# Palliative Care and End of Life Issues: A Pharmacist's Perspective

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#### Disclosure

• I do not have commercial or financial relationships to disclose relating to the content of this presentation.

## Objectives

- Describe the roles and responsibilities of the pharmacist in palliative care
- Assess, recommend, and treat pain and common symptoms encountered in the palliative care setting
- Discuss advance directives commonly encountered in palliative care, and their effect on patient care
- Understand the concept of a "dignified death," and how the pharmacist can assist the patient and family in achieving optimal outcomes

#### Definition of Palliative Care

- WHO: "Palliative care is the active total care of patients whose disease is not responsive to curative treatment. Control of pain, other symptoms, psychological, social, and spiritual problems is paramount. The goal of palliative care is achievement of the best possible quality of life for patients and their families."
- NHPCO: "Treatment that enhances comfort and improves the quality of an individual's life during the last phase of life. No specific treatment is excluded...."
- "Hospice care" is palliative care provided to patients during the last months of life

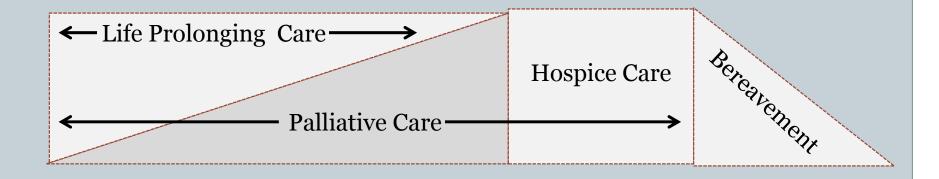
## Old Way of Thinking

Active
Aggressive
Intent

Palliative Intent
T
H

Adapted from: Frager G. Pediatric Palliative Care: Building the Model, Bridging the Gaps. 1996, Journal of Palliative Care, 12 (3):9-10.

## New Way of Thinking



Adapted from: Frager G. Pediatric Palliative Care: Building the Model, Bridging the Gaps. 1996, Journal of Palliative Care, 12 (3):9-10.

# ASHP Statement on the Pharmacist's Role in Hospice and Palliative Care

- Palliative care should be provided in conjunction with curative care at the time of diagnosis of a potentially terminal illness
- Palliative care alone may be indicated when attempts at a cure are judged to be futile
- Admissions to hospice and/or palliative care programs often come too late for optimal services to be provided
  - Length of stay
    - Mean: 50 days; Median: 25 days

#### The Pharmacist's Responsibilities

- Assessing the appropriateness of medication orders and ensuring the timely provision of effective medications for symptom control.
- Counseling and educating the hospice team about medication therapy.
- Ensuring that patients and caregivers understand and follow the directions provided with medications.

#### The Pharmacist's Responsibilities

- Providing efficient mechanisms for extemporaneous compounding of nonstandard dosage forms.
- Addressing financial concerns.
- Ensuring safe and legal disposal of all medications after death.
- Establishing and maintaining effective communication with regulatory and licensing agencies.

#### Symptom Management

- Pain
- Nausea and Vomiting
  - CINV
  - Generalized N/V
- Bowel Issues
  - Constipation & Bowel Obstruction
  - Diarrhea
- Anxiety
- Depression

- Delirium
- Oral Complications
  - Xerostomia and mucositis
- Dyspnea
- Death rattle/terminal secretions
- Insomnia
- Anorexia/Cachexia

## General Approach to Symptom Management at End-of-Life

- Search for cause of symptom
  - History, physical, laboratory (as appropriate)
- Treat underlying cause (if reasonable)
- Treat the symptom
- Re-evaluate frequently

## Pharmacotherapy in Palliative Care

- Essential for many symptoms
- Non-symptom based drugs may be no longer appropriate or desired
- Data often limited
  - Pharmacokinetic/pharmacodynamic differences
  - Goals of treatment differ
- May need unusual routes of administration and/or dosage forms

