

Introduction to Pharmacist's Role in Palliative Care

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How to start Pharmacy Student Pain and Palliative Care Education

- Build Pharmacist Role in Pain Management
 - Look for unmet needs
 - Improve pain control
 - Improve side effect management
 - Improve Safety
- Find mentors and advocates
 - Physicians, pharmacists, and/or nurses
 - Pharmacy Administration has to be open to new pharmacist roles

Pharmacy Student Pain and Palliative Care Education

- History of Pain Management Pharmacist Service at UC Davis Medical Center
 - My UCSF Pharmacy Residency Pain Management Rotation 1988 with:



Peter Koo, Pharm.D.

Clinical Pharmacist Specialist in Pain Management and **my mentor!**

- I started Operating Room Pharmacy at UC Davis Medical Center 1993
- I began working with Anesthesia Pain Service 1993. Develop credibility!
- Transition from patient monitoring service with physician to pharmacist consult only service
- Transition from nurses requesting consult to physicians requesting consult

Pain Management Pharmacist Service Evolution

- Focus on Patient Controlled Analgesia and Epidural Analgesia initially
- Focus on Surgical Pain Control initially
- Over time developed credibility with multiple groups of physicians from many specialties at UC Davis including Hematology/Oncology, Internal Medicine, Orthopedic Surgery, Neurosurgery, Trauma Surgery, Surgical Oncology, and Urology.

Palliative Care Pharmacist Role

- Provision of Pharmaceuticals
- Optimizing Medication Regimens
- Education and Drug Information
- Patient Safety
- Administrative/Formulary Management

Palliative Care Pharmacist Role

- Provision of Pharmaceuticals
 - Stock formulations for unique patients
 - Compound noncommercially available medications

Palliative Care Pharmacist Role

- Optimizing Medication Regimens
 - Recommend Appropriate Drug Therapy
 - Perform Opioid Conversion Calculations
 - Recommend Appropriate Dosing Strategies
 - Anticipate Potential Complications – have alternative medication regimen planned.

Palliative Care Pharmacist Role

- Education and Drug Information
 - Update staff on new Clinical Practice Guidelines
 - Educate patients, families, and caregivers on appropriate use of medications
 - Participate in family meetings to address medication concerns

Palliative Care Pharmacist Role

- Patient Safety
 - Medication Reconciliation
 - Investigate Medication Errors
 - Screen for Drug Abuse and Diversion

Palliative Care Pharmacist Role

- Administrative/Formulary Management
 - Develop and maintain a medication formulary
 - Implement quality improvement projects
 - Develop pain and symptom management protocols to optimize medication use

Palliative Care Terminology

- **Palliative Care (defined by World Health Organization)**

“An approach that improves the quality of life of patients and their families facing life-threatening illness, through the prevention, assessment, and treatment of pain and other physical, psychosocial, and spiritual problems.”

- **Hospice (defined by Merriam-Webster)**

- a facility or program designed to provide a caring environment for meeting the physical and emotional needs of the terminally ill

Palliative Care Terminology

- Pain (defined by International Association for the Study of Pain)

“An unpleasant sensory and emotional experience associated with actual or potential tissue damage.”

- Acute Pain

- Recent sudden onset
- Usually has obvious cause
- Short Duration (less than 1 month)
- Characteristic behavior such as crying, moaning, grimacing

- Chronic Pain

- Persistent (generally greater than 3 months or beyond expected healing time)
- Usually due to chronic disease or condition (often more difficult to treat)
- May cause prolonged functional impairment (physical and psychological)
- May or may not be associated with characteristic behavior (insomnia, depression)

Palliative Care Terminology

- Somatic Pain

- Pain originating from somatic nociceptors located in structures such as ligaments, bones, and blood vessels.
- Descriptor: Dull
- Example: Blunt trauma from hammer hitting thumb

- Visceral Pain

- Pain originating from organ-level nociceptors or visceral cavities resulting in diffuse pain.
- Descriptor: aching, pressure
- Example: Myocardial Infarction

- Neuropathic Pain

- Pain caused by a primary lesion or dysfunction of the nervous system.
 - Peripheral neuropathic pain (Example: Vincristine toxicity)
 - Central neuropathic pain (Example: Spinal Cord or Brain Tumor)
 - Descriptor: Burning, pins and needles

