PAINWEEK®

Getting the drug into the patient: Exploring alternate routes of medication administration

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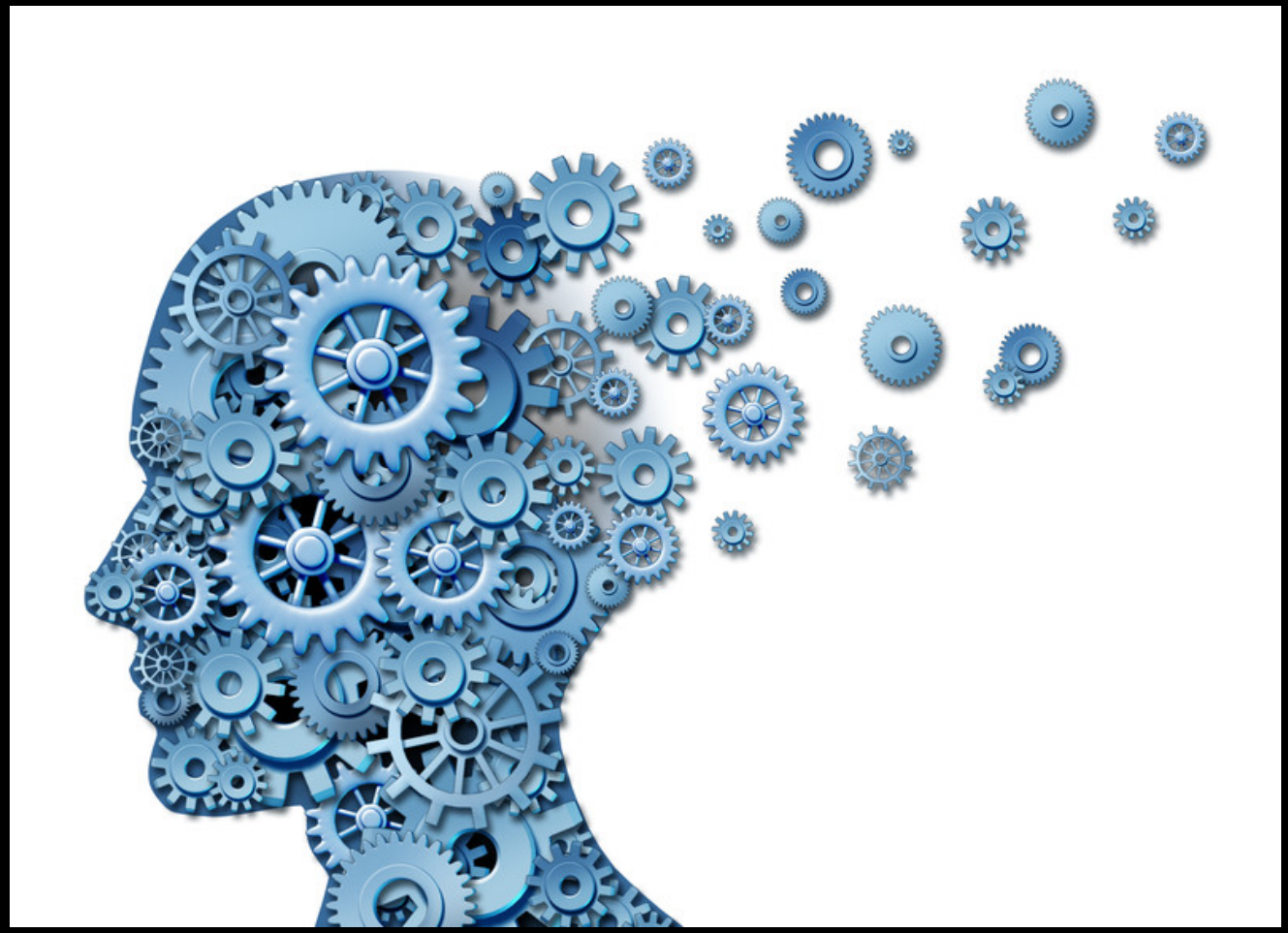
Disclosure

- Nothing (so boring…)

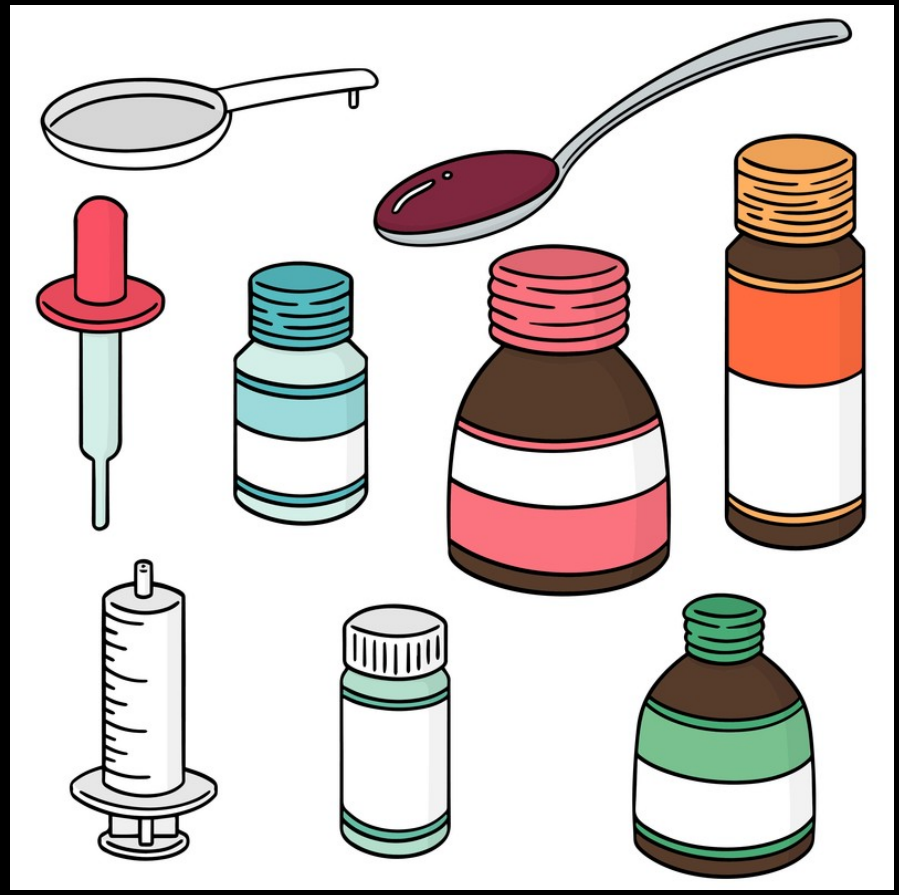


Learning Objectives

- Identify alternate routes of medication administration, in addition to the oral route.
- Describe the benefits and limitations of transmucosal, transdermal, topical and rectal medication administration.
- Describe evidence that supports and refutes the use of compounded topical medications.

