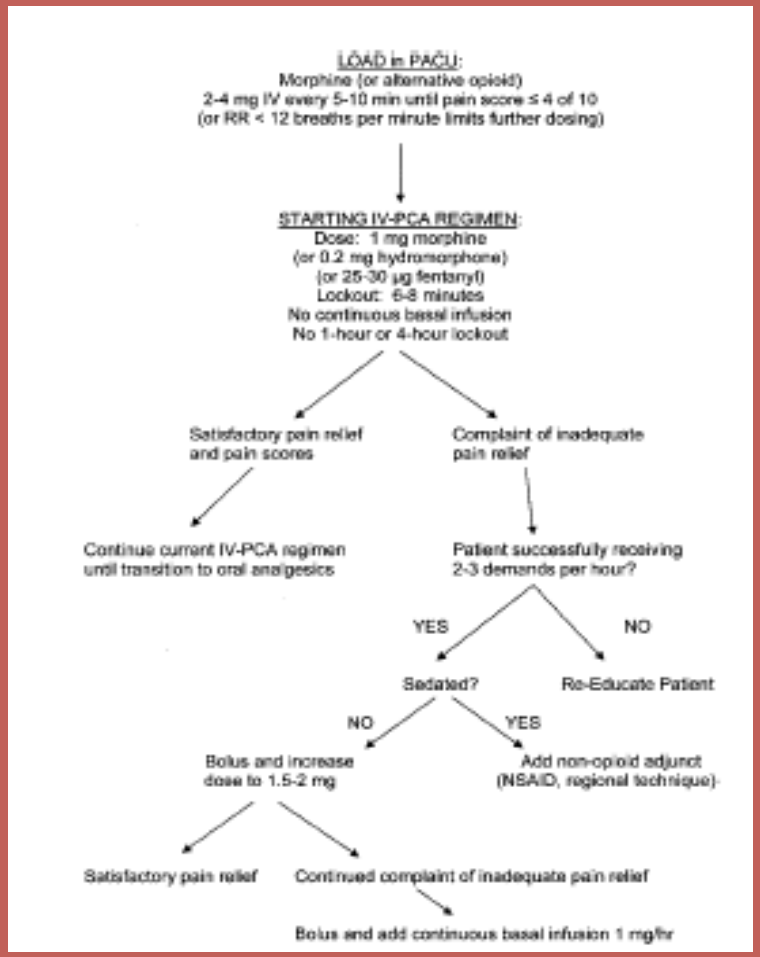
Conflicting studies exist regarding PCA providing better analgesia than IM injections. Regardless, patients prefer and are more satisfied with the IV vs IM route.

IM vs. IV PCA - Effective Analgesia



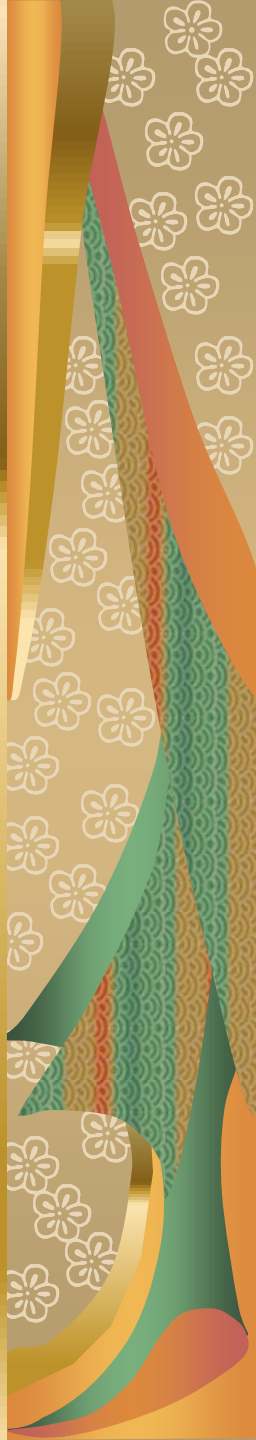
1. Individualize dosage and titrate to MEAC
2. Maintain constant opioid concentration and avoid peaks/troughs

Algorithm for IV PCA with Opioid Naïve Patients



Advantages of PCA

- Patient has a sense of control
- Painless
- Reduces demands on nursing
- Frequent boluses limit plasma drug fluctuations
- Adjustable to meet individual patient needs



