

Opioids and Pain Management: Allergies, Conversions, Dysphagia.... *Oh My!*

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Roadmap

- ▶ Define and differentiate true opioid allergies from adverse reactions
- ▶ Understand and apply opioid conversions to our hospice/palliative care population
- ▶ Review the available non-oral routes of opioid administration
- ▶ Strategize how to best manage a patient's pain when confronted with special considerations

Opioid Allergies

Pop Quiz!

- ▶ Which of the following is considered a True Allergy to Morphine?
- A. Itching
 - B. Respiratory Depression
 - C. Angioedema
 - D. Tachycardia

Allergy Types...What's in a name?

Adverse Effect (Common)

Predictable effects based on mechanism of action

Common reactions: N/V, Constipation, Drowsiness

Severe reactions: Addiction, Respiratory depression

Pseudo-Allergy

Unpredictable, hypersensitivity reactions that could occur after 1st dose

Common: Itching, Headache

Severe: Hives

True Allergy (Rare)

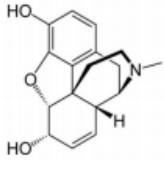
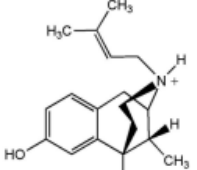
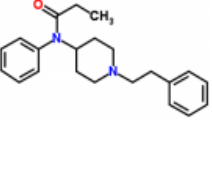
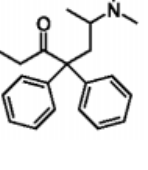
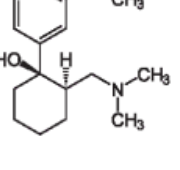
Immune mediated hypersensitivity reaction; requires prior exposure or repeat dosing

Common: Difficulty Swallowing, Headache

Severe: Angioedema (swelling of face, lips/tongue), Maculopapular rash, Hypotension, Shock

Opioid Classifications

Chemical Classes of Opioids (Updated 10/1/2018)

PHENANTHRENES	BENZOMORPHANS	PHENYLPIPERIDINES	DIPHENYLHEPTANES	PHENYLPROPYL AMINES
				
MORPHINE	PENTAZOCINE	FENTANYL	METHADONE	TRAMADOL
CROSS-SENSITIVITY RISK				
PROBABLE	POSSIBLE	LOW RISK	LOW RISK	LOW RISK
*Agents lacking the 6-OH group of morphine, possibly decreases cross-tolerability within the phenanthrene group				
**6-position is substituted with a ketone group and tolerability is similar to hydroxylation				

Jeffrey Fudin, BSPHarm, PharmD, DAIPM, FCCP, FASHP, FFSMB
http://paindr.com/resources/quick_references/ (See "Opioid Chemistry")

Opioid Classifications

Opioid Name	Class	Derivative(s)
Morphine	Phenanthrene	Buprenorphine* Codeine Hydrocodone* Oxycodone* Hydromorphone* Naloxone* Oxymorphone*
Fentanyl	Phenylpiperidine	Meperidine
Methadone	Diphenylheptane	Propoxyphene
Tramadol	Phenylpropylamine	Tapentadol

*decreased cross-tolerability within class

Fudin J. Chemical Classes of Opioids. Pain Dr. http://paindr.com/wp-content/uploads/2018/02/Opioid-Structural-Classes-Figure_updated-2018-02.pdf. Updated February 8, 2018.

So your patient can't tolerate morphine, what's next?

- ▶ First, determine what type of allergy/reaction
- ▶ Then ask what opioids the patient has taken in the past
 - ▶ If True Allergy → Switch to an opioid in another class and monitor
 - ▶ If Pseudo-Allergy → Switch to an opioid in another class OR add histamine blocker
 - ▶ If Adverse Reaction → Monitor closely and adjust dose as necessary
- ▶ In ALL cases, continued monitoring is KEY due to cross-reactivity risks
 - ▶ When in doubt, ask a Pharmacist for help!

Opioid Conversions

The Case of the Conversion Conundrum

- ▶ 60 yo female admitted to hospice with dx of Stage 4 breast cancer
- ▶ CC: Back pain; Rating 10/10; Describes as stabbing and burning
- ▶ Hx: Diabetes, Non-smoker, 5'5" 105 lbs.

- ▶ Current meds:
 - ▶ Morphine ER 30mg PO q8h
 - ▶ Morphine IR 10mg PO q2h prn BTP (using 5 doses/day)

The Case of the Conversion Conundrum

- ▶ What are our conversion options?

- ▶ Where do we start?