Alternate (non-oral) Routes of Administration

- Transmucosal
  - Sublingual, buccal, intranasal
- Rectal
- Transdermal
- Topical
- Parenteral
  - Intramuscular, intravenous, subcutaneous
- Neuraxial
  - Epidural, intrathecal



Morphine

Route	Formulation	Strengths
Oral	Tablet	15, 30 mg
	Solution	10 mg/5 ml, 20 mg/5 ml, 100 mg/5 ml
	Tablet ER	15 30, 60, 100, 200 mg
	Tablet ER 12-hour abuse-deterrent	15, 30, 60 mg
	Capsule extended-release 24 hour	10, 20, 30, 40, 45, 50, 60, 75, 80, 90, 100, 120, 200 mg
Rectal	Rectal suppository	5, 10, 20, 30 mg
Parenteral	Injection	Variety of concentrations

Ibuprofen

Route	Formulation	Strengths
Oral	Capsule	200 mg
	Tablet	100, 200, 400, 600, 800 mg
	Tablet Chewable	100 mg
	Suspension	50 mg/1.25 ml, 100 mg/5ml
Topical	Cream	10%
Parenteral	Intravenous	10 mg/ml, 800 mg/200 ml, 800 mg/8 ml

Gabapentin and Nortriptyline

Route	Formulation	Strengths
GABAPENTIN		
Oral	Capsule	100, 300, 400 mg
	Tablet	300, 600, 800 mg
	Solution	250 mg/5 ml, 300 mg/6 ml
	Suspension	25 mg/ml
Topical	Cream	10%
NORTRIPTYLINE		
Oral	Capsule	10, 25, 50, 75 mg
	Solution	10 mg/5 ml

Transmucosal Drug Delivery in the Oral Cavity

- Transmucosal refers to the route of administration in which the drug is diffused through the mucous membrane.
- This can refer to inhalation, nasal, sublingual, buccal, vaginal, rectal, or ocular routes.
- Situations when oral route of administration may not be available:
  - Obstructing GI tract tumors
  - Bowel obstruction
  - Dysphagia
  - Odynophagia
  - Frequent nausea or vomiting
  - Diminished level of consciousness in a dying patient

Transmucosal Drug Delivery in the Oral Cavity

- Advantages:
  - Absorption bypasses hepatic first pass metabolism*
  - Absorption bypasses drug degradation in the GI tract*
  - Fast onset of drug action
  - Useful when patient is unconscious
  - Simple and non-invasive (relative to parenteral)
  - Easily administered by caregivers
  - Avoids risk of infection that may be associated with parenteral administration
  - Avoids pain associated with parenteral administration

  - *unless the medication does eventually access the GI tract

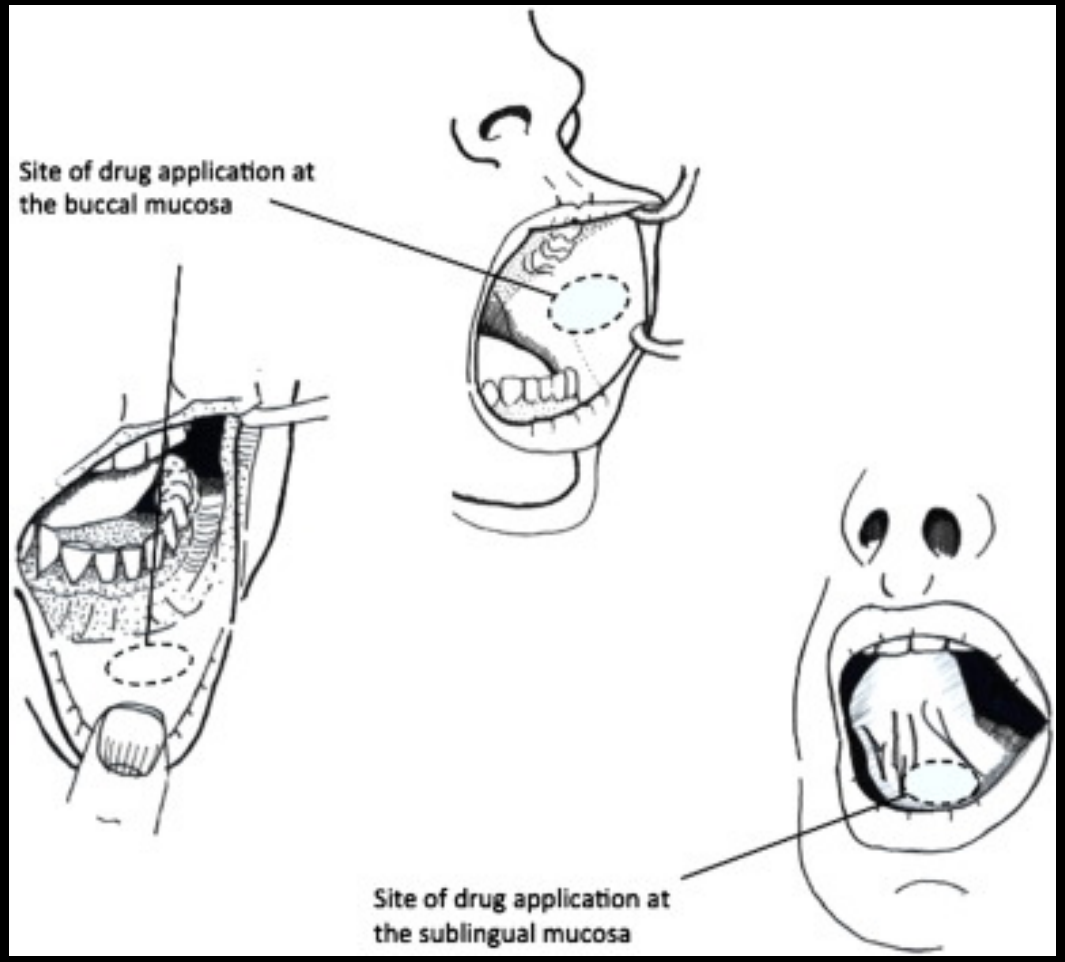
Lam JKW, et al. Advanced Drug Delivery Reviews 2014;73:50-62.

Transmucosal Drug Delivery in the Oral Cavity

- Characteristics of medications amenable to transmucosal administration:
  - Good lipophilicity and water solubility at physiological pH
  - High potency
  - Must not cause local irritation in the oral cavity
  - Clear clinical benefit in developing medication for TM delivery
  - Drug must overcome:
    - Intrinsic enzyme activity
    - Relative permeability of the oral mucosa
    - Small fluid volume for dissolution and absorption
  - Must allow for accurate and convenient dose measurement
  - Ability of patient to handle drug delivery system

Lam JKW, et al. Advanced Drug Delivery Reviews 2014;73:50-62.

Transmucosal Drug Delivery in the Oral Cavity



- Sublingual
  - Under the tongue
  - The floor of the mouth
- Buccal
  - Inner cheek
  - Buccal pouch between the cheeks and gums
- Dosage formulations
  - Oral films and wafers
  - Tablets and lozenges
  - Liquids

Transmucosal Fentanyl

- Abstral (fentanyl) sublingual tablet
- Actiq (fentanyl citrate) oral transmucosal lozenge and generics
- Fentora (fentanyl citrate) buccal tablet
- Lazanda (fentanyl) nasal spray
- Onsolis (fentanyl) buccal soluble film
- Subsys (fentanyl) sublingual spray

Buprenorphine

- Belbuca Buccal Film – 75, 150, 300, 450, 600, 750, 900 mcg
- Probuphine Implant – 74.2 mg
- Subutex Sublingual Tablet – 2, 8 mg

- Buprenorphine/naloxone film
  - Bunavail buccal film – 2.1/0.3, 4.2/0.7, 6.3/1 mg
  - Suboxone sublingual film – 2/0.5, 4/1, 8/2, 12/3 mg
  - Zubsolv sublingual tablet – 0.7/0.18, 1.4/0.36, 2.9/0.71, 5.7/1.4, 8.6/2.1, 11.4/2.9 mg

High Concentrate Oral Solution Formulations

- Dexamethasone 1 mg/ml
- Prednisone 5 mg/ml
- Methadone 10 mg/ml
- Morphine 20 mg/ml
- Oxycodone 20 mg/ml
- Sertraline 20 mg/ml
- Haloperidol 2 mg/ml
- Lorazepam 2 mg/ml
- Diazepam 5 mg/ml
- Alprazolam 1 mg/ml

