PHARMACOLOGICAL APPROACHES TO TREATING CHRONIC PAIN IN THE PRIMARY CARE SETTING

WE'RE ALL FAMILY (MEDICINE) CONFERENCE
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LEARNING OBJECTIVES AND DESCRIPTION

- Evaluate chronic pain complaints, including assessing risk for substance use and screening for mental health
- Explore the various pharmacologic treatment options for chronic pain including opioid and non-opioid options with a review of the CDC Guidelines
- Understand the PA role in medications for opioid use disorder (MOUD)

PAs in all fields are challenged by the complaint of pain. As we work in fields with objective measures, the subjective assessment and treatment of pain is challenging, made even more so as we find ourselves caught between wanting to help people feel better, patient satisfaction metrics, the exploding opioid epidemic, and state and federal guidelines regarding opioid prescriptions. This presentation is geared towards helping primary care PAs navigate the murky waters of pain management with attention screening for other health conditions, utilization of non-opioid pain relievers, and the basics of opioid medication management. There will also be a brief discussion of opioid use disorder and medications for treatment. This presentation is meant to be a companion to the *Non-Pharmacologic Approaches to Treating Chronic Pain in the Primary Care Setting* lecture.

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PAIN

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BASICS

- Central Nervous System (CNS)
  - Brain and Spine
- Peripheral Nervous System (PNS)
  - Thermoreceptors → temperature
  - Photoreceptors → light
  - Chemoreceptors → chemical
  - Mechanoreceptors → pressure, touch, proprioception, vibration
  - Nocioceptors → pain

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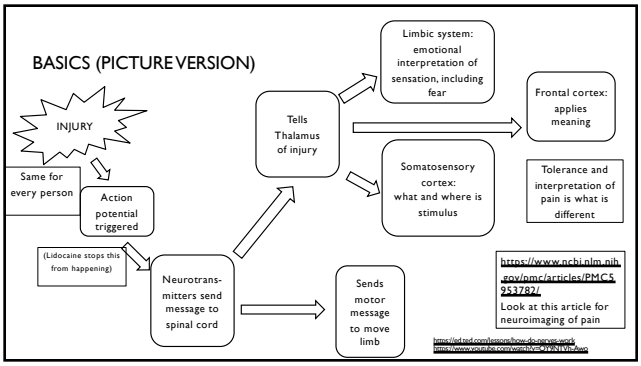
BASICS (PICTURE VERSION)



https://ed.ted.com/lessons/how-do-nerves-work
https://www.youtube.com/watch?v=2VXNYVh4wo

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BASICS (TEXT VERSION)

1. If sensory receptors in the skin detect pain or a change in temperature, they transmit an impulse (signal), which ultimately reaches the brain.
2. The impulse travels along a sensory nerve to the spinal cord.
3. The impulse crosses a synapse (the junction between two nerve cells) between the sensory nerve and a nerve cell in the spinal cord.
4. The impulse crosses from the nerve cell in the spinal cord to the opposite side of the spinal cord.
5. The impulse is sent up the spinal cord and through the brain stem to the thalamus, which is a processing center for sensory information, located deep in the brain.
6. The impulse crosses a synapse in the thalamus to nerve fibers that carry the impulse to the sensory cortex of the cerebrum (the area that receives and interprets information from sensory receptors).
7. The sensory cortex perceives the impulse. A person may then decide to initiate movement, which triggers the motor cortex (the area that plans, controls, and executes voluntary movements) to generate an impulse.
8. The nerve carrying the impulse crosses to the opposite side at the base of the brain.
9. The impulse is sent down the spinal cord.
10. The impulse crosses a synapse between the nerve fibers in the spinal cord and a motor nerve, which is located in the spinal cord.
11. The impulse travels out of the spinal cord along the length of the motor nerve.
12. At the neuromuscular junction (where nerves connect to muscles), the impulse crosses from the motor nerve to receptors on the motor end plate of the muscle, where the impulse stimulates the muscle to move.

https://ed.ted.com/lessons/how-do-nerves-work
https://www.youtube.com/watch?v=2VXNYVh4wo

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TYPES OF PAIN

- Acute pain < 3-6 months, Chronic pain > 6 months
  - But different 'cut offs' depending who you ask
  - Acute: focus on treating source
  - Chronic: addressing effects/improving functionality
- Difference not really not well understood
  - Likely a spectrum

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2787756/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4731442/

