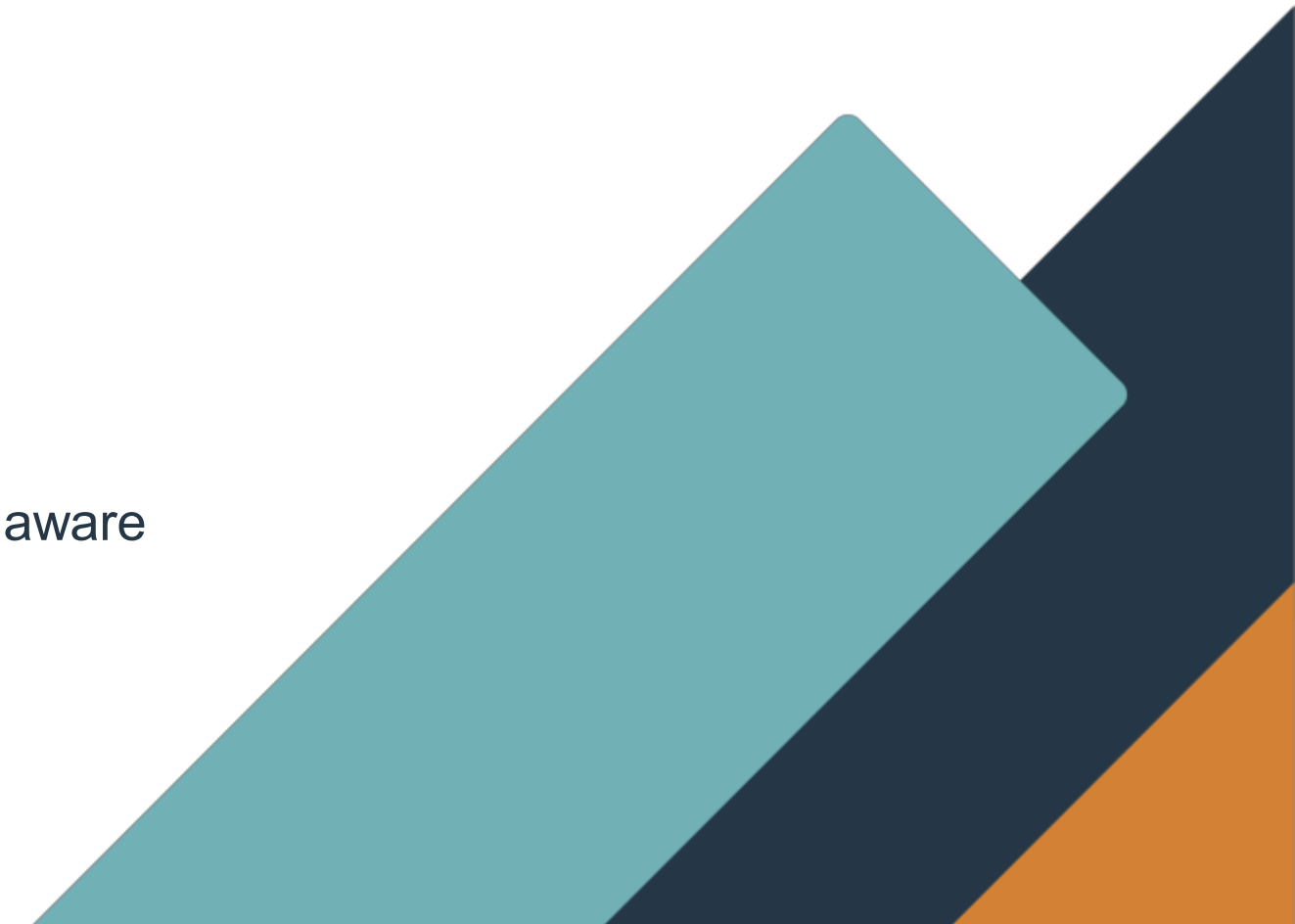
CareForum 2022

The WellSky® Conference

Alcohol withdrawal Management: What's new in 2022

Lisa L. Deal Pharm.D., FASHP, BCACP, B.S.N.

Director of Pharmacy SUN Behavioral Health Delaware



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Today's speaker

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SUN Behavioral Health Delaware

Disclosures

- Lisa L. Deal has no conflicts of interest to declare.

Agenda

1. Describe history of alcohol withdrawal(AW)
2. Discuss signs and symptoms of AW, including disruptive/psychotic patients
3. Recall CIWA scoring and other algorithms for scoring AW
4. Introduce treatment algorithms using benzodiazepines and other pharmacologic agents



KNOWLEDGE CHECK #1

What is the first known type of potable alcohol?

Historical Perspectives

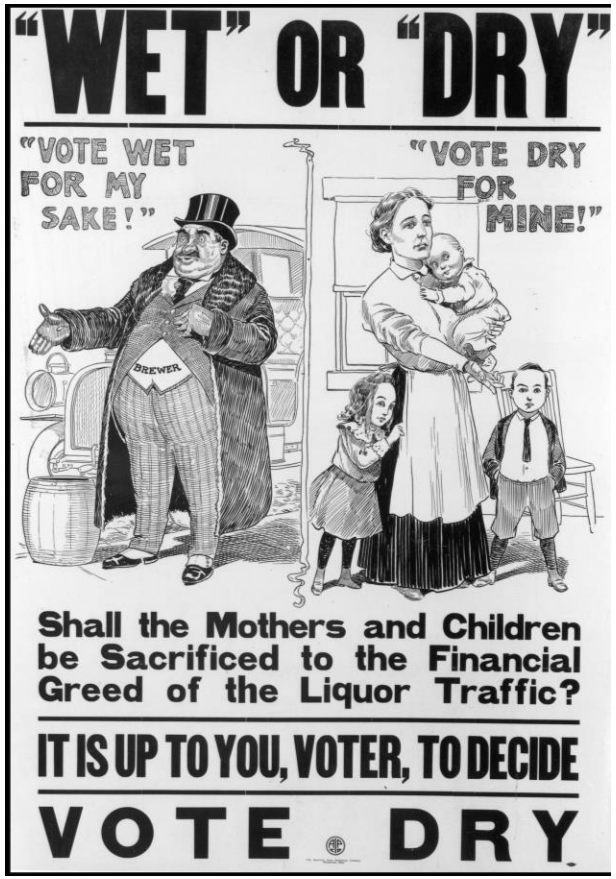
- In China, residue on pottery dating from around 5,000 years ago shows beer was brewed using barley and other grains

- A 3,900-year-old Sumerian poem honoring Ninkasi, the patron goddess of brewing, contains the oldest surviving beer recipe, describing the production of beer from bread made from barley

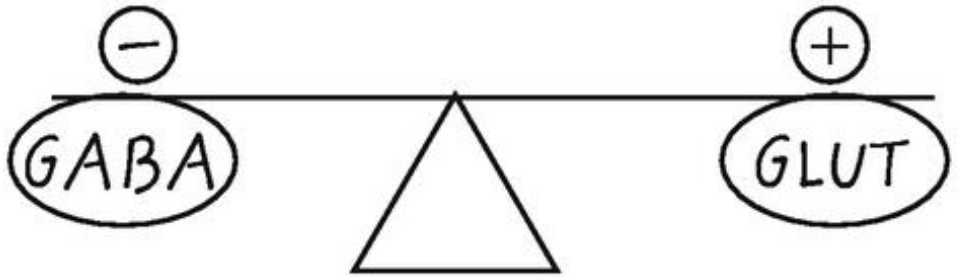
Li Liu et al, The origins of specialized pottery and diverse alcohol fermentation techniques in Early Neolithic China, Proceedings of the National Academy of Sciences (2019).

Historical Perspectives

- An uncontrollable, overwhelming and irresistible desire to consume alcohol was described by Benjamin Rush in 1784, and delirium tremens was independently described by both Pearson and Sutton in 1813
- The Temperance Movement suggested that anyone who consumed excessive amounts of alcohol would suffer from alcohol-related problems
  - Did NOT suggest that alcoholism could affect specifically vulnerable individuals



Gambino, Megan, Smithsonian Magazine. "During Prohibition, Your Doctor Could Write You a Prescription for Booze." October 7, 2013.
Clark, Patrick Michael, Rappahannock Magazine. "Drink the Dominion Dry: Prohibition Comes to Virginia". October, 2015, Volume 2, Issue 1.
Kamieniak, Ted, Fredericksburg: The Eclectic Histories for the Curious Reader. "The Pledge of Brotherhood".ialized pottery and diverse alcohol fermentation techniques in Early Neolithic China, Proceedings of the National Academy of Sciences (2019).