Opioid Conversion Chart

GENERIC NAME	SC, IV/24 hr	ORAL/24 hr
Morphine Sulfate	10 mg	30 mg
Oxycodone	-	20-30 mg
Hydromorphone	1.5	7.5 mg
Hydrocodone	-	30 mg
Oxymorphone	1 mg	10 mg
Codeine	130 mg	200 mg
Tramadol	-	150 mg

Fentanyl Patch Conversion

Age/Body Composition	Fentanyl patch (mcg/hr)	Morphine (mg)
Adult, normal wt, non-cachectic	100	180-200
Elderly & thin, non-cachectic	100	120
Cachectic patient	100	90

Example Fentanyl Patch Use Criteria



Yes No Question

1. Is the patient's BMI < 19? Current BMI _____
2. Is the patient able to swallow ANY medications (liquids, crushed, etc.).
3. Is the patient febrile? (Must monitor this on visits prior to ordering; drug will enter system must faster causing over sedation and other potential complications).
4. Is the patient's skin diaphoretic or sweaty?
5. Is the patient's prognosis less than 2 weeks? (transdermal delivery takes 1-3 days to take effect)
6. Is the fentanyl being used to treat neuropathic pain or bone pain? (Fentanyl is only effective for nociceptive pain.)

Methadone

- ▶ Most effective opioid for neuropathic pain
- ▶ Active N-methyl-D-aspartate (NMDA) receptor antagonist
 - ▶ Reduces CNS sensitization to pain/hyperalgesia
 - ▶ Reduces CNS amplification of pain sensation
- ▶ Few other known NMDA receptor antagonists:
 - ▶ Dextromethorphan
 - ▶ Ketamine
 - ▶ Memantine

When to Use Methadone

- ▶ Patients with rapidly escalating drug requirements (greater than 200 mg of morphine equivalents a day)
- ▶ Patients with dose-limiting side effects from other opioids
 - ▶ Nausea, constipation, hallucinations, myoclonus
- ▶ Patients having trouble swallowing pills who need long-acting pain control
- ▶ Moderate renal impairment

Morphine to Methadone Conversion

24 Hour Oral Morphine Equivalent	Morphine: Methadone Ratio per 24 Hours
<30 mg/24 hr	2:1
30 - 99 mg/24 hrs.	4:1
100-299 mg/24 hrs.	8:1
300-499 mg/24 hrs.	10:1
500-999 mg/24 hrs.	15:1
1000-1999 mg/24 hrs.	20:1
2000-2999 mg/24 hrs.	30:1
>3000 mg/24 hrs.	40:1

Methadone Dosing

1. Add up total oral morphine equivalents (OME)
2. Use morphine : methadone conversion factor
3. Divide daily dose into 2-3 doses per day
 - ▶ Patients on greater than 200 mg of morphine/day may need to cross-taper
4. Use breakthrough medication during titration
 - ▶ **Good rule of thumb:** 10% of the total daily dose of OME
5. Monitor daily for pain levels and new/worsening adverse effects
 - ▶ Increase total daily dose no more frequently than every 5 days

Methadone Administration

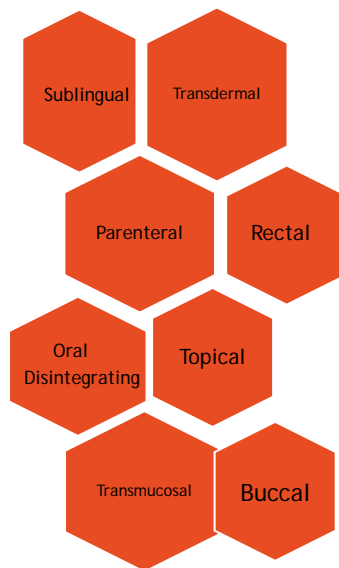
- ▶ Multiple dosage forms
 - ▶ Tablet (5 mg, 10 mg, 40 mg)
 - ▶ Liquid Concentration (10 mg/mL)
 - ▶ Injection (10 mg/mL)
- ▶ Well-absorbed from multiple routes of administration
 - ▶ Oral/Sublingual- tablets may be crushed
 - ▶ Rectal
 - ▶ Subcutaneous
 - ▶ Vaginal

The Case of the Conversion Conundrum

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- ▶ CC: Back pain; Rating 10/10; Describes as stabbing and burning
- ▶ 2nd Visit: Per her family, they are beginning to crush the Morphine ER tabs so she'll take them on schedule.

What's the best option for our patient?

