MAYO CLINIC

To taper or not to taper opioids: is that the only question?

Linda Huang, PharmD, BCPS
PGY-2 Pharmacy Resident in Ambulatory Care
Rochester, MN

Learning Objectives

- Identify indications to consider opioid tapering in chronic pain patients
- Compare potential opioid tapering strategies for patients with chronic pain using a patient case
- Describe considerations for successful opioid tapering

Introduction to Patient

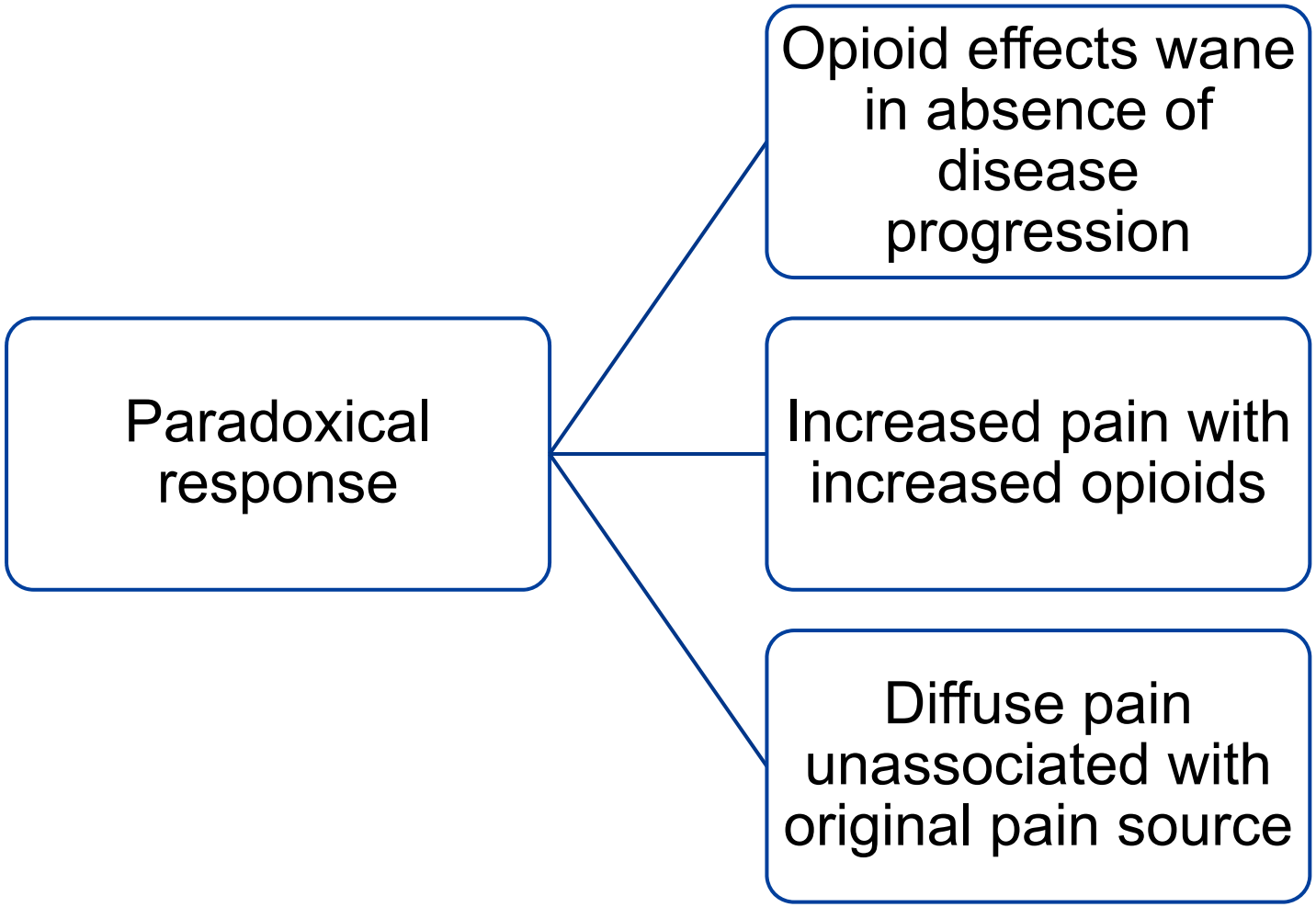
- 40 year old female presenting to pain rehabilitation clinic with complaints of back and joint pain for 7 years
- Complex medical history:
  - Over 20 medical diagnosis
  - Sees 8 different specialists
  - Highly resistant to medication changes
- Current opioid medications:
  - Oxycodone ER 15mg every 12 hours
  - Oxycodone 5 mg 3 times daily