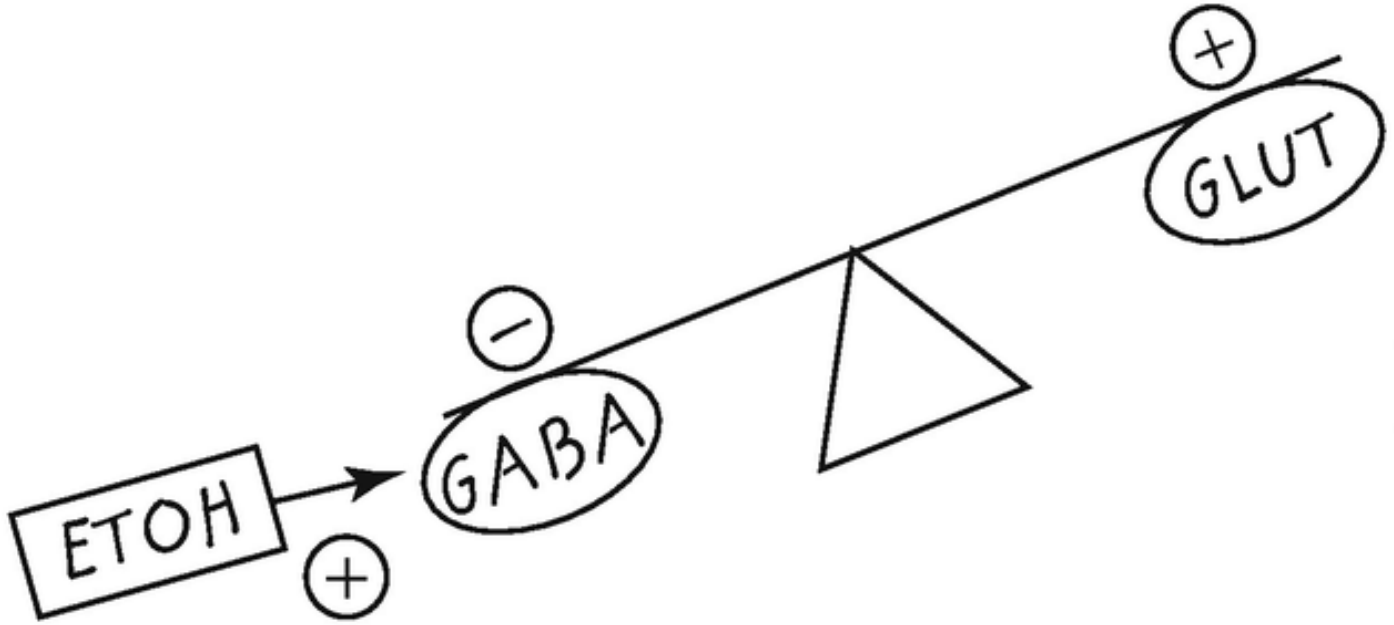
(Normal)

- GABA ≈ GLUT
- Normal balance of CNS inhibitory ⊖ and excitatory ⊕ neurotransmitters

Alcohol Withdrawal Mechanisms

Normal Resting State (Homeostasis)

Salottolo K, McGuire E, Mains CW, van Doorn EC, Bar-Or D. Occurrence, Predictors, and Prognosis of Alcohol Withdrawal Syndrome and Delirium Tremens Following Traumatic Injury. Crit Care Med. 2017 May;45(5):867-874.



Alcohol Intoxication

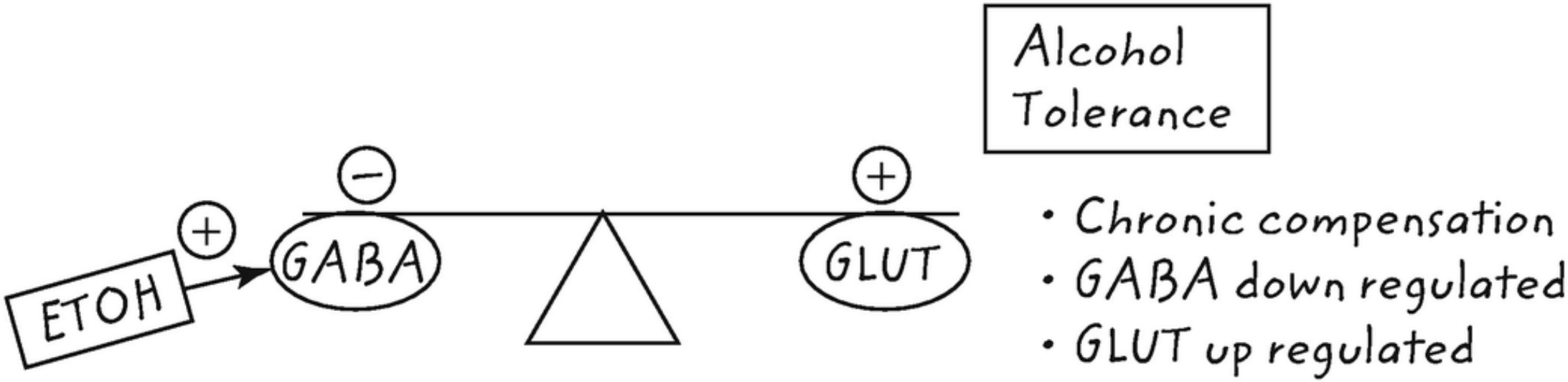
- ETOH $\xrightarrow{\oplus}$ GABA
- Alcohol stimulates increased inhibitory tone = sedation

GABA > GLUT

Alcohol Withdrawal Mechanisms

Alcohol Intoxication

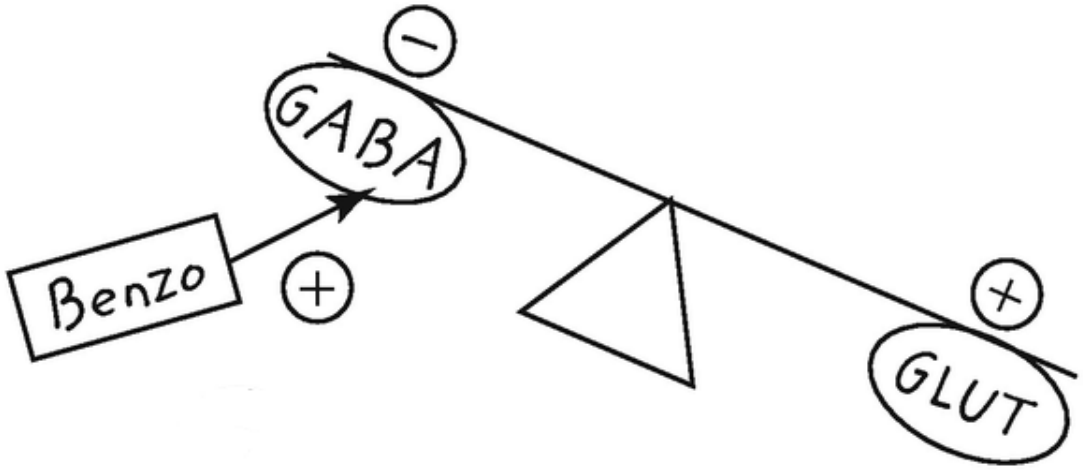
Salottolo K, McGuire E, Mains CW, van Doorn EC, Bar-Or D. Occurrence, Predictors, and Prognosis of Alcohol Withdrawal Syndrome and Delirium Tremens Following Traumatic Injury. Crit Care Med. 2017 May;45(5):867-874.



Alcohol Withdrawal Mechanisms

Alcohol Tolerance

Salottolo K, McGuire E, Mains CW, van Doorn EC, Bar-Or D. Occurrence, Predictors, and Prognosis of Alcohol Withdrawal Syndrome and Delirium Tremens Following Traumatic Injury. Crit Care Med. 2017 May;45(5):867-874.