High Concentrate Oral Solution Formulations

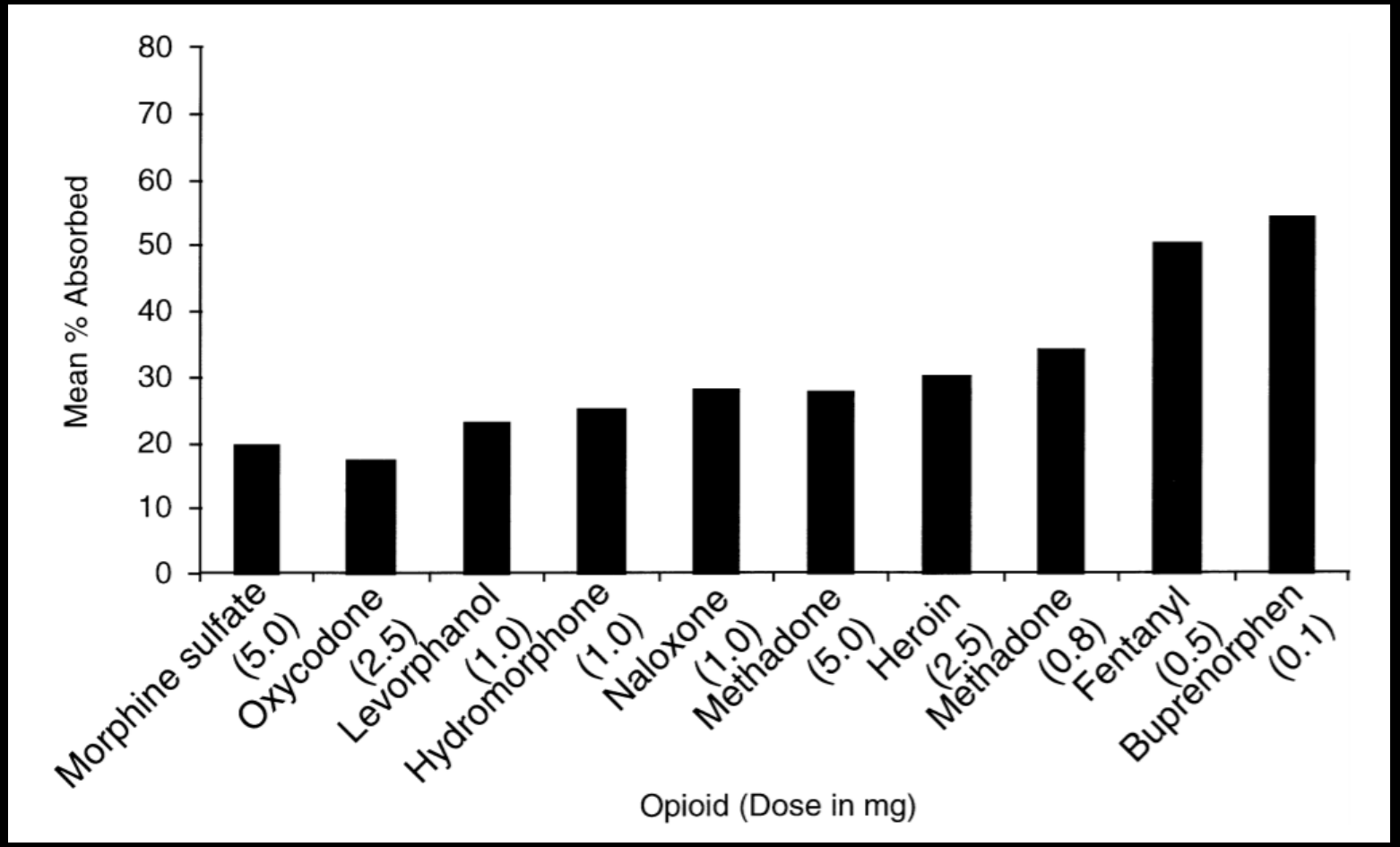
- Proper use of a highly concentrated oral solution
  - Recommend that it be mixed with liquid or semi-solid food such as water, juices, soda or soda-like beverages, applesauce or puddings
  - Use only the calibrated dropper provided with the product
  - Stir the liquid or food gently for a few seconds; the entire amount of the mixture (drug/liquid or drug/food) should be consumed immediately

But what if the patient can't SWALLOW?

High Concentrate Oral Solution Formulations

- Most studies have been done with sublingual administration of opioids
- Most hospice providers use concentrated oral solution of morphine, oxycodone or methadone for off-label sublingual or buccal administration in patients who are unable to swallow tablets or large quantities of solutions
- Instilling volumes > 2-3 ml will likely result in leakage out of the sublingual space

How much actually gets absorbed transmucosally?



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Coluzzi PH. *J Pain Symptom Manage*. 1998;16(3):184-92.

How much actually gets absorbed transmucosally?

- Hydrophilic opioids such as morphine and hydrocodone are poorly absorbed sublingually
- Bitter taste and burning sensation possible
- Preferable for patient to retain the drug sublingually for several minutes

- May be the best option given lack of other non-oral formulations available commercially

Rectal Route Advantages

- Simplicity
- Useful in patients with:
  - Nausea and vomiting
  - Dysphagia
  - GI obstruction
  - Malabsorption
  - Impaired neuromuscular function

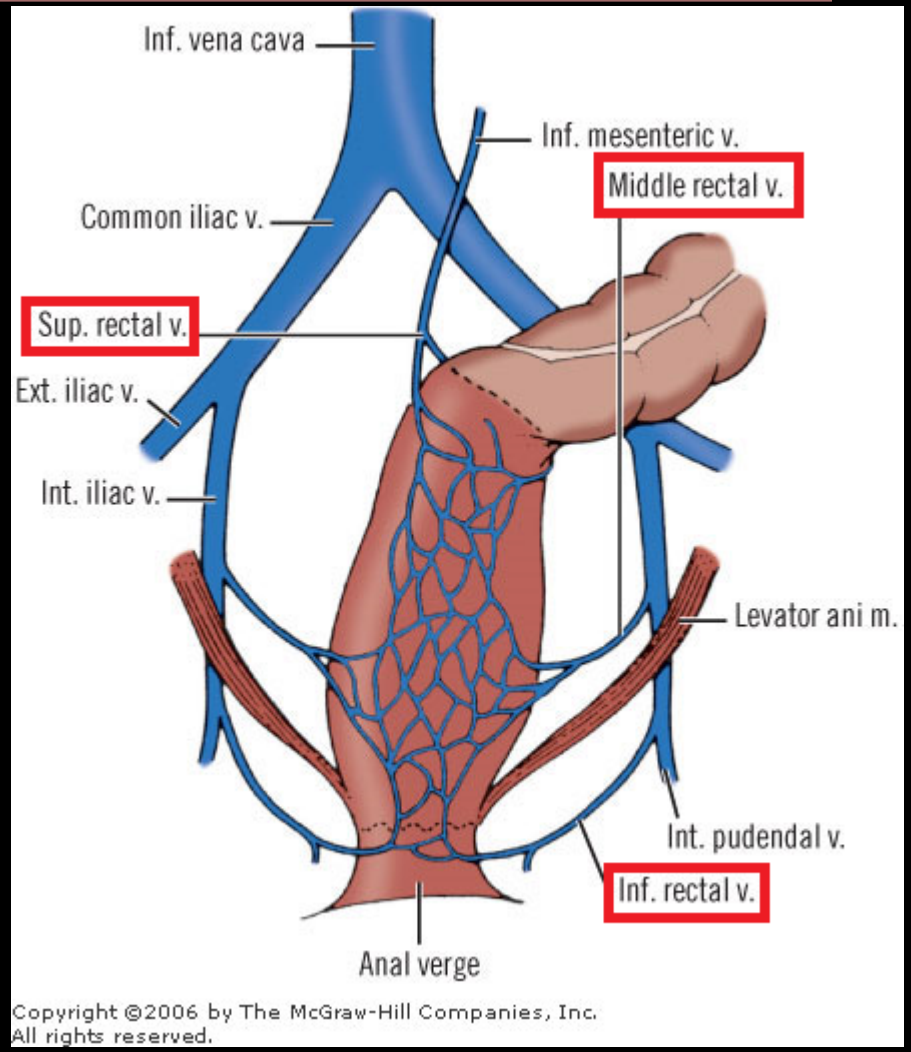
Rectal Route Disadvantages

- Bioavailability can be affected by multiple factors, including the small surface area of the rectum, insufficient fluid to dissolve tablets or capsules, and presence of feces that can limit absorption
- Should not be used in patients with impaction, constipation, or diarrhea
- Should not be used if placement of the suppository will cause pain (e.g., inflamed hemorrhoids, fissures, or lesions of the anus or rectum)
- Avoid in patients with neutropenia or thrombocytopenia due to risk of bleeding or infection
- Avoid route if repeated dosing is necessary
- Not useful if patient or caregivers are unwilling or unable to accept or administer medications rectally

Kestenbaum MG, et al. *Pain Med*. 2014;15(7):1129-53.

