Office and Hospital Detox Protocols

Launette Rieb
MD, MSc, CCFP, FCFP, DABAM, FASAM
Clinical Associate Professor,, Department of Family Practice, UBC
FMF 2016 - Vancouver
Faculty/Presenter Disclosure

Faculty: Launette Rieb
Relationship with commercial interests: None
Specifically, no pharmaceutical, medical device or communications company.

Teaching
- UBC, SPH, CPSBC, CFPC, various CME conferences (no pharma)

Research:
- NIDA – Canadian Addiction Med. Research Fellow

Clinical work:
- OrionHealth (Vancouver Pain Clinic) - CBI
- Orchard Recovery Centre
- St. Paul’s Hospital Immunodeficiency Clinic
Disclosure of Commercial Support

- No financial support or in-kind support for this program
- No potential conflicts of interest for Dr. Rieb
Mitigating Potential Bias

- There is no bias to mitigate
Disclaimer

- Please note the protocols shared in this presentation are suggestions only.
- They do not take the place of clinical judgment.
- I assume no liability for the use of these protocols.
Overview

- Differentiate the withdrawal syndromes of various substances
- Judge if an in-patient, residential, or office protocol for detoxification is in order
- Choose an appropriate detox protocol for the substance or combination of substances used by a patient
- Feel more confident when thinking of treating patients with substance use disorders
Case 1- A bit of everything

- Mr. Y = 24 yr retail clothing salesman presents with sleep difficulty due to “stress”, PMHx unremarkable aside from wrist injury

- Substance use history:
  - Nicotine x 10 yrs, now 1ppd
  - Marijuana x 8 yrs, weekends as teen, now 1 jnt hs
  - Caffeine x 8 yrs, currently 5-6 cups/d, rebound H/As
  - Alcohol 7 yrs – binging as a teen, now 4-8/night
  - Cocaine x 2 years, w/e binging, agitated + paranoid
  - Lorazepam 1 mg tid for anxiety and insomnia x 6 months
  - Oxycodone 10 mg qid for a work related mild wrist strain/sprain 4 months ago, crushing and snorting pills for the last month, first injected heroin use last weekend
Where to start?

- First make a diagnosis
  - Use? Substance Use Disorder? Pseudo-addiction?

- Is there physiologic dependence?
  - Is a withdrawal syndrome present?
  - How severe? Life threatening?

- What is the patient’s circumstance?
  - Support setting? Mental/physical health?
Residential Detox Needed?

- What risk factors may preclude out patient detox for some substances?
  - Mental health (suicidal, psychotic, etc.),
  - Physical health (cardiac, elderly, pregnancy, etc.)
  - Homelessness, lack of responsible caregivers
  - Polysubstance dep. (eg Alcohol + Benz)

- In hospital vs community detox facility?
Detox Protocols

- Caffeine
- Tobacco
- Alcohol
- Benzodiazepines
- Opioids
- Marijuana
- Stimulants
- Club drugs
Caffeine

- Coffee, black & green tea, chocolate, colas, energy drinks, pills
- Intoxication – 5+ below after 2+ cups coffee
  - Restlessness, nervousness, excitement
  - Insomnia, flushed face, diuresis, GI disturb
  - Muscle twitching, tachycardia/arrhythmia
  - Rambling thought/speech, inexhaustibility
  - Psychomotor agitation
- Must cause stress or impairment
  - Anxiety Disorder, Sleep Disorder, Withdrawal
Caffeine w/d Management

- \( \frac{1}{2} \text{ life} = 4-6h \) (however, 10 fold variation) so even just 1c/d can build up in a slow metabolizer and impact sleep and give headache on cessation

- Caffeine withdrawal (w/d) can include:
  - Headaches, irritability, impatience, restlessness
  - Sleep disturbance, dysphoria and fatigue

- Safe to taper all clients as outpatients (unless psychotic or compulsive use - admit)

- Taper as tolerated \( \frac{1}{2}c - 2c \ q1-2d \) outpatient

- Faster as in-patient if needed
Case: Why ask about caffeine?

- 37 year old female police officer, right knee cartilage defect, 2 surgeries, CNCP, isolated
- 6 months passive physio, T#3 1-2 q4h = 6-12/d
- ↑Anxiety with panic attacks and palpitations, insomnia, feels she is going “crazy”, mood ↓
- For this ↑doses of duloxetine, and lorazepam
- Caffeine: coffee 5 cups/d + 4 energy drinks
- Ask about size and content of each
- Each coffee = 3 shots espresso
- Caffeine = (15x160 mg/shot) + (4x160mg/edrink) + (12x15mg/T#3) = Total caffeine = 3,220 mg/d
Treatment of the Officer

- Taper off caffeine: In-patient cut in half and taper 2 shots/drinks q1d; Out-patient taper 1 shot/drink q1d, slow if headache++
- Change T#3 to codeine without caffeine (taper last), evaluate acetaminophen +NSAID
- Taper off lorazepam
- Taper duloxetine
- Initiate active physiotherapy, swimming
- Use offloading knee brace
- Re-engage with life
Tobacco - Nicotine w/d

- Stimulates nicotinic receptors
  - ↑ dopamine (DA), ↑noradrenaline (NOR)
- Withdrawal: 4+ after cessation of daily use
  - Dysphoria, insomnia, irritability, anxiety
  - Diff. concentrating, restless, decreased HR
  - Increased appetite or weight gain
- Likely physically dependent if smokes
  - 1ppd or more
  - 1st cig within 5 min of awakening
Nicotine w/d Management