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TYPES OF CHRONIC PAIN

- Nociceptive
  - Pain related to damage of somatic or visceral tissue
    - Ex: Arthritis
- Neuropathic
  - Pain related to damage of peripheral or central nerves
    - Ex: postheraptic neuralgia, diabetic neuropathy
- Nociplastic/hyperalgesic priming
  - Pain without identifiable nerve or tissue damage
    - Ex: fibromyalgia, IBS

Some forms of chronic pain can have components of all three

https://www.sciencedirect.com/science/article/pii/S1521694219300610
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2787756/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3217302/

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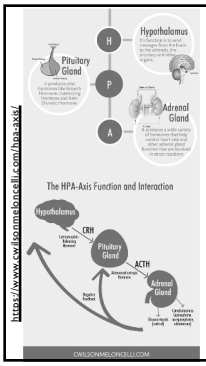

https://www.cwilsonmeloncell.com/hpa-axis/

BRIEF TANGENT: HPA

- Hypothalamus- Pituitary- Adrenal feedback loop
- Stress response
- With chronic stress→ linked to many long-term health issues
- Potential predisposition to chronic pain
- Adverse Childhood Experiences Study

2 Min Neuroscience: HPA Axis https://www.youtube.com/watch?v=QAeBKRaNri0

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DESCRIBE A MULTIMODAL APPROACH TO PAIN MANAGEMENT

ASSESS. MANAGE. MONITOR.

www.cdc.gov GUIDELINE FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN

https://www.cdc.gov/drugoverdose/providers/index.html

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WORLD HEALTH ORGANIZATION

- "…*WHO is deeply concerned about the opioid overdose crisis in the USA and about the risks and harms that can arise anywhere in the world from the misuse of medicines for pain management, including opioids. At the same time, WHO is well aware that in low- and middle-income countries, access to medicines for moderate and severe pain control remains very low. The Organization is fully committed to ensuring that children as well as adults with severe pain have access to effective pain control medication, including opioids when needed.*"
- Currently in process of revising guidelines for availability of controlled medicines and for pain control

  **Still in process*

https://www.who.int/news-room/detail/27-08-2019-who-revision-of-pain-management-guidelines

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APPROACH TO PAIN MANAGEMENT

CDC Guidelines

1. Nonpharmacologic and nonopioid treatments first
2. Treatment goals including realistic expectations – you won't be pain free
3. Before starting and periodically review risks/benefits
4. Start with immediate release first
5. Stay <50 MME, must justify >90 MME
6. Acute pain treatment: 7d or less of opioids
7. Chronic pain treatment: risk/benefit evaluation, consider tapering
8. Frequently evaluate risk for opioid related harm
9. PDMP review
10. Urine drug testing
11. Avoid opiates + benzos
12. Offer or refer for buprenorphine or methadone for those with OUD

https://www.cdc.gov/drugoverdose/pdf/prescribing/Guidelines_Factsheet-a.pdf

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ASSESSING PAIN

- Growing concern that the more we focus on pain, the "more pain" people have
  - Push to move from numeric scores, to functional pain score
- Acknowledge that in the past, didn't talk about psychosocial impact

Interesting podcast on reducing pain:
https://www.npr.org/2019/03/06/700743108/the-fifth-vital-sign

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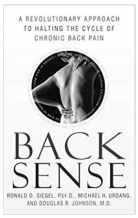
STARTING THE ASSESSMENT: ACT UP

- **Activities**: how is your pain affecting your life (i.e. sleep, appetite, physical activities, and relationships)?
- **Coping**: how do you deal/cope with your pain (what makes it better/worse)?
- **Think**: do you think your pain will ever get better?
- **Upset**: have you been feeling worried (anxious)/depressed (down, blue)?
- **People**: how do people respond when you have pain?



www.BackSense.org

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3841375/

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ASSESS FOR UNDERLYING DISEASE

- Rheumatologic evaluation
  - ESR/CRP, CPK, ANA, RF
- Infectious rule out (partly for source, partly owing to treatment)
  - HIV, RPR, Lyme, Hepatitis C, HSV, EBV
- Thyroid
- Vitamin
  - D, B12
- EMG/Nerve Conduction
- Muscle biopsy
- X-Ray
- CT
- MRI

Remember that imaging ≠ pain
~30% of 20yos have asymptomatic back pathology*

https://www.practicalpainmanagement.com/resources/diagnostic-tests/guide-chronic-pain-assessment-tools
https://www.mdedge.com/familymedicine/article/88929/musculoskeletal-disorders/suspect-smoothly-sike-approach-work
https://knowbook.com/rheumpain/ChronPainEdm.htm * https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4464799/