Current Role of Opioids in Chronic Pain

- Opioid have serious side effects but provide effective pain management
  - Most evidence for short term (< 12 weeks) nociceptive and neuropathic pain
  - Limited evidence for chronic, non-cancer pain
- CDC opioid guidelines have limited information on how to taper opioids

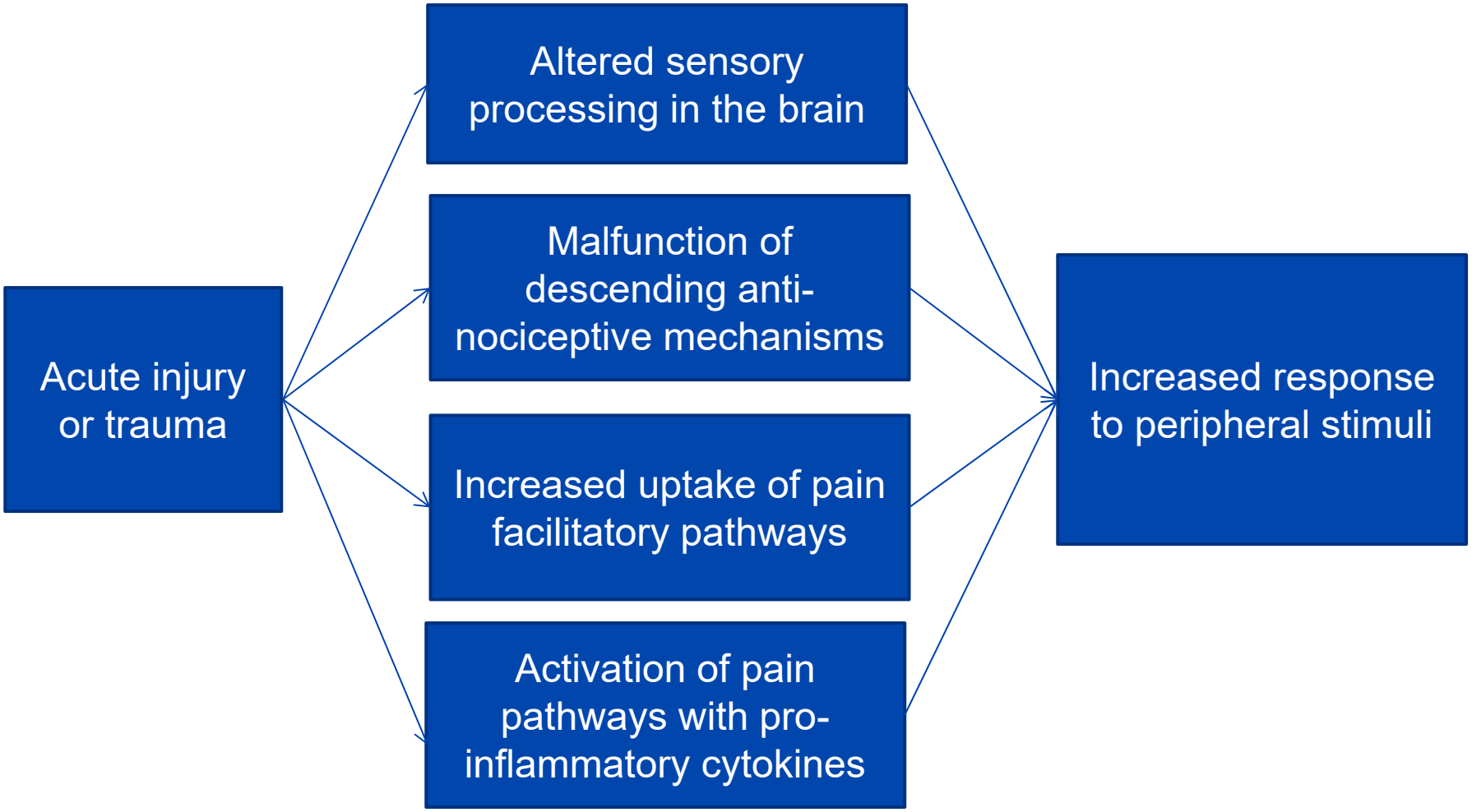
Noble M, Treadwell JR, Tregear SJ, et al. Cochrane Database Syst Rev. 2010;1:CD006605.
Dowell D, Haegerich TM, Chou R. *JAMA*. 2016; 315(15), 1624-1645.