Rx: Benzos -> Stimulate GABA

Alcohol Withdrawal

- Acute Excitation
- GABA < GLUT

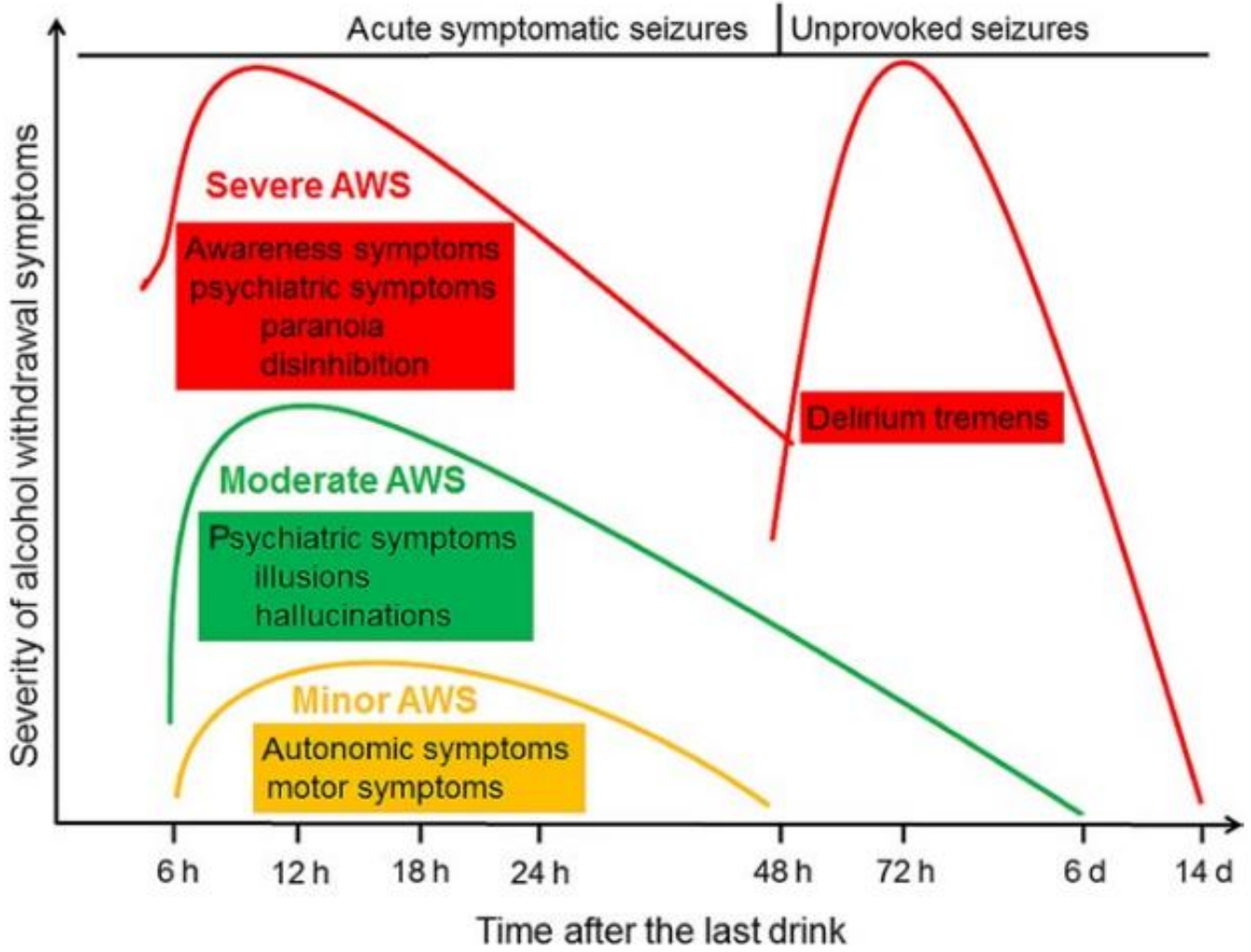
MAJOR	MINOR
DTs	Insomnia
Seizures	Tremors
Agitation	Tachycardia
Autonomic instability	Hypertension
Hallucinosis	

Alcohol Withdrawal Mechanisms

Acute Withdrawal

Salottolo K, McGuire E, Mains CW, van Doorn EC, Bar-Or D. Occurrence, Predictors, and Prognosis of Alcohol Withdrawal Syndrome and Delirium Tremens Following Traumatic Injury. Crit Care Med. 2017 May;45(5):867-874.

Symptom Time Course



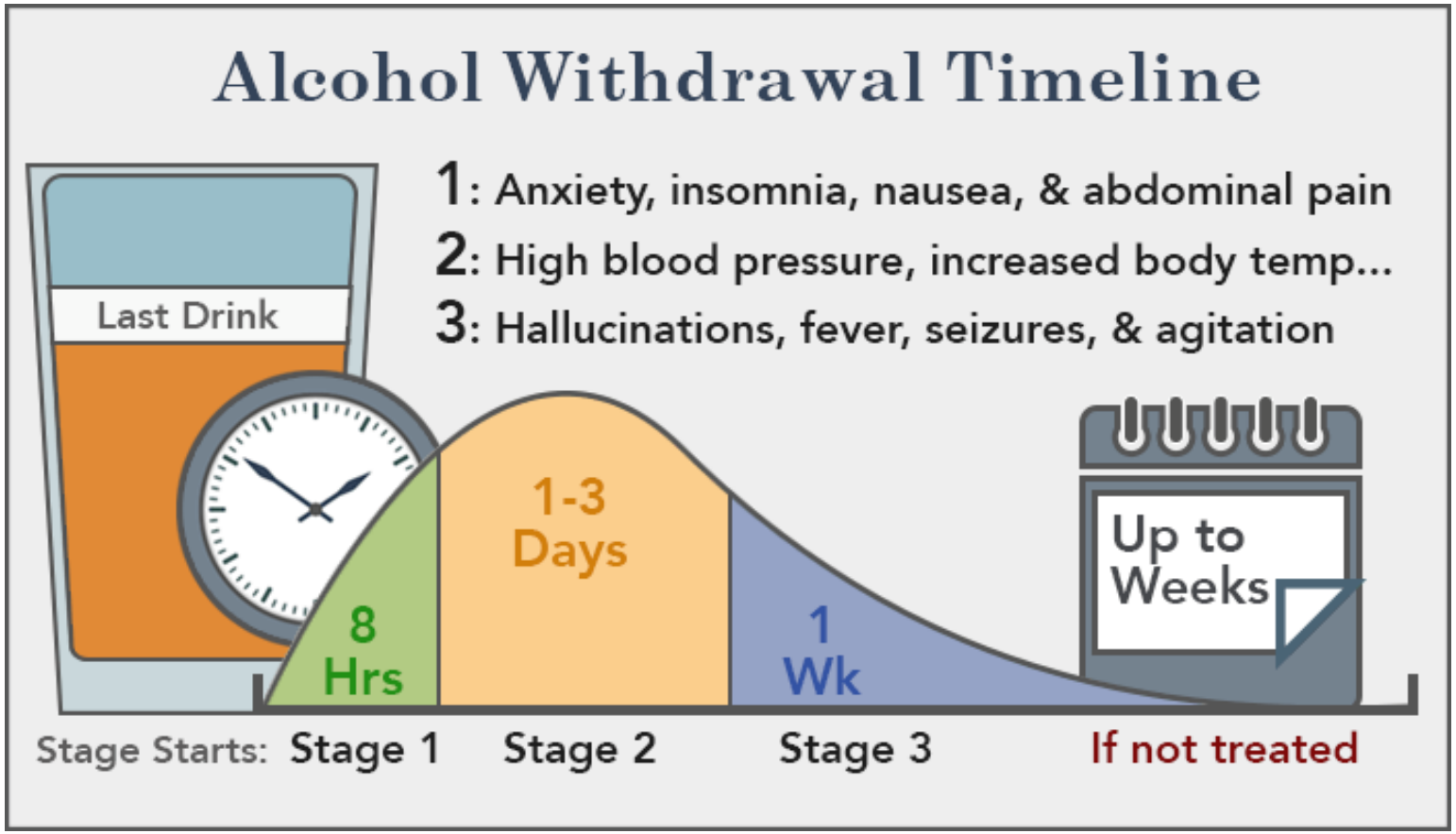
Kattimani, S., & Bharadwaj, B. (2013). Clinical management of alcohol withdrawal: A systematic review. Industrial psychiatry journal, 22(2), 100–108.

Differential Diagnoses For Severe Alcohol Withdrawal

Differential diagnosis	Comment
Hyponatremia	Due to poor oral intake, dehydration, and uremia; frequently presenting as hypoactive delirium
Hepatic encephalopathy	Jaundice, hematemesis, melena, icterus, flapping tremor, ascites, sleep–wake reversal
Pneumonia	Fever, cough, low arterial blood oxygen saturation, delirium before cessation of alcohol use
Encephalitis/Meningitis	Fever, meningeal signs, and focal neurological deficits; MRI/CSF abnormalities
Head injury	Being found unconscious, ear or nose bleeding, pinpoint pupils, focal neurological deficits
Thyrotoxicosis	History of thyroid illness; thyromegaly, exophthalmos, lagophthalmos
Lithium intoxication	History of psychiatric illness, drug overuse, diarrhea, fever, use of NSAID or diuretics
Atropine/Tricyclic intoxication	Fever, hot dry skin, dilated pupils
Psychosis	Hallucinations/delusions of long-standing duration, absence of clouding of sensorium
Antidepressant intoxication	Use of SSRI; diarrhea, myoclonus, jitteriness, seizures, altered sensorium
Subacute encephalopathy with seizures in AUD	Several days after alcohol cessation; complex/simple partial seizures with reversible motor deficits; in EEG focal slowing, periodic lateralized discharges; MRI with reversible T2w flair hyperintensities

Kattimani, S., & Bharadwaj, B. (2013). Clinical management of alcohol withdrawal: A systematic review. Industrial psychiatry journal, 22(2), 100–108.