Common Barriers to Treatment of Chronic Pain

Patient-Related

- **Exaggerated fear of addiction, tolerance, side effects**
- **Reluctance to report pain: stoicism, desire to “please” physician**
- **Concerns about “meaning” of pain (associate increased pain with worsening disease)**

Palliative Care Terminology

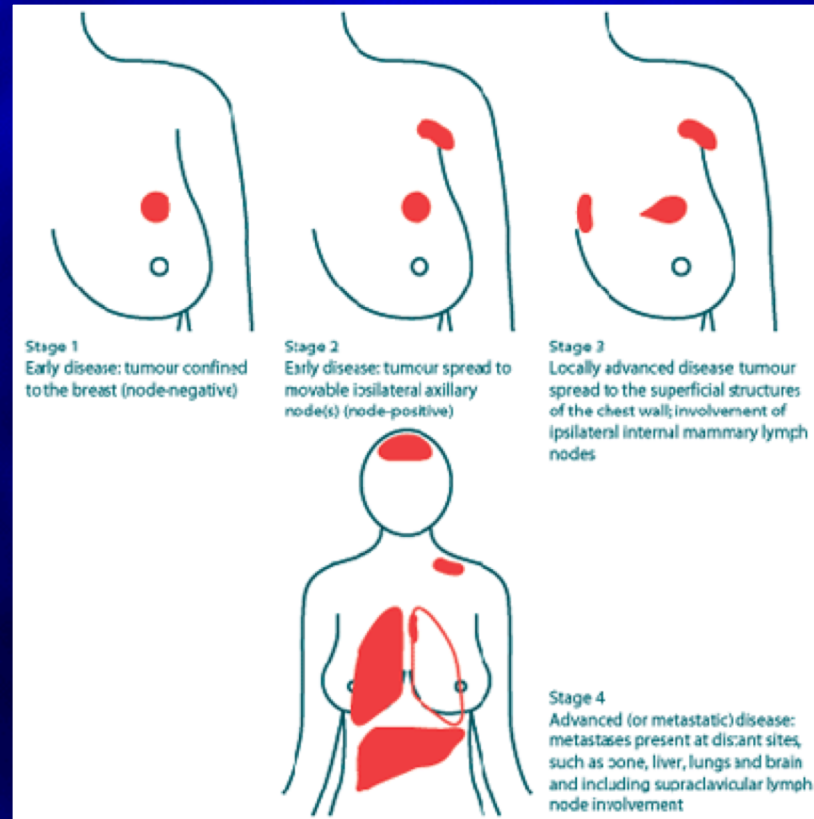
- Physical dependence

- Abstinence syndrome induced by administration of an antagonist or by dose reduction
- Assumed to exist after dosing for a few days but actually highly variable
- Usually unimportant if abstinence avoided
- Does not independently cause addiction

Palliative Care Terminology

- Tolerance
 - Diminished drug effect from drug exposure
 - Varied types: associative vs pharmacologic
 - Tolerance to side effects is desirable
 - Tolerance to analgesia seldom a problem in the clinical setting
 - Tolerance rarely “drives” dose escalation
 - Tolerance does not cause addiction