Opioid Hyperalgesia



Brush DE. *Journal of Medical Toxicology. 2012; 8*(4), 387-392.
Lee MM, Silverman MS, et al. Pain physician. 2011; 14, 145-161.

Central Sensitization



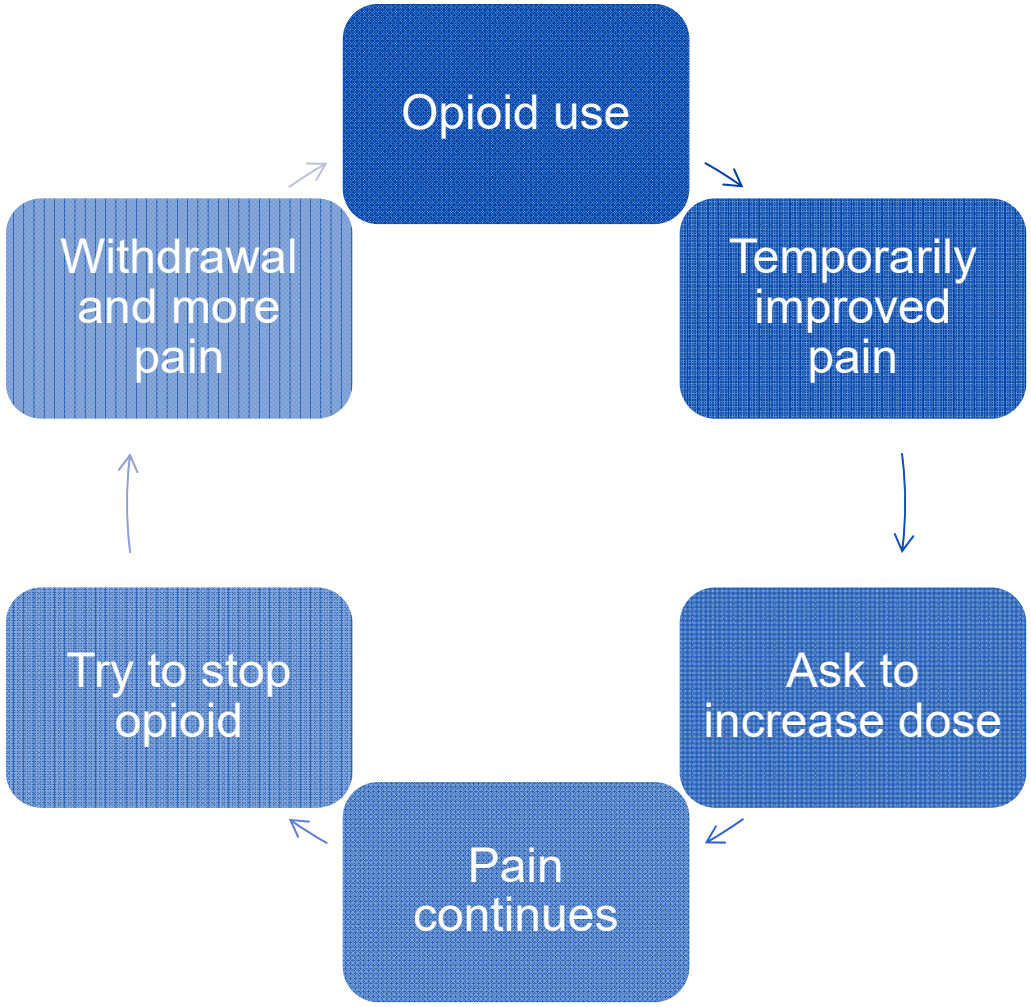
Nijs J, Van Houdenhove B, RA Oostendorp. Man Ther. 2010;15(2):135-141
van Wilgen CP, Keizer D. Pain Management Nursing. 2012;13(1), 60-65.