- Separate habit and physical dependence
  - 1st – record use and associated behaviors
  - 2nd – break up pattern (same # of cig still)
  - 3rd – designate smoke free areas (home, car)
  - 4th – build strategies to help once off
    - Exercise, relaxation, social

- 5th – taper by 1 cig q 1-2 d (count & carry)
  - NB Keep smoking frequency same (q1-2h)
Nicotine Replacement

- Nicotine **patch** $21, 14, 7$mg = 1, 2/3, 1/3 ppd
- Apply q am over muscle & hairless skin, rotate sites
- **Take off if chest pain, light headed, N or V**
- Some get more vivid dreaming
  - If nightmares occur $>3$ nights, remove patch for sleep
- Use each patch strength for 2-6+ wks, longer best
- **LR tip:** At end of taper can leave on final patch $2 - 3 + d$, or occlude half of 7mg patch to finish taper
- **LR tip:** If skin irritation - spray with steroid inhaler
- **LR tip:** If peels off - cover with transparent film
- Gum, inhaler, e-cigarette also effective
Nicotine - Antidepressant Tx

- Bupropion
  - DA and NOR reuptake inhibitor
  - Contraindicated with eating disorders, cocaine
  - 150 mg/d same efficacy as 300 mg/d
  - Stop smoking day 7 (+ nicotine replacement)
  - Can taper off bupropion after 3 months
  - Some feel a bit squirrely on this medication
  - 12 week quit rate 36%, 1yr quit rate 16.4%

- NB: ASAM guidelines use 2 agents at once
Nicotine Partial Agonist Tx

- Varenicline
- Partial nicotinic receptor agonist, ↑dopamine
- Contraindicated: renal impairment, pregnancy, suicidal or severe depression
- Dose: 0.5 mg/d x 3d, then 0.5 mg q12h
- 12 week quit rates ~44%, 1 yr quit rates same as bupropion or slightly better (22.1%)
- Dr. Rieb Tip: Ask patient not to smoke for 12+h prior to first dose, i.e. to be in withdrawal, then the medicine will relieve their withdrawal instead of precipitating it!
Canadian Low-risk Drinking Guidelines Ages 18-65

- 0 if contraindicated, 2d off/wk, 1/d least harm
- Females ≤ 10/wk, 2/d (rare event 3) max
- Males ≤ 15/wk, 3/d (rare event 4) max
- At risk of w/d if 40+ drinks/wk
Mechanisms of Alcohol

- **Acute consumption produces CNS sedation:**
  - ↓ glutamate
    - Blocks postsynaptic NMDA glutamate receptor
  - ↑ GABA
    - Binds to GABA1 receptors
  - Activates **opioid** system
    - ↑ dopamine
    - ↑ serotonin

- **Withdrawal produces opposite - CNS activation**
  - Wernicke-Korsakoff Syndrome (WKS)
  - Delirium tremens (DTs)
  - Tremor = best predictor of impending seizure
Alcohol Withdrawal

- W/d = 2+ occurring hrs/days after cessation
  - Autonomic hyperactivity, eg. HR >100, sweat
  - Hand tremor, insomnia, N or V, anxiety
  - Hallucinations, illusions (visual, aud., tactile)
  - Psychomotor agitation, grand mal seizures

- Both use and withdrawal can be dangerous

- Metabolism by ALD = 1 oz pure ETOH/3h
  = 1 standard drink per hour on average
Alcohol Lowering Strategies

- Keep a drinking diary
- Sip drinks, spread out drinking ≤1/hr
- Practice refusing drinks, measure your own
- Alternate alcoholic & non-alcoholic drinks
- Eat food and re-hydrate with water prior
- Social functions: Arrive late and leave early
- Increase other activities and interests
Alcohol Detoxification

- Tapering 1 to 2 drinks/d, unlikely to seize
- If ≤ 7 drinks/d can taper/stop “cold turkey”
  - If otherwise healthy: No seizure, DT, head inj.
- Residential detox or hospitalize if hx of...
  - ≥8 drinks/d - less if hx significant head injury
  - Seizure disorder, alcohol w/d seizures or DTs
  - Suicidal, psychosis, violence in w/d, pregnant
  - Cardiac/med conditions (MI, arrhythmias, etc)
  - Unstable social situation (homeless or alone)
• Benzodiazepines suitable choice for alcohol withdrawal (diazepam, chlordiazepoxide)
• Individualize dose based on w/d scales (eg. CIWA-Ar), comorbid illness (lorazepam or clonazepam for elderly or liver disease), hx w/d seizures
• Do not use b-blockers, neuroleptics, anti-epileptics as monotherapy
Cochrane: Benzos for ETOH

- Authors’ conclusion:
  - Benzodiazepines showed a protective benefit against alcohol withdrawal symptoms, in particular seizures, when compared to placebo and a potentially protective benefit when compared to other drugs.
  - No definite conclusion was possible because of the heterogeneity of the trials.
Protocol: CIWA - Ar

- **Symptom driven protocol for alcohol w/d:**
  - RN admin., decreases m&m, cost effective
  - **If score ≥ 10**
    - **Diazepam 20 mg PO q1-2 h until CIWA ≤ 8-10 (2-5mgIV/min up to 10-20mg q1h)**
    - If hx w/d sz use diazepam 20 mg q1h x3 minimum
    - Observe 2-4h after last dose, if CIWA <10 x 3 stop
    - Or **Lorazepam 2-4 mg SL q 1-2 h**
    - **If elderly, severe liver dis. lorazepam 1-2 mg tid-qid**
  - Prevention of Wernicke’s: thiamine 250mg IM/d x5d
  - **Hallucinations:** Haloperidol 2-5mgIM/PO q1-4H
  - **Nb.** Do not use together parenteral olanzapine and parenteral lorazepam
Benzodiazepine loading versus symptom-triggered treatment of alcohol withdrawal: a prospective, randomized clinical trial