Disadvantages of PCA

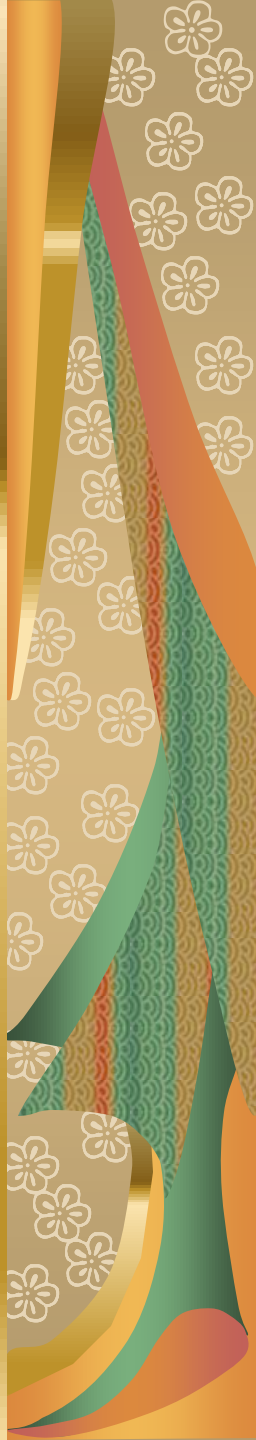
- Expense of equipment
- Requires the cooperation and comprehension of the patient
- Not appropriate for all age groups
- Patient must be able to use the demand button
- Hazards due to programming or delivery system

Contraindications

- Patient rejection – pt prefers to have staff manage pain
- Pt inability to safely comprehend use – mental impairment, language barrier
- Extremes of age
- Lack of appropriately trained nursing staff

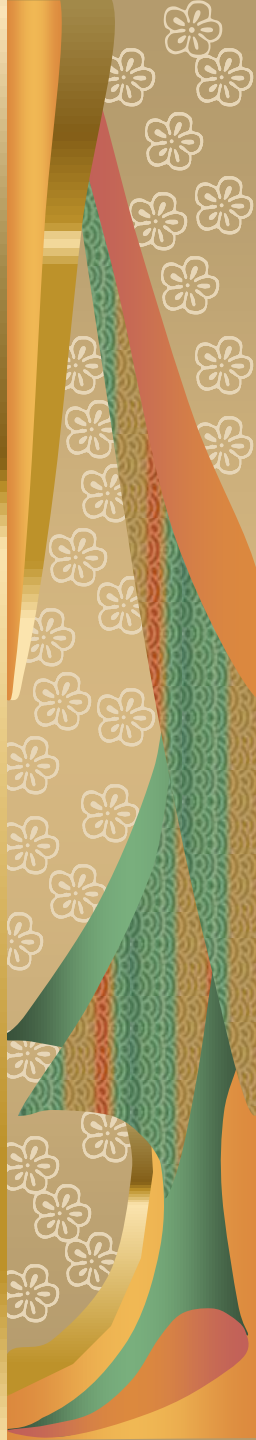
Proceed with caution:

- Marked metabolic disorders (sepsis)
- Severe fluid and electrolyte imbalances
- End-stage renal or hepatic disease
- Severe COPD
- Sleep apnea



PCA

- Morphine 1 mg / ml (5 mg/ml)
- Fentanyl 10 μg/ml (50 μg/ml)
- Hydromorphone 0.2 mg/ml (1 mg/ml and 5 mg/ml)
- No Meperidine



Morphine

- Inexpensive and "gold standard" for IV PCA
- Indicated for treatment of moderate to severe pain
- Comes in multiple forms (PO, IV, IM, PR)
- Metabolized: liver (CYP450:2D6) Excreted: kidney
  t1/2 = 2-4 hrs
- Slow-onset 10-15 min after IV bolus
- Metabolite – morphine-6-glucoronide causes analgesia, sedation, N/V, and respiratory depression
- Contraindicated with:
  - Allergy to morphine (rare and need to differentiate between this v. SE)
  - Hepatic dysfunction – increased accumulation
  - Renal dysfunction – metabolite accumulation; may have delay in profound resp depression; (avoid with Cr > 2 mg/dL)
  - Asthma – can exacerbate histamine release (also leads to pruritis)

Fentanyl

- Indicated for moderate to severe pain
- Synthetic, lipophilic opioid
- More expensive than morphine (must be prepared by pharmacist) and 100x more potent
- Forms – IV, transdermal patch, buccal
- Metabolized: liver (CYP450:3A4) Excreted: kidney
  t1/2 = 4 hrs
- Rapid onset – 1-5 min
- Non-sedating; rare pruritis
- No active metabolites → indicated in pts with renal/hepatic dysfunction
- Contraindication:
  - Allergy to fentanyl (differentiate from side effects)

HYDROmorphone (dilaudid)

- Indicated for moderate to severe pain
- More expensive than morphine (must be prepared by pharmacist)
- Semi-synthetic opioid derived from morphine (5x more potent than morphine)
- Forms – IV, PO, IM, PR
- Metabolized: liver (CYP450:3A4, 2C9) Excreted: kidney
  t1/2 = 2.3 hrs
- Onset – 10-15 min
- Non-sedating
- Metabolite – hydromorphone-3-glucuronide may cause euphoria when used in high doses
- Contraindication:
  - Hepatic impairment (4 fold increase in dose)
  - Renal impairment (2 fold increase in dose)

Normeperidine Toxicity

Pt. Group	Asympto -matic	Shaky Feelings	Tremors/ Twitches	Myoclonus Grand mal
N	19	20	9/9	8/2
Days of administration	1.2 (0.1) 1-2	8.0 (1.2) (1-22)	6.7 (1.9) (1-30)	5.9 (1.0) (3-10)
Rate of admin. (mg/day)	170 (18) (75-380)	350 (52) (59-1080)	370 (66) (46-1100)	420 (37) (260-540)