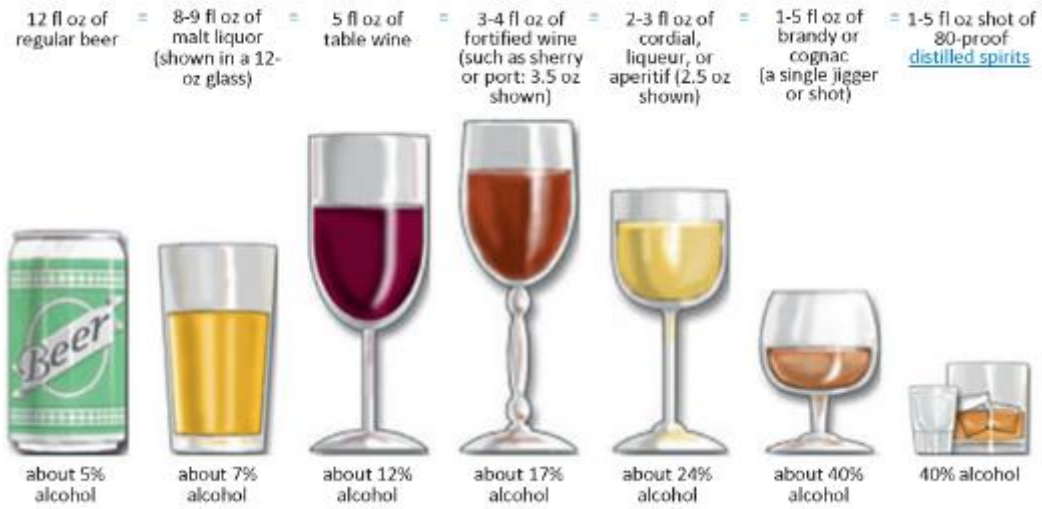
Understanding the DSM-5 Diagnostic Criteria for Alcohol Withdrawal



Schuckit MA. Recognition and management of withdrawal delirium (delirium tremens). N Engl J Med. 2014 Nov 27;371(22):2109-13.
Manasco A, Chang S, Larriviere J, Hamm LL, Glass M. Alcohol withdrawal. South Med J. 2012 Nov;105(11):607-12.
American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. DSM-5. Washington, DC: American Psychiatric Publishing, 2013

DSM-5 Diagnostic Criteria for Alcohol Withdrawal: Setting

- The person has been using significant amounts of alcohol for a significant amount of time
  - Note: Neither the amount nor the duration is specified by DSM-5
- The alcohol use either stops or is reduced



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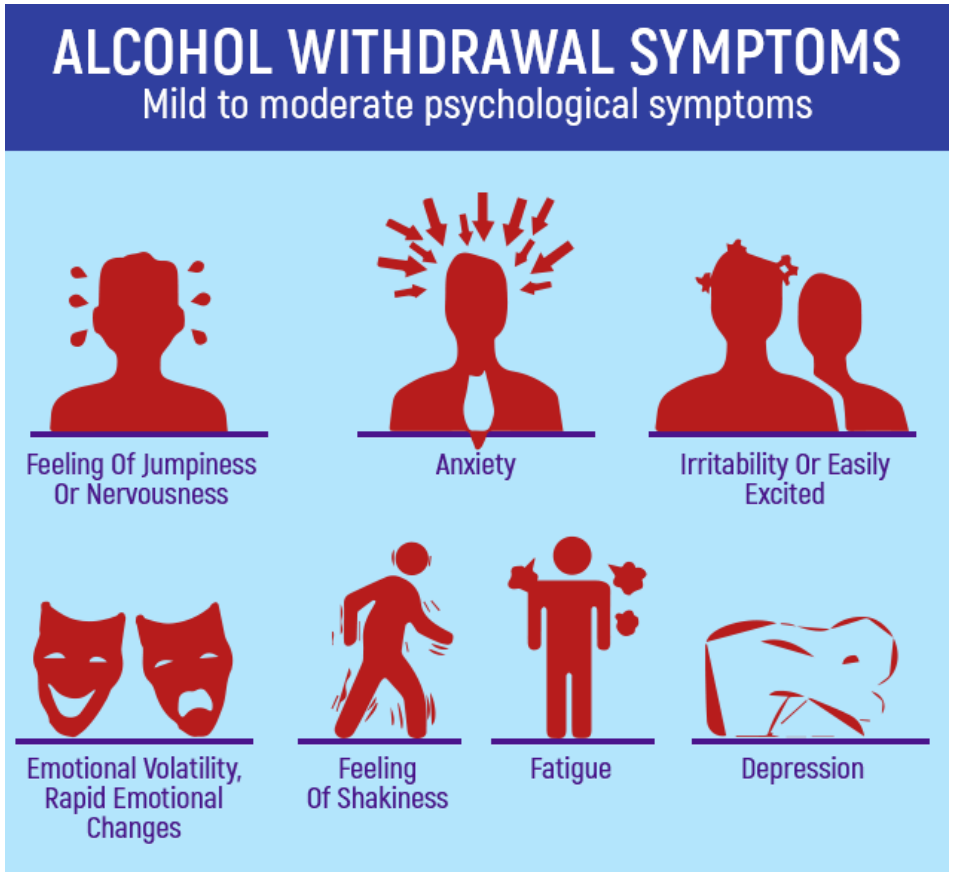
Manasco A, Chang S, Larriviere J, Hamm LL, Glass M. Alcohol withdrawal. South Med J. 2012 Nov;105(11):607-12.
American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. DSM-5. Washington, DC: American Psychiatric Publishing, 2013

DSM-5 Diagnostic Criteria for Alcohol Withdrawal: Sequence

- This again is stating the obvious, but the symptoms/ signs of alcohol withdrawal described below start soon after the alcohol use is stopped or reduced
  - How soon after?



Schuckit MA. Recognition and management of withdrawal delirium (delirium tremens). N Engl J Med. 2014 Nov 27;371(22):2109-13.
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American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. DSM-5. Washington, DC: American Psychiatric Publishing, 2013

DSM-5 Diagnostic Criteria for Alcohol Withdrawal: Signs & Symptoms

Eight clinical features are listed by DSM-5 that may be present in alcohol withdrawal

- **For the diagnosis, at least two of these eight should be present**
  - Autonomic hyperactivity (e.g., increased sweating, tachycardia)
- **Agitation, psychomotor**
  - Anxiety
  - Increased hand tremor
  - Insomnia
  - Nausea or vomiting
  - Transient visual, tactile, or auditory hallucinations or illusions
  - Generalized tonic-clonic seizures

As in all DSM diagnoses:

- There should be either distress or functional impairment
- The symptoms should not be due to another cause

DSM-5 Diagnostic Criteria for Alcohol Withdrawal: Delirium

Decreased attention and awareness

Disturbance in attention, awareness, memory, orientation, language, visuospatial ability, perception, or all these abilities that is a change from the normal level and fluctuates in severity during the day

No evidence of coma or other evolving neurocognitive disorders

Schuckit MA. Recognition and management of withdrawal delirium (delirium tremens). N Engl J Med. 2014 Nov 27;371(22):2109-13.
Manasco A, Chang S, Larriviere J, Hamm LL, Glass M. Alcohol withdrawal. South Med J. 2012 Nov;105(11):607-12.
American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. DSM-5. Washington, DC: American Psychiatric Publishing, 2013

Risk Factors for Severe AWS

- Prior episodes of severe AWS
- Older age
- Medical comorbidities
- Symptoms with detectable BAL
- Non-medical use of other sedatives

Benson G, McCallum J, Roberts NJ. Risk Factors for Severe Alcohol Withdrawal Syndrome in an Acute Hospital Population. J Addict Nurs. 2019 Jul/Sep;30(3):159-168.

KNOWLEDGE CHECK #2

What patient population is at greatest risk for severe alcohol withdrawal?

Clinical Institute Withdrawal Assessment for Alcohol–Revised (CIWA-Ar)