Disease Progression



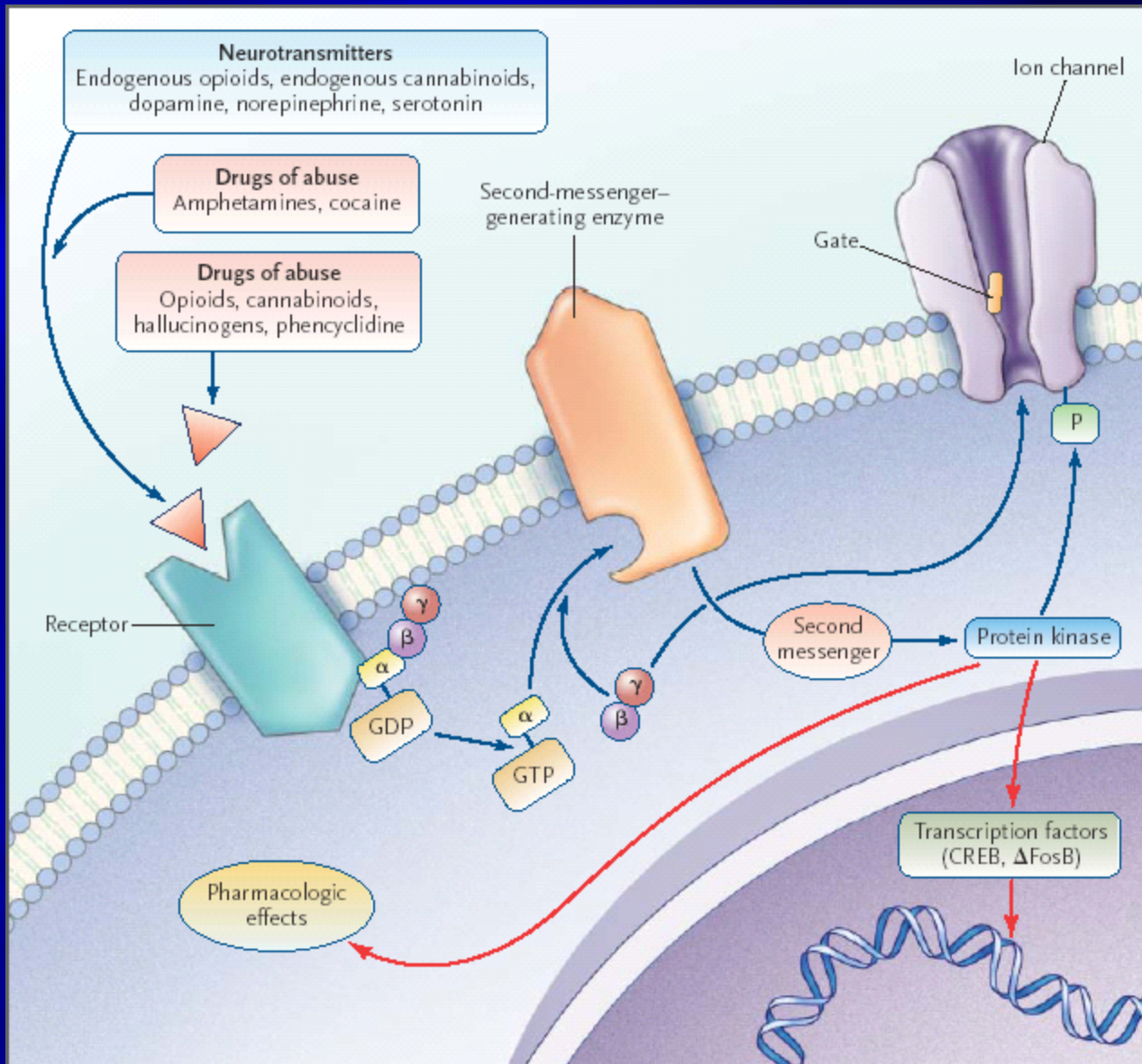
US Food and Drug Administration

Definition of Opioid Tolerance

- Opioid Tolerance occurs after a patient has taken the equivalent of 60 mg per day of oral morphine for one week.
- This equates to:
 - 40 mg oral oxycodone/day
 - 25 mcg/hr transdermal fentanyl

Palliative Care Terminology

- Addiction
 - Disease with pharmacologic, genetic, and psychosocial elements
 - Fundamental features
 - Loss of control
 - Compulsive use
 - Use despite harm
 - Diagnosed by observation of aberrant drug-related behavior



Palliative Care Terminology

- Pseudoaddiction
 - Aberrant drug-related behaviors driven by desperation over uncontrolled pain
 - Reduced by improved pain control
 - Complexities
 - How aberrant can behavior be before it is inconsistent with pseudoaddiction?
 - Can addiction and pseudoaddiction coexist?

Prevalence of Addiction in the General Population

- ◆ Approximately 10% (3% - 16%)
 - Relapse rate with long-term opioid use is unknown¹

Portenoy RK, Savage SR.
J Pain Sympt Manage.
1997;14(3):S27-35.