Kaiko RF et al, *Ann Neurol* 1983;13(2):180-5

IV PCA Opioid Therapy Initial Settings

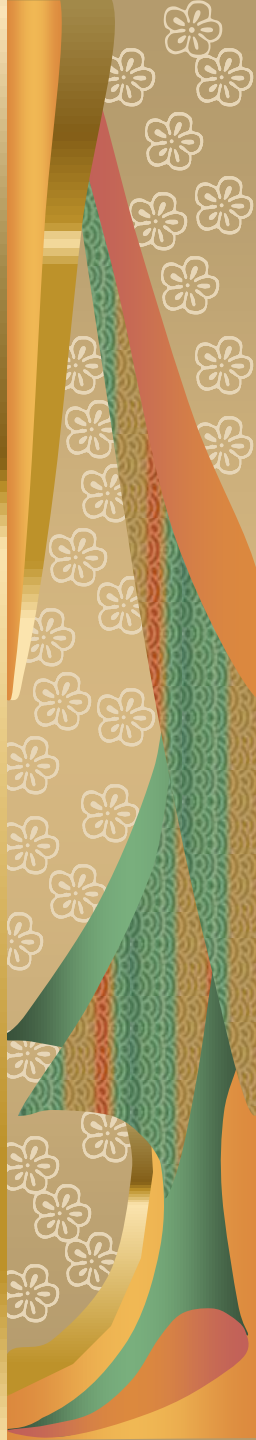
- Loading dose
- PCA Dose
- Lockout interval
- 4 hour maximum
- Bolus Dose for Rescue
- Continuous mode on or off
- Rate of continuous infusion
- “Smart” Features

Loading Dose

- The amount of drug required to achieve an initial level of analgesia (the minimum effective analgesic concentration - MEAC)
  - Large interpatient requirement differences
  - Total dose per patient impossible to predict
- Can be done via PCA machine for convenience but not really a PCA function
- Ideally done in PACU prior to PCA use

(Ex: morphine 2-4 mg IVP q5-10 min until pain<4/10 or RR<12)

- Omission may lead to failure to obtain good analgesia with PCA because MEAC may not be achieved → inc pain and anxiety



How is PCA demand dose determined?

- Demand dose - amount of medication the patient receives after a successful demand
- Ideal - consistent and satisfactory analgesia without excessive side effects
- Large Enough to have some effect perceptible to the patient (if not, they will tire of pressing the button, complain and/or lose faith in the system)
- Small Enough so that no 1 or 2 doses can take the patient from awake to severe respiratory depression
- One dose size DOES NOT fit all. Must re-evaluate needs of each individual

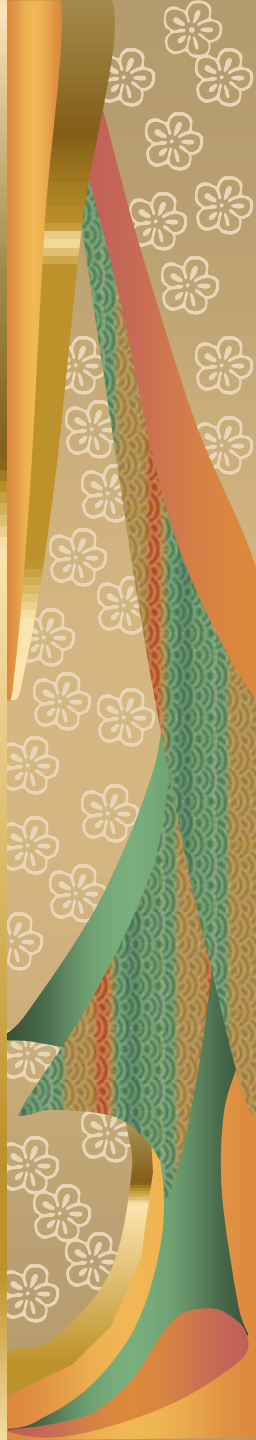
PCA GUIDELINES for HEALTHY PATIENTS

Incremental Doses		**Age**			
		7-16	16-40	40-70	>70 yrs
MSO4	mg	0.025/kg	1.5	1	0.5
	ml	0.025/kg	1.5	1	0.5
Hydromorphone	mg	0.003/kg	0.3	0.14	0.06
	ml	0.015/kg	1.5	0.7	0.3
Fentanyl	mcg	0.20/kg	15	10	5
	ml	0.020/kg	1.5	1	0.5

PCA Notes

Significant dose reductions should be made in the face of diagnoses that could impact on respiratory function or drug metabolism.

- Pulmonary disease
- Congestive heart failure
- Sleep apnea
- Closed head injury
- Hepatic or renal failure
- Altered mental status
- Lactating mothers



PCA Opioid Therapy- How is lockout interval determined?