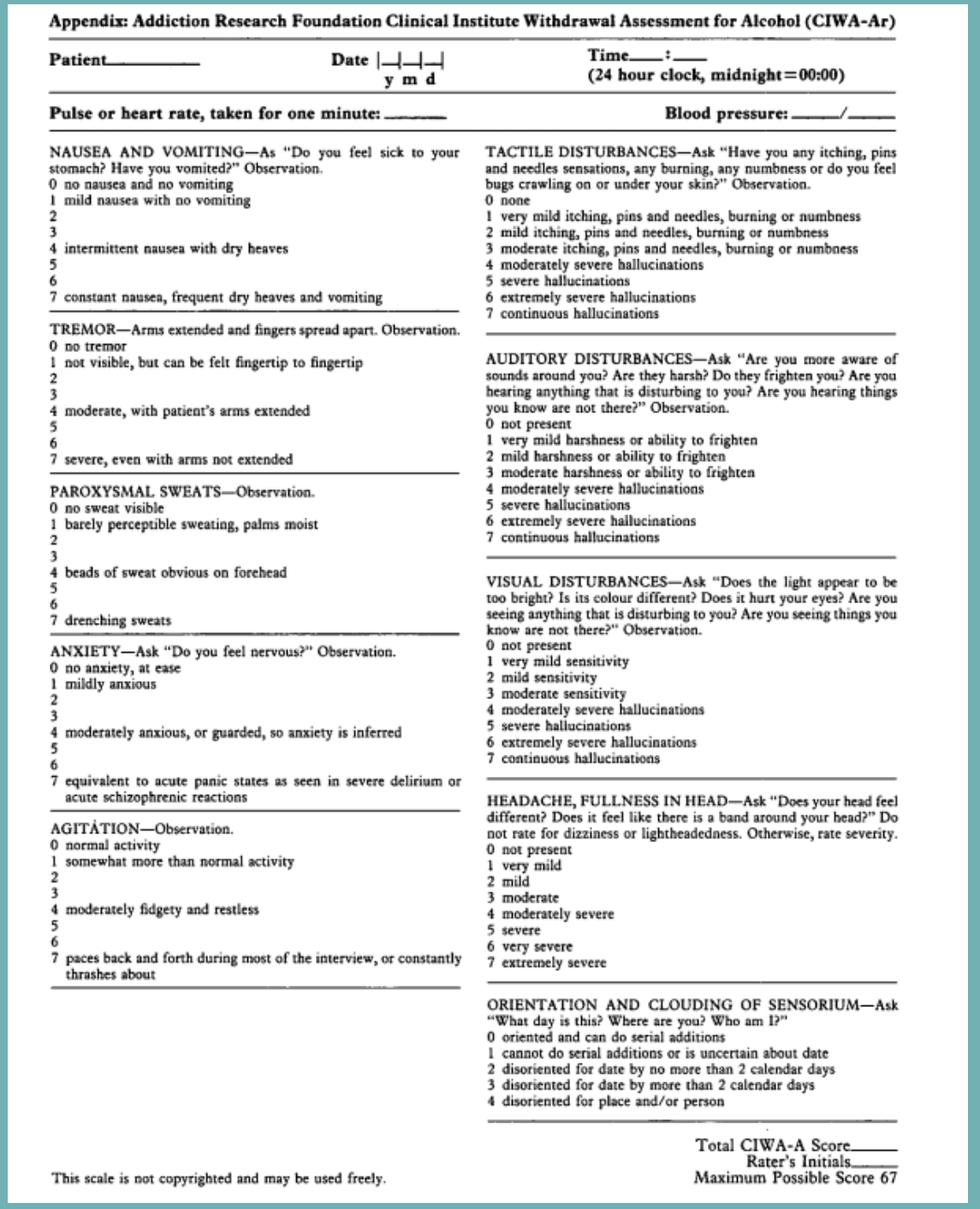
Maximum Score = 67

Severe >15

Moderate = 10-15

Moderate = 10-15

*Treatment at 8-10



Appendix: Addiction Research Foundation Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar)

Patient_____ **Date** |_|_|_|_| y m d **Time**___:___ **(24 hour clock, midnight = 00:00)**

Pulse or heart rate, taken for one minute: _____ **Blood pressure:** ____/____

NAUSEA AND VOMITING—As "Do you feel sick to your stomach? Have you vomited?" Observation.
0 no nausea and no vomiting
1 mild nausea with no vomiting
2
3
4 intermittent nausea with dry heaves
5
6
7 constant nausea, frequent dry heaves and vomiting

TREMOR—Arms extended and fingers spread apart. Observation.
0 no tremor
1 not visible, but can be felt fingertip to fingertip
2
3
4 moderate, with patient's arms extended
5
6
7 severe, even with arms not extended

PAROXYSMAL SWEATS—Observation.
0 no sweat visible
1 barely perceptible sweating, palms moist
2
3
4 beads of sweat obvious on forehead
5
6
7 drenching sweats

ANXIETY—Ask "Do you feel nervous?" Observation.
0 no anxiety, at ease
1 mildly anxious
2
3
4 moderately anxious, or guarded, so anxiety is inferred
5
6
7 equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions

AGITATION—Observation.
0 normal activity
1 somewhat more than normal activity
2
3
4 moderately fidgety and restless
5
6
7 paces back and forth during most of the interview, or constantly thrashes about

TACTILE DISTURBANCES—Ask "Have you any itching, pins and needles sensations, any burning, any numbness or do you feel bugs crawling on or under your skin?" Observation.
0 none
1 very mild itching, pins and needles, burning or numbness
2 mild itching, pins and needles, burning or numbness
3 moderate itching, pins and needles, burning or numbness
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

AUDITORY DISTURBANCES—Ask "Are you more aware of sounds around you? Are they harsh? Do they frighten you? Are you hearing anything that is disturbing to you? Are you hearing things you know are not there?" Observation.
0 not present
1 very mild harshness or ability to frighten
2 mild harshness or ability to frighten
3 moderate harshness or ability to frighten
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

VISUAL DISTURBANCES—Ask "Does the light appear to be too bright? Is its colour different? Does it hurt your eyes? Are you seeing anything that is disturbing to you? Are you seeing things you know are not there?" Observation.
0 not present
1 very mild sensitivity
2 mild sensitivity
3 moderate sensitivity
4 moderately severe hallucinations
5 severe hallucinations
6 extremely severe hallucinations
7 continuous hallucinations

HEADACHE, FULLNESS IN HEAD—Ask "Does your head feel different? Does it feel like there is a band around your head?" Do not rate for dizziness or lightheadedness. Otherwise, rate severity.
0 not present
1 very mild
2 mild
3 moderate
4 moderately severe
5 severe
6 very severe
7 extremely severe

ORIENTATION AND CLOUDING OF SENSORIUM—Ask "What day is this? Where are you? Who am I?"
0 oriented and can do serial additions
1 cannot do serial additions or is uncertain about date
2 disoriented for date by no more than 2 calendar days
3 disoriented for date by more than 2 calendar days
4 disoriented for place and/or person

Total CIWA-A Score_____
Rater's Initials_____
Maximum Possible Score 67

This scale is not copyrighted and may be used freely.

Sullivan et al., 1989J.T. Sullivan, K. Sykora, J. Schneiderman, C.A. Naranjo, E.M. SellersAssessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar) Br. J. Addict., 84 (1989), pp. 1353-1357.

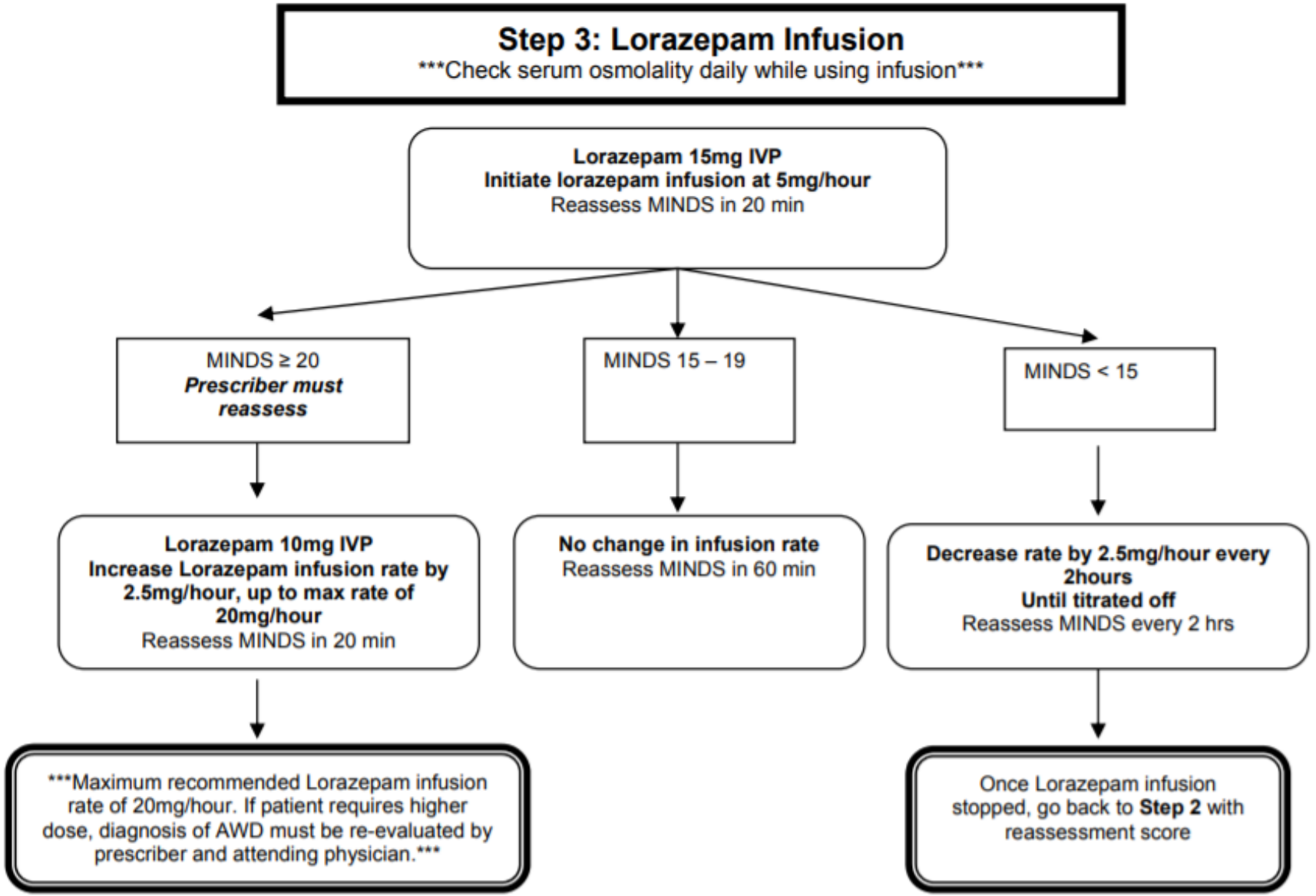
MINDS/mMINDS

- Symptom-based detoxification scale assessment tool (MINDS) and a single standardized high dose, diazepam-based treatment protocol (loading dose up to 80 mg diazepam)
- Use of a novel symptom-based assessment tool and a single high dose diazepam-based treatment protocol significantly decreased LOS, use of restraints, and transfer into the ICU compared to use of multiple older protocols without adversely impacting readmissions and mortality
  - This standardized treatment approach can be safely used to improve patient outcomes