José R. Maldonado, M.D. a,*, Long H. Nguyen, M.D. b, E. Merritt Schader, M.D. c, John O. Brooks III, Ph.D., M.D. d

aDepartment of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305-5718, USA
bAddiction Psychiatry, San Francisco VA-Medical Center, San Francisco, CA, USA
cCommunity Solutions, Morgan Hill, CA, USA
dSemel Institute at UCLA, Los Angeles, CA, USA

Received 3 March 2012; accepted 23 June 2012
Benzo loading vs symptom-triggered protocol n=47

- Load = diazepam 20 q2h x 3 doses PLUS added diazepam based on CIWA-Ar
- Symptom = CIWA-AR lorazepam 1-2mg q2h as per protocol (CIWA >=8)

Authors’ conclusion:
- This study did not reveal clear evidence of a clinical advantage for choosing either treatment
Benzo Fixed Dose protocol

- Fixed dose schedules - no hx of seizure/delerium
- Scoring over 8 on CIWA-Ar
- Diazepam 20 mg q1-2h x 3 doses
  - Stop if sedated, slurred speech, or RR < 10

Alternative medication:
- Lorazepam 2 mg dosed as above (elderly, liver problems or unknown LFTs, COPD/asthma)

Prevent Wernicke’s: parenteral thiamine 250mg/d x 5d
Anticonvulsants for alcohol withdrawal (Review)

2010

Minozzi S, Amato L, Vecchi S, Davoli M
Cochrane: Anticonvulsants for alcohol withdrawal

Authors’ conclusions:

- Results of this review do not provide sufficient evidence in favour of anticonvulsants for the treatment of AWS
  - Lack of evidence over placebo
- Some suggestions that carbamazepine may be more effective for treating [seizure] compared to benzodiazepines
Benzos vs Anticonvulsants


Gabapentin versus chlordiazepoxide for outpatient alcohol detoxification treatment.

Stock CJ, Carpenter L, Ying J, Greene T.

Alcohol Clin Exp Res. Author manuscript; available in PMC 2010 September 1.
Published in final edited form as:

Published online 2009 May 26. doi: 10.1111/j.1530-0277.2009.00986.x

A DOUBLE BLIND TRIAL OF GABAPENTIN VS. LORAZEPAM IN THE TREATMENT OF ALCOHOL WITHDRAWAL

Hugh Myrick, MD,1,2 Robert Malcolm, MD,2 Patrick K. Randall, PhD,2 Elizabeth Boyle, MSW,2 Raymond F. Anton, MD,2 Howard C. Becker, PhD,1,2 and Carrie L. Randall, PhD2
Office-based Withdrawal Management

- **Gabapentin** – Anticonvulsant
- Ca++ channel and GABA modulating
- 300 mg q6h = 1200 mg/d – days 1-3
- 300 mg q8h = 900 mg/d – day 4
- 300 mg q12h = 600 mg/d – day 5
- 300 mg hs = 300 mg/d – day 6

May be better than benzodiazepines: Less sedation/drinking/craving at some time points, no increased adverse events for out-patients

Exclude those with previous seizure or delirium
Phenobarbital for acute alcohol withdrawal: a prospective randomized double-blind placebo-controlled study.


METHODS: This was a prospective, randomized, double-blind, placebo-controlled study. Patients were randomized to receive either a single dose of i.v. phenobarbital (10 mg/kg in 100 mL normal saline) or placebo (100 mL normal saline). All patients were placed on the institutional symptom-guided lorazepam-based alcohol withdrawal protocol. The primary outcome was initial level of hospital admission (ICU vs. telemetry vs. floor ward).

RESULTS: There were 198 patients enrolled in the study, and 102 met inclusion criteria for analysis. Fifty-one patients received phenobarbital and 51 received placebo. Baseline characteristics and severity were similar in both groups. Patients that received phenobarbital had fewer ICU admissions (8% vs. 25%, 95% confidence interval 4-32). There were no differences in adverse events.
Phenobarb iv + lorazepam

- Bottom line:
- Patients receiving one dose of phenobarbital 10mg/kg in 100 ml of saline in emerg then put on a modified CIWA-Ar protocol using lorazepam 2 mg had reduced ICU admissions compared to those getting lorazepam alone (8% vs 25%)
Phenobarb for alcohol w/d

- Though not included in the previous study, the protocol may be useful for those on benzos (or phenobarbital) + alcohol
- Historic use in detox centres: phenobarbital loading protocol for those on high dose benzos/barbiturates + high dose alcohol
- Phenobarbital 120mg q1h until 3 of:
  - Nystagmus, slurred speak, labile, ataxic, drowsy
- Monitor closely – respiratory rate, dysinhibition thus risk of self harm
- Or can benzo load + CIWA + benzo taper

(Kahan M, and Wislon L. 2002)
Case: Alcohol + benzo w/d

- Mr. T = 45 year old man, alcohol use disorder
- Several withdrawal seizures in the past
- Drinking vodka - Two 26 oz. bottles/d
- Along with diazepam 100-200 mg/d
- Tx: Phenobarbitol loaded to 720 mg
- Felt “great”
- Thought he could fly – jumped out the window – caught by the ankle by guard
- Phenobarb slowly auto-tapers over days
The “Prediction of Alcohol Withdrawal Severity Scale” (PAWSS): Systematic literature review and pilot study of a new scale for the prediction of complicated alcohol withdrawal syndrome

