

# DO NOT CONFUSE

## NALOXONE

Can be bought without a prescription in many states



## NALTREXONE

Cannot be bought without a prescription

# [ USES ]



### NALOXONE

- Injected into a patient suffering from an opioid overdose
- Works rapidly to take the effect of the drug away
- It's now offered as a take-home kit for Fentanyl overdose

### NALTREXONE

- Is primarily used as alcohol and drug recovery treatment
- It has been in use for over 30 years
- Injected and slowly released into the body





# **Withdrawal Syndromes (alcohol, opioids, benzodiazepines, & forgotten/occult withdrawal)**

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# HAWAI'I HEALTH & HARM REDUCTION CENTER

*The New Chapter for Life Foundation and The CHOW Project*

Reducing Harm, Promoting Health,  
Creating Wellness and Fighting Stigma  
in Hawaii and the Pacific



# PRIMARY CARE *PLUS*

- Primary care with SUD informed staff
- Outpatient detoxification
- Addiction Medicine
- Occupational Health



I, MOSES, JP have no financial interests, arrangements, or relationships that could be perceived as a conflict of interest within the context of this presentation.

MANY MEDICATIONS DISCUSSED will be OFF LABEL ---- IF you are an APRN, PA, or other non-PHYSICIAN (MD/DO), ASSUME I AM speaking about an off label use. **You are responsible for understanding and remaining within your scope of practice.**

<https://www.americanmedspa.org/blogpost/1633466/316454/Off-label-Considerations-for-Mid-level-Practitioners>

## **DISCLOSURE STATEMENT**




# Ancillary Medications-----

## PLEASE!



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Withdrawal management (WM) refers to the medical and psychological care of patients who are experiencing withdrawal symptoms as a result of ceasing or reducing use of their drug of dependence.<sup>5</sup>



# syn·drome

/ˈsɪnˌdrɒm/

*noun*

1. a group of symptoms which consistently occur together, or a condition characterized by a set of associated symptoms.

"a rare syndrome in which the production of white blood cells is damaged"

- a characteristic combination of opinions, emotions, or behavior.

"the "Not In My Backyard" syndrome"



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Alcohol and benzodiazepines present a true medical emergency for detoxification.

Long-term alcohol users may have multiple “phases” of detoxification, therefore the most dangerous days for them may be **days 4 through 10**. consider the use of the **PAWWS** for long term medical management of detox and comorbidities.



# Alcohol

**Swillbowl (1532), Rumdum (19<sup>th</sup>  
Centruy), drunkard (1890),  
dipsomaniac (??)...inebriate, tosspot,  
sterwbum, shicker, etc.**

# Committed to their art





# stigma

<https://www.drugabuse.gov/nidamed-medical-health-professionals/health-professions-education/words-matter-terms-to-use-avoid-when-talking-about-addiction>

**Addict, user, abuser, junkie, alcoholic, drunk, part head, dipsomaniac, clean/dirty.....Please type any additional terms, whether derogatory or not, into the chat room please.**



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<https://www.aspenridgerecoverycenters.com/drug-street-names/>



# opioids

**Receptors- mu (brain), kappa (belly)**

**Tolerance – examine MME trends over  
past year (detox) or longer  
(treatment)**



# opioids

**Short term use of BUP?**

**Standard – benzos, Bentyl,  
hydroxyzine, Imodium (HATE IT),  
ondansetron, carbamazepine,  
topiramate, pregabalin**





## Office based detox

**Simple – pt with reasonable executive function does well**

**Well understood MOA for all FDA approved medications**

**MOSTLY FOR COMFORT- important?**



# Benzodiazepines

Usually very **LONG TERM** use

See underlying personality and mood disorders – if anxiety, reconfirm diagnosis

**THINK MONTHS, NOT DAYS**







# benzodiazepines

**This group is also very committed to their art, and appear for all intent and purpose, “inebriated.”**





# Alcohol and benzodiazepine similarities

Increased social acceptability, ease of access, both considered sedative hypnotic, abrupt cessation of either will decrease the seizure threshold, **making alcohol and benzos the most dangerous detox**





# Oldies But Goodies

- Medications that have a generally respected track record



## Chlordiazepoxide – Detox BZO

Librium (chlordiazepoxide HCl) has antianxiety, sedative, appetite-stimulating and weak analgesic actions. The precise mechanism of action is not known. The drug blocks EEG arousal from stimulation of the brain stem reticular formation, RESULTING IN DECREASED SEIZURE RISK.

SHORT TERM USE ONLY – DANGER OF USE WITH ALCOHOL

Drowsiness, dizziness, nausea, constipation, blurred vision, or headache may occur

May use fixed, symptom triggered, or tapering dosage.

## Ancillary Medications



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## Clonidine-benzos, alcohol, opioids

Clonidine attenuates opiate withdrawal syndrome, via reduction in catecholamine activity in the brain, most probably at the locus ceruleus. Clonidine and locus ceruleus lesions, in animals with alcohol dependency as with the opiates, modify alcohol withdrawal. Both alcohol loading and withdrawal from steady alcohol use alter catecholamines in man and animals. Clonidine's potential to treat alcoholics in withdrawal is reviewed.