- Definition: the time, following the end of the delivery of one dose, during which the machine will not administer another dose despite further pt demands
  - Should reflect time necessary for pt to appreciate effect of demand dose before another delivered.
  - Dose must circulate and cross the blood brain barrier
- Ideal interval related to drug used and size of bolus demand dose
- Practically – common intervals are 5-12 min
- Once reached MEAC, no appreciable major differences in time of onset among opioids

IV PCA Opioid Therapy- How is lockout interval determined?

- Typical error is lockout intervals that are too long
- Promotes patient frustration and does not add to safety
- 7 minutes often ideal for most of our opioids with IV properly set up
- 15 minutes too long for IV PCA
- Large demand doses with long lockouts increases risk of side-effects (resp depr)

IV PCA Opioid Therapy Function of the 4 hour limit?

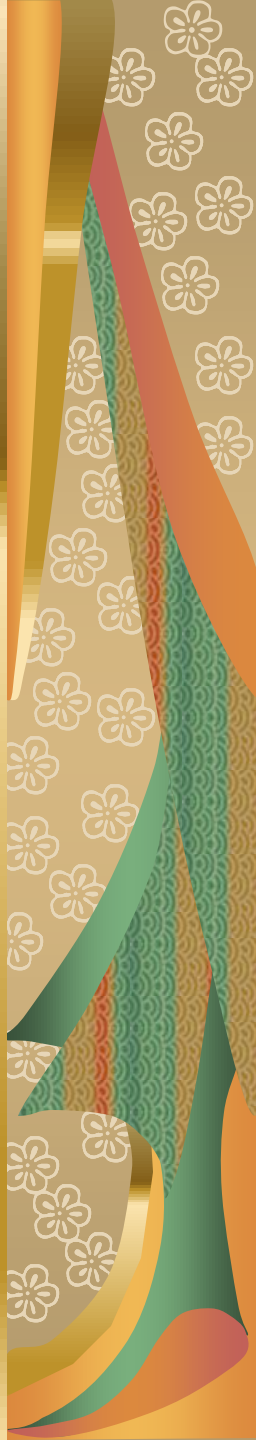
- Required by the FDA to approve a PCA device
- Generally Superfluous - no sufficient evidence to prove that inclusion of this limit has reduced side effects
- Properly set PCA dose, lockout interval should provide all the safety you need

4 hour limit- can something good come of it?

- Should not be used to punish the patient or limit the dose to a particular number
- Should instead be a trigger for nursing personnel to assess patient and invite physician to do the same

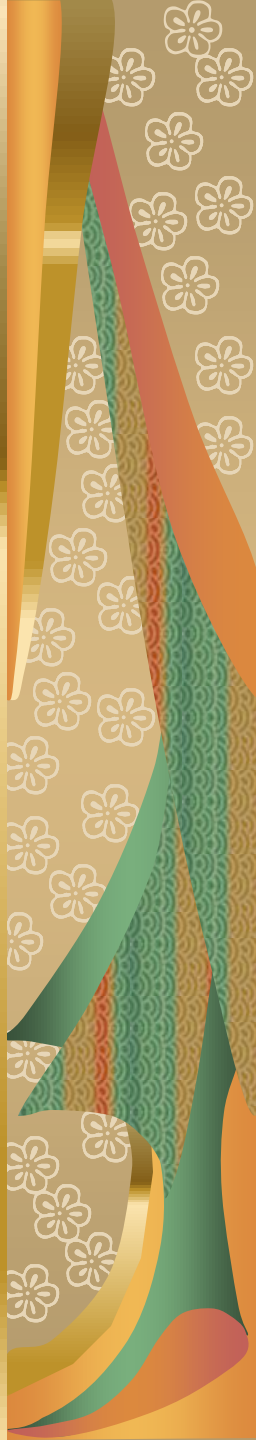
4 hour limit reached- what may be going on?

- IV infiltrated or blocked
- Carrier too slow
- Incorrect dilution of opioid drug
- Lockout too long for patient
- PCA dose too small for patient
- A new painful problem which requires diagnosis- hematoma, obstruction etc.



4 hour limit- a reasonable way to set it

- Choose other settings first
- Calculate how the maximum the patient can get in 4 hours based on the dose and lockout
- Set the 4 hour limit to 70% of that amount

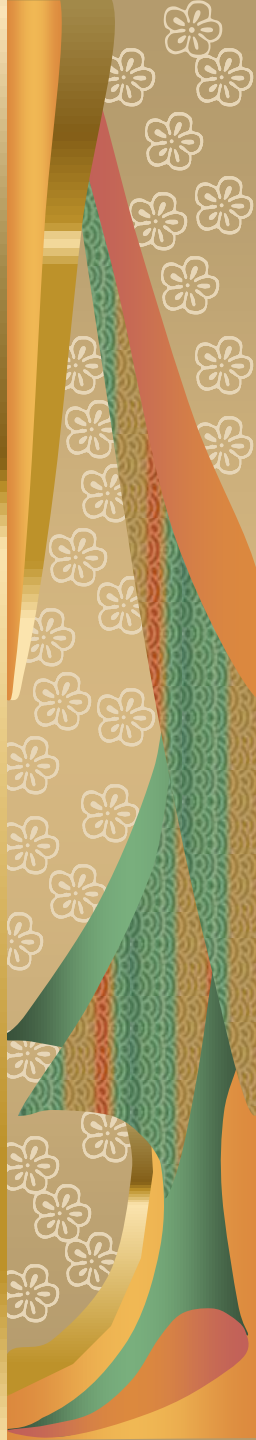


4 hour limit- who can really benefit

- Elderly
- Lung Disease
- Cardiac Disease
- Meperidine Use
- Anyone whose frail medical status undermines the basic safety of PCA therapy

Continuous Infusion- On or off?