Opioid Therapy and Chemical Dependency

- Risk of addiction: Evolving view
 - Acute pain: unlikely
 - Cancer pain: unlikely
 - Cancer Survivor: evolving view
 - Chronic noncancer pain:
 - Surveys of patients without abuse or psychopathology show rare addiction
 - Surveys that include patients with abuse or psychopathology show mixed results

Palliative Care Goals

- Provide relief from pain and other distressing symptoms.
- Affirm life and regard dying as a part of the life cycle.
- Intend neither to hasten or postpone death.
- Offer a **support** system to help patients live as actively as possible until death.
- Offer a support system to help the family cope during the patient's illness and in their own bereavement, including the needs of children.
- Use a team approach to address the needs of patients and their families, including bereavement counseling, if indicated.
- Enhance the quality of life that may also positively influence the course of a patient's illness.
- Palliative care does not preclude aggressive treatment of an illness, and provides comfort to patients and their loved ones.

Palliative Care Pharmacotherapy

- Illness seen commonly in Palliative Care
 - Cancer
 - End Stage Renal Disease
 - End Stage Hepatic Disease
 - End Stage Lung Disease
 - End Stage Heart Disease

Palliative Care Pharmacotherapy

- Palliative Care Challenges
 - Pediatrics
 - Cognitively Impaired
 - Non-Verbal
 - Difficulty Swallowing
 - Impaired Renal Function
 - Impaired Hepatic Function

Palliative Care Pharmacotherapy

- Palliative Care Pharmacist Opportunities
 - Opioid equianalgesic conversions
 - Pain Management
 - Medication Selection
 - Dose titration
 - Side effect management
 - Symptom Management
 - Medication Selection
 - Dose adjustments for decreased hepatic and renal function