Diagnosis associated with Central Sensitization

Medical Diagnosis	Characteristic of Disorder	Present in subgroup
Chronic low back pain		X
Temporomandibular disorders		X
Chronic whiplash	X	
Myofascial pain syndrome		X
Osteoarthritis		X
Rheumatoid arthritis		X
Fibromyalgia	X	
Chronic fatigue symptom	X	
Postural orthostatic tachycardia syndrome	X	
Chronic headache		X
Irritable bowel syndrome	X	

Nijs J, Van Houdenhove B, RA Oostendorp. Man Ther. 2010;15(2):135-141

Cycle of Opioid Dependence



Department of Veterans Affairs. VA/DoD Clinical Practice Guideline for Opioid Therapy for Chronic Pain. 2017.

Opioid Tapering Indications

- No relief or functional improvement
- Deterioration in function
- Adverse effects
- Pain improvement or resolution
- Nonadherence with opioid agreement
- Concurrent high risk medications or comorbidities
- Prolonged treatment with unclear benefit-harm balance

Dowell D, Haegerich TM, Chou R. *JAMA*. 2016; 315(15), 1624-1645.
HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics. 2019.

Question

- Which of the following scenarios would NOT be an indication for considering opioid tapering to a patient?
  - A. Filling opioids from other providers seen on PDMP
  - B. Complains that oxycodone makes them feel “put under”
  - C. Stable pain management with low dose opioids with maintained functional improvement
  - D. Upcoming surgery to address pinched nerve

Morphine Milligram Equivalence (MME)

Opioid	Conversion Factor
Codeine	0.15
Fentanyl transdermal	2.4
Hydrocodone	1
Hydromorphone	4
Morphine	1
Oxycodone	1.5
Tapentadol	0.4

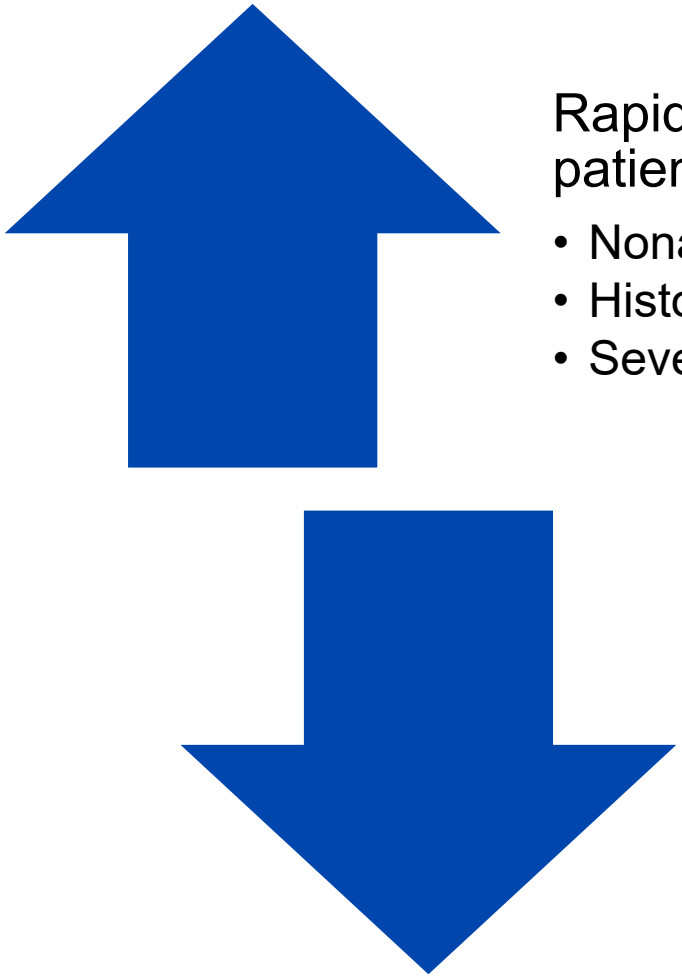
Dowell D, Haegerich TM, Chou R. *JAMA*. 2016; 315(15), 1624-1645.

Examples of Opioid Tapering Recommendations

Veterans Affairs Slow Taper	• 5-20% reduction every 4 weeks
Veterans Affair Fast Taper	• 5-20% reduction every week
Canadian Guidelines	• Start taper at 10% of total daily dose every 1-14 days • Slow taper to half the previous rate once one-third of original dose is reached
Berna C, et al.	• 10% decrease of the original dose every 5 to 7 days until 30% of the original dose • Then weekly decrease by 10% of the remaining dose

Department of Veterans Affairs. VA/DoD Clinical Practice Guideline for Opioid Therapy for Chronic Pain. 2017.
Berna C, Kulich RJ, Rathmell JP. Mayo Clinic Proceedings 2015; 90 (6) 828-842)
Kahan M, Wilson L, Mailis-Gagnon A, Srivastava A. *Can Fam Physician*. 2011;57(11):1269-76, e419-28.

