

Using Evidence Based Medicine to Ethically Provide End of Life Symptom Control



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Disclosures

- I do NOT have any financial disclosures
- I WILL be discussing off label prescribing



Objectives

- Discuss strategies for treating intractable pain
 - Why the Doctrine of Double Effect matters here
- Review mechanisms and treatments for nausea
- How to fix constipation fast
- Comprehensive approach to dyspnea treatment

Opioid Pain Management Pearls



[Scrub's Pain Clip](#)

Wait, Which Medicine?

Generic Name	IV	Short PO	Long PO
Codiene		T3	
Hydrocodone		Norco Vicodin Lortab	Zohydro ER
Oxycodone		Oxycodone Percocet Roxicodone	Oxycontin
Morphine	Morphine	MSIR Roxanol	MS Contin Oramorph SR Kadian
Hydromorphone	Dilaudid	Dilaudid IR Palladone	Palladone SR Jurnista
Fentanyl	Fentanyl	Actiq Sublimaze (nasal/buccal)	Duragesic (patch)

Pain Pearls

- IV to PO dosing 1:3
- Time to Onset and Duration for morphine
 - IV 6-10 minutes and lasts 2 hours
 - IM 30 minutes and lasts 2 hours
 - PO 60 minutes and lasts 4 hours
- Common Conversions
 - PO hydrocodone = PO morphine
 - PO oxycodone is 1.5 x stronger than PO morphine
 - IV hydromorphone is 5-7 x stronger than IV morphine

Choosing the Med and the Dose

- Morphine IV weight based dosing 0.1mg/kg
- Fentanyl IV weight based dosing starts at 1-2 mcg/kg
- Hydromorphone IV dosing starts at 0.015 mg/kg

- Morphine more renal metabolism
- Hydromorphone and fentanyl more liver

Doctrine of Double Effect

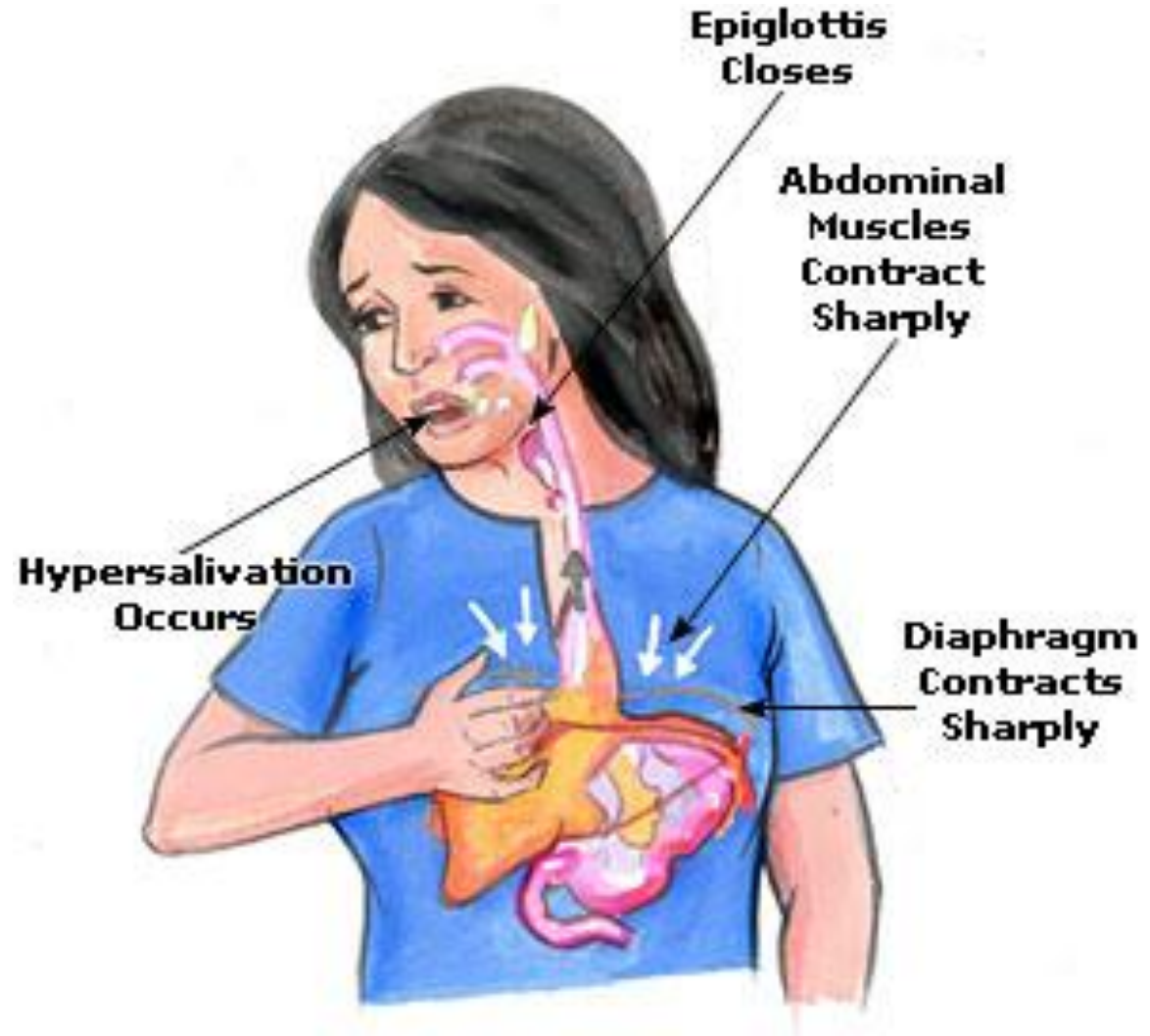
- The permissibility of an action that causes a serious harm, even death, as a side effect of promoting some good end
- Treating pain versus euthanasia/physician assisted suicide