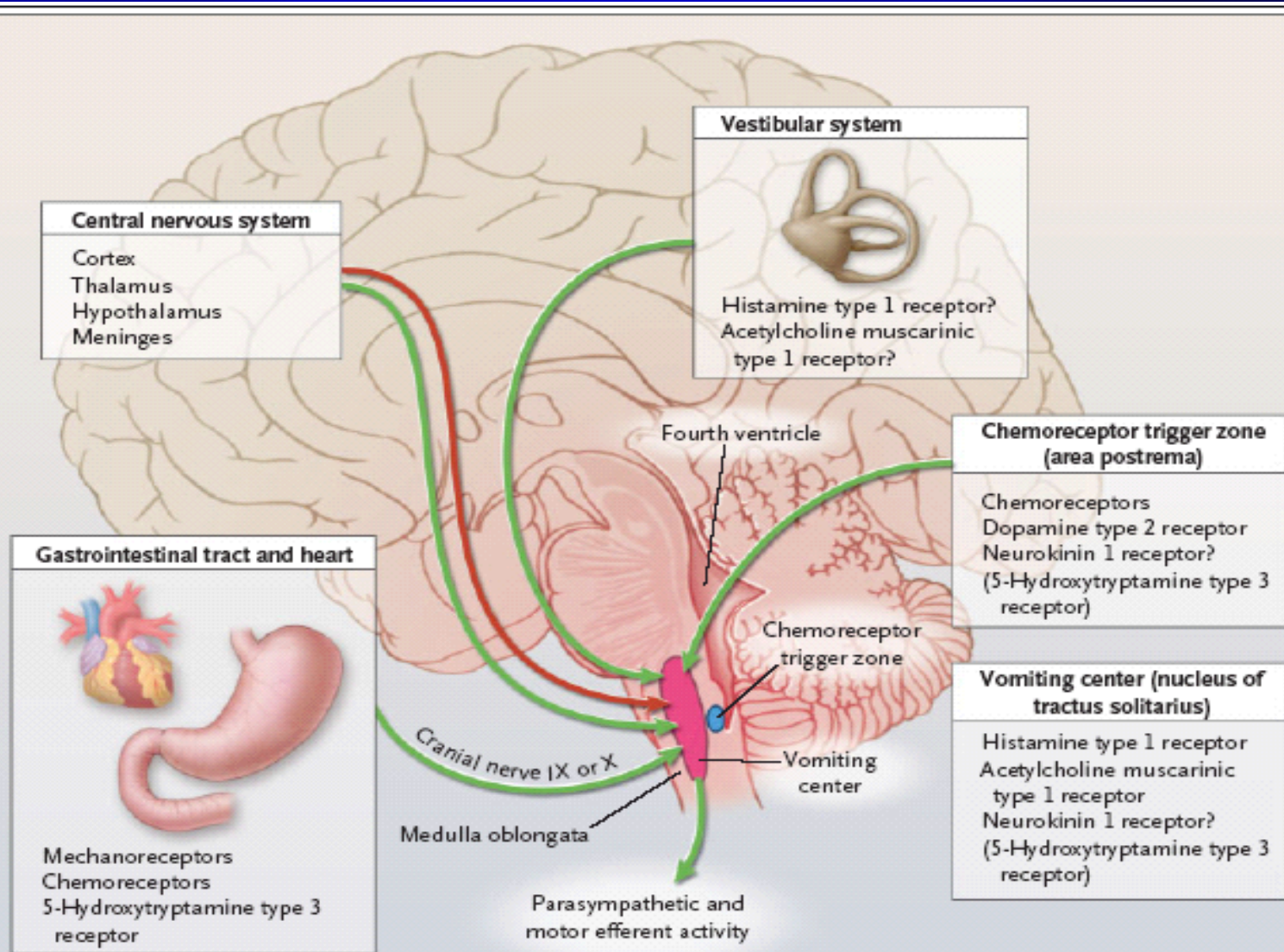
Patient with Severe Nausea/Vomiting

- Patient with Breast Cancer Taking Extended Release Morphine 90 mg po TID for Chronic Severe Pain. Pain Score = 3/10 Comfortable.
- Having Difficulty with nausea/vomiting for past two days. HR 120 BP 145/95 RR 20
- Pain has increased to 10/10
- Important PMH: Patient started course of Chemotherapy two days ago that includes Doxorubicin.

Opioid-Induced Nausea and Vomiting

- Constipation
 - Opioids decrease GI motility
- Medications
 - Opioids stimulate chemoreceptor trigger zone
- Movement
 - Opioids stimulate vestibular apparatus

Nausea Mechanisms



Comparative Opiate Agonist Dosage with Oral or Parenteral Administration

Equianalgesic Dose (in mg)*

<u>Opiate Agonist</u>	<u>Oral</u>	<u>IM</u>
Morphine	30	10
Hydromorphone	7.5	1.5
Oxycodone	20	—
Methadone	20 (acute)	10 (acute)
Levorphanol	4 (acute) 1 (chronic)	2 (acute) 1 (chronic)
Fentanyl	—	0.1 (acute)
Oxymorphone	—	1
Meperidine	300	75

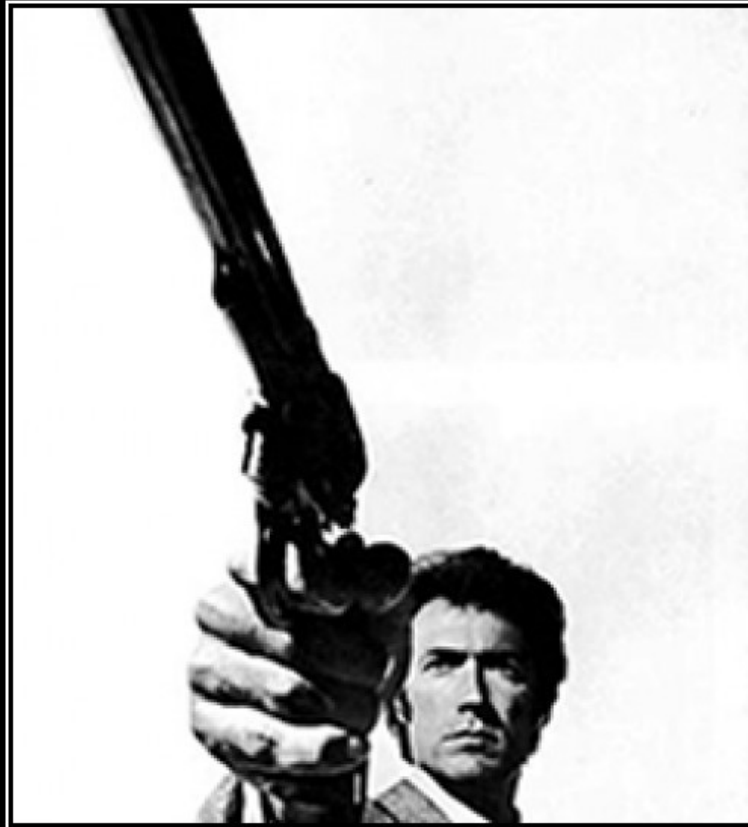
Opioid Conversion Calculators

- <http://www.globalrph.com/narcotic.cgi>
- <http://http://www.hopweb.org>.
- <http://www.painphysicians.org/calc/Calculator.php>
- <http://www.lexi.com>
- <http://medicalconverters.com>