Factors Impacting Rate of Taper



Rapid tapers may be indicated in high risk patients

- Nonadherence or risky behaviors
- History of substance abuse or overdose
- Severe co-morbidities

Gradual tapers hypothesized to be better tolerated

- Allows patient to adjust to new dose prior to next reduction
- Patient anxiety over decreasing opioids
- Very high daily MME at baseline
- Duration of treatment longer than a year

HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics. 2019.

Opioid Tapering Speed Statistics

- Cohort review of commercial and Medicare Advantage insured patients from 2008-2017
- Patient covariates associated with tapering:
  - Female sex
  - Baseline dose > 300 MMEs/day
- Mean maximum dose reduction was 27.6% per month
- 18.8% of patients had a maximum tapering rate exceeding 40% per month

Fenton JJ, Agnoli AL, et al. *JAMA network open*. 2019; *2*(11), e1916271-e1916271.

Opioid Taper Prescribing Recommendations

Prescribe for short intervals frequently

Maintain dose for adverse symptoms, decreased function, or significant worsening of pain or mood

Addressing increased risk for overdose if abruptly return to previously prescribed higher dose

- Consider need for naloxone

Kahan M, Wilson L, Mailis-Gagnon A, Srivastava A. *Can Fam Physician*. 2011;57(11):1269-76, e419-28.
HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics. 2019.

Additional Opioid Considerations

Fentanyl or buprenorphine Patches	• Decrease by smallest increment available • Can utilize two patch strengths to reach appropriate MME daily dose
Extended release versus immediate Release	• Lack of trials comparing tapering success • Extended release agents are associated with higher risk of overdose
Rescue “as needed” medications	• May not require tapering if using less than once daily • Consider stabilizing opioid dose prior to taper

Miller M, Barber CW, Leatherman S, et al. JAMA Intern Med. Apr 2015;175(4):608-615.

Patient Directed Tapering Strategies

Darnall BD, et al.

- Reduced median MME from 288 to 150 in 4 months
  - Dose reduced up to 5% for up to 2 dose reductions in month 1
  - In months 2 to 4, reduce dose up to 10% per week
- Clinical follow-up at least monthly

EMPOWER – currently enrolling

- Dose reduce by 5% monthly
- Will have 3 arms: CBT group, peer-led group, taper only

Darnall BD, Ziadni MS, et al. *JAMA internal medicine.* 2018;*178*(5), 707-708.
Darnall BD, Mackey SC, et al. *Pain Medicine*. 2019.

CBT = cognitive behavioral therapy

Tapering Example #1

- Patient taking hydromorphone 4 mg every 6 hours for past month post-surgery. Family history of substance abuse.
  - Total daily MME: 64

Week	1	2	3	4	5
Hydromorphone Dose	4 mg every 8 hours	2 mg every 8 hours	2 mg every 12 hours	2 mg daily	None
MME percent reduction	25%	25%	12.5%	12.5%	12.5%

Tapering Example #2

- Patient taking fentanyl patch 50mcg/hr every 72 hours and 5-325 hydrocodone/acetaminophen every 8 hours PRN for past 10 years. Patient is nervous about decreasing opioids.
  - Total daily MME: 135

Month	1	2	3	5	7	9	11
Fentanyl Dose	37.5 mcg/hr	25 mcg/hr	12.5 mcg/hr	None	None	None	None
Hydrocodone /APAP Dose	1 tablet every 8 hours	1 tablet every 8 hours	1 tablet every 8 hours	1 tablet every 8 hours	1 tablet every 12 hours	1 tablet daily	None
Percent Reduction	22%	22%	22%	22%	4%	4%	4%

Question

- Current opioid medications:
  - Oxycodone ER 15mg every 12 hours
  - Oxycodone 5 mg 3 times daily
- What is an appropriate first step in tapering this patient's medications?
  - A. Continue Oxycodone ER, stop oxycodone
  - B. Decrease Oxycodone ER to 15 mg daily for 1 week, continue oxycodone
  - C. Continue Oxycodone ER, switch to oxycodone 2.5mg 5 times daily for 3 days
  - D. Decrease Oxycodone ER to 15mg in the morning and 10 mg in the evening for 1 month, continue oxycodone