Understanding and Treating Nausea



Defining Nausea & Vomiting

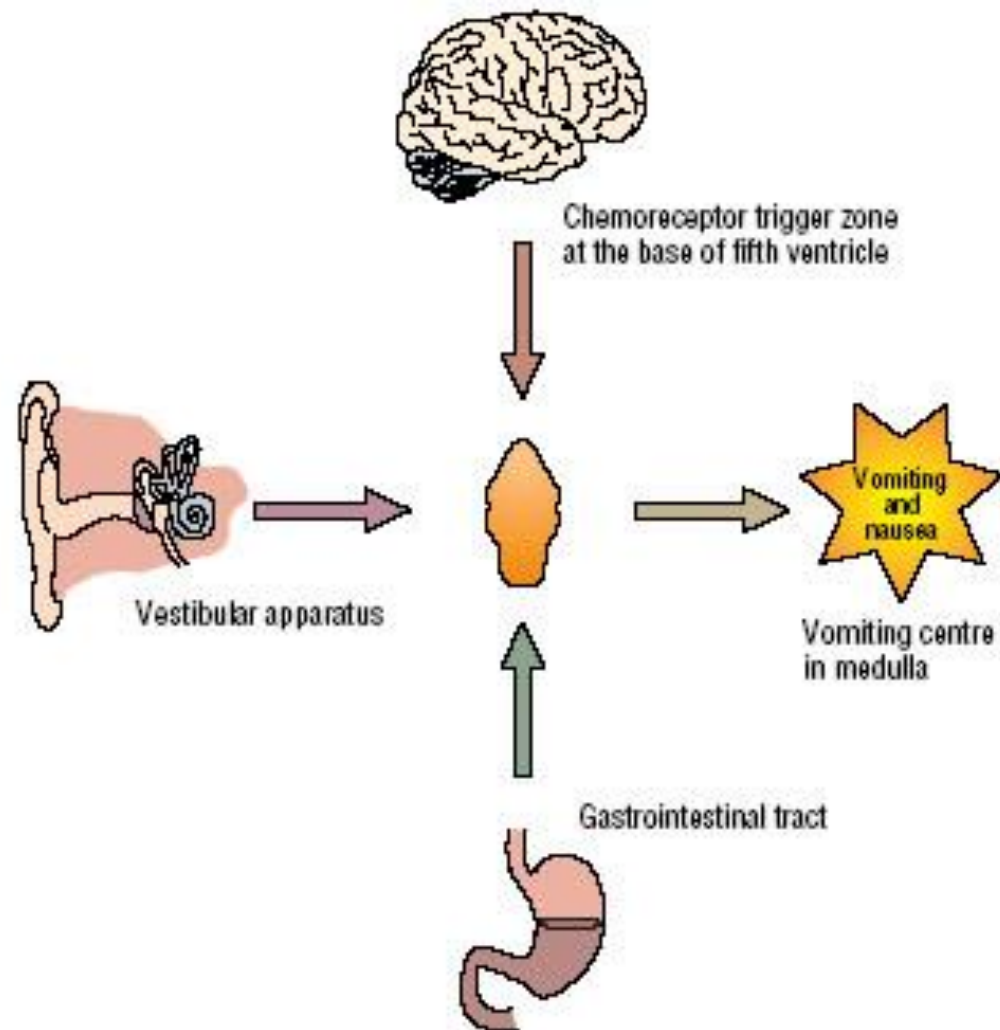
- Nausea
 - Subjective sensation
 - Stimulation
- Vomiting
 - Neuromuscular reflex