Equianalgesic Table

PO (mg)	Analgesic	SC/IV/IM (mg)
30	Morphine	10
10	Oxymorphone	1
4	Hydromorphone	1.5
20	Oxycodone	14
(2-8)	Methadone	(2-8)
-	Fentanyl*	100 µg/hr parenteral or transdermal $\equiv$ 4 mg/hr morphine parenteral
	* chronic	

Equianalgesic Conversions Require Basic Math



BASIC MATH

Because the difference between six and five can be very
damned important.

Equianalgesic Conversions

Example:

- **Patient with a total 24-hr dose of Morphine ER 270 mg PO**
- **What is the equivalent 24-hour dose of IV morphine?**

Equianalgesic Conversions

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- **Patient with a total 24-hr dose of Morphine ER 270 mg PO**
- **What is the equivalent 24-hour dose of IV morphine?**
- $$\frac{\text{Morphine 30 mg PO}}{\text{Morphine 10mg IV}} = \frac{\text{Morphine 270 mg PO}}{X}$$
- **X = morphine 90 mg IV per 24 Hours**

Equianalgesic Conversions

Example:

- **Patient with a total 24-hr dose of Morphine ER 270 mg PO**
- **What is the equivalent 24-hour dose of IV morphine?**
- $$\frac{\text{Morphine 30 mg PO}}{\text{Morphine 10mg IV}} = \frac{\text{Morphine 270 mg PO}}{X}$$
- **X = morphine 90 mg IV per 24 Hours**
- **Determine starting IV dose of morphine based on above.
Consider starting at 3- 4 mg/hr IV Morphine after getting patient comfortable with Bolus doses of IV Morphine.**

Opioid Conversion for Nausea/Vomiting

- Patient with Breast Cancer Taking Extended Release Morphine 90 mg po TID for Chronic Severe Pain. Now admitted for severe nausea
- Opportunity for pharmacist to help
- Nausea
 - Triggered by Doxorubicin
 - Exacerbated by opioid withdrawal
- Convert patient to IV/SC Morphine
- Suggest Antiemetic Regimen

Opioid Conversion for Nausea/Vomiting

- Patient with Breast Cancer Taking Extended Release Morphine 90 mg po TID for Chronic Severe Pain. Now admitted for severe nausea
- Challenge: Patient has no IV Access
 - Subcutaneous Route limited to 2 ml/hr maximum infusion rate. Patient may need concentrated formulation.
 - Suggest Morphine 5 mg/ml concentration for Subcutaneous infusion. Dose = 4 mg/hr = 0.8 ml/hr

Opioid Conversion for Nausea/Vomiting

- Patient with Breast Cancer Taking Extended Release Morphine 90 mg po TID for Chronic Severe Pain. Now admitted for severe nausea
- Challenge: Suggest Antiemetic Regimen
- Promethazine 25 mg PO/PR Q 6 hours prn
- Scopolamine Patch 1.5 mg Change Q 72 hours

Opioid Conversion for Delirium

- Patient with Breast Cancer Taking Morphine 4 mg/hr SC for Severe Pain. Pain under control with SC morphine. Nausea under control with Scopolamine
- Patient stable for 2 days and then noted to having jerking movements in extremities as well as mild confusion.
- Patient noted to have decreasing urine output
- Serum Creatinine = 3.0

Opioid Conversion for Delirium

- Patient with Breast Cancer Taking Morphine 4 mg/hr SC for Severe Pain. Pain under control with SC morphine. Nausea under control with Scopolamine
 - What could be causing myoclonus?
 - What could be causing delirium?