Answer

- Total Daily MME: 67.5
  - Oxycodone ER 15mg every 12 hours
  - Oxycodone 5 mg 3 times daily

Month	1	2	3	4	5	6	7	8	9
Oxycodone ER Morning Evening	 15 10	 10 10	 10 5	 5 5	 5 0	 0 0	 0 0	 0 0	None
Oxycodone dose	5 mg every 8 hours	5 mg every 8 hours	5 mg every 8 hours	5 mg every 8 hours	5 mg every 8 hours	5 mg every 8 hours	5 mg every 12 hours	5 mg daily	None
Percent Reduction	11%	11%	11%	11%	11%	11%	7.5%	7.5%	7.5%

Opioid Withdrawal Symptoms

Early Symptoms* (Hours to Days)

- Anxiety/Insomnia
- Rapid Respirations
- Dilated Pupils

Late Symptoms* (Days to Weeks)

- Fever/Chills
- Muscle Tremors/Aches
- Gastrointestinal Upset
- Autonomic Symptoms

Prolonged Symptoms (weeks to months)

- Irritability/Fatigue
- Bradycardia
- Insomnia
- Decreased body temperature

*Consider use of clinical instruments such as clinical opioid withdrawal scale (COWS)

Wesson DR, Ling W. *J Psychoactive Drugs.* 2003;35(2):253-259
ASAM. National practice guideline for the use of medications in the treatment of addiction involving opioid use. 2015.

Potential Adjuvant Medications for Opioid Withdrawal

Autonomic Symptoms
- Clonidine
- Baclofen, gabapentin, or tizanidine

Anxiety
- Hydroxyzine

Runny nose/eyes
- Diphenhydramine

Muscle Aches
- NSAIDs
- Acetaminophen
- Topical creams/ointments

Insomnia
- Trazodone

Abdominal Cramping
- Dicyclomine

Gowing L, Farrell MF, Ali R, White JM. *Cochrane Database Syst Rev.* 2014;3:Cd002024.
Chou R, Fanciullo GJ, Fine PG, Adler JA, et al. J Pain. 2009;10(2):113-30. DOI: 10.1016/j.jpain.2008.10.008.

Mental Health Considerations

- Treating comorbid psychiatric conditions improve likelihood of tapering success
- Depressive symptoms predict taper dropout
- Referring to behavioral specialist for patients with severe mental illness or are at risk of suicide

Ballantyne JC, Sullivan MD, Kolodny A. Archives of internal medicine. 2012; 172(17), 1342-1343.
HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics. 2019.

Substance Use Disorder

- Psychiatric illness that may require referral to addiction specialist
- Consider using validated screening tools and the DSM-5 criteria to identify candidates
- Should be considered throughout tapering process

Patient Perspectives - Barriers

- Emotional burden
- Fear of medical abandonment
- Lack of provider trust
- Patient perceived functional limitations
- Previous opioid tapering experiences
- Inadequate resources
- Psychological conditions

Frank JW, Levy C, et al. *Pain Medicine.* 2016; *17*(10), 1838-1847.
Henry SG, Paterniti DA, et al. The Journal of Pain. 2019; 20(2), 181-191.
Kennedy LC, Binswanger IA, et al. Pain medicine. 2018; 19(11), 2201-2211.

Patient Perspectives – Improved Experience

- Empathizing with patient's experience
- Preparation for opioid tapering process
- Start taper when patient is ready to "buy in"
- Individualized tapering
- Consider opioid support group

Sullivan MD, Turner JA, et al. *The Journal of Pain*. 2017; *18*(3), 308-318.
Frank JW, Levy C, et al. *Pain Medicine*. 2016; *17*(10), 1838-1847.
Henry SG, Paterniti DA, et al. The Journal of Pain. 2019; 20(2), 181-191.
Kennedy LC, Binswanger IA, et al. Pain medicine. 2018; 19(11), 2201-2211.