José R. Maldonado a,*, Yelizaveta Sher b, Judith F. Ashouri c, Kelsey Hills-Evans d, Heavenly Swendsen e, Sermsak Lolak f, Anne Catherine Miller g
PAWSS - a new in-pt screening tool for alcohol

- Lit review: no tool validated in medically ill
- Analyzed factors associated with complicated alcohol w/d (AWS)
- 10 items found that correlated
- Tested and validated during CIWA-Ar n=68
- In this pilot sample the sensitivity, specificity, and positive and negative predictive values of PAWSS were 100%, using the threshold score of 4
- First validated tool in medically ill patients
Prediction of Alcohol Withdrawal Severity Scale (PAWSS)

Maldonado et al., 2014

Part A: Threshold Criteria:
1. Have you consumed any amount of alcohol (i.e., been drinking) within the last 30 days?
   OR did the patient have a “+” BAL upon admission?
   IF the answer to either is YES, proceed with test:

Part B: Based on patient interview:
2. Have you ever experienced previous episodes of alcohol withdrawal?
3. Have you ever experienced alcohol withdrawal seizures?
4. Have you ever experienced delirium tremens or DT’s?
5. Have you ever undergone of alcohol rehabilitation treatment?
   (i.e., in-patient or out-patient treatment programs or AA attendance)
6. Have you ever experienced blackouts?
7. Have you combined alcohol with other “downers” like benzodiazepines or barbiturates during the last 90 days?
8. Have you combined alcohol with any other substance of abuse during the last 90 days?

Part C: Based on clinical evidence:
9. Was the patient’s blood alcohol level (BAL) on presentation > 200?
10. Is there evidence of increased autonomic activity?
    (e.g., HR > 120 bpm, tremor, sweating, agitation, nausea)

Total Score: ___

Notes: Maximum score = 10. This instrument is intended as a SCREENING TOOL. The greater the number of positive findings, the higher the risk for the development of alcohol withdrawal syndromes. A score of ≥ 4 suggests HIGH RISK for moderate to severe AWS; prophylaxis and/or treatment may be indicated.
N=403, group A PAWSS ≤3; group B ≥ 4
PAWSS cutoff of 4, the tool’s sensitivity for identifying complicated AWS is 93.1% specificity is 99.5%, PPV 93.1%; NPV 99.5%
Excellent inter-rater reliability
Conclusion: PAWSS has excellent predictive value among medically ill hospitalized patients, helping clinicians identify those at risk for complicated AWS and allowing for prevention and timely treatment of complicated AWS.
Magnesium for alcohol withdrawal (Review)

Sarai M, Tejani AM, Chan AHW, Kuo IF, Li J
Cochrane: Magnesium

Authors’ conclusions:

- There is insufficient evidence to say if magnesium is beneficial or harmful in the treatment or prevention of alcohol withdrawal syndrome.
Ongoing Management of AUDs

Q: Abstinence is a requirement of which medication used in the ongoing management of alcohol use disorders?

A) Acamprosate
B) Disulfiram
C) Naltrexone
D) Gabapentin
E) None of the above
Benzodiazepines
Evidence for Use

- Only real indication is for alcohol withdrawal
- Poor evidence for Generalized Anxiety Disorder, Obsessive Compulsive Disorder, Post Traumatic Stress Disorder, Major Depressive Disorder (including augmentation), or schizophrenia
- May be indicated for short term therapy in insomnia or acute anxiety short term (i.e. panic disorder) but note that needs CBT alongside and can create refractory anxiety – not a monotherapy indication
- **Contraindicated** with opioids, alcohol, sedatives
**Benzodiazepines**

- **Binds to GABA-BNZ receptors** allowing chloride to enter
- Withdrawal criteria same as for alcohol
- Both use and w/d can be life threatening
- W/d may last weeks, occasionally months
  - High dose, long duration, short acting benzos, also high neuroticism, female gender, and mild to moderate alcohol use are all risks for difficult or prolonged w/d
  - Meta-analysis on tapering protocols inconclusive of the best rate – best to engage patients, some promise with substitute therapies

(Parr JM. 2008 and Schweitzer E. 1990)
Benzodiazepine – withdrawal

- Discuss with patients what to expect:
  - Anxiety symptoms – irritability, insomnia, panic attacks, poor concentration
  - Neurological symptoms – ringing in the ears, blurred vision, distorted perception, depersonalization
- Let them know if they get shaky to stop taper
  - Tremor is clearest sign pre-seizure
  - Need to reassess, perhaps take extra dose
Benzo Tapering - Long

- Abrupt cessation of $\geq$ diazepam 50 mg/d
  - Risk seizure, psychosis or delirium
  - Consider residential tx if abrupt cessation $>80$mg

- **Office management: Convert to long acting benzo**
  - Smooth blood level decreases symptoms
  - **Diazepam** can be used if young and healthy
  - Beware of daytime sedation, warn about driving
  - **Clonazepam** may be a good alternative for w/d from alprazolam or triazolam
  - **Lorazepam** if cirrhosis, elderly or unknown LFTs
Benzo Tapering - Long

- Give 75% in **diazepam** equivalent and divided q8h
  - Plus breakthrough prn doses of the original benzo
- Reassess in 1-2 days as in-pt, (1 wk out-pt), establish dose
- Taper diazepam by 5-10% q 1-2 weeks
  - No regular breakthroughs
  - If short term use – faster, if long term – slower
  - Can initially drop faster if dose over 50 mg/d
- Trazodone 50 hs or propranolol 10-20 tid may help decrease prolonged w/d symptoms, as can a neuromodulator
Benzo Tapering – Long

- Alternatively you can substitute in the diazepam 25% per week while decreasing the other benzodiazepine, then taper
- Since there may not be perfect cross tolerance some find this more comfortable
- Some find lorazepam more anxiolytic and diazepam more sedating
- Diazepam allows the dose to go lower before discontinuing since comes as 2 mg – can split
Ashton Protocol

- Dr. Heather Ashton from the UK
- Protocol for very slow benzo conversion and taper of diazepam (can apply the same principle to opioid tapering if needed)
- May use for highly sensitive patients
  - Those on for many years
  - Elderly
  - Failed conventional tapering
If the person has been on a short acting benzo for a long time, can taper this.