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FACTORS ASSOCIATED WITH CHRONIC PAIN

Modifiable

- Mental health
- Medical co-morbidities
- Smoking
- Alcohol
- Obesity
- Physical activity level
- Sleep
- Nutrition
- Employment status

Non-Modifiable

- Age
- Sex (F>M)
- Cultural background
- Socioeconomic status
- History of trauma (ACEs)
- Heritable factors (including genetics and epigenetics)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4590163/

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MEDICATIONS FOR PAIN

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WHERE DO THE DRUGS WORK

https://www.researchgate.net/figure/Therapeutic-modulation-of-the-pain-processing-pathway-Abbreviations-NMDA_fig1_315934301

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MEDICATIONS: FIRST START

- Acetaminophen
- NSAIDs/COX-2 inhibitors
- Antidepressants- Dose same range as would to treat mental health complaints
  - Tricyclics (TCAs)
  - SNRIs
    - Duloxetine (Cymbalta) is the only MH med FDA approved for pain related complaint
  - NDRI (Buproprion)
  - SSRIs
    - Less efficacy for pain, better if associated MH complaint

https://www.cdc.gov/drugoverdose/training/nonopioid/index.html, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2729622/, https://www.practicalpainmanagement.com/treatments/pharmacological/non-opioids/use-antidepressants-multimodal-pain-management

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MEDICATIONS: FIRST START

- Anticonvulsants: all used for migraine prophylaxis for years as well as neuropathic pain
  - Gabapentin: 1800-3600mg total daily dose;
  - Pregabalin: 50-600mg total daily dose
  - Increasing rates of abuse of gabapentin in particular
- Topical agents: Lidocaine, Capsaicin, Topical NSAIDs
- Interventional approaches
  - Epidural or intraarticular glucocorticoid injections
  - Arthrocentesis
  - Trigger point injections
    - You can do this!

https://www.cdc.gov/drugoverdose/training/nonopioid/index.html, https://www.cochrane.org/CD007938/SYMPT_gabapentin-chronic-neuropathic-pain-adults, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3161452/, https://www.nejm.org/doi/full/10.1056/NEJMp1704631 - reviews concerns about increasing Rx rates

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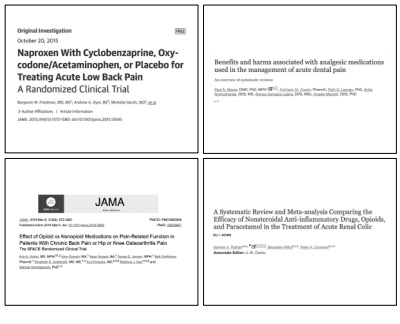
ALL STUDIES SHOWING NSAIDS +/- APAP DO BETTER THAN OPIOIDS

But it's the 'branding' effect



Original Investigation

October 20, 2015

Naproxen With Cyclobenzaprine, Oxycodone/Acetaminophen, or Placebo for Treating Acute Low Back Pain

A Randomized Clinical Trial

Benefits and harms associated with analgesic medications used in the management of acute dental pain

An overview of systematic reviews

JAMA

Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain

The SPACE Randomized Clinical Trial

A Systematic Review and Meta-analysis Comparing the Efficacy of Nonsteroidal Anti-inflammatory Drugs, Opioids, and Paracetamol in the Treatment of Acute Renal Colic

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NOVEL THERAPEUTICS

- Alternatives to Opioids (ALTO)
  - Acute pain management in ED setting
  - http://www.painfree-ed.com/
- Ketamine
  - Evidence for some pain conditions, concerns about lack of standardization with infusion clinics
    - Consensus guidelines exist https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6023575/