- Constant rate infusion given regardless of pt activating demand or not
- Depends on drug
- Common for fentanyl
- For morphine and hydromorphone
  - Not routine
  - Initial set-up - DO NOT use continuous with opioid naïve pts
    - Rarely required
    - Markedly increase risk of respiratory depression

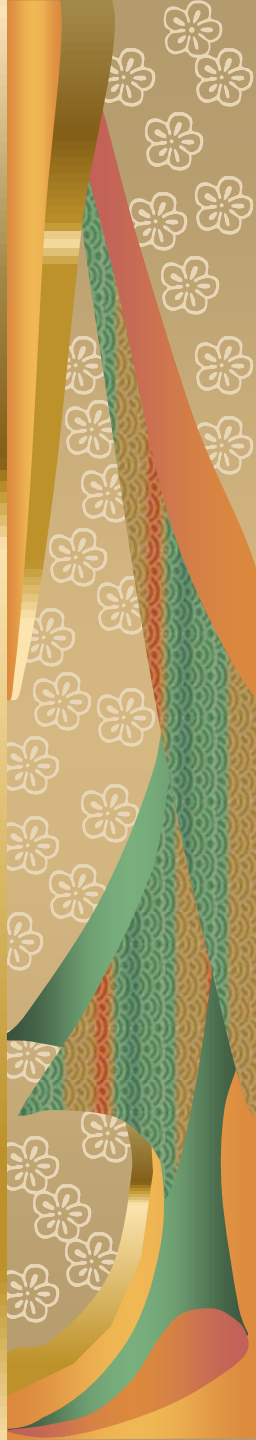


Continuous Infusion- On or off?

- Depends on clinical setting
- Very safe in Critical Care Areas
- More questionable in other settings because it is not patient controlled and undermines the basic safety of the PCA
- Can be used safely outside ICU when done right
- Depends also on magnitude of trauma and health of patient
- Can improve sleep and diminish painful awakenings

Continuous Infusion

- Start an infusion if:
  - Inadequate analgesia over >6 hours
  - Opioid-tolerant patient
- Infusion rate based on hourly use over previous 6 hours
  - Opioid-naïve 25-50% of hourly requirement
  - Opioid-tolerant 50-75% of hourly requirement

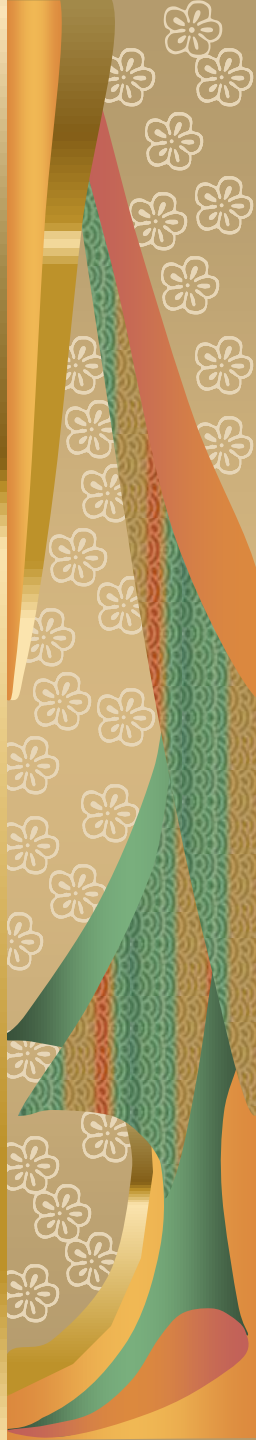


Rate of Continuous: Morphine and Hydromorphone

- One “PCA dose” per hour quite safe in less monitored setting
- Twice that amount questionable in unmonitored setting

Rate of Continuous: Fentanyl

- 10-20 mcgs per hour reasonable and often necessary because of short effect of drug