Options for Dysphagia



Non-oral opioid routes of administration

Preferred Routes (Most supporting data)

- IV/Subcutaneous
- Transdermal patch
- Enteral*

Not as Preferred (Mixed supporting data)

- Sublingual**
- Buccal
- Rectal**
- Topical

Non-Preferred (little supporting data)

- Intramuscular
- Vaginal
- Intranasal

*Rarely used in hospice setting

**Used often in hospice despite mixed data

Sublingual ("under the tongue")

Definition: *Absorption of medication into blood through tissues underneath the tongue*

- ▶ Favors lipophilic drugs

Advantages:

- ▶ Great option for concentrated liquids
- ▶ Rapid onset of action

Disadvantages:

- ▶ Limited volume
- ▶ Burning/bitter taste

Buccal (Transmucosal)

Definition: *Absorption of medication into blood through tissues by placement between gums and cheek*

- ▶ Favors lipophilic drugs

Advantages:

- ▶ Well studied
- ▶ Rapid onset of action

Disadvantages:

- ▶ High price point
- ▶ Eating, drinking or smoking can affect absorption

Transmucosal Immediate Release Fentanyl (TIRF)

- ▶ Indicated for breakthrough cancer pain
- ▶ Advantage: Rapid onset of pain relief without a needle
- ▶ Disadvantages: Cost prohibitive; difficult to titrate

Available products:

- ▶ Fentanyl citrate lozenge (Actiq)
- ▶ Fentanyl sublingual tablet (Abstral)
- ▶ Fentanyl sublingual spray (Subsys)
- ▶ Fentanyl buccal tab (Fentora)
- ▶ Fentanyl buccal soluble film (Onsolis)

Parenteral Routes ("outside the intestine")

Definition: *Injection or infusion of medication directly into the body; avoiding skin/mucous membranes*

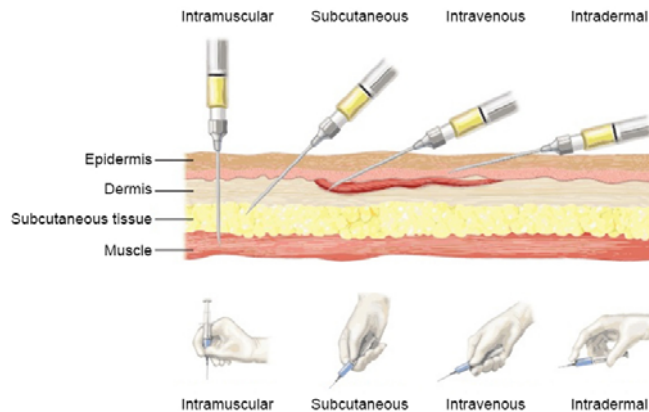


Figure 6 Structure of the skin and subcutaneous layers and common routes of parenteral drug administration.

https://www.dovepress.com/cr_data/article_fulltext/s99000/99651/img/DDDT-99651-F06.jpg

Parenteral Routes

Definition: *Injection or infusion of medication directly into the body; avoiding skin/mucous membranes*

IV = Intravenous (larger volume)

Advantages: Widely accepted

- ▶ Rapidly escalating doses; can be adjusted in minutes
- ▶ Great choice for pts who already have venous access
- ▶ Avoids first pass metabolism

Disadvantages:

- ▶ Limited availability (IV opioid shortage; equipment)
- ▶ Requires higher level of care/nurse training

Parenteral Routes

Subcut/SQ = Subcutaneously (smaller volume)

Advantages:

- ▶ Ease of use by clinicians/caregivers
- ▶ Less restrictions on mobility

Disadvantages:

- ▶ Max of 5 ml/hr. infusion rate
- ▶ Avoid use with immunocompromised patients

Parenteral Routes

IM = Intramuscularly

Advantages:

- ▶ Readily available
- ▶ Ease of administration

Disadvantages:

- ▶ Pain at injection site
- ▶ Variable absorption; difficult to achieve therapeutic blood levels

Transdermal Route (Patches)

Definition: *Absorption across the skin for systemic distribution*

- ▶ Favors lipophilic drugs

Advantages:

- ▶ Ease of use; favorable compliance
- ▶ Extended duration of action (3 days)
- ▶ Less adverse effects (minimal N/V, constipation, etc.)