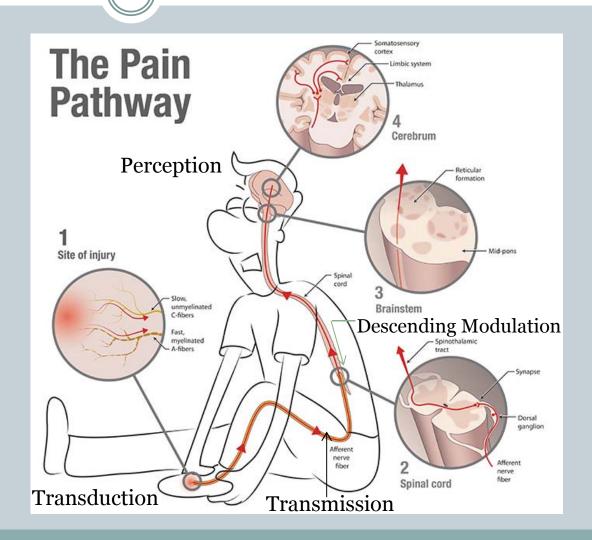
# Pain Management



#### Pain Pathway

"An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage

It's what the patient says it is!



Feeling Pretty Remarkable. Preventing Chronic Pain. Available at: http://www.feelingprettyremarkable.com/blog/preventing-chronic-pain

#### Pain Management

#### Types of pain

- Nociceptive
  - Transient in response to noxious stimulus
- Inflammatory
  - Tissue damage occurs despite nociceptive defense
- Neuropathic
  - Spontaneous pain and hypersensitivity to pain, associated with damage to or pathologic changes in the periphery or CNS
- Functional
  - ➤ Pain sensitivity due to an abnormal processing or functioning of the CNS in response to normal stimuli

#### Pain Assessment

- P-Palliative, precipitating
- Q-Quality
- R-Radiating
- S-Severity
- T-Timing
- U-You

#### Pain Terms Defined

#### Addiction

Continued repetition of a behavior despite adverse consequences

#### Physical Dependence

 Normal adaptive state that results in withdrawal symptoms if the drug is abruptly stopped or decreased

#### Tolerance

 Process by which the body continually adapts to the substance and requires increasingly larger amounts to achieve the original effects

#### Pseudo-addiction

 A drug-seeking behavior that simulates true addiction, which occurs in patients with pain who are receiving inadequate pain medication

#### General Approach to Treatment

#### Effective treatment

- Evaluate cause, duration, intensity
- Selection of an appropriate treatment modality

#### Two common approaches

- Based on pain severity
- Based on mechanism responsible for the pain

#### Goal

 Reduce peripheral sensitization, subsequent central stimulation and amplification associated with windup, spread, and central sensitization

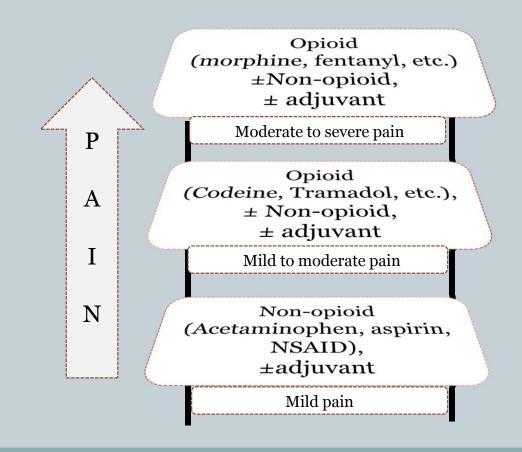
## Pain Treatment Paradigm

- Physical
  - o Heat, cold, ultrasound, TENS, massage, exercise
- Behavioral
  - Imagery
  - Distraction
  - Relaxation
  - Cognitive behavioral therapy
- Pharmacotherapy
- Surgical
- Regional/Spinal Anesthesia



## Pharmacotherapy

- Non-opioids
  - APAP & NSAIDs
- Opioids
  - Mu Agonists
  - Partial Agonists
  - o Tramadol?
- Adjuvants
  - Topical Agents
    - × Lidocaine
    - × NSAIDs
  - Antidepressants
    - × TCAs
    - × SNRIs
  - Anticonvulsants
    - Gabapentin, Pregabalin



World Health Organization. WHO's Cancer Pain Ladder for Adults. Available at: http://www.who.int/cancer/palliative/painladder/en/

## **Choosing Analgesics**

- Type of pain
- Efficacy of analgesics for indication
- Route(s) available
- Renal and hepatic function