PAIN CONDITION	MEDICATION
Headache/Migraine	1. Prochlorperazine 10 mg IV or Metoclopramide 10 mg IV + Diphenhydramine 25-50 mg IV 2. Repeat dose of either medication in Step 1 with Step 3 3. Ketorolac 15 mg IV or Ibuprofen 600-800 mg PO and/or Acetaminophen 1000 mg PO 4. Sumatriptan 6 mg SQ or 25-50 mg PO 5. Magnesium 2g IV over 60 min 6. Dexamethasone 10 mg IV 7. Rescue therapy: Ketamine per protocol or 8. Haloperidol 3-5 mg IM/IV 9. Consider Valproate Sodium 1000 mg IV x 1 in conjunction with neurology consultation *Recommend waiting 45 min – 1 hour between therapies
Back Pain	1. Ketorolac 15 mg IV or Ibuprofen 400-800 mg PO 2. Acetaminophen 1000 mg PO 3. Lidocaine 5% topical patch to most painful area 4. Dexamethasone 10 mg IV or PO 5. Trigger point injection 2 mg lidocaine 2% + Bupivicaine .5% 1:1 mix IM in site of maximal pain 6. Ketamine 0.3 mg/kg IVPB over 20 min, then continuous drip 0.15 mg/kg/hr x 1-2 hours if needed 7. Gabapentin 300mg-600mg (if neuropathic component) *Any of the above therapies can be combined except giving ketamine and lidocaine concomitantly
Renal Colic	1. Ketorolac 15 mg IV 2. Lidocaine 2% 1.5 mg/kg IBW IV over 10- 20 min 3. Acetaminophen 1000mg PO 4. Ketamine per protocol
Undifferentiated Abdominal Pain	1. Ketorolac 15 mg IV 2. Dicyclomine 20 mg PO 3. Acetaminophen 1000 mg PO 4. Reglan 10 mg IV (may help with nausea/cramping in gastroparesis, cyclic vomiting) 5. Haloperidol 2.5-5 mg IV/IM (may help with nausea/cramping in gastroparesis, cyclic vomiting) 6. Topical capsaicin or methylsalicylate/menthol cream to abdomen (may be beneficial in cyclic vomiting, cannabis induced hyperemesis) 7. Ketamine 0.3 mg/kg IVPB over 20 min, then continuous drip 0.15 mg/kg/hr x 1-2 hours if needed 8. Lidocaine 2% 1.5 mg/kg IBW IV over 10- 20 min
Dental Pain	1. Ketorolac 15 mg IV or Ibuprofen 600-800 mg PO 2. Acetaminophen 1000 mg PO 3. Dental nerve block: 1-2ML lidocaine 2% + Bupivicaine 0.5% 1:1 mix

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OPIOIDS FOR PAIN CONTROL

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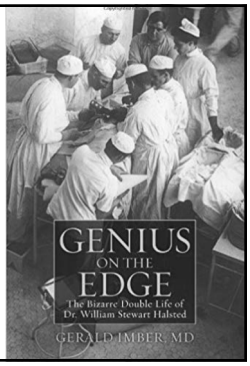
OPIOIDS VS NARCOTICS

- Chemical class: Opioid vs opiate
- Opiates are from poppy plants
- Opioid means they act like an opiate
- Functional class: Narcotic analgesic
- Opium → Morphine → Heroin (to get off morphine)



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BEFORE STARTING OPIOIDS

- Discussion of risks/benefits
  - Review that unlikely to be ever pain free
  - Set functional treatment goals
    - Not recommended for diffuse muscle pain like fibromyalgia or chronic migraine (1)
- Screen EVERYONE for risk factors
  - Including short term use, planned surgery, pregnant
  - **Problem: what to do if they screen positive?** (2)

1- https://accpl.org/pdfs/documents/publications/jpeariforpractice/CoreEntrustables-Opioid-Therapy-Acute-Chronic-Pain-jcph1276.pdf
2- https://www.drugabuse.gov/nidamed-medical-health-professionals/science-to-medicine/screening-substance-use/in-pain-management-setting
Image from https://www.practicalpainmanagement.com/resource-centers/opioid-prescribing-monitoring/risk-assessment-safe-opioid-prescribing-tools

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OPIOID "CONTRACT"

- Single pharmacy for all meds
- No prescriptions from other providers
- ROI for all providers
- Can go to ER for treatment of acute pain
  - But can't be discharged with pain Rx
- Random drug screens
- Pill counts
- PDMP review
- Involvement in psychosocial support programs

*marijuana positive on tox screens(?)