Causes of Nausea & Vomiting

- Metastases
- Meningeal irritation
- Movement
- Mental anxiety
- Medications
- Mucosal irritation
- Mechanical Obstruction
- Motility
- Metabolic
- Microbes
- Myocardial





Pathway

-  Chemoreceptor trigger zone
-  Vestibular
-  Vomiting centre pathways
-  Gastric stasis

Potentially beneficial drugs

- Dopamine and 5-HT₃ serotonin receptors
- Cholinergic muscarinic receptors
- Histamine and cholinergic muscarinic receptors
- Dopamine and 5-HT₄ serotonin receptors





- Dopamine Antagonists
 - Haloperidol, Prochlorperazine, Droperidol, Thiethylperazine, Promethazine, Perphenazine, Trimethobenzamide
- Acetylcholine Antagonists (anticholinergics)
 - Scopolamine
- Histamine Antagonists (antihistamines)
 - Diphenhydramine, Meclizine, Hydroxyzine
- Serotonin Antagonists
 - Ondansetron, Granisetron



- Prokinetic Agents
 - Metoclopramide
- Antacids
 - H₂ receptor antagonists
 - Cimetidine, Famotidine, Ranitidine
 - Proton pump inhibitors
 - Omeprazole, Lansoprazole
- Cytoprotective Agents
 - Misoprostol
- Others
 - Dexamethasone, Tetrahydrocannabinol



Table 1 – Relative Affinities of selected antiemetic agents to various receptors

	DA ₂ Antago- nist	H ₁ Antago- nist	M ₁ Antago- nist	5-HT _{2A} Antago- nist	5-HT _{3A} Antago- nist	5-HT _{3B} Antago- nist	5-HT _{3C} Antago- nist	5-HT ₄ Antago- nist	NK-1 Antago- nist	CB-1 Modula- tor	MOR Antago- nist
Scopolamine	-----	+	++++	-----	-----	-----	-----	-----	-----	-----	-----
Diphenhydramine	-----	++++	++	-----	-----	-----	-----	-----	-----	-----	-----
Promethazine	++	++++	+++	-----	-----	-----	-----	-----	-----	-----	-----
Hydroxyzine	-----	++++	++	-----	-----	-----	-----	-----	-----	-----	-----
Prochlorperazine 	++++	++	++	+	-----	-----	-----	-----	-----	-----	-----
Droperidol	++++	+	-----	+	-----	-----	-----	-----	-----	-----	-----
Haloperidol 	++++	+	-----	+	-----	-----	-----	-----	-----	-----	-----
Metoclopramide 	+++	-----	-----	-----	-----	++	-----	+++	-----	-----	-----
Ondansetron	-----	-----	-----	-----	-----	++++	-----	-----	-----	-----	-----
Hyoscine	-----	-----	-----	-----	-----	++++	-----	-----	-----	-----	-----
Levomepromazine	+++	+++	+++	++++	-----	-----	-----	-----	-----	-----	-----
Aprepitant	-----	-----	-----	-----	-----	-----	-----	-----	++++	-----	-----
Dronabinol	-----	-----	-----	-----	-----	-----	-----	-----	-----	++++	-----
Naloxone	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	++++
Ondansetron 	-----	-----	-----	-----	+	++	-----	-----	-----	-----	+
Granisetron	-----	-----	-----	-----	+++	+++	+++	-----	-----	-----	-----
Dolansetron (Hy- drodolasetron)	-----	-----	-----	-----	++	++++	-----	-----	-----	-----	-----
Palonosetron	-----	-----	-----	-----	++++	-----	-----	-----	-----	-----	-----
Mirtazapine	-----	+	+	+++	-----	+	-----	-----	-----	-----	-----
Olanzapine	+	+	+	++++	-----	++	-----	-----	-----	-----	-----

Constipation



"WORST CASE OF CONSTIPATION I'VE EVER SEEN."