- Safety (NSAID vs. Cox-2
- Drug interactions
- Cost
- Patient and/or family preference

## **Opioid Analgesics**

- Classified by receptor activity (stimulate opioid receptors  $\mu, \kappa$ ,  $\delta$ ) in CNS), usual pain intensity treated, and duration of action
- Pure agonists
  - Three classes
  - Bind to μ receptor and have no "ceiling"
- Partial Agonists
  - Butorphanol, pentazocine, nalbuphine
  - Partially stimulate μ-receptor and anatgonize the κ-receptor
    - Reduced analgesic efficacy with a ceiling-dose
    - × Reduced side effects at the μ-receptor
    - × Psychometric side effects due to κ-receptor antagonism
    - Possible withdrawal in patients dependent on pure agonists

## **Classes of Opioids**

Class I (Phenanthrenes)	Class II (Phenylpiperidines)	Class III (Phenylheptalamines)
Natural	Fentanyl	Methadone
Codeine	Meperidine	Propoxyphene (Disc)
Morphine		
Semisynthetic		
Hydrocodone		
Hydromorphone		
Oxycodone		
Oxymorphone		

#### Self-Assessment

- The best opioid option for a patient with a true morphine allergy is?
  - A) hydromorphone
  - o B) oxymorphone
  - o C) oxycodone
  - o D) fentanyl

#### Self-Assessment

- The best opioid option for a patient with a true morphine allergy is?
  - A) hydromorphone
  - o B) oxymorphone
  - o C) oxycodone
  - O) fentanyl

## Opioid Switch

- Why switch?
  - Lack of efficacy
  - Development of intolerable side effects
  - Change in patient status
    - Inability to use specific dosage formulations
    - **Transition of care**
  - Other practical considerations
    - Availability of opioid, or dosage formulation
    - Cost or formulary issues
    - Patient, family preferences (morphobia)

## Equianalgesic Doses of Selected Opioids

#### **Equianalgesic Opioid Dosing**

#### Equianalgesic Doses (mg)

		` `;
Drug	Parenteral	Oral
Morphine	10	30
Buprenorphine	0.3	0.4 (sl)
Codeine	100	200
Fentanyl	0.1	NA
Hydrocodone	NA	30
Hydromorphone	1.5	7.5
Meperidine	100	300
Oxycodone	10*	20
Oxymorphone	1	10
Tramadol	100*	120

\*Not available in the US McPherson ML. Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing. Amer Soc of Health-Systems Pharm, Bethesda, MD, 2010. Copyright ASHP, 2010. Used with permission. NOTE: Learner is STRONGLY encouraged to access original work to review all caveats and explanations pertaining to this chart.

## **Opioid Chart Issues**

- Unidirectional vs. bidirectional?
  - $\circ$  -A=B
  - But does B=A?
- Based on single-dose conversion data or multipledose conversion data?
- Pharmacogenomics
- Influence of age?

#### Steps in Opioid Conversion

- Globally assess the patient and pain complaint
- Determine the total daily dose of the current opioid
- Decide which opioid to switch to (or formulation)
  - Consult an opioid conversion chart
- Individualize dose based on assessment info
- Patient follow-up and continued reassessment

#### Setting Up Conversions

- Calculate total daily dose (TDD) of current opioids
- Set up conversion ratio between old opioid (and route of administration) and new opioid (and route of administration as follows:

```
\frac{\text{"X"}mg\ TDD\ new\ opioid}{mg\ TDD\ current\ opioid} = \frac{equianalgesic\ factor\ new\ opioid}{equianalgesic\ factor\ current\ opioid}
```

Or

 $\frac{\text{"X"}\textit{mg TDD new opioid}}{\textit{equianalgesic factor of new opioid}} = \frac{\textit{mg TDD current opioid}}{\textit{equianalgesic factor current opioid}}$ 

#### **Conversion Calculations**

- Cross multiply, solve for "x"
- Three choices:
  - Reduce calculated dose due to lack of complete cross-tolerance
  - Begin with calculated dose
  - o (Rarely) increase calculated dose
- Decide how many times per day you're going to dose the new opioid; divided by the appropriate dosing interval, and select a dosage that is available in that strength