Question

- Which of the following should be considered prior to starting opioid tapering in a patient?
  - A. Depression
  - B. Screening for opioid use disorder
  - C. Opioid withdrawal symptom counseling
  - D. Benefit and risk discussion
  - E. All of the above

Look Back on Patient

- In addition to pain, patient had complaints of:
  - Gastrointestinal distress
  - Migraines
  - Poor sleep
  - Dry mouth and eyes
- You have successfully tapered patient off of opioids…

Full Patient Medication List

- Acetaminophen 1000mg every 6 hours as needed for muscle and joint pain
- Albuterol 90mcg/actuation 2 puffs 4 (four) times a day.
- Amlodipine 5mg daily
- Ascorbic acid 1000mg daily
- acetaminophen-aspirin-caffeine 1 tablet every 6 hours as needed for headaches
- Belimumab 200 mg under the skin every 7 days
- Benzocaine 20% mucosal gel use as needed for mouth sores
- Acetaminophen-butalbitol-caffeine 1-2 tablets as needed
- Caffeine 200 mg by mouth daily as needed for migraine.
- Calcium carbonate 750mg 2-4 tablets daily as needed for esophageal discomfort
- Calcium carbonate 600mg with Vitamin D3 500 unit 2 capsules daily
- Citracal Calcium+D Chew 2 tablets daily
- Calcium-vitamin D3-vitamin K 650 mg-12.5 mcg-40 mcg tablet 2 tablets daily.
- Camphor-methyl salicyl-menthol patch daily as needed
- Capsaicin-menthol 0.025-1.25 % adhesive patch daily as needed
- Cetirizine 10mg daily
- Cholecalciferol 2,000 units daily
- Clindamycin 1 % lotion twice daily as needed
- Cyanocobalamin 1,000 mcg tablet daily
- Cyclobenzaprine 5mg twice daily
- Dapsone 100 mg tablet daily
- Diclofenac 4 times daily as needed
- Dicyclomine 40mg twice daily as needed (capsules and suspension
- Diphenhydramine 25 mg capsule daily as needed
- Duloxetine 60mg daily
- Ferrous sulfate 325mg daily
- Fluticasone 50mcg/actuation 2 sprays in both nostrils
- Fluticasone furoate/vilanterol 200-25mcg/actuation 1 puff every morning
- Furosemide 20mg twice daily as needed
- Gabapentin 100mg three times daily
- Ginger root 550mg daily
- Glucosamine/chondroitin 2000-1200mg/30mL liquid take 10mL daily
- Albuterol/ipratropium 0.5-2.5mg/3mL nebulize as needed
- Ketoconazole 2% cream topically daily
- Lidocaine 4% patch topically as needed
- menthol-methyl salicylate cream topically as needed
- Lidocaine 2% mucosal solution take 5mL daily as needed
- Lifitegrast 5 % ophthalmic solution 1 drop 2 (two) times a day
- Lysine 1000mg 2 times daily
- Magnesium hydroxide 400mg daily
- Magnesium oxide 400mg at bedtime
- Meclizine 25mg as needed for vertigo
- Melatonin 1mg/4mL drops, take 2 mL by mouth at bedtime as needed
- Melatonin 5 mg tablet at bedtime.
- Melatonin-chamomile flower 3-500 mg-mcg tablet at bedtime
- Melatonin+L-Theanine+Botanicals" 1 tablet daily
- Menthol 4% gel apply 4 times daily as needed
- Menthol-camphor gel as needed
- Menthol-zinc oxide apply as needed
- Metronidazole cream two times daily
- Mometasone 0.1% ointment two times daily
- Multivitamin 1 tablet daily
- Mupirocin 2% 3 times daily as needed
- Mycophenolate 200mg/mL suspension take 1500mg 2 times daily
- Nitroglycerin 0.4 mg sublingual tablet as needed
- Nortriptyline 25 mg capsule at bedtime
- Nystatin 100,000 unit/gram ointment 3 times daily
- Nystatin 100,000 unit/mL suspension, take 500,000 Units 4 (four) times a day.
- Olopatadine 0.1 % ophthalmic solution 1 drop into both eyes 2 times daily
- Fish oils 1200mg daily
- Ondansetron 8mg every 8 hours as needed
- Pantoprazole 40mg twice daily before meals
- Peg 400-propylene glycol ophthalmic solution 4 times daily as needed
- Prednisone 20mg daily
- Pregabalin 225mg 2 times daily
- Promethazine 25mg every 6 hours as needed
- Pseudoephedrine 120mg every 12 hours
- Ranitidine 300mg 2 times daily
- Rizatriptan 10mg as needed
- Saliva stimulant gel as needed
- Simethicone 125mg 4 times daily as needed
- Sucralfate 1g 4 times daily (oral and liquid)
- Sumatriptan 50mg daily as needed
- Tizanidine 4mg three times daily
- Triamcinolone 0.1% cream 2 times daily
- Tumeric 550mg daily
- Umeclidinium 62.5 mcg/actuation 1 puff daily
- Vitamin B12/CoQ10/Goji Berry vitamin daily
- GABA/Lemon Balm/L-theanine vitamin daily
- “Nerve” vitamins – 8 tablets twice daily
- Probiotic 4 tablets at bedtime
- Xylitol 550 mg buccal tablet daily