https://www.drugabuse.gov/sites/default/files/SamplePatientAgreementForms.pdf

https://www.fda.gov/media/114694/download

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KEEP IN MIND

- Opiates metabolized by cytochrome P450 pathway, primarily CYP3A4 and CYP2D6 enzymes
  - Methadone involves 6 different enzymes
  - Codeine and Tramadol contraindicated in under 12yo in part because of this
  - Remember that Tramadol has serotonergic properties
- FDA also calls attention to opiate naïve vs tolerant
  - No long-acting meds for opiate naïve (e.g. OxyContin, patches, methadone)
  - Define tolerant as having been on one of the following for >1wk
    - 60mg oral morphine/day, 25mcg fentanyl patch/hour, 30mg oxycodone/day, 60mg hydrocodone/day, 8mg hydromorphone

https://accpl.org/pdfs/documents/publications/jpeariforpractice/CoreEntrustables-Opioid-Therapy-Acute-Chronic-Pain-jcph1276.pdf, https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-restricts-use-prescription-codeine-pain-and-cough-medicines-and, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2704133/

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START LOW, GO SLOW

- Start with immediate-release/short acting opioids first- less risk of unintentional overdose
- Lowest possible dose, for shortest possible duration of action
- Really want less than 50 MME
- Everyone with opioid prescription should also get prescription for naloxone
  - They don't have to fill it

Washington State Interagency Guide on Prescribing Opiates for Pain
http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf

Miller, et al. Prescription opioid duration of action and the risk of unintentional overdose among patients receiving opioid therapy. JAMA. 2015.
https://pubmed.ncbi.nlm.nih.gov/25686208/

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MME

- Morphine Milligram Equivalents
- Calculate dose of all pain meds
- Per CDC, keep daily MME <50; must justify >90MME
- Use MME to help when changing between meds
- Remember, you can prescribe methadone and buprenorphine for PAIN ONLY

https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf

https://www.aafp.org/dam/AAFP/documents/patient_care/pain_management/conversion-table.pdf

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MED = Morphine Equivalent Dose

http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf

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LONG-ACTING OPIATES

- Limited evidence that long acting actually do a better job of pain control
  - May work better for some patients but not all
  - Easier dosing regimen, but different pharmacokinetics
  - Higher risk of overdose if misused (crushed, snorted, chewed, extra dose)
- May still need immediate-release meds for breakthrough pain.
  - Doses should provide approximately 5% to 20% of the total daily dose or 25% to 30% of the single-standing dose.

https://pcoa.org/pdf/documents/publications/pearls/practice/CoreEntrustables-Opioid-Therapy-Acute-Chronic-Pain-ceh1276.pdf
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1069064/

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STICKY POINT

- Want patient to use Acetaminophen/Ibuprofen for primary pain control and opioids only for more severe pain
- Hydrocodone – only comes with acetaminophen or ibuprofen
- Oxycodone – Most euphoric but comes by itself
- Morphine IR – probably best BUT more 'flags' when prescribing

Note: pediatric patients should NEVER get codeine or tramadol products

https://emergencymedicinecases.com/opioid-misuse-emergency-medicine/
https://pediatrics.aappublications.org/content/138/5/e20161742
https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-restricts-use-prescription-codeine-pain-and-cough-medicines-and

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CURRENT OPIOID MISUSE MEASURE (COMM)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2955853/

MONITORING TREATMENT

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URINE DRUG SCREENS

- Point of Care (POC)
  - Variety of tests, different sensitivities/specificities
- Confirmatory
  - Remember, you want a POSITIVE test for meds pt is prescribed
  - Gas chromatography-mass spectrometry needed to confirm positive tests (e.g. employment, probation)
- Faked samples
  - Witnessed collections, pH, specific gravity, creatinine

https://www.drugabuse.gov/sites/default/files/files/UrineDrugTesting.pdf
https://www.mdedge.com/familymedicine/article/159567/addiction-medicine/how-accurate-are-point-care-urine-drug-screens
https://www.mayoclinicproceedings.org/article/S0025-6196(11)61120-8/fulltext

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Drug	How soon after taking drug will there be a positive drug test?	How long after taking drug will there continue to be a positive drug test?
Marijuana/Pot	1-3 hours	1-7 days *Can be positive for >30 days in heavy users*
Crack (Cocaine)	2-6 hours	2-3 days
Heroin (Opiates)	2-6 hours	1-3 days
Speed/Uppers (Amphetamine, methamphetamine)	4-6 hours	2-3 days
Angel Dust/PCP	4-6 hours	7-14 days
Ecstacy	2 to 7 hours	2 - 4 days
Benzodiazepine	2 -7 hours	1 - 4 days
Barbiturates	2 - 4 hours	1 - 3 weeks
Methadone	3 - 8 hours	1 - 3 days
Tricyclic Antidepressants	8 - 12 hours	2 - 7 days
Oxycodone	1 - 3 hours	1 - 2 days

https://www.fda.gov/medical-devices/drugs-abuse-tests/drugs-abuse-home-use-test

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UDS/TOX SCREEN: FALSE POSITIVE