#### Self-Assessment

• Convert Morphine 5mg IV every 4 hours + 0.5mg IV every 2 hours prn (used 6 doses in 24 hours) to oral oxycodone

#### **Equianalgesic Opioid Dosing**

Equianalgesic Doses (mg)

Drug	Parenteral	Oral
Morphine	10	30
Buprenorphine	0.3	0.4 (sl)
Codeine	100	200
Fentanyl	0.1	NA
Hydrocodone	NA	30
Hydromorphone	1.5	7.5
Meperidine	100	300
Oxycodone	10*	20
Oxymorphone	1	10
Tramadol	100*	120

\*Not available in the US McPherson ML. Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing. Amer Soc of Health-Systems Pharm, Bethesda, MD, 2010. Copyright ASHP, 2010. Used with permission. NOTE: Learner is STRONGLY encouraged to access original work to review all caveats and explanations pertaining to this chart.

#### Self-Assessment

TDD =33mg IV morphine

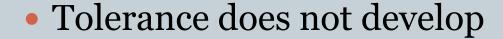
$$\frac{33mg\ IV\ morphine}{10mg\ IV\ morphine} = \frac{\text{"X"}mg\ oxycodone}{20mg\ oral\ oxycodone}$$

- X=66mg oral oxycodone
- Reduce by 25-50% for cross tolerance
  - o 66mg x 0.75=49.5mg daily; 66mgx0.5=33mg daily
- Available as 5mg, 10mg, 15mg, 20mg, 30mg
- Dose: 5-10mg every 4 hours

# Symptom Managment



## **Opioid Induced Constipation**



- Prevention is key!
  - Stimulant laxative cornerstone of therapy
  - Stool softener offers no benefit
- Golden rule
  - "The hand that writes for the long acting opioid, is the hand that writes for the breakthrough opioid, is the hand that orders the laxative"

## Nausea/Vomiting

#### Chemoreceptor Trigger Zone (CTZ)

Dopamine, 5HT3, Neurokinin-1

# Gastrointestinal Tract (GI)

Dopamine, 5HT3

#### **Cerebral Cortex**

Dopamine, 5HT3, Neurokinin-1

#### **Vomiting Center**

Acetylcholine, Histamine, 5HT2

#### **Vestibular Nerve**

Acetylcholine, Histamine

Nausea & Vomiting

Adapted from: Chisholm-Burns MA, Wells BG, Schwinghammer TL, et al. Palliative Care. In: Pharmacotherapy Principles and Practice. 2013. 45.

#### 11 M's of Emesis

- Metastases (cerebral, liver)
- Meningeal irritation
- Movement
- Mentation (anxiety)
- Medications (opioids, chemo)
- Mucosal irritation

- Mechanical obstruction
- Motility
- Metabolic (hypercalcemia, hyponatremia, hepatic/renal failure
- Microbes
- Myocardial

Education in Palliative and End-of-Life Care for Oncology. Self-Study Module 3p: Symptoms; Nausea/Vomiting. Available at: http://www.cancer.gov/cancertopics/cancerlibrary/epeco/selfstudy/module-3/module-3p-pdf

#### Managing N/V

Etiology	Pathophysiology	Therapy
Meningeal Irritation	Increased ICP	Steroids
Movement	Vestibular stimulation	Anticholinergics
Mentation (anxiety)	Cortical	Anxiolytics
Metastases	<ul> <li>Increased ICP</li> <li>Direct Chemoreceptor Trigger Zone (CTZ) effect</li> <li>Toxin buildup</li> </ul>	Steroids Mannitol Anti-Dopamineric Antihistamine
Motility	GI tract, CNS	Prokinetic agents Stimulant laxatives

Goldstein NE, Morrison RS. Use of Medications to Prevent and Treat Nausea and Vomiting Unrelated to Chemotherapy. In: Evidence Based Practice of Palliative Medicine. 2013: 143.