Causes of Constipation

- Medications
- Decreased mobility
- Ileus
- Mechanical obstruction
- Malignancy
- Metabolic abnormalities
- Spinal cord compression
- Dehydration
- Autonomic dysfunction



Management Options

- Stimulant laxatives
 - Prune juice, Casanthranol
 - Senna
 - Bisacodyl
- Osmotic laxatives
 - Lactulose or sorbitol
 - Milk of magnesia
 - Magnesium citrate
- Detergent laxatives
 - AKA stool softeners
 - Sodium docusate
 - Calcium docusate
- Prokinetic agents
 - Metoclopramide
- Lubricant stimulants
 - Glycerin suppositories
 - Oils (mineral or peanut)
- Large-volume enemas
 - Warm water
 - Soap suds



Opioid Constipation

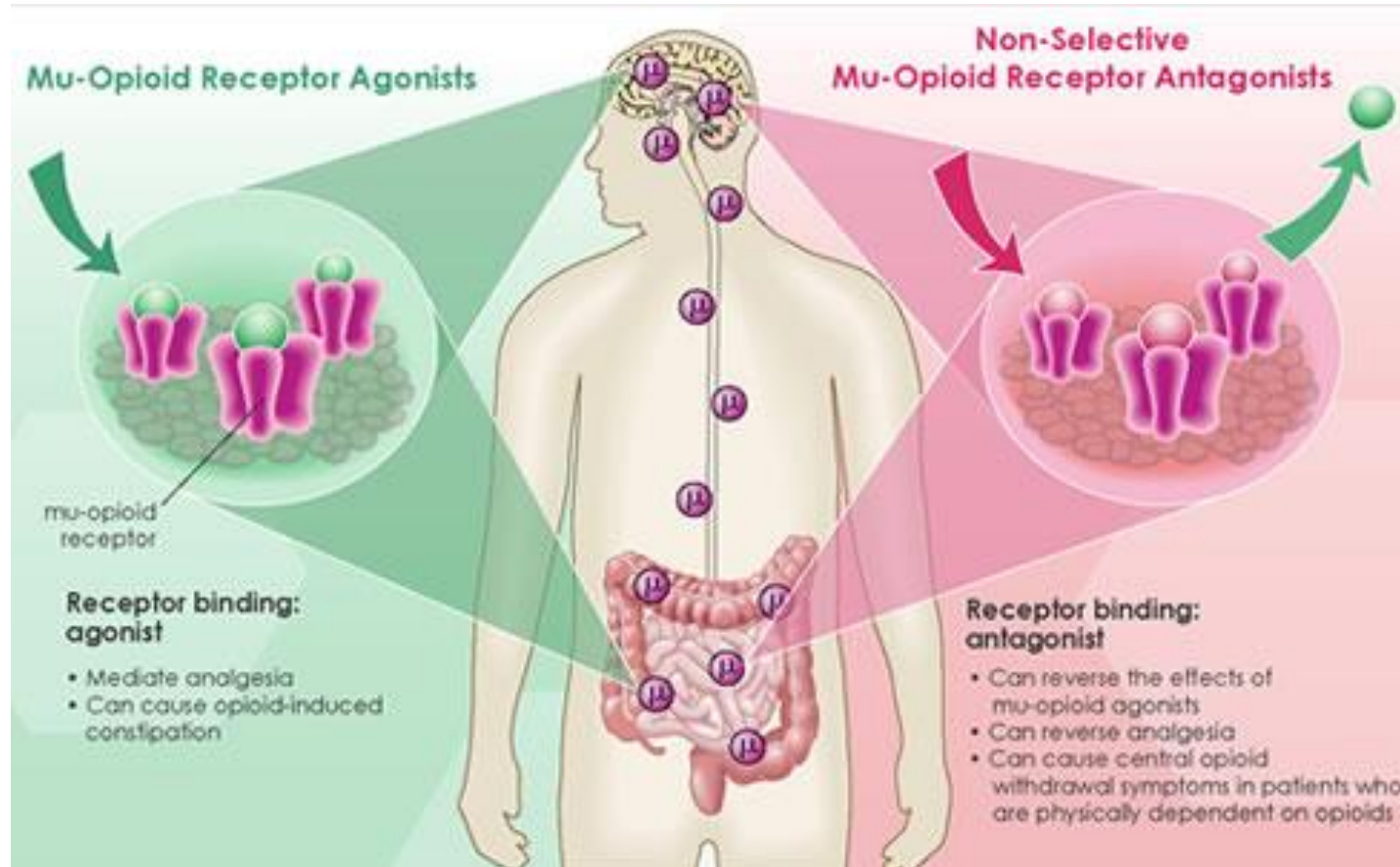
- Occurs with ALL opioids
- Never develop tolerance to this side effect
- Dietary interventions alone not sufficient
- Avoid bulk-forming agents
 - Fiber doesn't fix this!