Drug Tested	Cross-Reactivity
Amphetamines	Atenolol, buproprion, labetalol, ranitidine, trazodone
Barbiturates	Ibuprofen, naproxen, phenytoin
Benzodiazepines	Oxaprozin, Sertraline
Cannabinoids	Ibuprofen, naproxen, pantoprazole
LSD	Amitriptyline, buproprion, buspirone, fluoxetine, haloperidol, metoclopramide, risperidone, sertraline, trazodone, verapamil
Opioids	Amisulpride, fluoroquinolones, quetiapine, rifampicin, verapamil, dextromethorphan
Oxycodone	Codeine, hydrocodone, hydromorphone

https://www.mdedge.com/psychiatry/article/131220/addiction-medicine/strategies-preventing-and-detecting-false-negatives
https://www.uspharmacist.com/article/urine-drug-screening-minimizing-false-positives-and-false-negatives-to-optimize-patient-care
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3505132

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COMPLICATIONS & SIDE EFFECTS OF CHRONIC OPIOID USE

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COMPLICATIONS OF CHRONIC OPIOID USE

- Constipation
- Allodynia
- Hyperalgesia
- Opioid induced androgen (dysfunction)
- Sleep apnea → may cause or exacerbate

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OPIOID INDUCED CONSTIPATION

- GI side effects by κ-receptors in the stomach/small intestine and μ-receptors in the small intestine/proximal colon
- All patients should be on bowel regimen if on opioids
- Peripherally acting μ-opioid receptor antagonists (PAMORAs)
  - Movantike
  - Symproic
  - Relistor

https://www.gastrojournal.org/article/S0016-5085(18)34782-6/fulltext

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ALLODYNIA VS HYPERALGESIA

Allodynia

- Pain in response to non-painful stimulation
- Pain in response to touch and/or temperature and/or movement

https://www.ncbi.nlm.nih.gov/pubmed/19461836
https://www.painphysicianjournal.com/current/pdf?article=MTQ0Ng%3D%3D&journal=60
https://www.youtube.com/watch?v=zfqgi-sWZPQ

Hyperalgesia

- Excessive/increased level of pain to painful stimulation
- E.g. papercut feels like cut finger off
- Opioid Induced Hyperalgesia (OIH)

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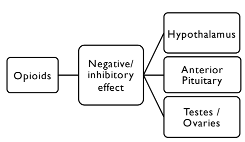
OPIOID-INDUCED ENDOCRINE DYSFUNCTION
OPIOID INDUCED ANDROGEN DEFICIENCY (OPIAD)

- Impacts hypothalamus → gonadotrophin-releasing hormone (GnRH) → alters luteinizing hormone (LH) → alters testosterone // estrogen, progesterone
- Symptoms include infertility, decreased sexual function, loss of muscle mass, mood changes, osteoporosis



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4590093/ https://www.ncbi.nlm.nih.gov/pubmed/27586511
https://www.mascc.org/assets/documents/pain_Impact_Opioids_Endocrine_Katz.pdf
https://d3i71xaburhd42.cloudfront.net/09cf2c10ef79d13186a26bbde8b69d3c45c9e60f/2-Figure1-1.png

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BENEFITS OF WASHOUT

- Opiate free period
- Thought is that it "resets" receptors
- Reduces tolerance so safety component

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STOPPING OPIOIDS

- "If I hurt this bad while on the medicine, how bad will I be off the meds?"
- But if no better after 3 months, likely not going to be any different
- Dose reduction **≤10% every 1-2 weeks**
- Clinical Opioid Withdrawal Scale
- Ultra-rapid detox under sedation NOT recommended
  - But is advertised

FDA cautioned about avoiding abrupt withdrawal 4/2019
https://www.fda.gov/drugs/fda-drug-safety-podcasts/fda-identifies-harm-reported-sudden-discontinuation-opioid-pain-medicines-and-requires-label-changes

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ASSESSING WITHDRAWAL

- Use Clinical Opioid Withdrawal Scale (COWS)
- Similar to CIWA in that free and easy to use