#### Managing N/V

Etiology	Pathophysiology	Therapy
<ul><li>Metabolic</li><li>Hepatic/renal failure</li><li>Hypercalcemia</li></ul>	CTZ	Anti-dopaminergic Antihistamines Rehydration Steroids
Mechanical Obstruction	Constipation, tumor, fibrotic stricture	<ul> <li>Treat constipation</li> <li>Reversible: surgery</li> <li>Irreversible: Manage fluids; decrease oral intake; octreotide</li> </ul>
<ul><li>Medications</li><li>Opioids</li><li>Chemotherapy</li></ul>	CTZ Vestibular effect GI tract	Anti-dopaminergic Antihistamines Anticholinergics Prokinetic agents Anti-5HT3 Steroids

Goldstein NE, Morrison RS. Use of Medications to Prevent and Treat Nausea and Vomiting Unrelated to Chemotherapy. In: Evidence Based Practice of Palliative Medicine. 2013: 143.

#### Managing N/V

#### Mirtazepine

- Antagonizes 5HT3 receptor
- Refractory symptoms
- Olanzapine
  - Efficacy demonstrated in small case reports
- Cannabanoids
  - Efficacious for those with cancer and AIDS
  - Delirium and sedation, especially in older adults
- Lorazepam, diphenhydramine, haloperidol, metoclopramide (ABHR) suppositories/gels
  - No evidence to support efficacy

#### Dyspnea

• Commonly seen in patients with heart failure and

pulmonary issues

- Potential causes
  - Muscle wasting
  - Acid/base disturbance
  - Anxiety
  - Obstruction



#### Treatment of Dyspnea

#### Non-pharmacologic

- Minimize need for exertion
- Reposition upright
- Avoid strong odors
- Use fans or open windows
- Adjust temperature/humidity

#### Pharmacologic

- Opioids
- Benzodiazepines
- Bronchodilators
- Oxygen?

#### Self-Assessment

#### • True or False?

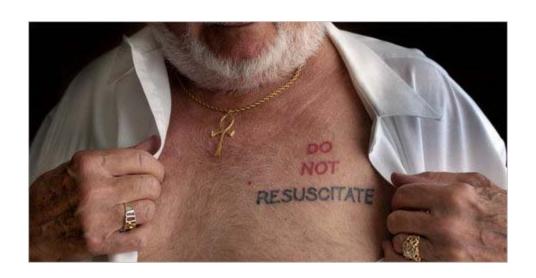
 Opioids do not improve dyspnea through inhibition of the respiratory drive; rather, opioids improve dyspnea without causing significant deterioration in respiratory function.

#### Self-Assessment

#### • **True** or False?

 Opioids do not improve dyspnea through inhibition of the respiratory drive; rather, opioids improve dyspnea without causing significant deterioration in respiratory function.

### Advance Directives



#### **Advance Directives**

Document	Description
<ul><li>Substantive Directives</li><li>Living will</li><li>Five wishes</li><li>Personal wishes statement</li></ul>	Allows a patient to specify wishes for future care May include a section to designate a proxy decision maker
<ul> <li>Process Directives</li> <li>Health care power of attorney</li> <li>Heath care proxy</li> <li>Durable power of attorney for health care</li> </ul>	Designates a surrogate decision-maker Does not specify wishes for care
Physician Orders for Life Sustaining Treatment	Physician orders regarding CPR, antibiotics and artificial nutrition/hydration Travels with a patient and is legally valid as an order in transit
Code status	Specifies whether to perform CPR in event of decompensation

Goldstein NE, Morrison RS. Effective Advance Care Plans and How they Differ From Advance Directives. In: Evidence Based Practice of Palliative Medicine. 2013: 259.