Modified Minnesota Detoxification Scale (MINDS)	
PARAMETER (Patient receives score based on real-time assessment)	SCORE
Pulse (beats per minute)	
<90	0
90-110	1
>110	2
DIASTOLIC blood pressure (mmHg)	
<90	0
90-110	1
>110	2
***Tremor** – Assess with patient's arms extended and fingers spread.	
Absent	0
Slightly visible or can be felt fingertip to fingertip	2
Moderate – Noticeably visible with arms extended	4
Severe – Noticeable even with arms not extended	6
Sweat	
Absent	0
Barely; Moist palms	2
Beads visible	4
Drenching	6
***Hallucinations** – Feeling crawling sensations over skin (tactile), hearing voices when no one has spoken (auditory), or seeing patterns, lights, beings, or objects that are not there (visual).	
Absent	0
Mild – Mostly lucid, sporadic/rare hallucinations	1
Moderate/Intermittent – Hallucinating at times (when first waking up or in between conversations/patient care) with moments of lucidity but able to be reoriented	2
Severe, continuous while awake	3
***Agitation** – Assess using the Richmond Agitation-Sedation Scale (RASS)	
Normal activity or sedated (RASS of 0 or less)	0
Somewhat > normal (RASS of +1)	3
Moderately fidgety, restless (RASS of +2)	6
Pacing, thrashing (RASS of ≥+3)	9
***Orientation**	
Oriented x3 (person/place/time OR at patient's baseline OR too sedated to assess orientation)	0
Oriented x2	2
Oriented x1	4
Disoriented	6
***Delusions** – Unfounded ideas that can be related to suspicions or paranoid thoughts, i.e. patient believes their things have been stolen, or they are being persecuted unjustly	
Absent of unable to assess	0
Present	6
Seizures	
Not actively seizing	0
Actively seizing	6
TOTAL	
***If unable to assess a parameter secondary to over sedation or mechanical ventilation, score = 0**	

Littlefield AJ, Heavner MS, Eng CC, et al. Correlation Between mMINDS and CIWA-Ar Scoring Tools in Patients With Alcohol Withdrawal Syndrome. Am J Crit Care. 2018;27(4):280-286. doi:10.4037/ajcc2018547

MINDS



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Brief Alcohol Withdrawal Scale (BAWS)

	0 None	1 Mild	2 Moderate	3 Severe	Score
Tremor	No tremor	Not visible, but can be felt	Moderate, with arms extended	At rest, without arms extended	
Diaphoresis/ Sweats	No sweats	Mild, barely visible	Beads of sweat	Drenching sweats	
Agitation	Not present (RASS = 0 or less)	Increased activity (RASS = 1)	Restless, fidgety (RASS = 2)	Restless, pacing, thrashing in bed (RASS = 3 or 4)	
Confusion/ Orientation	Oriented to person, place, time	Disoriented to time (e.g., by more than 2 days or wrong month or wrong year) or to place (e.g., name of building, city, state), but not both	Disoriented to time and place	Disoriented to person	
Hallucinations (visual, auditory, tactile)	None	Mild (vague report, reality testing intact)	Moderate (more defined hallucinations)	Severe (obviously responding to internal stimuli, poor reality testing)	
				TOTAL	

Rastegar DA, Applewhite D, Alvanzo AAH, Welsh C, Niessen T, Chen ES. Development and implementation of an alcohol withdrawal protocol using a 5-item scale, the Brief Alcohol Withdrawal Scale (BAWS). Subst Abus. 2017 Oct-Dec;38(4):394-400.

SHOT Protocol

SHOT Scale

Sweating	0 – No visible sweating 1 – Palms moderately moist 2 – Visible beads of sweat on forehead
Hallucinations "Are you feeling, seeing, or hearing anything that is disturbing to you? Are you seeing or hearing things you know are not there?"	0 – No hallucinations 1 – Tactile hallucinations only 2 – Visual and/or auditory hallucinations
Orientation "What is the date, month, and year? Where are you? Who am I?"	0 – Oriented 1 – Disoriented to date by one month or more 2 – Disoriented to place or person
Tremor Extend arms and reach for object. Walk across hall (optional).	0 – No tremor 1 – Minimally visible tremor 2 – Mild tremor 3 – Moderate tremor 4 – Severe tremor

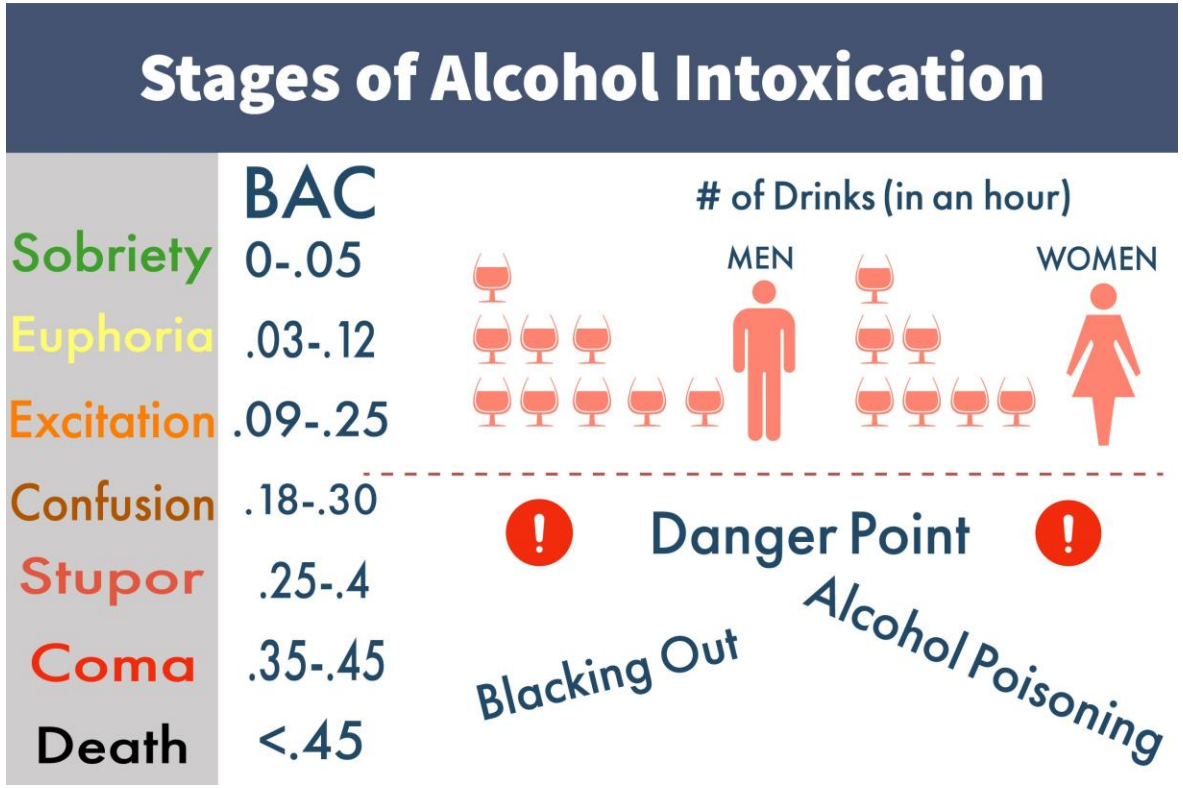
- Score of 2+ indicates need for benzodiazepines
- Discontinue treatment when score < 2 on two consecutive occasions

META:PHI 2015

Gray S, Borgundvaag B, Sirvastava A, Randall I, Kahan M. Feasibility and reliability of the SHOT: A short scale for measuring pretreatment severity of alcohol withdrawal in the emergency department. Acad Emerg Med. 2010 Oct;17(10):1048-54.