Rectal Route (PR)

- The rectum constitutes the terminal 15-19 cm of the large intestine
- Studies have shown minimal migration of renal preparations, leaving the total area for drug absorption a 6-8 cm section of “smooth pipe”
- Three veins:
  - Superior rectal vein empties into portal vein and subsequently into the liver
  - Middle and inferior veins return to the inferior vena cava
    - Medications administered into the lower part of the rectum avoid “first-pass” metabolism



Warren DE. *J Pain Symptom Manage*. 1996;11(6):378-87.
https://gregorzorn.com/delivery-methods/cannabis-suppositories-taking-your-medicine-down-under/

Rectal Route Considerations

- Bioavailability of drugs given rectally is highly variable and influenced by the site of insertion
- Drugs administered through the rectum, especially opioids, are dosed similarly as when given orally
- There are a limited number of commercially available drugs specifically manufactured for rectal administration

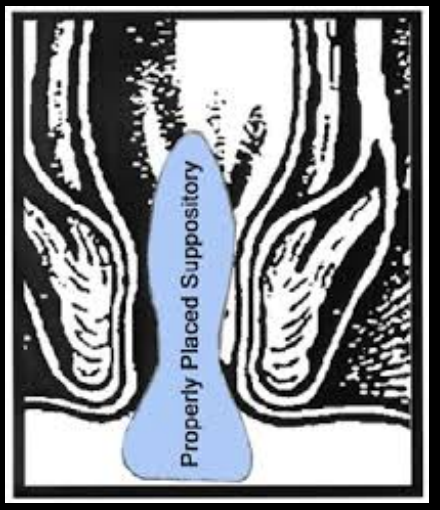
Rectal Route Administration

- Rectum should be emptied prior to insertion as stool interferes with drug absorption
- Insert the drug about a finger's length into the rectum and place against the rectal wall
- Pointy end goes in first, or blunt end?
- 10 ml warm water can be inserted via syringe to assist dissolution of the suppository or suspension
- Keep volume of drug preparation less than 60 ml to avoid spontaneous expulsion before absorption

Rectal Rocket – Whoa Nelly!

- Hydrocortisone and lidocaine
- Treatment of hemorrhoids

- The suppository does not get lost in the rectum but stays at the point of insertion.
- It addresses both internal and external hemorrhoids at the time.
- The patient can pass gas without losing the suppository.



Rectal Formulations

Therapeutic Class	Medications
Opioids	***Morphine, hydromorphone*** Methadone, oxycodone, codeine, tramadol
Acetaminophen/NSAIDs	***Acetaminophen, indomethacin*** Diclofenac, ibuprofen, naproxen, aspirin
Skeletal Muscle Relaxant	Baclofen
Anesthetic	Lidocaine
Laxatives	***Glycerin, sodium phosphates, mineral oil, bisacodyl, docusate***
Anti-convulsants	Phenobarbital, phenytoin, carbamazepine, valproic acid, lamotrigine, carbamazepine
Corticosteroids	Hydrocortisone, prednisolone, dexamethasone
Anxiolytics	Diazepam, lorazepam, midazolam, clonazepam
Anti-emetics	***Prochlorperazine, promethazine*** Chlorpromazine, metoclopramide, haloperidol
Antihistamine	Diphenhydramine

Commercially available

True or False

- ANY tablet or capsule can be inserted rectally, resulting in the expected therapeutic effect.

True or False

- ANY tablet or capsule can be inserted rectally, resulting in the expected therapeutic effect.

Macy Catheter

- FDA cleared to provide rectal access to administer liquids/medications.
- Facilitates quick and effective symptom management.
- Easy and safe for clinicians to use.
- Requires minimal training.

https://www.macycatheter.com/

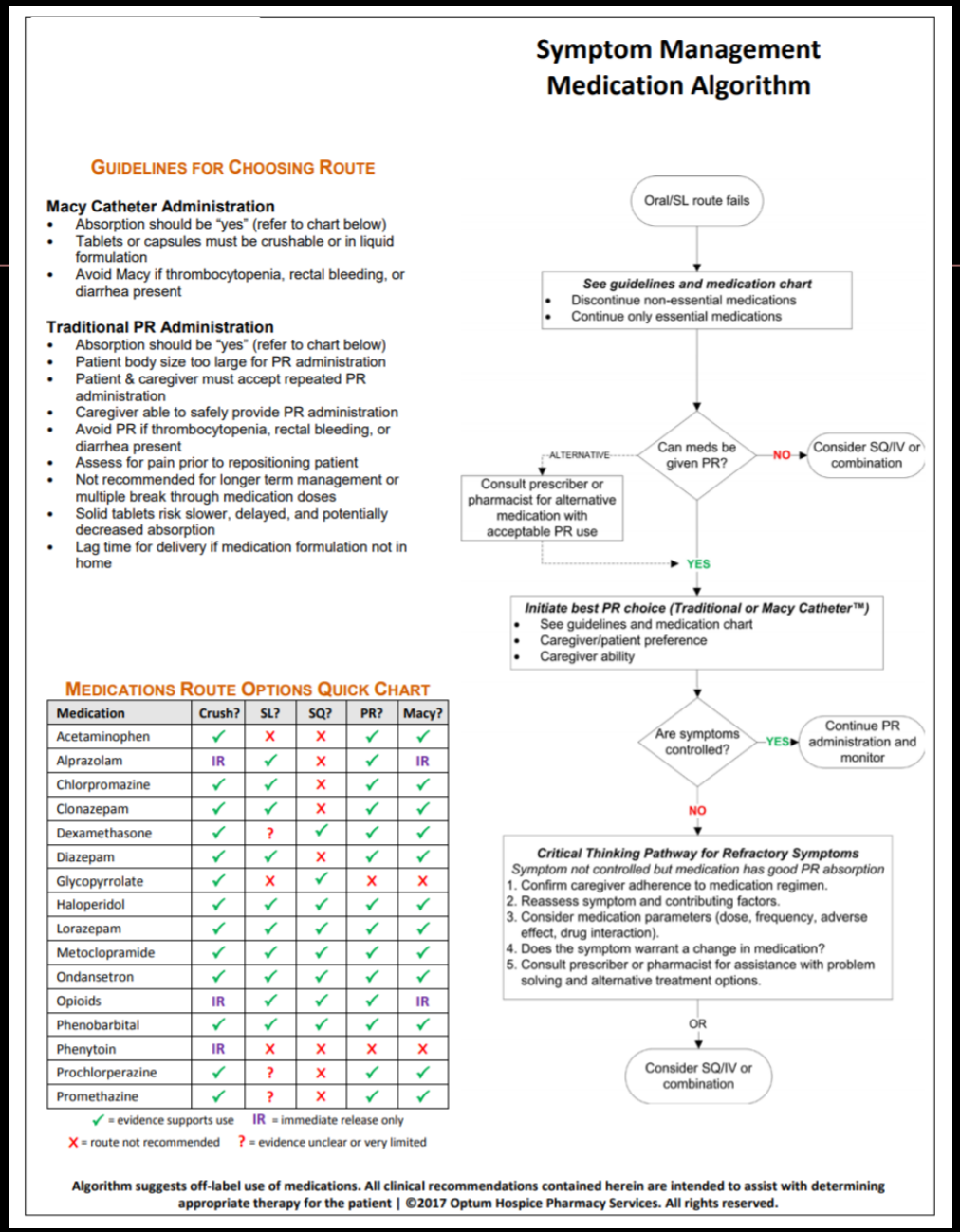
Oral Dosage Formulations that Should Not Be Crushed