Resting Pulse Rate _____ beats/minute *Measured after patient is sitting or lying for one minute* 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	**GI Upset** *over last 1/2 hour* 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting
Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.* 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	**Tremor** *observation of outstretched hands* 0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds	**Yawning** *Observation during assessment* 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute
Pupil size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	**Anxiety or Irritability** 0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable or anxious 4 patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiate withdrawal is scored* 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	**Gooseflesh skin** 0 skin is smooth 3 piloerrection of skin can be felt or hairs standing up on arms 5 prominent piloerrection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Initials of person completing assessment: _____

Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal

†https://www.dcmhsrtc.psu/sites/default/files/files/ClinicalOpiateWithdrawalScale.pdf

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NEONATAL ABSTINENCE SYNDROME (NAS)

- Recommended against withdrawing from opioids in pregnancy
  - Higher risk of relapse- more dangerous for fetus/infant
  - Not good evidence about medication supervised withdrawal
- In pregnancy- PLAIN buprenorphine (no naloxone) or methadone
- In infant- morphine or methadone is first line (most evidence)

CNS	GI	Autonomic
• Inconsolability • High-pitched crying • Skin excoriation • Hyperactive reflexes • Tremors • Seizures	• Poor feeding • Excessive sucking • Feeding intolerance • Vomiting • Diarrhea	• Sweating • Fever • Nasal stuffiness • Sneezing • Tachypnea • Mottling

Abbreviations: CNS, central nervous system; GI, gastrointestinal

Reports of gabapentin NAS increasing

https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions/Committee-on-Obstetric-Practice/Opioid-Use-and-Opioid-Use-Disorder-in-Pregnancy
https://solutions.aap.org/DocumentLibrary/docwebinars/2017%20Dec%20Neonatal%20Abstinence%20Syndrome.pdf https://www.bmj.com/content/358/bmj.j3326

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RELEVANT LEGISLATIVE HISTORY

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"WAR ON DRUGS"

- Harrison Narcotics Tax Act, 1914
- "An Act To provide for the registration of, with collectors of internal revenue, and to impose a special tax on all persons who produce, import, manufacture, compound, deal in, dispense, sell, distribute, or give away opium or coca leaves, their salts, derivatives, or preparations, and for other purposes."
- Interpreted to mean that physicians could prescribe narcotics to patients in the course of normal treatment, but not for the treatment of addiction, which was not a disease but a **moral failing**

http://www.drugpolicy.org/blog/today-100th-anniversary-harrison-narcotics-tax-act
US v Doremus (1919) https://supreme.justia.com/cases/federal/us/249/86/

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DRUG ADDICTION TREATMENT ACT (DATA) 2000

- Part of the Children's Health Act of 2000, permitted only physicians to prescribe buprenorphine in treatment settings other than OTPs.
  - OTP: Opioid Treatment Program, traditionally "methadone clinics"
- Created DEA X-Waiver
  - Separate number required
  - Only used for buprenorphine (Suboxone) prescriptions **for OUD**
  - Had to have 8 hours of mandated training from federally approved providers
    - ASAM, AAAP, AMA, AOA, APA; later approved AAPA and AANP

https://www.samhsa.gov/medication-assisted-treatment/statutes-regulations-guidelines

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MENTAL HEALTH PARITY AND ADDICTION EQUITY ACT (MHPAEA) 2008

- The Paul Wellstone and Pete Domenici Mental Health Parity and Addiction Equity Act of 2008 (MHPAEA)
- Prevents group health plans and health insurance issuers that provide mental health and substance use disorder (MH/SUD) benefits from imposing less favorable benefit limitations on those benefits than on medical/surgical coverage

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COMPREHENSIVE ADDICTION AND RECOVERY ACT (CARA) 2016

- Grants to FQHCs to improve treatment
- Pharmacists to dispense naloxone
- Expanded DEA-X waiver to PAs/NPs
  - But required 24 hours of specialized CME credit compared to 8hrs for physicians
- Grants for treatment of pregnant/postpartum women

https://www.asam.org/advocacy/issues/opioids/summary-of-the-comprehensive-addiction-and-recovery-act

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ADDICTION

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EVERYONE ON CHRONIC OPIOID PAIN MEDICINE WILL BECOME ADDICTED

BUT DIFFERENCE BETWEEN SUBSTANCE USE DISORDER AND "JUST" PHYSICALLY DEPENDENT

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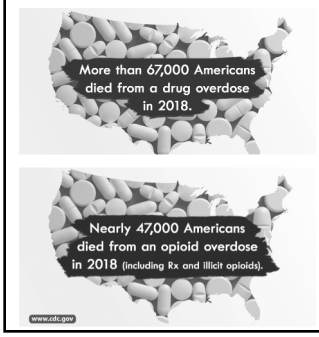