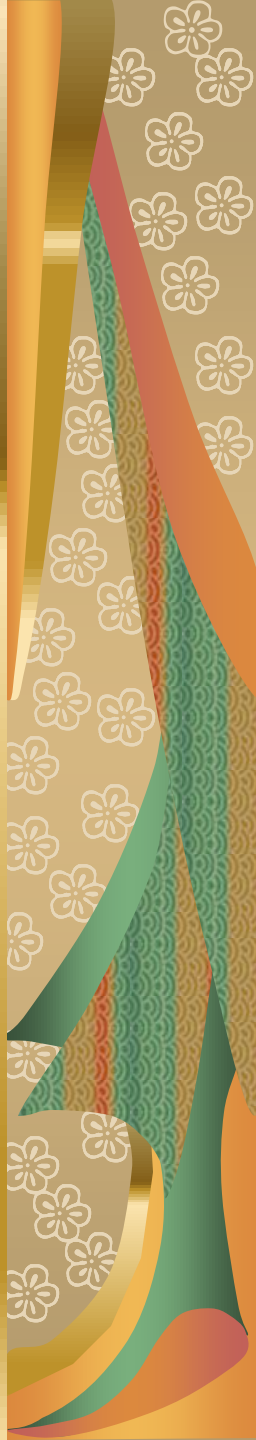


Reports from the machine

- Look at the ratio of total button pushes to successful deliveries
- Also look at total number of deliveries
- Goal is demand: delivery = 1:1
- Case: Patient reports dissatisfaction with PCA, but made only 13 attempts in 24 hours and all were successful 1:1 -> Educate patient

Reports from the machine

- Case: Patient reports satisfaction, pushed button 120 times and got 60 successful deliveries
- Case: Patient Satisfied, pushed button 25 times and got 13 deliveries



IV PCA Opioid Therapy
Modification of PCA Demand Dose

- Decrease if a single dose puts patient to sleep repeatedly - somnolence preceeds respiratory depression
- Increase if patient tells us that 2 consecutive doses given over one lockout do little to relieve pain
- Alternative in latter situation is to “miniload” the patient under your direct observation and then see if old PCA dose starts to work
- Increase by about 50% each time, decrease by about 40%

Modification of Lockout

- Should not be necessary
- Decrease if patient give you a story that makes sense
- “I feel better when I press it, but I have to wait too long to press it again”
- Not less than 6 minutes

Modification of 4 hour limit

- As needed
- Can cancel or increase if it is reached and re-evaluation shows patient just needed more opioid

Adding a continuous

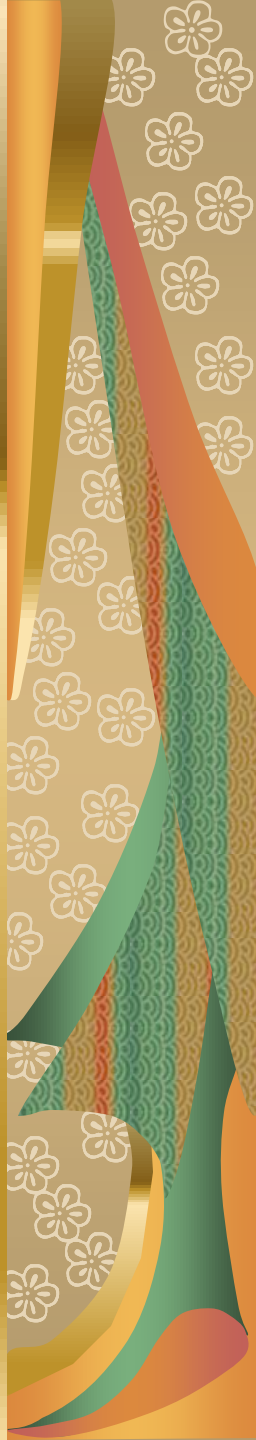
- Can be much safer AFTER the first day
- Note total use for day and comfort level
- Make some assumptions
- Make an educated guess about the total use for the next day
- Are you anticipating pain levels going down or up?
- Quite safe to give about a third to a fourth of this as continuous
- No need to change other settings

Monitoring with IV PCA

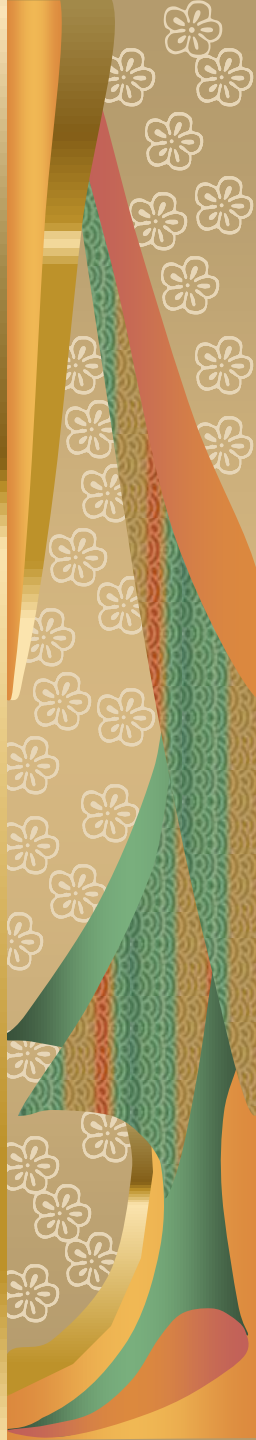
- Pain scores - at rest and with movement
- Sedation scores
- Respiratory rate - decreases in rate may be a late and unreliable sign of resp depression
- Total amount of opioid delivered
- Onset of any side-effects and treatment delivered
- Regular monitoring of oxygen saturation with high risk individuals - COPD, sleep apnea, s/p major surgery, or those on continuous infusions (O_2 sats may be unreliable on those with supplemental O_2)

When is PCA discontinued?