Major improvements were in pulse, blood pressure and composite alcohol withdrawal scores. Side effects were minor and mainly included mild sedation, or postural hypotension.

# Ancillary Medications



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## Barbiturates – Detox BZO, etoh

**Conclusion:** Barbiturates provide effective treatment for alcohol withdrawal syndrome. In particular, they show promise for use in the emergency department and for severe withdrawal in the intensive care unit. Respiratory depression does not appear to be exceedingly common. Additional studies are needed to clarify the role of barbiturates in alcohol withdrawal syndrome.

SHORT TERM USE ONLY – DANGER OF USE WITH ALCOHOL

Drowsiness, dizziness, nausea, constipation, blurred vision, or headache may occur

May use fixed, symptom triggered, or tapering dosage.



# Ancillary Medications

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## Ondansetron – antiemetic

- MOA - serotonin (5-HT<sub>3</sub>) receptor antagonist, which decreases vagal stimulation
- First line antiemetic for most withdrawal syndromes
- Adverse effects
  - QT prolongation
  - serotonin syndrome
  - headache
  - constipation

## Ancillary Medications





## Folic Acid - Vitamin

**Folic acid** supplementation has been postulated to be a therapeutic option for correcting hyperhomocysteinemia and therefore for reducing the risk of seizures in patients undergoing **alcohol withdrawal**.

An important mechanism in alcohol-induced injury is biomolecular oxidative damage. Folic acid is supplied to chronic alcoholic patients in order to prevent this situation, as this is the main vitamin deficiency that they suffer from. The decreased concentration of serum folic acid may occur in 80% of alcoholics.

# Ancillary Medication







## Thiamine - Vitamin

Routine use of thiamine is recommended because the development of Wernicke encephalopathy or Wernicke-Korsakoff syndrome is disastrous in these patients and can remain unrecognized.

Role in axonal conduction, particularly in acetyl cholinergic and serotonergic neurons. A reduction in the function of these enzymes leads to diffuse impairment in the metabolism of glucose in key regions of the brain, resulting in impaired cellular energy metabolism.

Rare ADR

Dosage: 100 mg tab, 1 tab po qd

Thiamine has no effect on the symptoms or signs of alcohol withdrawal or on the incidence of seizures or DTs.

# Ancillary Medications



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## Hydroxyzine Pamoate (Not HCL) - Antihistamine

MOA for anxiety - competes with histamine for binding at H1-receptor sites on the effector cell surface. The sedative properties of hydroxyzine occur as a result of suppression of certain subcortical regions of the brain. Secondary to its central anticholinergic actions, hydroxyzine may be effective as an antiemetic

ADR/SE - Dry mouth (pilocarpine?)

- Drowsiness (usually transitory, improves with tolerance)
- Involuntary motor activity (tremor, convulsions) usually with doses considerably higher than those recommended
- Clinically significant respiratory depression has not been reported at recommended doses

## Ancillary Medications



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## Alprazolam - benzodiazepine

Alprazolam (Xanax) - psychoactive drugs that work to slow down the central nervous system by activating GABA receptors. This provides a variety of useful tranquilizing effects. Aside from relieving symptoms of alcohol withdrawal, benzodiazepines are also commonly prescribed to treat insomnia, muscle spasms, involuntary movement disorders, anxiety disorders, and convulsive disorders.

ADR/SE - Drowsiness, dizziness (these effects will be less pronounced after a few days, avoid driving a car or engaging in other dangerous activities if these occur); GI upset (take drug with food); fatigue; depression; dreams; crying; nervousness

Although benzodiazepines have gotten their reputation tarnished over the past 15 years, they are still useful in many cases. As with opioids, I never start a person on benzodiazepines without an exit strategy. When I have a polysubstance abuser, I generally try to address all substance recovery at the same time, including nicotine. The transition from one benzo to another using topiramate is beyond the scope of this lecture, he may see me afterwards as it is off label.

## Ancillary Medications



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# PROGRESSIVES IN COMMON USE

- Medications that have no current indication for withdrawal, but are used daily by specialists in addiction medicine
- ....provider open to risk but has supportive evidence



## Topiramate – Anti-seizure

### WITHDRAWAL and MOOD MANAGEMENT – OFF LABEL!

1. Blocks voltage-dependent sodium and calcium channels.
2. Inhibits the excitatory glutamate pathway while enhancing the inhibitory effect of GABA.
3. Moreover, it inhibits carbonic anhydrase activity. (The relevant mechanism of action responsible for efficient migraine prophylaxis remains to be determine)

Tiredness, drowsiness, dizziness, loss of coordination, tingling of the hands/feet, loss of appetite, bad taste in your mouth, diarrhea, and weight loss may occur

MANY CURRENT RESEARCH STUDIES ON OTHER USES FOR THIS MEDICATION. IT IS ALREADY SHOWING PROMISE IN WEIGHT LOSS, ALCOHOL/OPIOID/BENZO WITHDRWAL AND MOOD DISORDERS