- Extended-release or delayed-release formulations
- Slow-release formulations
- Medications that are mucous membrane irritants
- Enteric-coated formulations
- Film-coated or wax-coated formulations
- Lozenges or effervescent tablets
- Liquid-filled formulations
- Medications where exposure to the powder may cause toxicities or teratogenicity

www.ismp.org/tools/donotcrush.pdf

Analgesics

- Acetaminophen
- Aspirin
- Carbamazepine
- IR Diclofenac, Naproxen
- Ibuprofen
- Ketamine
- Lamotrigine
- Dexamethasone
- IR opioids



Symptom Management Medication Algorithm

Guidelines for Choosing Route

Macy Catheter Administration
- Absorption should be "yes" (refer to chart below)
- Tablets or capsules must be crushable or in liquid formulation
- Avoid Macy if thrombocytopenia, rectal bleeding, or diarrhea present

Traditional PR Administration
- Absorption should be "yes" (refer to chart below)
- Patient body size too large for PR administration
- Patient & caregiver must accept repeated PR administration
- Caregiver able to safely provide PR administration
- Avoid PR if thrombocytopenia, rectal bleeding, or diarrhea present
- Assess for pain prior to repositioning patient
- Not recommended for longer term management or multiple break through medication doses
- Solid tablets risk slower, delayed, and potentially decreased absorption
- Lag time for delivery if medication formulation not in home

Medications Route Options Quick Chart

Medication	Crush?	SL?	SQ?	PR?	Macy?
Acetaminophen	✓	X	X	✓	✓
Alprazolam	IR	✓	X	✓	IR
Chlorpromazine	✓	✓	X	✓	✓
Clonazepam	✓	✓	X	✓	✓
Dexamethasone	✓	?	✓	✓	✓
Diazepam	✓	✓	X	✓	✓
Glycopyrrolate	✓	X	✓	X	X
Haloperidol	✓	✓	✓	✓	✓
Lorazepam	✓	✓	✓	✓	✓
Metoclopramide	✓	✓	✓	✓	✓
Ondansetron	✓	✓	✓	✓	✓
Opioids	IR	✓	✓	✓	IR
Phenobarbital	✓	✓	✓	✓	✓
Phenytoin	IR	X	X	X	X
Prochlorperazine	✓	?	X	✓	✓
Promethazine	✓	?	X	✓	✓

✓ = evidence supports use IR = immediate release only
X = route not recommended ? = evidence unclear or very limited

Oral/SL route fails

See guidelines and medication chart
- Discontinue non-essential medications
- Continue only essential medications

Can meds be given PR?
- NO → Consider SQ/IV or combination
- ALTERNATIVE → Consult prescriber or pharmacist for alternative medication with acceptable PR use
- YES

Initiate best PR choice (Traditional or Macy Catheter™)
- See guidelines and medication chart
- Caregiver/patient preference
- Caregiver ability

Are symptoms controlled?
- YES → Continue PR administration and monitor
- NO

Critical Thinking Pathway for Refractory Symptoms
Symptom not controlled but medication has good PR absorption
1. Confirm caregiver adherence to medication regimen.
2. Reassess symptom and contributing factors.
3. Consider medication parameters (dose, frequency, adverse effect, drug interaction).
4. Does the symptom warrant a change in medication?
5. Consult prescriber or pharmacist for assistance with problem solving and alternative treatment options.

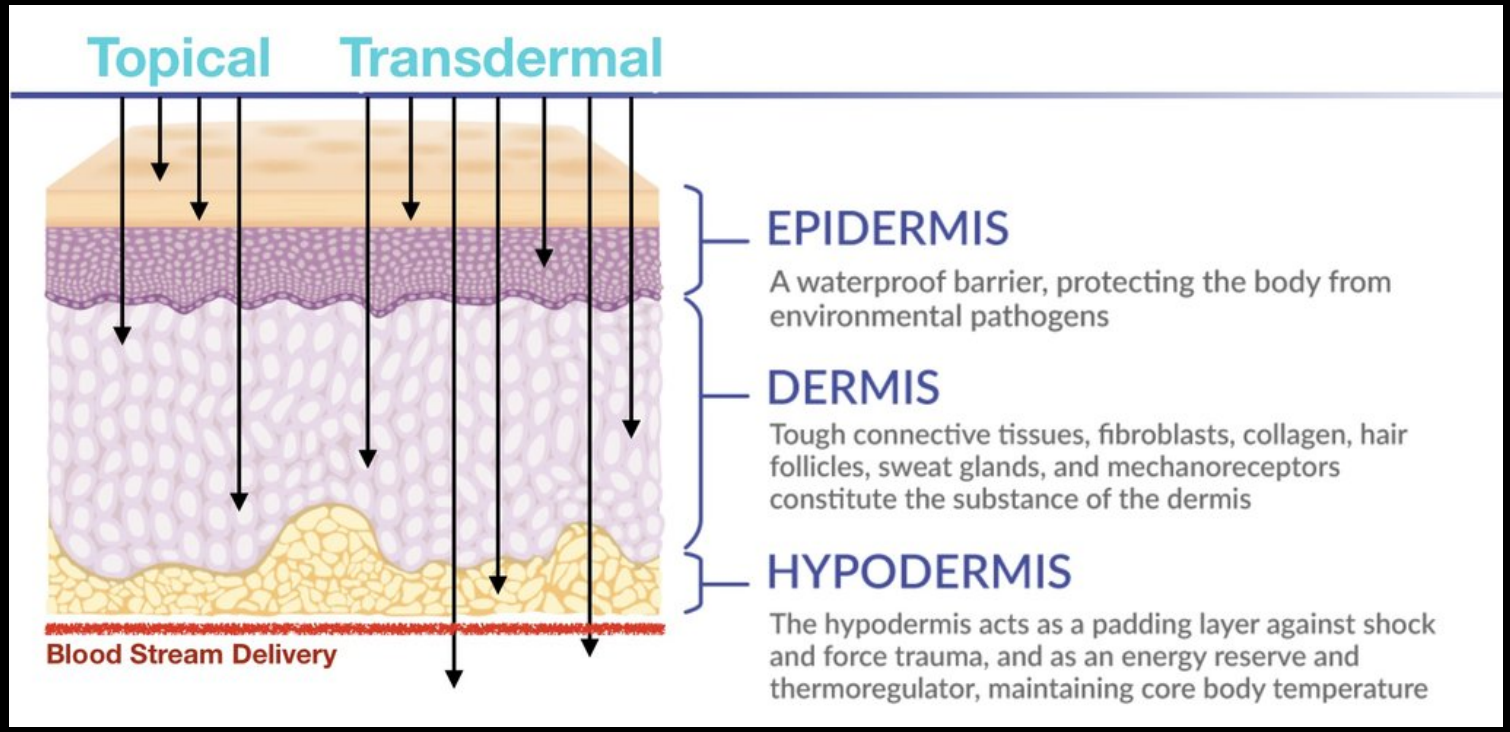
OR

Consider SQ/IV or combination

https://www.macycatheter.com/wp-content/uploads/2019/11/Optum-Symptom-Management-Algorithm.pdf

Transdermal vs. Topical Medications

- Transdermal
  - Fentanyl
  - Buprenorphine
- Topical
  - Lidocaine
  - Counterirritants
  - Capsaicin
  - NSAIDs
  - Others



https://4phive.com/blogs/news/basically-transdermal

Topicals

- Commercially available products
  - Lidocaine (topical patch, gel)
  - Counterirritants (gels, creams, patches)
  - NSAID (diclofenac – patch, drops)
- Compounded
  - Gels (intended for systemic absorption)
  - Pastes (e.g., Magic Butt Paste – 2:2:1:1 [A&D:zinc oxide:lidocaine:PEG ointment])
  - Sprays for topical use (lidocaine, metronidazole, morphine/intrasite gel)