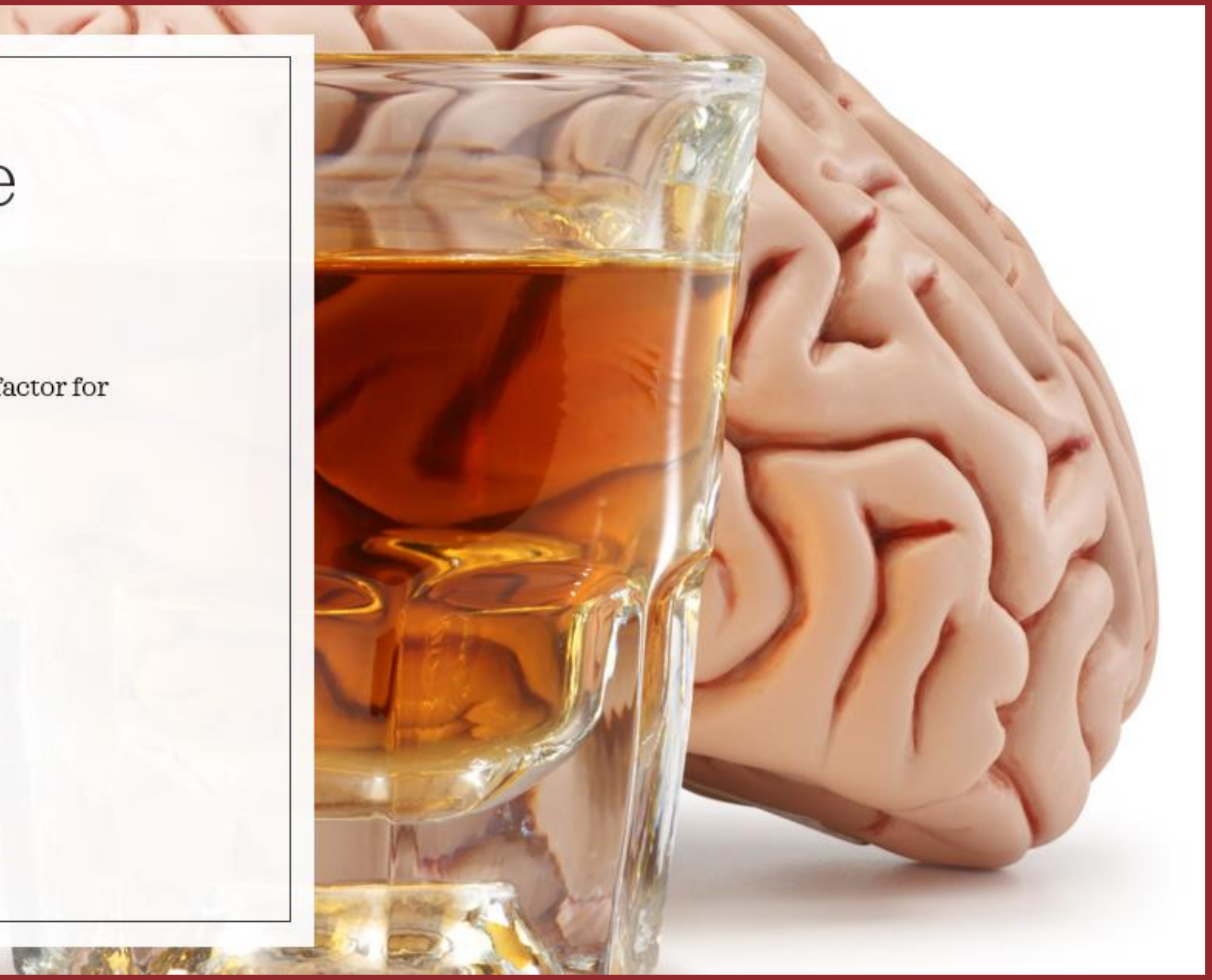
Withdrawal Intoxication Assessment

- Serum alcohol levels cannot predict withdrawal threshold



Knowledge Check #3

- What is the single greatest risk factor for intoxication?



Therapeutics

- Work Up
- Treatment
  - Benzodiazepines
  - Barbiturates
  - Anticonvulsants
  - α2-adrenergic agonists
  - Vitamins
  - Fluids

Benzodiazepines

Medication	Typical Route of Admin.	Onset of Action	Half-Life	Metabolism
Chlordiazepoxide	Oral	15-30 mins	5-30 hrs, 200 hrs	Phase I & II 3A4
Lorazepam	Oral, IV	<15 mins (IV) 15-30 mins (PO)	12-18 hrs	Phase II
Diazepam	Oral, IV	<15 mins	30-60 hrs, 100 hrs	Phase I & II 2C19, 3A4
Oxazepam	Oral	30-60 mins	8-14 hrs	Phase II

Melton ST, Kirkwood CK. Anxiety Disorders: Generalized Anxiety, Panic, and Social Anxiety Disorders. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey L. eds. Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York, NY: McGraw-Hill; 2017.

Taper versus Symptom-Triggered Treatment

Symptom-triggered therapy

- Benzodiazepines are given only when the patient has symptoms of alcohol withdrawal
  - No symptoms, no medication
  - Depends on validity of assessment

Fixed schedule therapy

- Benzodiazepine is given at fixed intervals even if symptoms are absent

Symptom-triggered lorazepam treatment for AW resulted in administration of **lower total doses of medication** for a **shorter duration of treatment** and was **as safe as the fixed tapering dose**

Sachdeva A, Chandra M, Deshpande SN. A comparative study of fixed tapering dose regimen versus symptom-triggered regimen of lorazepam for alcohol detoxification. Alcohol Alcohol. 2014 May-Jun;49(3):287-91. doi: 10.1093/alcalc/agt181. Epub 2014 Jan 8. PMID: 24407777.

Barbiturates

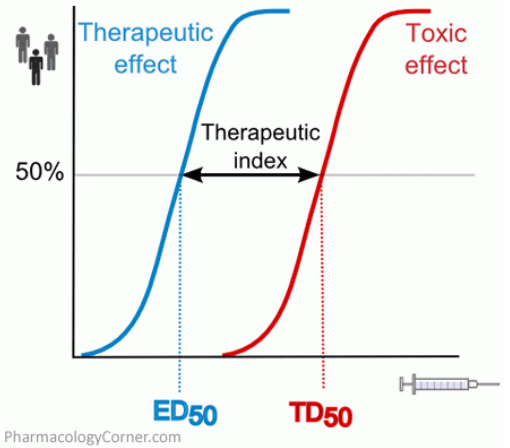
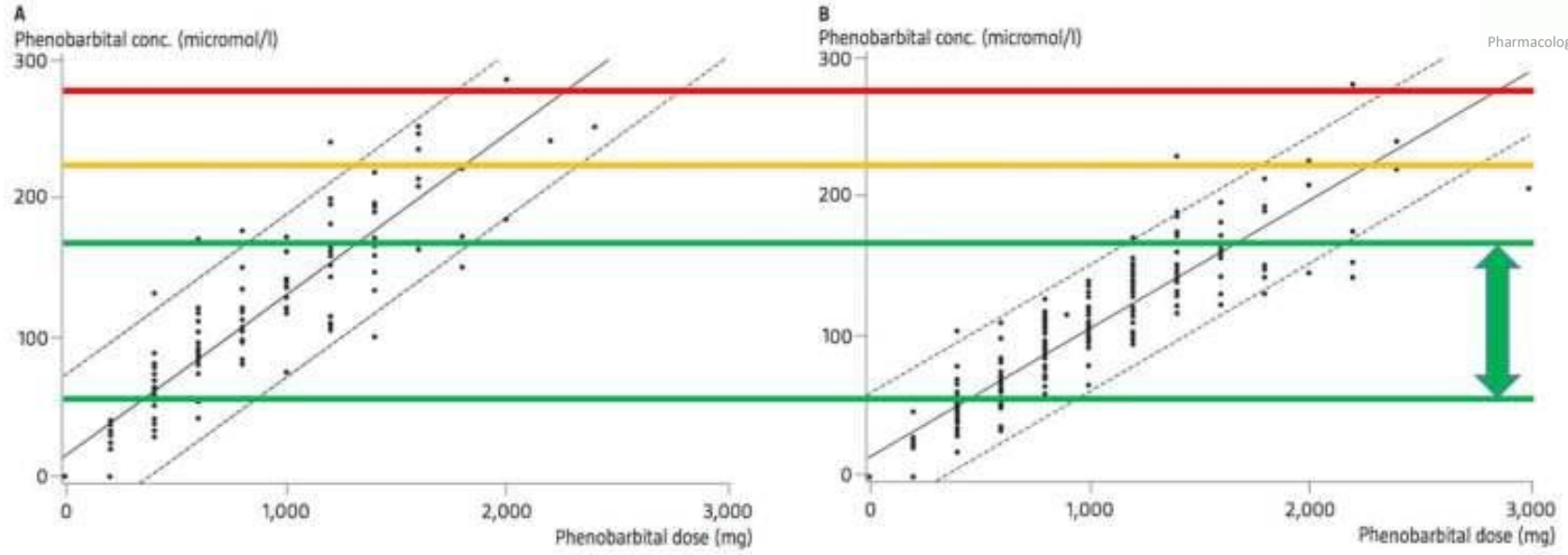


FIGURE 1

Relation between plasma phenobarbital concentration (micromol/l) and phenobarbital dose (mg), including best fitting linear relation and 95% confidence limits estimated under the linear assumption (212 males **(A)** and 136 females **(B)**).



Relationship between cumulative phenobarbital dose and plasma phenobarbital concentration among patients treated for alcohol withdrawal. Green lines indicate the therapeutic range of phenobarbital concentration for *epilepsy* (**64-172 uM/L = 15-40 ug/ml**), the orange line indicates the level at which mild signs of toxicity are usually noted such as atatxia and nystagmus (**215 uM/L = 50 ug/ml**) and the red line indicates the lowest level which has been associated with stupor or coma (**>280 uM/L = 65 ug/ml**). Please note however that the ideal phenobarbital concentration for the treatment of alcohol withdrawal remains unclear. If the patient's weights were taken into account, these relationships would be even more tightly linear. Note that based on this data, one gram of phenobarbital would achieve a reasonable phenobarbital level in nearly all patients.

Tangmose et al 2010 PMID 20682131

Tangmose K, Nielsen MK, Allerup P, Ulrichsen J. Linear correlation between phenobarbital dose and concentration in alcohol withdrawal patients. Dan Med Bull. 2010 Aug;57(8):A4141. PMID: 20682131.