# Ancillary Medications



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## Topiramate – Anti-seizure

### WITHDRAWAL and MOOD MANAGEMENT – OFF LABEL!

- Alprazolam is successful in reducing anxiety but has a high addictive/misuse potential.
- Topiramate is a novel anticonvulsant which has been used as a mood stabilizer.
- Other anticonvulsants, such as carbamazepine and valproate, have been used in alcohol and benzodiazepine withdrawal.
- Topiramate has recently been used in alcohol, cocaine and opiates withdrawal.
- There has been also one report of topiramate use in midazolam withdrawal.
- (In our case of a patient with recurrent major depressive disorder, subthreshold anxiety disorder and addiction to alprazolam, topiramate appears to be efficient and safe in alprazolam withdrawal)

## Ancillary Medications





# gabapentin

- **CONCLUSIONS AND RELEVANCE** These data, combined with others, suggest gabapentin might
- be most efficacious in people with AUD and a history of alcohol withdrawal symptoms. Future
- studies should evaluate sleep changes and mood during early recovery as mediators of
- gabapentin efficacy.
  
- **Downloaded From: <https://jamanetwork.com/> on 11/01/2021**





# Carbamazepine

- **Conclusion:** Carbamazepine has demonstrated safety, tolerability and efficacy in treatment of moderate to severe symptoms of alcohol withdrawal in the inpatient setting. However, trials of carbamazepine provide inconclusive evidence for prevention of alcohol withdrawal seizures and DTs in comparison with benzodiazepines. Benzodiazepines remain the primary treatment of moderate to severe AWS.





- All FDA approved medications are to be used as PART of a comprehensive treatment program that includes and mutual support groups
- Buprenorphine and Naltrexone both show promise in multiple harm reduction studies
- Buprenorphine treatment may be initiated by any prescriber who completed special training required by the DATA 2000 (stay tuned for COVID driven changes)

## Summary





# A little out there

- **Hold onto your license and check your malpractice insurance**



# UGLY SLIDE, BUT YOU GET THE IDEA

n (%) TABLE 1 - Trends in the Use of Medications for Alcohol Withdrawal Syndrome

2016	2017	2018	2019	Overall=96,050		
Patients	21,490	23,390	24,690	26,480	0	
Benzodiazepines		23,970 (112)	26,950 (115)	27,790 (113)	29,470 (111)	108,180 (113)
Lorazepam	8030 (37)	6740 (29)	6300 (26)	5720 (22)	26,790 (28)	
Midazolam	4330 (20)	3870 (17)	3520 (14)	3110 (12)	14,830 (15)	
Diazepam	4680 (22)	4100 (18)	3420 (14)	2770 (10)	14,970 (16)	
Oxazepam	600 (3)	60 (0)	70 (0)	40 (0)	770 (1)	
Temazepam	680 (3)	510 (2)	340 (1)	1540 (6)	3070 (3)	
Alprazolam	1850 (9)	1590 (7)	1390 (6)	4880 (18)	9710 (10)	
Chlordizepoxide		3940 (18)	3770 (16)	3620 (15)	3290 (12)	14,620 (15)
Haloperidol	9940 (46)	10,930 (47)	11,250 (46)	11,650 (44)	43,771 (46)	
Clonidine	9040 (42)	9900 (42)	10,430 (42)	11,020 (42)	40,391 (42)	
Hydroxyzine		1750 (8)	1700 (7)	1610 (7)	1400 (5)	6460 (7)
Baclofen	1270 (6)	1490 (6)	1560 (7)	1660 (8)	5980 (6)	
Phenobarbital		1040 (5)	1250 (5)	1600 (6)	1650 (6)	5540 (6)





# **N-acetylcysteine**

**NAC may correct glutamate dysregulation**

- **NAC for SUDs: Emerging evidence**
- Several recent reviews have described the efficacy of NAC for SUDs and other psychiatric disorders. Here we summarize the current research examining the efficacy of NAC for stimulant (ie, cocaine and methamphetamine), alcohol, cannabis, and tobacco use disorders



# *N*-acetylcysteine

- **Abstract**
- Background
- Neonatal abstinence syndrome (NAS) is a significant problem. Opioid withdrawal induces oxidative stress and disrupts glutamate and glutathione homeostasis. We hypothesized that *N*-acetylcysteine (NAC) administered during acute opioid withdrawal in neonatal rats would decrease withdrawal behaviors and normalize CNS glutathione and glutamate.



# ***KRATOM***

- **NIH is notably silent**
- **Used safely as a leaf in many areas of the world, primarily Southeastern Asia**
- **GABA and norepinephrine modulation are most likely for positive effects, negative effects invariably outweigh positive for this agent**



# ***Medical Cannabis***

- **NO**

<https://c'mon guys, seriously?>



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JP Moses, NUR 0020, 2016





# How do clients get to see providers?

NEW Patients MUST be worked up by Medical Assistant and presented to a PROVIDER for scheduling.

**Kelli K. is the lead on this initiative and will coordinate compliance with Dr. Wang and Case Management.**





The End!