Disadvantages:

- ▶ Difficult titration; especially in hospice setting
- ▶ Increased temp can increase absorption
- ▶ Loss of appetite/weight leads to decreased absorption

Transdermal Opioid Options

- ▶ Fentanyl patch (Duragesic) \$\$
- ▶ Buprenorphine patch (Butrans) \$\$\$

Rectal Route- Traditional

Definition: *Absorption by rectum blood vessels and into circulatory system for distribution to organs/systems.*

Advantages:

- ▶ Helpful in N/V and GI obstruction
- ▶ Multiple options: Suppositories, Tablets (whole mixed with lubricating jelly), Liquid

Disadvantages:

- ▶ Not popular with caregivers
- ▶ Avoid with constipation or diarrhea
- ▶ Limited surface area for absorption

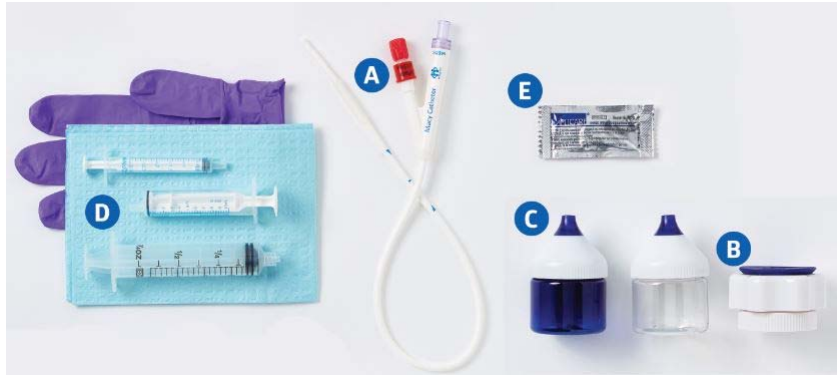
Pop Quiz!

Which of the following long acting opioids can be given rectally?

- A. Oxycodone ER tabs
- B. Morphine sulfate ER tabs
- C. Methadone
- D. Fentanyl
- E. Both B & C

Rectal Route- Macy Catheter

Rectal administration of oral medications (tabs/liquids) via catheter tubing with two-valved med port and balloon inflation port. Kit comes with system to crush meds for insertion into med port.



<https://catalogcontent.medline.com/wp-content/uploads/2019/04/Curated-Kit-Items-Hospi-Macy-Catheter.jpg>

Rectal Route- Macy Catheter

Advantages:

- ▶ Rapid symptom control with minimal medication waste
- ▶ Discreet administration
- ▶ More cost effective than parenteral route

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- ### Disadvantages:
- ▶ Contraindicated with rectal tumors/lesions or diarrhea
 - ▶ Poor data on rectal absorption of certain medications
 - ▶ Patient/caregiver preference

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Topical (Transdermal gels)

Definition: *Application of a drug in gel, ointment, cream, foam, lotion to superficial surface of the skin.*

Advantages:

- ▶ Ease of use with dysphagia/combativeness
- ▶ Painless

Disadvantages:

- ▶ Variable absorption rates; poor bioavailability data
- ▶ Costly due to compounding fees
- ▶ Caregiver confusion

Alternate Routes: Onset of Action

Route	Example Opioid(s)	Time to Initial Analgesic Effect
IV	Morphine	30-60 secs
Sublingual	Morphine, Methadone	3-5 mins
Buccal	Fentanyl	3-5 mins
IM	Morphine, Meperidine	10-20 mins
Subcut	Hydromorphone	15-30 mins
Rectal	Methadone	5-30 mins
Transdermal	Fentanyl	Variable; mins to hrs.
Topical	Morphine	Variable; mins to hrs.

Available from LexiComp Online Drug database: <https://online.lexi.com/lco/action/home>

Back to our Conversion Conundrum...

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- ▶ CC: Back pain; Rating 10/10; Describes as stabbing and burning
- ▶ Hx: Diabetes, Non-smoker, 5'5" 105 lbs.

- ▶ 2nd Visit: Per her family, they are beginning to crush the Morphine ER tabs so she'll take them on schedule.

What's the best option for our patient?

How do we keep our patient comfortable?

- A. Advise the family to continue crushing the Morphine sulfate ER and monitor closely for adverse reactions
- B. Speak with clinical pharmacist for recommendations to convert Morphine over to Methadone
- C. Convert patient over to Morphine IR tabs or Morphine sulfate 100 mg/5ml concentrate scheduled given via sublingual or rectal route
- D. Stop the Morphine sulfate ER and advise family to give Morphine IR on an as needed basis only
- E. B or C; depending on family preference

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Methadone Conversion

- ▶ Methadone equianalgesic dosing ratio: 8:1
- ▶ 140 divided by 8 = 17.5mg per day
- ▶ Dose reduce by 25% = 13.125 mg
 - ▶ When switching between opioids
 - ▶ Round up to 15 mg (severe pain) or down to 10 mg (Pt is not in pain)

Discontinue Morphine ER; Start: Methadone 5 mg SL q8h
 Morphine Liquid (20mg/mL) 10-20mg SL q2h prn
 breakthrough pain
 Monitor daily for 5 to 7 days

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Questions



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