If highly sensitive/symptomatic, consider compounding the medication in a liquid vehicle as an inpatient:

- E.g. Lorazepam 1 mg/ml – 1 ml hs x 1 d
  - 0.9 mg/ml – 1 ml hs x 1 d
  - 0.8 mg/ml – 1 ml hs x 1 d, etc. until off
- Note – same volume taken each night
- As an out patient can go slower
Some medications have been tried in withdrawal for symptomatic therapy:

- SSRI for depressive symptoms
- TCAs, melatonin, trazodone for insomnia
- Propranolol for severe palpitations, gastric upset
- Muscle relaxants

No real good evidence for this but is clinically relevant in engaging patients in withdrawal

- Novel studies being done with pregabalin, gabapentin, and other anti-epileptics
Pharmacological assisted benzodiazepine discontinuation

1\textsuperscript{st} line: Phenobarbital
- Acts as a weak agonist at GABA receptor
- Long t1/2, minimal withdrawal, generally well-tolerated and effective
- Dosing: 30 – 60 mg bid – qid

2\textsuperscript{nd} line:
- Gabapentin 100 – 300 mg tid
- Pregabalin 50 – 75 mg qhs – tid

(Dr Mark Weiner, Ann Arbor, Mich., Pain Recovery Solutions)
Effects of pregabalin on subjective sleep disturbance during withdrawal from long term benzodiazepine use

- N = 282
- Pregabalin dose 315 mg/day (mean)
- Decrease in insomnia scores (week 12)
  - Pregabalin: 55.8 +/- 18.9
  - Placebo: 25.1 +/- 18.0
- Improvements in anxiety symptoms

(Rubio G et al, Eur Addict, Jun 2011)
Papaver Somniferum
Dose-related risk of opioid overdose

Risk of adverse event

Dose in mg MED

<20 mg/day  20-49 mg/day  50-99 mg/day  >=100 mg/day

Risk Ratio

0  1  2  3  4  5  6  7  8  9  10

Dunn 2010
Bohnert 2011
Gomes 2011
Zedler 2014

Courtesy
Gary Franklin
Prescription Opioids

“Watchful Dose”

in morphine equivalent daily dose (MEDD)

90 mg US CDC and CPSBC

120 mg Worksafe BC & Washington state law

200 mg Canadian Opioid Use Guidelines (old)

At 120 mg MEDD: Addiction = 122 x RR

Analgesia only in 1 out of 4 respond to opioids and then only 20-30% drop in pain – Yet we chase the fantasy of perfect analgesic control!
Prescription Opioid Involved Overdoses
Washington State

Age-adjusted rate per 100,000

- Blue line: Deaths
- Red line: Hospitalizations
Opioids

Bind to opioid receptors

- Relieving pain (psychological and physical)
- ↑ dopamine (DA) in pleasure centres (ventral tegmental area ➔ nucleus accumbens)
- ↓ noradrenalin (NOR) in the fight or flight centres (locus coeruleus and amygdala), calming
- Affects brainstem (OD from respiratory depr.)
- Can produce dysphoria, sedation, impaired judgment, constipation, weight gain, erectile dysfunction (from decreased testosterone)
Opioid Use Can Cause Pain
Opioid can cause pain

- Opioid-induced hyperalgesia, withdrawal induced hyperalgesia, and withdrawal-associated injury site pain (WISP) at healed injury sites...
  - May all be dose dependent
  - And withdrawal episode dependent
  - WISP lasts 2+ wks on average and mean pain 8/10

Treatment:
- Opioid lowering, rotation, elimination
- NMDA antagonists, NSAIDs, gabapentinoids

(Mao, 2006; Hooten, 2015; Angst, 2003, Rieb, 2016)
Opioid Withdrawal

- **DSM-5...**3+ within minutes to days of stopping:
  - Dysphoria
  - N or V
  - muscle aches
  - lacrimation or rhinorrhea
  - diarrhea
  - yawning
  - fever
  - insomnia
  - Pupillary dilatation, piloerection or sweating
Withdrawal Hyperalgesia

- When opioids are tapered or stopped the pain relieving properties cease but the opioid induced hyperalgesia pushback continues for a time with worsened hyperalgesia, known as:
  - Opioid-abstinence hyperalgesia
  - Opioid withdrawal hyperalgesia
  - Withdrawal induced hyperalgesia (WIH)

- Is dose dependent
- May worsen with repeated exposure and w/d
  (Younger J 2008, Hooten WM 2010)

- LR tip: Beware old injury sites may hurt temporarily
Opioid Withdrawal

Withdrawal is not life threatening

- Unless patient has a history of seizures, is dehydrated, suicidal or pregnant

- Warn patients of OD risk post detox
Mrs. Winslow's

Soothing Syrup

For Children Teething
When to Suggest Opioid Taper from Legally Obtained Meds?