#### **POST**

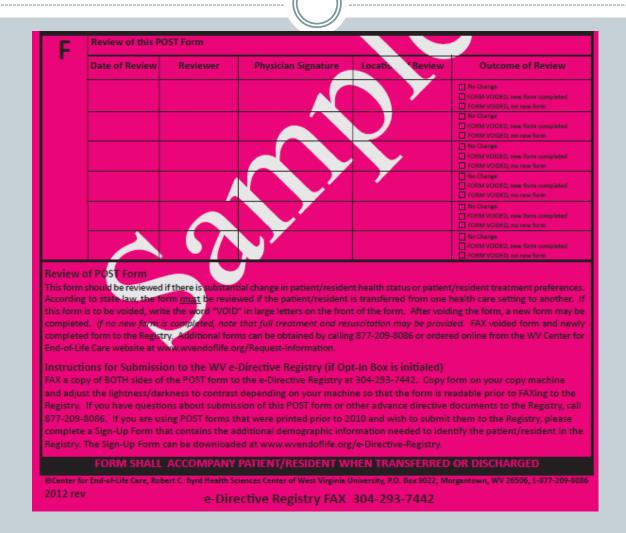
West Virginia Physician Orders	Last Name/First/Middle Initial  Address  City/State/Zip	
for Scope of Treatment (POST)		
This is a Physician Order Sheet based on the person's medic		
condition and wishes. Any section not completed indicates for treatment for that section. When need occurs, <u>first</u> follow the orders, then contact physician.	The same of First Service Selection and the same of th	
B Comfort Measures Treat with dignity and Use medication by any route, positioning, oxygen, suction and manual treatment of a	MEDICAL INTERVENTIONS: Person has pulse and one is breathing.  Comfort Measures Treat with dignity and respect. Keep clean, warre, and dry.  Use medication by any route, positioning, wound care and other measures to relieve pain and suffering	

	POS	ST	
C Check One Box Only in Each Calumn	MEDICALLY ADMINISTERED FLUIDS AND NUTRITION  No IV fluids (provide other measures to assure comfort)  IV fluids for a trial period of no longer than  IV fluids long-term if indicated  Other Orders	Oral fluids and nutrition must be offered at l No feeding tube Feeding tube for a trial period of no long Feeding tube long-term	1000
D	significantly deteriorates, I give permission	g statement: If I lose decision making capacity to my MPOA representative/surrogate to mak coordance with my expressed wishes for such a o	e decisions and to
		DST form, do not resuscitate card, living will an abmitted to the WV e-Directive Registry and re FAX - 304-293-7442	
	Signature of Patient/Resident, Parent of Minor, or Guardian/MPOA Representative/Surrogate (Mandatory)		Date
	Signature of Physician		
	Physician Name (Print Full Name)	Physician Phone Number	
	Physician Signature (Mandatory)	Date and Time	
	FORM SHALL ACCOMPANY PATIENT/RESIDENT	WHEN TRANSFERRED OR DISCHAR	tGED
SCenter fo 2012 rev	e-Directive Registry FA		06. 1-877-209-8086

#### **POST**

E	Patient/Resident (Parent for Minor Child) Preferences as a Guide for this POST Form					
-	Advance Directive (Living Will or MPOA)  Organ and Tissue Document of Gift  Court-appointed Guardian  Health Care Surrogate Selection  MPOA/Surrogate/Court-appointed Guardian/Parent		NO YES - Attach copy NO YES - Attach copy of documentation NO YES - Attach copy of documentation NO YES - Attach copy of documentation The Minor Contact Information			
	Name	Address		Phone		
	Preparing Form					

#### **POST**



#### Self-Assessment

- Which of the following is false regarding most Physician Orders for Life Sustaining Treatment (POLST) forms?
  - They contain orders regarding CPR
  - They contain orders regarding artificial nutrition/hydration
  - They contain orders regarding antibiotics
  - They contain orders regarding care of delirium

#### Self-Assessment

- Which of the following is false regarding most Physician Orders for Life Sustaining Treatment (POLST) forms?
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  - They contain orders regarding care of delirium

## Honoring Patient Wishes and the "Dignified Death"

- Step 1: Prepare for the conversation
- Steps 2 and 3: Determine what the patient knows and wants to know
- Step 4: Deliver any new information
- Step 5: Notice and respond to emotions
- Step 6: Determine goals of care and treatment priorities
- Step 7: Agree on a plan

#### 5 Things to Say Before Death

- I love you
- Please forgive me
- I forgive you
- Thank you
- Good-bye

#### Good-Bye For Now

- In my Father's house are many mansions: if it were not so, I would have told you. I go to prepare a place for you. And if I go and prepare a place for you, I will come again, and receive you unto myself; that where I am, there ye may be also. John 14: 2-3 (KJV)
- And God shall wipe away all tears from their eyes; and there shall be no more death, neither sorrow, nor crying, neither shall there be any more pain: for the former things are passed away. Rev 21:4 (KJV)

#### Questions?



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