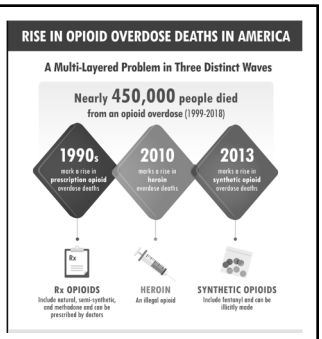

https://www.cdc.gov/drugoverdose/data/analysis.html

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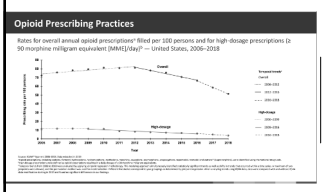

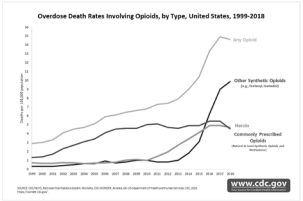

WE ARE STARTING TO SEE CHANGES

BUT LIKELY PUSHING TOWARDS OTHER ALCOHOL / OTHER DRUGS
AND NO IDEA HOW COVID-19 PANDEMIC WILL IMPACT THESE TRENDS

https://www.cdc.gov/drugoverdose/pdf/pubs/CDC_2019_Surveillance_Report_DataSummary_presentation.pdf.

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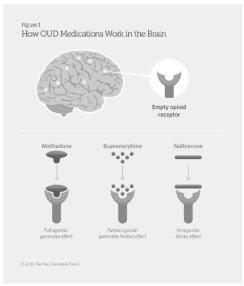

https://bit.ly/37UKaNY

MEDICATION OPTIONS (MAT/MOUD)

- **Methadone**
  - Full agonist
  - Slow build to necessary dose
  - Half life of several days
  - Cautions/complications: prolonged QT, dental issues, can only get through OTP
- **Buprenorphine**
  - Partial Agonist
  - Faster build to necessary dose
  - Cautions/complications: higher street value, must be DEA X-Waivered
- **Naltrexone**
  - Antagonist
  - Pill or Injection
  - Cautions/Complications: must be opioid/alcohol free for 7-10 days before starting

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LEGISLATION AND MEDICINE

- More laws re: prescribing habits
  - E.g. "3 day rule"
  - Max number of pills/rx
  - Max number of refills/rx
- Increasing number of cases against providers
  - But only when deviate significantly from standard of care
- BUT fear is impacting treatment of cancer pain and trauma

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WE'VE COVERED A LOT

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TAKE HOME POINTS

- Screen every patient – no guessing who will have / has a problem
- Develop procedural skills
- Get your DEA X-waiver
- Develop a balanced approach to pain management
  - Connect with community services/providers to help support patients outside of the exam room
- Make sure your employer allows you to keep that balance
  - Medicine is not customer service
  - We still need to do what is best for patient in the long term

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TRAINING AND PODCASTS

- CDC Trainings for Providers https://www.cdc.gov/drugoverdose/training/index.html
- NIDA https://www.drugabuse.gov/nidamed-medical-health-professionals/health-professions-education/opioid-pain-management-cmesces
- Washington State Interagency Guide on Prescribing Opiates for Pain http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf
- EM Basic http://embasic.org/wp-content/uploads/2016/12/EMBasic-Prescription-Opioid-Overdose-Podcast-Shownotes-with-checklist.pdf
- Hidden Brain: Lazarus Drug https://www.npr.org/2018/10/26/661011560/life-death-and-the-lazarus-drug-confronting-americas-opioid-crisis
- Invisibilia: The Fifth Vital Sign https://www.npr.org/programs/invisibilia/701219878/the-fifth-vital-sign
- ACEP Frontline
  - https://podcasts.apple.com/us/podcast/dr-kathryn-hawk-from-yale-medicine-on-opioid-overdoses/id1063793120?i=1000454359099
  - https://podcasts.apple.com/us/podcast/opioids-head-to-washington-alto-legislation-treatment/id1063793120?i=1000459140308
  - https://podcasts.apple.com/us/podcast/the-challenges-and-approach-to-behavioral-health-in-the-ed/id1063793120?i=1000457857242
- Last Day series https://www.lemonadamedia.com/show/last-day/
  - ☆ Especially listen to episode 6: magic formula

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THANK YOU!

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