- Patient on opioids without significant improvement in pain and function
- Safety sensitive position
- Spread of pain in the absence of disease progression - hyperalgesia
- Other SUDs where harm reduction not viable
- Patient requests to come off
- N.B. If not physically dependent then no taper needed
Opioid Tapering - Long

- Conventional wisdom is to convert short acting opioids to long acting then taper. Sometimes short is needed to add back in at the end due to dose strength.

- Convert to long acting (same drug less 25% - 50%, rest is given as short acting PRN, re-evaluate daily).
  - Once on just long acting: Taper ~5-10% per 1-14 d
  - Symptom management like the CINA protocol.

- If rotating opioids beware of conversion.
  - Lack of cross tolerance with some opiates.
Opioid Tapering – Short

- Sometimes easiest to simply taper what the patient is currently using
  - E.g. Percocet 16-20/d, taken 6 tid +/- 2/d

- If it is a dual agent first switch to eliminate the ASA or acetaminophen (bloodwork?)
  - E.g. Oxycodone 5 mg 18/d

- Next spread out the daily dose evenly based on the ½ life of the medication
  - E.g. Oxycodone 5 mg 5/4/4/5 spread q6h
Opioid Tapering – Example

- Next taper the medication – drop can be q4-14d as out-pt, and drop daily as in-pt or faster if d/c needed (other symptom mngt may be needed)
- Oxycodone 5 mg 4/4/4/5 spread q6h
- Oxycodone 5 mg 4/4/4/4 spread q6h
- Oxycodone 5 mg 4/3/4/4 spread q6h
- Oxycodone 5 mg 4/3/3/4 spread q6h
- Oxycodone 5 mg 3/3/3/4 spread q6h
- Oxycodone 5 mg 3/3/3/3 spread q6h...
- Continue this pattern until 0/0/0/1, then off
Case 2 - Mr. C. - 2015

- 66 year old carpenter, 2014 compression #L1
- 2004 left ankle # at work
- Degenerative changes in low back and neck – non-surgical, “fibromyalgia” x 20 years, depression, sleep apnea, insomnia
- Oxycodone 160mg/d = 240 MEDD
- MMP 2015: Tapered off in 6 1/2 weeks
- Pain in ankle and back about the same, slightly worse in neck/headaches (acetaminophen rebound headaches?)

- Very happy to be off oxy: Mentally clear, and morning erections for the first time in a decade!
Opiate Addiction

Abstinence
- Counseling
- Peer Support
- Residential Treatment

Medications
- Agonist
  - Methadone
  - Buprenorphine
- Antagonist
  - Naltrexone
COWS

- Clinical Opiate Withdrawal Scale
- Health practitioner administered
- Cows score above 8-10 can initiate meds – either a clonidine protocol or buprenorphine
Opioid w/d Management

- Clonidine protocol
- For use when you cannot (or will not) prescribe opioids, e.g. street opioid use
- Often works best for short acting opioids like heroin, codeine, morphine, oxycodone, etc.

- If outpatient and no reliable caregiver, then daily dispensed from a pharmacy
Opioid w/d Management

- **Environment:** Safe, minimal: caffeine, exercise, spice, hot bath/shower/sauna

- **Clonidine 0.1mg qidx4d, tidx1d, bidx1d, hsx1d prn**
  - Test dose 0.1mg, BP pre & 1-2h post in the office can be done – OK if BP >90/60,
  - if BP lower - give clonidine 0.05 mg tabs
- **Decreases temperature dys-regulation (hot/cold flashes) and NOR (insomnia & anxiety)**
- Warn pts of *postural hypotension, driving*
- Use with medications on next slide
Opioid w/d Management,

- Gabapentin 300 – 600 mg tid, prn for anxiety, insomnia, and pain *
- +/- Trazodone 50 mg 1-2 tabs hs for insomnia
- Loperamide 2 mg after loose stool, 8/d max
- Dimenhydrinate 25mg 1-2 tid N+V
- Ibuprofen 400 mg q 6-8h for pain
- Acetaminophen 500mg q6h for pain
- * Substitutions:
  - quetiapine 25 mg ½ -1 bid - tid and 1-2 hs
  - diazepam 5 mg qid x 4d, tid x1d, bid x1d (classic, but more dangerous if opioids continue, diversion)
Opioid Substitution: Methadone

- **Methadone** can be used for pts with an opioid use disorders and/or pain, and for detox
  - Dose *once daily* to eliminate withdrawal and block other opioids – may be sufficient
- **Methadone used for pain** dosed *q6-8h*
- If on methadone at admission - Lower the dose by 25%+ on and give the rest in 5 mg prn doses, witnessed ingestion, hold if sedated
## Morphine to Methadone

<table>
<thead>
<tr>
<th>24 hour total oral morphine</th>
<th>Oral morphine to methadone conversion ratio</th>
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<tbody>
<tr>
<td>&lt;30 mg</td>
<td>2:1</td>
</tr>
<tr>
<td>31-99 mg</td>
<td>4:1</td>
</tr>
<tr>
<td>100-299 mg</td>
<td>8:1</td>
</tr>
<tr>
<td>300-499 mg</td>
<td>12:1</td>
</tr>
<tr>
<td>500-999 mg</td>
<td>15:1</td>
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<tr>
<td>&gt;1000 mg</td>
<td>20:1</td>
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</tbody>
</table>

Methadone for Detox

- MD must be trained – College course, license
- Only for highly tolerant patients on high dose opioids (not those on high dose methadone)
- Methadone 20 mg with 5mg prn q4h up to 30mg max day 1 – witnessed by RN, hold if drowsy or no w/d
- Then taper 5 mg daily until off
- LR Tips: Can taper last 5 mg by 1/d, and/or switch to buprenorphine patch at end of taper for sensitive individuals
- Or switch to bup/nx at end for maintenance
Defining dosing pattern characteristics of successful tapers following methadone maintenance treatment: results from a population-based retrospective cohort study