Bowel Regimen with Opioids

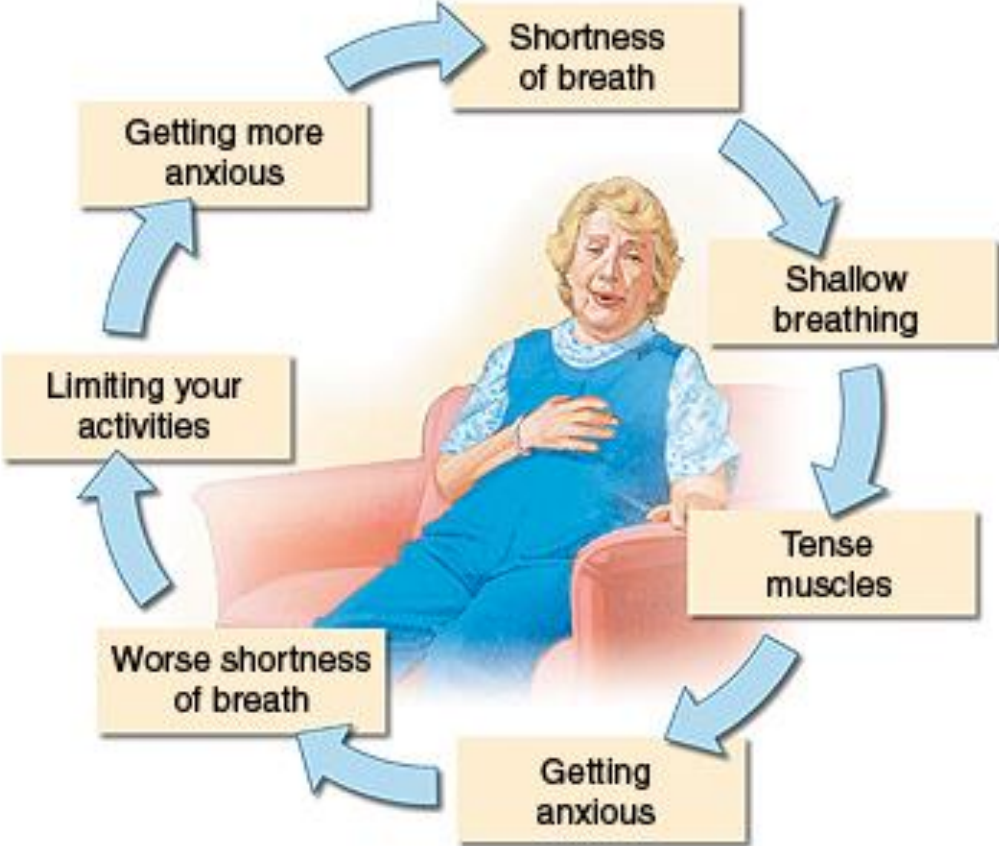
- All patients on opioids should have combo plan
 - Softner plus stimulant
 - Senna + docusate sodium scheduled (Senna S)
- Lactulose prn

Methylnaltrexone

- Relistor 8-12mg subcutaneous
 - Peripherally acting opioid antagonist
 - Does not cross blood brain barrier