- Hopefully the patient will do it for you
- Daily use falls by 2/3
- Patient unable to use PCA effectively or appropriately (i.e. onset of confusion)
- Oral Route becomes practical
- Patient ambulating for 24 hours



Parenteral to PO Conversions



Parenteral to PO Conversions

- Worth memorizing some basic ones
- Useful for cancer pain and other nociceptive pain which will last beyond the practicality of IV administration
- Especially useful when good control established with a level or slightly diminishing PCA opioid dose

Equianalgesic Doses of Opioid Analgesics

	Equianalgesic Dose (mg)		Starting Oral Dose	
	Oral	Parenteral	Adults (mg)	Children (mg/kg)
Morphine-like agonists				
Morphine	30	10	15 – 30	0.3
Hydromorphone	7.5	1.5	4 – 8	0.06
Oxycodone	20	—	15 – 30	0.3
Methadone	20	10	5 – 10	0.2
Levorphanol	4	2	2 – 4	0.04
Fentanyl	—	0.1	—	—
Oxymorphone	—	1	—	—
Meperidine	300	75	Not recommended	
Mixed agonist-antagonists				
Nalbuphine	—	10	—	—
Butorphanol	—	2	—	—
Dezocine	—	10	—	—
Partial agonist				
Buprenorphine	—	0.4	—	—

With permission from American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain;* 1999:14.

Converting to Oral Opioids

- determine the 24 hour IV morphine requirement
  - example: 2 mg/h = 48 mg/24h
- multiply x 3 to get equivalent PO dose
  - (48 mg x 3 = 144 mg PO per 24h)
- reduce by 30-60%
  - (144 mg - 38% = 90 mg per day)
- Divide by # of doses per day
  - 90 mg/day = MS Contin 30 mg q8h
- Reduce by 33% if using oxycodone
  - 90 mg/day = 60 mg/day of oxycodone
  - = 2 Percocet 5/325 q4h, ATC
  - = Oxycontin 30 mg q12h or 20 mg q8h

Sample strategy 2

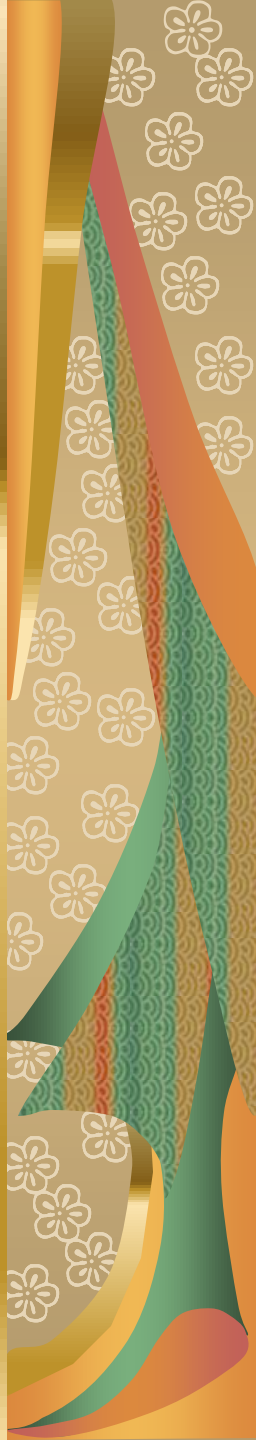
- Patient has been using PCA dilaudid 40 mg/day and pain is 1/10 at rest and 3/10 with movement
- Plan conversion to morphine equivalents: 40 x 5 = 200 mg IV morphine/day = 600 mg PO morphine
- Give 50% of total or 300 mg conservatively, as long acting oral morphine (MS Contin) 100 mg PO q8hrs
- Make available other half (300 mg) as either: morphine immediate release 60 mg or dilaudid 16 mg PO q2-3 hrs prn pain

Sample strategy (cont)

- Make clear to patient that the slow release is to be taken by the clock, not skipped, and is non-negotiable
- Make provisions for side effects. Constipation will the worst and most recalcitrant with long term use
- Address nausea as you would anyone- often diminishes with time
- Oversedation- low dose amphetamine