DELIRIUM

- Acute onset of days to hours
- Fluctuating course
- Disturbance or disorientation that is not accounted for by an established dementia
- Reduced ability to focus, sustain or shift attention
- Generally a reversible condition

Table 1. Clinical Features of Delirium.*

Acute onset

- Occurs abruptly, usually over a period of hours or days
- Reliable informant often needed to ascertain the time course of onset

Fluctuating course

- Symptoms tend to come and go or increase and decrease in severity over a 24-hour period
- Characteristic lucid intervals

Inattention

- Difficulty focusing, sustaining, and shifting attention
- Difficulty maintaining conversation or following commands

Disorganized thinking

- Manifested by disorganized or incoherent speech
- Rambling or irrelevant conversation or an unclear or illogical flow of ideas

Altered level of consciousness

- Clouding of consciousness, with reduced clarity of awareness of the environment

Cognitive deficits

- Typically global or multiple deficits in cognition, including disorientation, memory deficits, and language impairment

Perceptual disturbances

- Illusions or hallucinations in about 30 percent of patients

Psychomotor disturbances

Psychomotor variants of delirium

Hyperactive

- Marked by agitation and vigilance

Hypoactive

- Marked by lethargy, with a markedly decreased level of motor activity

Mixed

Altered sleep–wake cycle

- Characteristic sleep-cycle disturbances
- Typically daytime drowsiness, nighttime insomnia, fragmented sleep, or complete sleep-cycle reversal

Emotional disturbances

Common

- Manifested by intermittent and labile symptoms of fear, paranoia, anxiety, depression, irritability, apathy, anger, or euphoria

* Additional details are provided in Table 2 in the Supplementary Appendix.

Treatment of Delirium in Cancer Patient

- Delirium
 - Reversible Causes
 - Medications
 - Dehydration
 - Infection

Potential Mechanisms of Morphine Metabolite Toxicity

Morphine-6-Glucuronide

- **Drowsiness**
- Nausea and Vomiting
- Coma
- Respiratory Depression

Morphine-3-Glucuronide

- Agitation
- **Myoclonus-Seizures**
- Hyperalgesia
- **Delirium**

Mercadante,S *Palliative Medicine* 1999;13:95-104

Increased Plasma Morphine Metabolites in Terminally Ill Cancer Patients with Delirium

- Investigators looked at 131 consecutive hospice patients
- 8 patients had blood samples drawn before and after development of delirium
- Plasma concentrations of M-6-G and M-3-G significantly increased after development of delirium within the same patient.

Morita, T et al. J Pain Symptom Manage 2002;23:107-113

Table 3. Precipitating Factors or Insults That Can Contribute to Delirium.

Drugs

- Sedative hypnotics
- Narcotics
- Anticholinergic drugs
- Treatment with multiple drugs
- Alcohol or drug withdrawal

Primary neurologic diseases

- Stroke, particularly nondominant hemispheric
- Intracranial bleeding
- Meningitis or encephalitis

Intercurrent illnesses

- Infections
- Iatrogenic complications
- Severe acute illness
- Hypoxia
- Shock
- Fever or hypothermia
- Anemia
- Dehydration
- Poor nutritional status
- Low serum albumin level
- Metabolic derangements (e.g., electrolyte, glucose, acid–base)

Surgery

- Orthopedic surgery
- Cardiac surgery
- Prolonged cardiopulmonary bypass
- Noncardiac surgery

Environmental

- Admission to an intensive care unit
- Use of physical restraints
- Use of bladder catheter
- Use of multiple procedures
- Pain
- Emotional stress
- Prolonged sleep deprivation

Pharmacologic Treatment of Delirium

Table 4. Pharmacologic Treatment of Delirium.

Class and Drug	Dose	Adverse Effects	Comments
Antipsychotic Haloperidol	0.5–1.0 mg twice daily orally, with additional doses every 4 hr as needed (peak effect, 4–6 hr) 0.5–1.0 mg intramuscularly; observe after 30–60 min and repeat if needed (peak effect, 20–40 min)	Extrapyramidal symptoms, especially if dose is >3 mg per day Prolonged corrected QT interval on electrocardiogram Avoid in patients with withdrawal syndrome, hepatic insufficiency, neuroleptic malignant syndrome	Usually agent of choice Effectiveness demonstrated in randomized, controlled trials ^{20,37} Avoid intravenous use because of short duration of action
Atypical antipsychotic Risperidone Olanzapine Quetiapine	0.5 mg twice daily 2.5–5.0 mg once daily 25 mg twice daily	Extrapyramidal effects equivalent to or slightly less than those with haloperidol Prolonged corrected QT interval on electrocardiogram	Tested only in small uncontrolled studies Associated with increased mortality rate among older patients with dementia
Benzodiazepine Lorazepam	0.5–1.0 mg orally, with additional doses every 4 hr as needed*	Paradoxical excitation, respiratory depression, oversedation	Second-line agent Associated with prolongation and worsening of delirium symptoms demonstrated in clinical trial ³⁷ Reserve for use in patients undergoing sedative and alcohol withdrawal, those with Parkinson's disease, and those with neuroleptic malignant syndrome
Antidepressant Trazodone	25–150 mg orally at bedtime	Oversedation	Tested only in uncontrolled studies

* Intravenous use of lorazepam should be reserved for emergencies.