Dyspnea



Defining Dyspnea

- Described as shortness of breath, smothering, inability to get air, or suffocation
- Only patient self report is reliable
- Looks like fear
- Does not correlate to RR, pO₂, or blood gas

- 21-78% of cancer pts, 56% in COPD, 68% in HIV, 61-70% in CHF, 70% in dementia

Causes of Dyspnea

- Anxiety
- Airway obstruction
- Bronchospasm
- Hypoxemia
- Pleural effusion
- Pneumonia
- Pulmonary edema
- Pulmonary embolism
- Thick secretions
- Anemia
- Metabolic
- Stress

Management of Dyspnea

- Treat underlying cause
- Symptomatic management
 - Oxygen
 - Opioids
 - Anxiolytics
 - Nonpharmalogical

Oxygen

- To treat symptom, not pulse ox
- Symbol of medical care
- Don't obstruct ability to communicate if able to communicate at end of life
- Fan may be just as effective



Opioids

- Central and peripheral action
 - Decrease chemoreceptor response to hypercapnia
 - Increase peripheral vasodilation
 - Decrease anxiety and subjective dyspnea
- Small doses
 - Morphine IV 2-5 mg q10-30 minutes prn
- Ethical intent is to relieve dyspnea

Anxiolytics

- Small doses
- Safe in combination with opioids (in small doses)
- Lorazepam 0.5-1 mg IV q30 minutes prn

Nonpharmacologic

- Introduce humidity
- Reposition/elevate head
- Educate/support family

- Consider treating secretions
 - Atropine or scopolamine or glycopyrrolate

Palliative Care Resources

- Palliative Fast Facts
 - <https://www.mypcnow.org/fast-facts>
- EPEC education
 - <http://bioethics.northwestern.edu/programs/epec/>

Topics Covered on Fast Facts

- Prognostication
 - Dementia
 - Liver Failure
 - COPD
 - CHF
 - AIDS
 - After CPR
- Symptom control
 - Nausea
 - Diarrhea / Constipation
 - Dyspnea
- Pain management
 - Chronic pain
 - Malignant pain
 - Equianalgesic dosing
- Syndrome of imminent death
- Opioids at the end of life
- Terminal extubation
- Medical futility

Calculating Opioid Dose Conversions

Authors: [Robert M Arnold MD](#) , [David E Weissman MD](#)

Category: [Pain: opioids](#)

Introduction A variety of published conversion tables exist to provide clinicians a rough guide for making calculations when switching between different opioid routes or preparations. Listed below are methods for common conversions using standard published conversion ratios. The examples assume a change in drug or route at a time of stable pain control using equianalgesic doses. See [Fast Fact #2](#) about conversions involving transdermal fentanyl; [Fast Fact #75](#) and [Fast Fact #86](#) about methadone; and [Fast Fact #181](#) about oxycodone.

Caution: Published values in equianalgesic tables should be considered a rough clinical guide when making dose conversions; substantial inter-individual variation exists. The final prescribed dose needs to take into account a patient's age, renal, pulmonary and hepatic function; their current pain level and opioid side effects such as sedation; as well as prior and current opioid use.

Opioid Equianalgesic Conversion Ratios for use with the following examples:

Morphine 10 mg parenteral = Morphine 30 mg oral = Hydromorphone 1.5 mg parenteral = Hydromorphone 7.5 mg oral (see Reference 1).

A. Change route, keeping drug the same (eg oral to IV morphine)

Example: Change 90 mg q12 Extended Release Morphine to Morphine by IV continuous infusion

1. Calculate the 24 hour current dose: $90\text{mg q } 12 = 180\text{ mg Morphine}/24\text{ hours}$
2. Use the oral to parenteral equianalgesic ratio: $30\text{ mg PO Morphine} = 10\text{ mg IV Morphine}$
3. Calculate new dose using ratios: $180/30 \times 10 = 60\text{ mg IV Morphine}/24\text{ hours}$ or $2.5\text{ mg}/\text{hour}$ infusion
4. Some experts recommend starting the new opioid at 75% of the calculated dose to account for inter-individual variation in first pass clearance.

B. Change drug keep the same route (eg po morphine to po hydromorphone)

Questions and Comments

*“To cure, occasionally
To relieve, often
To comfort, always”*

Hippocrates