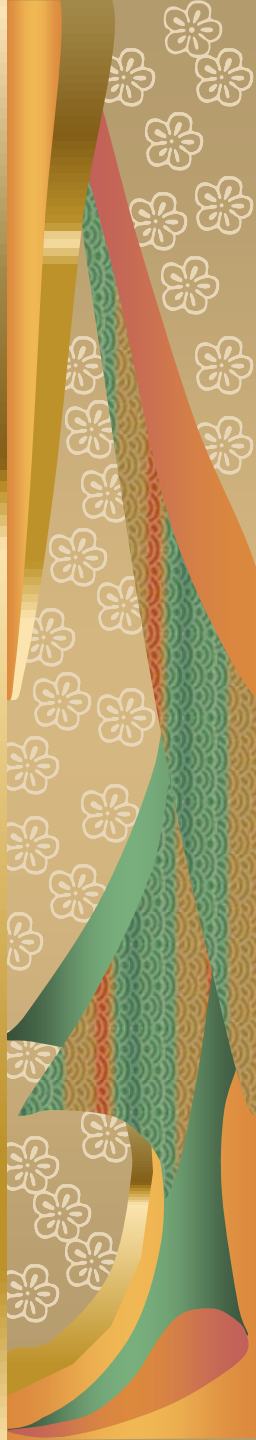
Conversion from Oral to Parenteral

- Use same numbers in opposite direction
- Use IV PCA
- You can and should give a third of the expected daily dose as a continuous infusion



Problems with IV PCA-Failure

- Are the settings correct? (Programming errors are the most common operator errors and tend to occur with cartridge changes rather than initial set-up)
- Proper patient education?
- Did you consider preoperative tolerance?
- Did you fail to get a history of substance abuse/dependence?
- Are you seeing alcohol withdrawal?
- Is a major psychiatric diagnosis being missed? (dependent pd)



Problems with IV PCA-Failure

- Is there coexisting anxiety that needs to be treated? -> high anxiety highly related to higher pain scores with PCA use and may be associated with frequent unsuccessful demands
- Would a non-steroidal co-analgesic be helpful?
- Have you correctly assessed ongoing and new surgical problems?
- Family interference? Friend selling the drug on the street?

Pain with movement, well controlled at rest

- A classical result of IV PCA Opioid Therapy, especially after major orthopedic procedures
- Non-steroidal agents may help, especially ketorolac, which has its own problems
- A major advantage of continuous regional analgesia

Routine non-steroidals

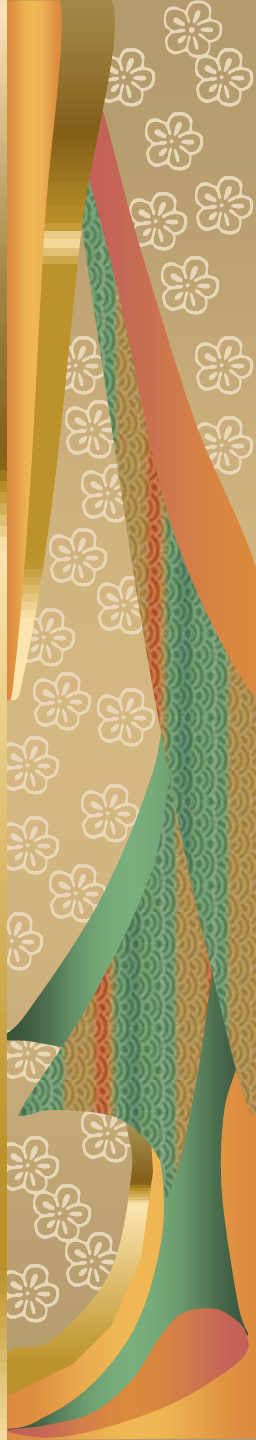
- Should almost all acute pain patients be treated with either acetaminophen or a non-steroidal on an around the clock basis, when practical and with respect for the toxicities of these drugs? Use both together?
- Would probably reduce side effects of opioids, improve analgesia with movement

Routine Non-steroidals-Adjunct to PCA, etc

- Confidence in the COX-2 inhibitors, celecoxib, may increase surgeon comfort with non-steroidals in the post-op period
- Renal toxicity still a possibility
- Renal toxicity of all NSAID less likely if patient is well hydrated, not in heart failure, and not medically diuresed

Other investigational enhancements to IV PCA Analgesia

- Low dose ketamine added, being done for ICU patients at UCS Norris Cancer Institute
- Anxiolytics added or on a separate PCA



Management of Side Effects - Nausea and Vomiting

- Dose related
- Risk factors: female, h/o motion sickness, h/o PONV
- Administration of one anti-emetic/one-receptor site
  ➲ 30% reduction
- Combo zofran ($5HT_3$ antag) + droperidol (D_2 antag)
  ➲ 90% reduction
- Tx options:
  - Ondansetron, droperidol, promethazine, dexamethasone, scopolamine patch, propofol infusion, naloxone infusion v. low-dose IVP (0.6 mcg/ml) with morphine
  - Change opioid

Management of Side Effects - Pruritis

- Mechanism not fully understood - may be mediated by μ-receptor not histamine
- Incidence = 5%
- Incidence higher in:
  - Middle-aged - 40% in 40-49 y/o
  - Post C-section -25%
- 50% lower incidence in PCA vs epidural route
- Treatment:
  - Change opioids
  - Naloxone, naltrexone, droperidol
  - Lack of evidence for: propofol, IV ondansetron,IM hydroxyzine, epidural clonidine