Opioid Conversion for Delirium

- Patient with Breast Cancer Taking Morphine 4 mg/hr SC for Severe Pain. Pain under control with SC morphine. Nausea under control with Scopolamine
 - Which opioid analgesic should we use for this patient?
 - What should we do with the patient's scopolamine?

Opiate Pharmacology

- Opiates with Active Metabolites
 - morphine
 - meperidine
 - codeine
 - hydrocodone
 - oxycodone
 - oxymorphone
 - Propoxyphene

Opiate Pharmacology

- Opiates with Active Metabolites
 - Morphine to M6G and M3G
 - Meperidine to Normeperidine
 - Codeine to Morphine
 - Hydrocodone to Hydromorphone
 - Oxycodone to Oxymorphone
 - Oxymorphone to 6-OH-OXM
 - Propoxyphene to norpropoxyphene
 - Hydromorphone to H3G

Equianalgesic Table

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-	Fentanyl*	100 µg/hr parenteral or transdermal $\equiv$ 4 mg/hr morphine parenteral
	* chronic	

Opioid Conversion Calculators

- <http://www.globalrph.com/narcotic.cgi>
- <http://opioidcalculator.practicalpainmanagement.com/>
- <https://medicalconverters.com/analgesic-converter>

*<http://www.hopweb.org>

*<http://www.lexi.com>

*Login required for access.

Opioid (Narcotic) Analgesic Converter

Opioid (Narcotic) analgesic converter	
Note: ALL METHADONE CALCULATIONS REMOVED - Check out the new advanced version for methadone related conversions....	
Converting From:	
Step 1:	Select a narcotic analgesic to convert
Step 2:	(Enter total daily dose in mg)
Incomplete cross-tolerance correction	
Step 3: Reduction for incomplete cross tolerance:	% ? (Usual range: 25 - 75% reduction)
Converting To:	
Step 4:	Select a narcotic analgesic to convert
Calculate the equivalent dose Reset	
 Results	
Based on your selections above, here is the result: Equivalent dose for opiate selected in Step 4 above: Reduction for incomplete cross tolerance: % Chronic oral morphine equivalent dose is: mg (Note: If morphine was chosen, the conversion factor used was for chronic dosing only.) Ideally, we recommend our desktop program for much greater control over these conversions).	

Practical Pain Management Opioid Calculator



Opioid Calculator

What do you want to do?

➡ Calculate an opioid starting dose for an opioid-naive patient.

➡ Perform an opioid conversion-dose calculation.



Opioid Analgesic Converter

Analgesic Converter

References

These buttons are for adding and removing any additional drugs



Choose an Analgesic to convert from:

Hydromorphone(mg) PO

Total Daily Dose:

16

Choose an Analgesic to convert to:

Morphine(mg) PO

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Convert

Here is your result:

120 mg daily of Morphine

120 mg Total

Equianalgesic Conversions

Example:

- **Patient with a total 24-hr dose of Morphine IV 90**
- **What is the equivalent hourly dose of transdermal fentanyl?**
- $\frac{\text{Morphine 4 mg/hr IV}}{\text{Fentanyl 100 mcg/hr transdermal}} = \frac{\text{Morphine 4mg/hr IV}}{\text{X}}$
- **X = Fentanyl 100 mcg/hr transderamal**
- **Determine starting dose of fentanyl based on above. Consider starting at 75-100 mcg/hr.**

Palliative Care Pharmacist Role

- Provision of Pharmaceuticals
- Optimizing Medication Regimens
- Education and Drug Information
- Patient Safety
- Administrative/Formulary Management

Online Resources

- painEDU.org (online pain textbook)
- ampainsoc.org (American Pain Society)
- painmed.org (American Academy of Pain Medicine)
- cancer.org (American Cancer Society)
- https://www.youtube.com/watch?v=Wm_3Y6IvGTA

Arigato