Let's meet Betty

- Betty is a 68-year-old woman admitted to hospice with a diagnosis of lung cancer with wide-spread metastasis, including bone involvement.
- S/P MI 3 months ago, and shingles across her trunk
- Lesions have dried and cleared, but she c/o "horrendous" pain
  - Burning, sharp, jabbing
  - Skin is exquisitely sensitive, even the air hurts her skin
- Post-herpetic neuralgia
  - Age > 50, severe rash and pain with initial illness, concurrent chronic illnesses, face or torso affected, antiviral therapy delayed for more than 72 hours after rash appeared

Let’s consider our options

- What can we offer Betty for management of her post-herpetic neuralgia?
  A. Methadone with morphine for breakthrough pain
  B. Topical capsaicin cream or patch
  C. Topical lidocaine patch
  D. Systemic adjuvant analgesic therapy (e.g., gabapentin or an antidepressant)

Let's consider our options

- What can we offer Betty for management of her post-herpetic neuralgia?
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  - C. Topical lidocaine patch
  - D. Systemic adjuvant analgesic therapy (e.g., gabapentin or an antidepressant)

Possibly, especially if she requires systemic therapy for her cancer

Causes burning on application, which lasts about 2 weeks. 40-50% of patients cannot tolerate

Topical Lidocaine

- Lidocaine is an amide-type local anesthetic agent that penetrates the skin after application sufficient to produce an analgesic effect, but not enough to cause complete sensory block
  - Lidoderm and generics – 5% lidocaine (12 hours on, 12 hours off)
  - ZTLido – 1.8% lidocaine (bioequivalent to Lidoderm)
  - OTC – IcyHot Lidocaine Patches plus Menthol; Salonpas Lidocaine 4%; Aspercreme Lidocaine patch (cannot exceed 4%, usually applied 8-12 hours)

Poor Elsie!

- Elsie is an 88-year-old woman with CHF, CAD with stent, diastolic heart failure, hypertension, diabetes (on insulin), CKD stage 4 and seizure disorder.
- 5’5”, 155 pounds
- Receiving oxycodone 5 mg prn, uses 2-4 times per day
- Pain is primarily due to post-herpetic neuralgia in her perianal area and back, and painful diabetic neuropathy
- Oxycodone not working particularly well, makes her sleepy and confused
- Would a lidocaine patch be appropriate for Elsie?

Good luck with that!

- Consider lidocaine gel
- Available in a variety of strengths (2, 3, 4, 5%)
- Apply 2-4 times per day to affected area

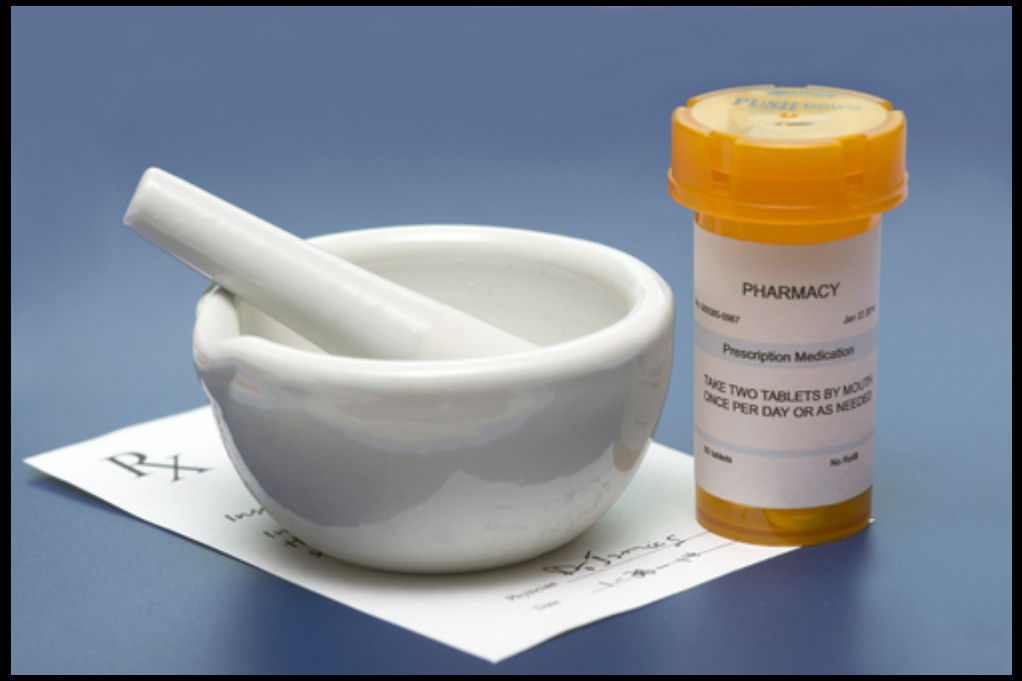
- Topical lidocaine may be a beneficial therapeutic option for particular pain scenarios
  - Pain that is fairly superficial
  - Preferably for an FDA-approved indication (post-herpetic neuralgia)
  - Consider need for systemic therapy
  - Consider lidocaine gel for tricky areas!

What CAN be compounded?

Compounded Medications

- A compounded preparation is needed when no commercially manufactured medication is available to adequately address a patient's medical needs
- Physicians
  - Compounds offer flexibility to prescribe doses and delivery systems that are designed for individual patient needs
- Patients
  - Provide much-needed release when commercially manufactured medications are ineffective or cannot be tolerated.
  - Useful when a non-commercially available strength is needed.
    - Morphine 1 mg/ml oral solution
    - Methadone 50 mg/ml oral solution
    - Oxycodone 40 mg/ml oral solution

What SHOULDN'T be compounded?



Compounded Topical Pain Creams

- Compounded Topical Pain Creams: Review of select ingredients for safety, effectiveness, and use (2020)
- The National Academies of Sciences Engineering Medicine
- https://www.nap.edu/catalog/25689/compounded-topical-pain-creams-review-of-select-ingredients-for-safety?utm_source=NASEM+News+and+Publications&utm_campaign=313f503b6c-Final_Book_2020_07_22_25689&utm_medium=email&utm_term=0_96101de015-313f503b6c-105966349&goal=0_96101de015-313f503b6c-105966349&mc_cid=313f503b6c&mc_eid=c381f6dbeb

Clinical Evidence for the Topical Application of Single-Ingredient Compounded Pain Preparations

- Active pharmaceutical ingredient
- Does available evidence suggest effectiveness when used on intact skin?
- Is there evidence of systemic absorption?
- Is there evidence to conclude that the active ingredient is safe?
- What were the demographics of the populations studied?
- What adverse effects have been described?
- Comments

Compounded Topical Pain Creams: Review of select ingredients for safety, effectiveness, and use (2020)
The National Academies of Sciences Engineering Medicine

Clinical Evidence for the Topical Application of Single-Ingredient Compounded Pain Preparations

- Amitriptyline
- Baclofen
- Bupivacaine
- Cannabidiol
- Carbamazepine
- Clonidine
- Cyclobenzaprine
- Dexamethasone
- Doxepin
- Gabapentin
- Ketamine
- Lidocaine
- Meloxicam
- Memantine
- Naproxen
- Nifedipine
- Orphenadrine
- Pentoxifylline
- Topiramate
- Tramadol

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Clinical Evidence for the Topical Application of Single-Ingredient Compounded Pain Preparations

- Of the 20 active ingredients reviewed, 3 individual ingredients and one two-drug combination demonstrate potential clinical effectiveness
- Doxepin - evidence of effectiveness
- Lidocaine – evidence of effectiveness
- Naproxen – inconsistent evidence, but demonstrates potential effectiveness for certain types of pain
- Pentoxifylline/clonidine combination has limited evidence of effectiveness in one pain model
- Data inadequate – safety, risks, extent of absorption

Compounded Topical Pain Creams: Review of select ingredients for safety, effectiveness, and use (2020)
The National Academies of Sciences Engineering Medicine

Compounded Topical Pain Creams

- Military treatment facility
- 399 patients with localized pain classified by their MD as neuropathic, nociceptive or mixed (back/butt; neck; limb; other location)

Group	Compounded Product
1 – Neuropathic pain	Ketamine, gabapentin, clonidine, lidocaine
2 – Nociceptive pain	Ketoprofen, baclofen, cyclobenzaprine, lidocaine
3 – Mixed neuropathic/nociceptive	Ketamine, gabapentin, diclofenac, baclofen, cyclobenzaprine, lidocaine
4 – Placebo	Placebo

Brutcher RE et al. Ann Int Med 2019;170:309-318.