Bohdan Nosyk¹,², Huiying Sun³, Elizabeth Evans², David C. Marsh⁴, M. Douglas Anglin², Yih-Ing Hser² & Aslam H. Anis³,⁵

¹ BC Centre for Excellence in HIV/AIDS, Vancouver, British Columbia, Canada. ² UCLA Integrated Substance Abuse Programs, Semel Institute for Neuroscience and Human Behavior, Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine, Los Angeles, CA, USA. ³ Centre for Health Evaluation and Outcome Sciences, Vancouver, British Columbia, Canada. ⁴ Northern Ontario School of Medicine, Sudbury, Sudbury, British Columbia, Canada. ⁵ School of Population and Public Health, University of British Columbia, Vancouver, British Columbia, Canada
Results for those tapered off MMT in BC

- 646/4183 sustained successful tapers = 13%
- Younger, males, better tx adherence, lower mean max weekly doses
- Longer tapers better
  - 12-52 weeks vs <12 weeks OR 3.58
  - >52 weeks vs <12 weeks OR 6.68
- More gradual, stepped tapering schedule
  - 25-50% vs <25% of taper weeks OR 1.61
Patterns of Methadone Dose Tapering (Most successful checked)

Opioid Substitution - Bup

- **buprenorphine/naloxone** (bup/nx) can be used for pts with an opioid use disorders or detox
- **Dose once daily** to eliminate withdrawal and block other opioids – may be sufficient
- **Bup/nx used for pain +/- SUD** can be dosed q6-8h
- **Bup/nx currently off label for pain alone** though can argue physiologic dependence, tolerance
Precipitated Withdrawal

- Buprenorphine/naloxone – bup/nx – a "partial agonist" in vitro, but is really a full agonist at the mu opioid receptor in vivo
  - slightly better than morphine for receptor saturation and pain relief
  - Has higher AFFINITY for the mu opioid receptor than anything but fentanyl thus will kick off other opioids and put the person into withdrawal until the buprenorphine is high enough to relieve withdrawal
  - kappa receptor antagonist, may help mood
Buprenorphine for the management of opioid withdrawal (Review)

Gowing L, Ali R, White JM
Authors’ conclusions

Buprenorphine is more effective than clonidine or lofexidine for the management of opioid withdrawal. Buprenorphine may offer some advantages over methadone, at least in inpatient settings, in terms of quicker resolution of withdrawal symptoms and possibly slightly higher rates of completion of withdrawal.
Buprenorphine/nx for Detox

Clinician must do 6 hour on-line training
- Ensure person is in w/d (COWS≥10)
- 1-2mg test dose, if no precipitated w/d
- Then 2 mg q2h until symptoms abate
- Max 8 mg day 1, max 16 mg day 2
- Then taper by 1-2 mg /d
- E.g. 8/8/6/4/2/1 or 8/7/6/5/4/3/2/1
- Tip: Buprenorphine patching (20mcg/h) 1 d pre bup/nx can ↓ precipitated w/d
- LR Tip: Post bup/nx add patch, ↓w/d
Conversion from High-Dose Full-Opioid Agonists to Sublingual Buprenorphine Reduces Pain Scores and Improves Quality of Life for Chronic Pain Patients


Retrospective chart review of patients on over 200 MEDD converted to Suboxone - pain scores dropped 51% on average, 8/10 to 4/10
Pre- and postconversion pain scores by pre-conversion morphine equivalents dosage

Average 4 point drop!  

Naltrexone – opioid antagonist

- Post detox use naltrexone 50mg/d po for those with OUD
  - can block 0.5+ gm of heroin IV or equivalent
- Start 1-2 wks after last short acting opioid (3-4 wks post methadone)
  - ¼ pill day 1; ½ pill day 2; 1 pill day 3 onwards
  - Witnessed ingestion is best
- Contraindicated cirrhosis, OD risk high once d/c
- Use for first 6-12 months of sobriety from OUD
- Analgesia with non-opioids or get consult
Naloxone Take Home Kits

- Nasal or injectable naloxone kits given to people prescribed opioids for pain or addiction
- Train Pt and others living with them
- Can save lives in OD situations
- Sometimes Pt uses it on a friend
- Find out what is available/allowable in your area
Case – Escalating doses

- Mr. D = 47 year old married at home father, degree is psychology,
- No family history of SUD, dad a gambler late in life
- Age 19: L4-5 discectomy for prolapse
- Post-op give Tylenol #3
  - He mixed these with ETOH to get high
- 10 years later – recurrent disc – surgery
- Initially successful then increasing low back pain over the next year
Mr. D, con’t

- GP managed
  - Tried different medications, low dose at 1st
  - Hydromorphone short acting up to 80 mg/d
    - Would run out early, would crush and smoke
  - Fluoxetine 60 mg/d
  - Lorazepam 4 mg/d
  - Pain still unmanageable on above regime
  - Referred on
Mr. D., con’t

- Multidisciplinary hospital based pain clinic
  - Medications altered, various medications combined
  - Opioids were increased over time to the level below:
    - Fentanyl Patch 150 mcg/h q2 d (prescribed q3d)
    - +/- fentanyl solution 100 mcg/2ml vile 3-5/d
    - Fentanyl film 600 mcg bid = 1200 mcg/d
    - Tramadol (24h) 50 mg ii bid = 6 tabs/d = 300 mg/d
    - Methadone tablets 60 mg bid = 120 mg/d
    - Hydromorphone - short acting 80 mg/d (snorting)
    - Morphine equivalent dose = 1,830+ mg/d
Mr. D., con’t