Patient's medications related to complaints

- Acetaminophen 1000mg every 6 hours as needed for muscle and joint pain
- Acetaminophen-aspirin-caffeine 1 tablet every 6 hours as needed for headaches
- Acetaminophen-butalbitol-caffeine 1-2 tablets as needed
- Caffeine 200 mg by mouth daily as needed for migraine.
- Camphor-methyl salicyl-menthol patch daily as needed
- Capsaicin-menthol 0.025-1.25 % adhesive patch daily as needed
- Cyclobenzaprine 5mg twice daily
- Diclofenac gel 4 times daily as needed
- Dicyclomine 40mg twice daily as needed (capsules and suspension
- Diphenhydramine 25 mg capsule daily as needed
- Duloxetine 60mg daily
- Gabapentin 100mg three times daily
- Ginger root 550mg daily
- Glucosamine/chondroitin 2000-1200mg/30mL liquid take 10mL daily
- Lidocaine 4% patch topically as needed
- menthol-methyl salicylate cream as needed
- Lifitegrast 5 % eye drops 1 drop twice daily
- Melatonin 5 mg tablet at bedtime.
- Melatonin 1mg/4mL drops, take 2 mL by mouth at bedtime as needed
- Melatonin-chamomile 3-500 mg-mcg tablet at bedtime
- Melatonin+L-Theanine+Botanicals" 1 tablet daily
- Menthol 4% gel apply 4 times daily as needed
- Menthol-camphor gel as needed
- Menthol-zinc oxide apply as needed
- Nortriptyline 25 mg capsule at bedtime
- Olopatadine 0.1 % ophthalmic solution 1 drop into both eyes 2 times daily
- Fish oils 1200mg daily for inflammation
- Peg 400-propylene glycol ophthalmic solution 4 times daily as needed
- Pregabalin 225mg 2 times daily
- Rizatriptan 10mg as needed
- Saliva stimulant gel as needed
- Sumatriptan 50mg daily as needed
- Tizanidine 4mg three times daily
- Turmeric 550mg daily
- Vitamin B12/CoQ10/Goji Berry vitamin daily
- GABA/Lemon Balm/L-theanine vitamin daily
- Xylitol 550 mg buccal tablet daily

Patient's Pain Related Medications

- Acetaminophen
- acetaminophen-aspirin-caffeine
- Camphor-methyl salicyl-menthol patch
- Capsaicin-menthol patch
- Cyclobenzaprine
- Diclofenac gel
- Duloxetine
- Gabapentin
- Lidocaine 4% patch
- Menthol cream
- menthol-methyl salicylate cream
- Menthol-camphor gel
- Nortriptyline
- Pregabalin
- Rizatriptan
- Sumatriptan
- Tizanidine

Patient Follow-Up

- Discussed medications' relation to pain management
  - Potential of improved pain now that off of opioids
  - Presence of central sensitization
- Discussed relationship of pain to other medication related diagnosis
  - Possibility of medication induced migraines
  - Decrease polypharmacy

Medications Stopped

Pain/Sleep Medications

- Acetaminophen
- Cyclobenzaprine
- Tizanidine
- Nortriptyline
- Melatonin

Migraine Medications

- Acetaminophen-bultabitol-caffeine
- Sumatriptan

Tapering off:

- Lorazepam
- Gabapentin
- Pregabalin

Vitamins/Supplements Used for Pain

- Turmeric
- Fish oils
- Ginger Root

Over the counter Medications

- Topical benzocaine and menthol products
- Lidocaine cream and patches

Re-evaluate need for:

- Eye drops for dry eyes
- Salivating tablets

Takeaway Points

- Conduct thorough review of patient indications for tapering off of opioids
- Dedicate time to have an open conversation with patients regarding their pain medication regimen
  - Counsel on potential of having equal or less pain without opioids
- Utilize adjuvant medication therapy appropriately

Questions & Discussion