Concentrations of ingredients

- Ketamine 10%
- Gabapentin 6%
- Clonidine 0.2%
- Lidocaine 2%
- Ketoprofen 10%
- Baclofen 2%
- Cyclobenzaprine 2%
- Diclofenac 3%
- Lipophilic base carrier

Apply to affected area 3 times per day.

Amount applied determined by size of the area (set by investigators – 4 rotations of container for 5x5 area)

Brutcher RE et al. Ann Int Med 2019;170:309-318.

So WILL a little dab do ya?

- Primary outcome – average pain score 1 month after treatment
  - Positive categorical response was a reduction in pain score by ≥ 2 points (0-10) WITH a satisfaction score of ≥ 3 on a 5-point satisfaction scale
- Data collected by phone by a trained, blinded investigator not involved in patient care
  - 1 month (24-40 days)
  - 3 months (75-110 days)
- 399 started trial, 390 completed
  - 202 assigned to a study drug, 197 to placebo

Brutcher RE et al. Ann Int Med 2019;170:309-318.

Drum roll please….

- No change in pain score at 1 month between drug and placebo for any group
  - Neuropathic pain – 0.1 point reduction in pain
  - Nociceptive pain – 0.3 point reduction in pain
  - Mixed pain – 0.3 point reduction in pain
- SF-36 measures did not differ between the groups

Brutcher RE et al. Ann Int Med 2019;170:309-318.

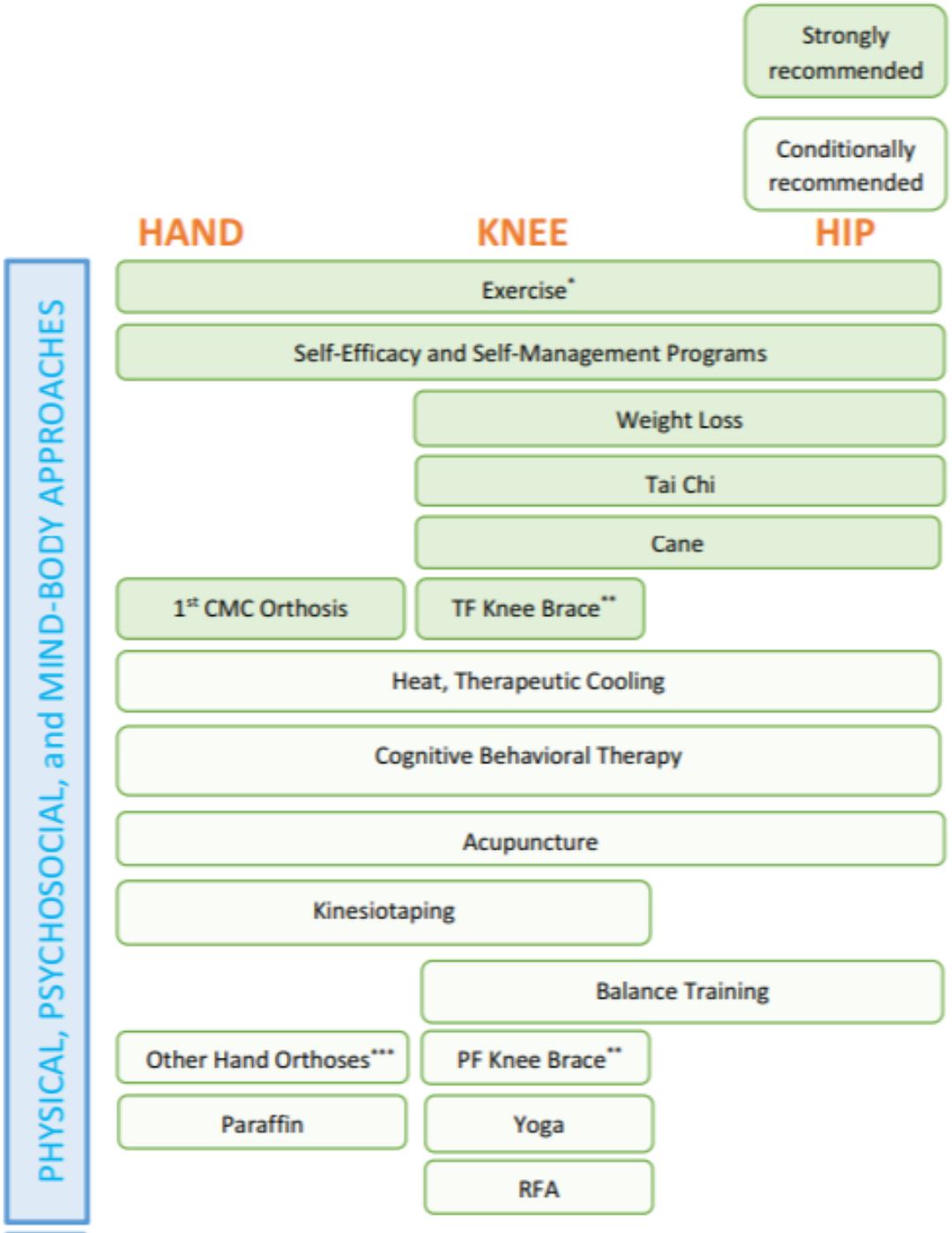
ABH Gel for Nausea (oh please…)

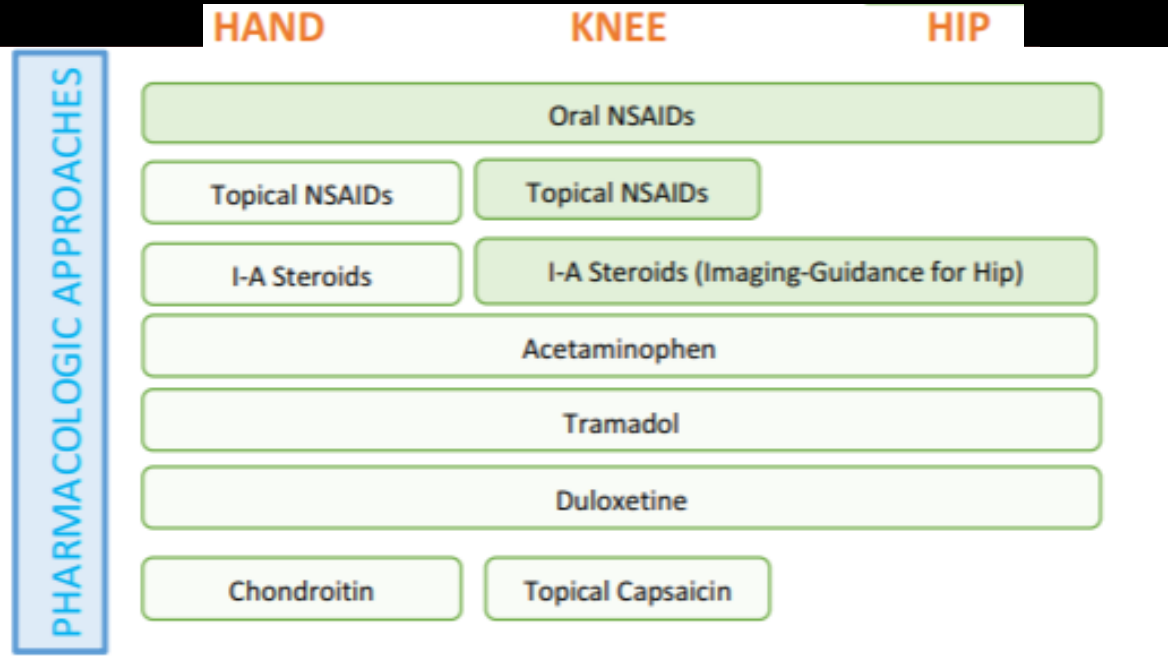
- Study 1
  - Healthy volunteers applied standard 1.0 ml dose
  - 2 mg lorazepam, 25 mg diphenhydramine, 2 mg haloperidol in PLO
  - Rubbed on inner wrist
  - No lorazepam or haloperidol detected in any sample; diphenhydramine in very small, variable amount
- Study 2
  - Randomized, double-blind, placebo-controlled, crossover, noninferiority clinical trial
  - Difference in nausea score on 0-10 scale at baseline and 60 minutes
  - ABH gel vs. placebo
  - Placebo group noninferior to intervention group

Smith TJ, et al. J Pain Symptom Manage 2012;43:961-966.
Fletcher DS, et al. J Pain Symptom Manage 2014;48:797-803.