- Other medications
  - Fluoxetine 80 mg/d (adverse rxn - duloxetine)
  - Diazepam 2.5 mg bid (+still using lorazepam)
  - Decongestant with pseudoephedrine 2 tabs/d
  - Caffeine pills and energy drinks

- He still felt pain, otherwise felt “Great!”
- Function: ran triathlons, others see sedation
- Total cost to wife’s insurance = $3,000/wk
Mr. D., con’t

- Voluntary admission to a medically supervised residential treatment facility: education, 12 step, group, 1:1, CBT, etc.
- Methadone and fluoxetine same dose at 1st
- Stopped tramadol on admission
- Stopped all fentanyl after 2 d taper
- Added quetiapine 25 mg q6h
- No withdrawal seen
Mr. D., con’t

- Tapered the methadone over 3 weeks to 5 mg tid
- Dose held until in withdrawal
- Switched to buprenorphine patch 10 mcg initially – not quite enough
- Then over to sublingual bup/nx titrated to 6 mg/d where he has been maintained successfully
Mr. D., followup

Follow-up 12 months post admission to recovery

- **Meds**
  - Bup/nx 6 mg/d
  - Fluoxetine 60 mg/d and tapering
  - Quetiapine 125 mg/d and tapering
- Has attended 12 step daily, has a sponsor
- No relapses or slips, despite divorcing
- No more pain issues
- GAF 95/100
Mr. D., Reflections

- Primary pain disorder or substance use disorder?
- Opioid induced hyperalgesia?
- How can the opioids besides methadone be stopped abruptly without withdrawal?
- How can bup/nx and 12 step combined control both the pain and addiction issues?
And new “Spice” = synthetic cannabinoids
THC binds to CB1 and CB2 receptors
- ↑DA, is a CNS stimulant and depressant
- Changes perception, memory, motivation, movement, reflexes, BP, pain, appetite,
W/d reported <25%
- Dysphoria, irritability, restlessness, insomnia, anorexia, anxiety, sweating, tremor & craving
- Supportive care, drug free environment
- **Trazadone** 50 mg hs for insomnia if needed
Stimulants

- **Cocaine** (incl. “crack” and free “base”) is a DA, 5HT, & NOR reuptake inhibitor
- **Methamphetamine** ("crystal meth", "jib"); amphetamine ("speed"), and PCP
  - direct agonists to these receptor sites and have a longer $\frac{1}{2}$ life
- W/d includes 2+: Fatigue, vivid dreams, hypersomnia or insomnia, incr. appetite, psychomotor retardation or agitation
- 3 phase w/d: Crash, dysphoria, extinction
Stimulants, cont.

- Use can be life threatening, w/d is not
- Treatment is largely environmental support
  - Change of scene, rest, eat, calm, no triggers
  - No proven drug tx
- If agitated an atypical antipsychotic can be used
  - Eg Quetiapine 25 mg tid-qid, the dose can be titrated up to effect (caution – lower sz thresh.)
- Avoid benzos
- Generally avoid stimulant substitution
Designer Drugs and Inhalants

- **MDMA** “Ecstasy”- hallucinogen & stimulant +
  - Intox = bruxism & dry mouth (soother sign), ^HR, hyperthermia (dancing), rhabdomyolysis
  - Or water overload, hyponatremia, brain damage
  - w/d = like cocaine + muscle aches. No Rx.

- **GHB** – sed/hyp: w/d similar to benzo 3-15d
  - diazepam or phenobarbital to tx (monitor)

- **Inhalants** – Use dangerous w/d mild, rarely...
  - disorientation, halluc., psychosis, seizures
  - Supportive care (no clear Rx - phenobarb?)
Treatment Options

Q: Which of the following is not considered “treatment” for alcohol dependence?

A) Medically supervised detoxification
B) Alcohol and drug counselors (1:1, group)
C) Residential recovery programs
D) Recovery houses, therapeutic communities
E) Self help groups (AA, Alateen, 16 step, RR)
Case – A little bit of everything

 Mr. Y = 24 yr retail clothing salesman presents with sleep difficulty due to “stress”, PMHx unremarkable aside from wrist injury

 Substance use history:
   Nicotine x 10 yrs, now 1ppd
   Marijuana x 8 yrs, weekends as teen, now 1 jnt hs
   Caffeine x 8 yrs, currently 5-6 cups/d, rebound H/As
   Alcohol 7 yrs – binging as a teen, now 4-8/night
   Cocaine x 2 years, w/e binging, agitated + paranoid
   Lorazepam 1 mg tid for anxiety and insomnia x 6 months
   Oxycodone 10 mg qid for a work related mild wrist strain/sprain 4 months ago, crushing and snorting pills for the last month, first injected heroin use last weekend
Highlights

- Patients with physiologic dependence who need to come down or off a substance can be assisted by a variety of approaches:
  - Replacement and tapering
  - Symptom management
  - Agonist therapy
  - Antagonist therapy
  - Education and non-pharmacologic options
Key References


- This site provides the CIWA form: [https://umem.org/files/uploads/1104212257_CIWA-Ar.pdf](https://umem.org/files/uploads/1104212257_CIWA-Ar.pdf)
- This site calculates the CIWA – Ar online for you [www.mdcalc.com/ciwa-ar-for-alcohol-withdrawal/](http://www.mdcalc.com/ciwa-ar-for-alcohol-withdrawal/)
Thank you!