Diclofenac

- Available formulations
  - –1% (Rx, OTC) topical gel
    - 32 g/day over all affected joints; 16 g/day to any single joint of the lower extremities; 8 g/day to any single joint of the upper extremities
  - –1.5%, 2% topical solution (Rx)
    - **1.5%** - Apply 10 drops topically and spread around front, back, and sides of each affected knee; repeat until 40 drops have been applied; apply 4 times daily
    - **2%** - Apply 40 mg (2 pump actuations) topically to affected knee 2 times a day
  - –1.3% transdermal patch (Rx)
    - Apply one 1.3% topical system (180 mg) to the most painful site twice daily





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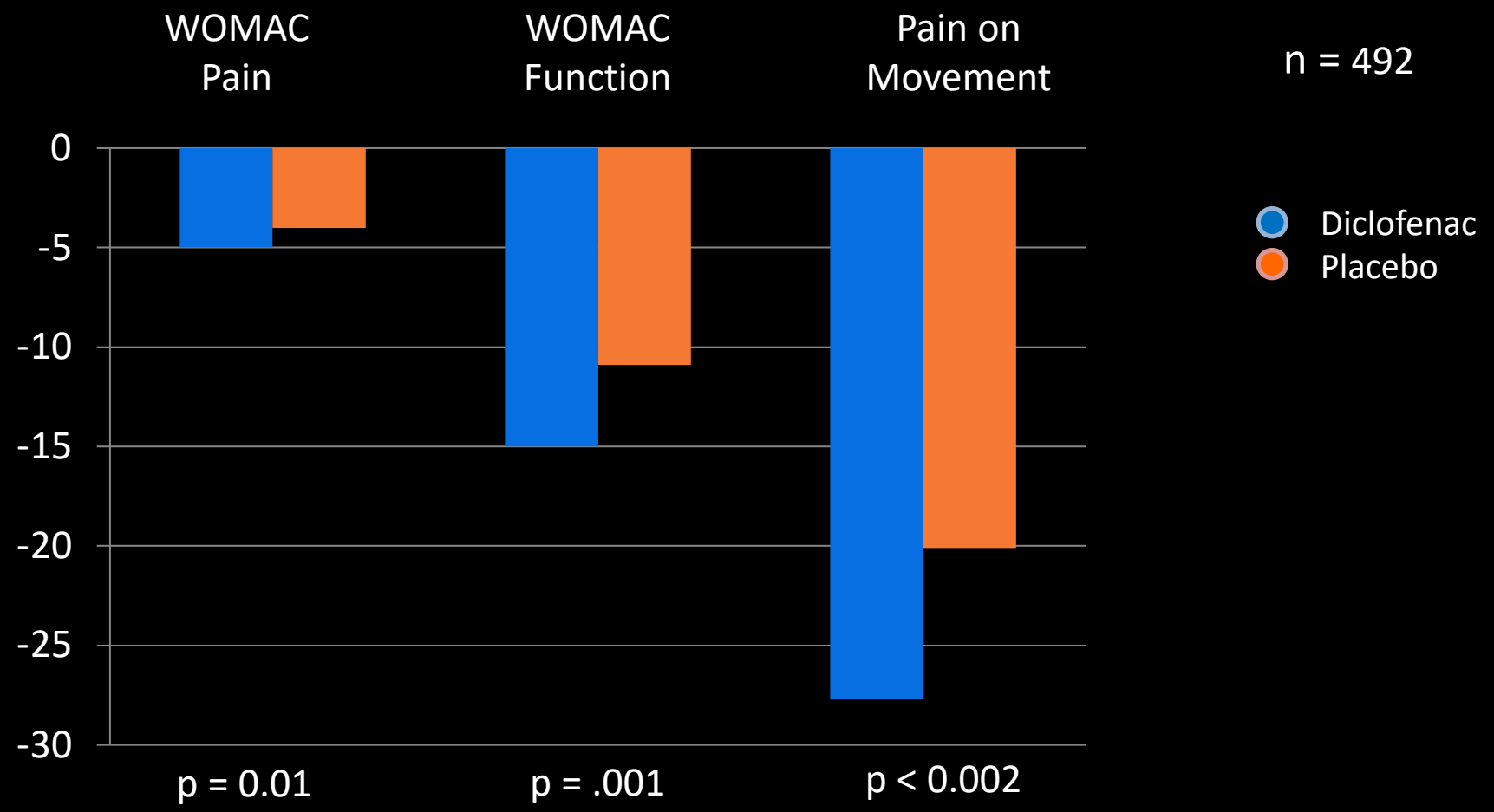
DOI 10.1002/acr.24131

Diclofenac gel (Voltaren® Gel) in OA of the knee



PAINWEEK®

Barthel HR, Haselwood D, Longley S 3rd et al. Semin Arthritis Rheum. 2009; 39(3):203-12.

Topical Cannabinoids

- Transdermal CBD has been shown to reduce inflammation and pain-related behaviors in rat models of arthritis
- Potential applications in wound care
  - THC and CBD are lipophilic compounds
  - Readily absorbed through all classes of cutaneous wounds
  - Case series of patients with pyoderma gangrenosum
    - Topical THC/CBD oil
    - Clinically significant pain reduction in 2/3 patients
    - Opioid sparing effect

Hammell DC, et al. Eur J Pain 2016;20(6):936-48.
Maida V, et al. J Pain Symptom Manage 2017;54(5):732-36.

Mucositis

- What does the data show?
  - Despite its prevalence, data does not support the use of magic mouthwash
    - RCT comparing the efficacy of 3 mouthwashes (chlorhexidine, salt and soda, and magic mouthwashes, including lidocaine, diphenhydramine, and aluminum hydroxide) found no difference in pain rating or time to cessation of symptoms
    - Lack of standardization - no set formula, compounded differently by individual pharmacies
    - Lidocaine and alcohol can cause oral numbness and dysgeusia
    - Unnecessary exposure to antimicrobials and steroids
- Common compounds
  - 2% morphine mouthwash
    - 20 mg morphine sulfate diluted in 100 ml of water
    - 10 ml po q3h PRN
  - Ketamine 4 mg/ml in artificial saliva or flavored drink (oral rinse)
  - Doxepin mouthwash

Wound Pain

- Topical opioids
  - Topical 0.1% morphine gel
    - Add 1 ml of 10 mg/ml morphine injection solution to 8 g hydrogel in a plastic container, thoroughly mix (final concentration 1 mg/ml)
    - After cleansing, apply the gel mixture directly to the exposed tissue of the wound or apply to clean gauze and firmly apply to the wound
    - Apply 2-3 times daily or with every dressing change
- Topical ketamine
  - Topical 1% ketamine gel

Intranasal Ketamine

- Pharmacokinetics
  - Bioavailability ~50% following nasal administration
  - Time to Cmax 20-40 minutes
  - $T_{1/2}$ 7-12 hours
- Many potential advantages over oral/IV dosing
- Data supporting its use in the ED
- Potential role in cancer-related pain

PAINWEEK®

Getting the drug into the patient: Exploring alternate routes of medication administration

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