Phenobarbital

- One important caveat is that **phenobarbital is synergistic with benzodiazepine,** so toxicity could occur at lower phenobarbital levels in the presence of benzodiazepine.
- IV administration is preferred in the critical care arena
  - Allows for more rapid achievement of peak drug levels
- **Rapid absorption decreases the risk of dose stacking** (administering multiple doses before the first dose has had time to act fully, leading to excessive dosing).
  - When given intravenously, the drug distributes within <30 minutes

Prediction of phenobarbital level from cumulative dose

Conventional units (USA):

Phenobarbital level in ug/ml = 1.5(Dose in mg/kg)

SI units:

Phenobarbital level in uM/L = 6.6(Dose in mg/kg)

-Internet Book of Critical Care, by @PulmCrit

interpretation of phenobarbital levels

	Conventional Units (ug/ml)	SI units (uM/L)
Therapeutic Range, Epilepsy	15-40 ug/mL	64-172 uM/L
Mild signs of toxicity usually noted (e.g. ataxia, nystagmus)	>50 ug/mL	>215 uM/L
Severe toxicity can occur (e.g. stupor/coma)	>65 ug/mL	>280 uM/L
Therapeutic range, Monotherapy for EtOH withdrawal	~10-40 ug/mL (??)	~43-172 uM/L (??)

This table is only intended to provide a rough concept of phenobarbital levels. The optimal phenobarbital levels in treatment of alcohol withdrawal remains unclear. Ultimately, doses need to be titrated based on clinical response. For example, patients with alcohol withdrawal will often have an excellent clinical response at phenobarbital levels which are *below* the traditional therapeutic range for epilepsy.

-The Internet Book of Critical Care, by @PulmCrit

Tangmose K, Nielsen MK, Allerup P, Ulrichsen J. Linear correlation between phenobarbital dose and concentration in alcohol withdrawal patients. Dan Med Bull. 2010 Aug;57(8):A4141. PMID: 20682131.

Phenobarbital for Alcohol Withdrawal

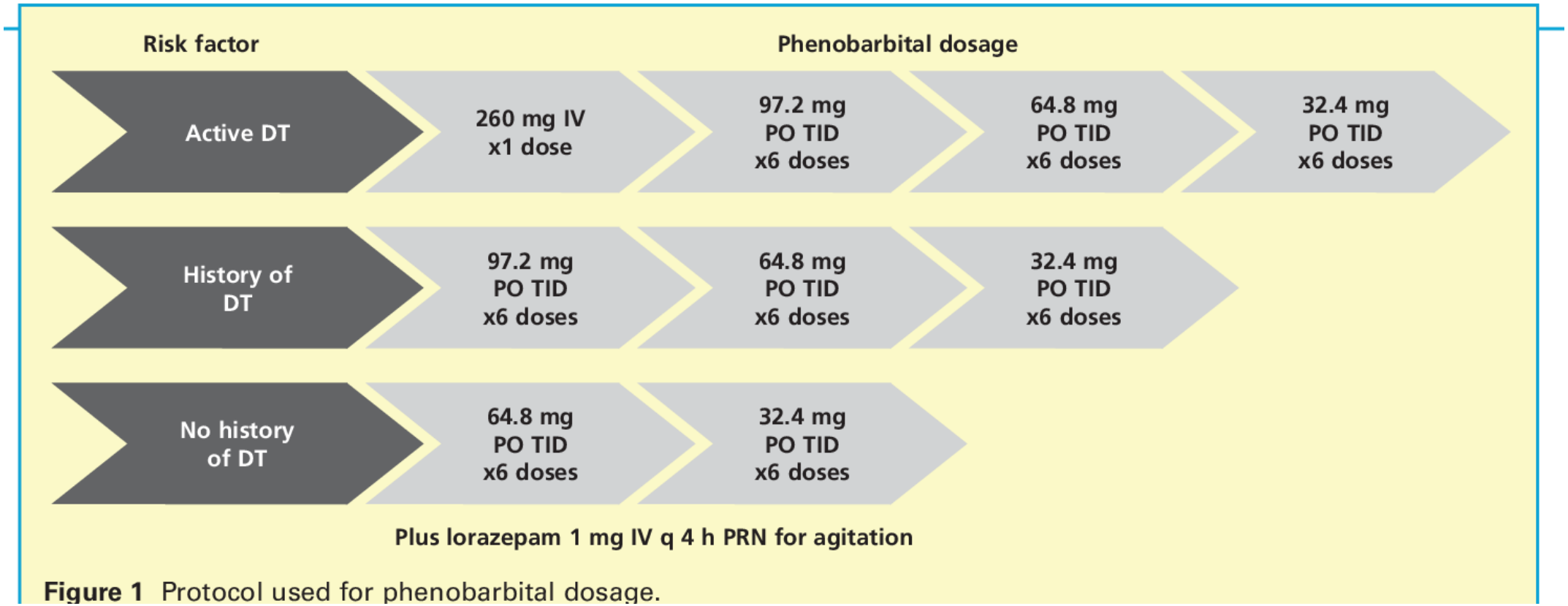
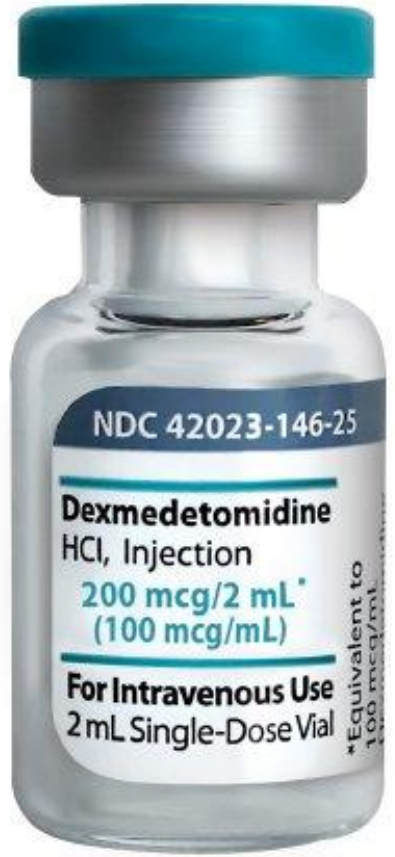


Figure 1 Protocol used for phenobarbital dosage.

Tidwell, W., Thomas, T.L., Pouliot, J.D., Canonico, A.E., & Webber, A.J. (2018). Treatment of Alcohol Withdrawal Syndrome: Phenobarbital vs CIWA-Ar Protocol. American Journal of Critical Care, 27, 454–460.

Dexmedetomidine for Alcohol Withdrawal (Adjunct)

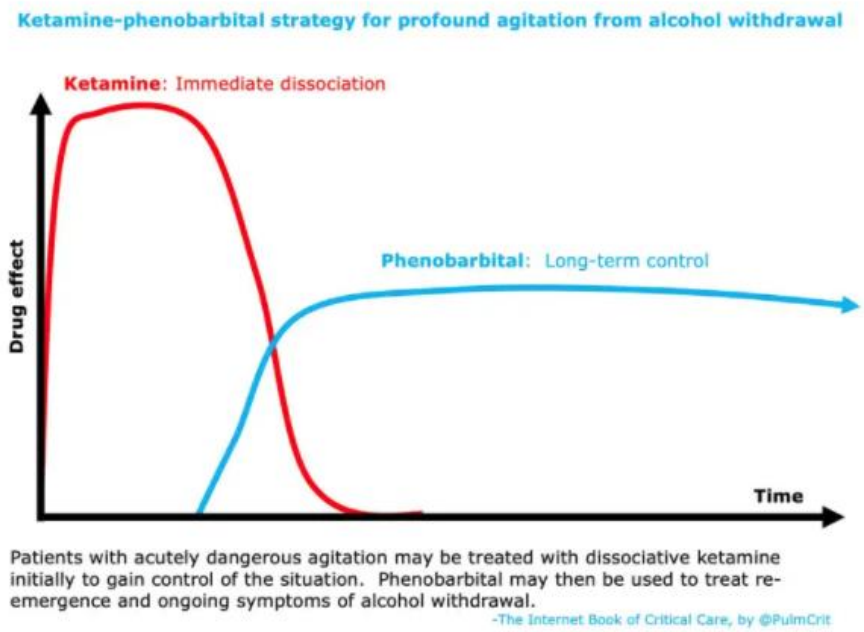
- Overall, evidence supporting use of **dexmedetomidine as an adjunct agent for alcohol withdrawal symptoms** is limited to low quality data of mostly retrospective studies and 2 randomized controlled trials
- Although there are limited data supporting its use, the 2020 ASAM guideline recommends its use as an **adjunct to benzodiazepine therapy for hyperactivity and anxiety symptoms** that are not controlled with benzodiazepines alone, and for patients in the ICU experiencing resistant alcohol withdrawal symptoms
  - Cost
  - Hypotension
  - Bradycardia



Benson G, McCallum J, Roberts NJ. Risk Factors for Severe Alcohol Withdrawal Syndrome in an Acute Hospital Population. J Addict Nurs. 2019 Jul/Sep;30(3):159-168.

Ketamine for Alcohol Withdrawal (Adjunct)

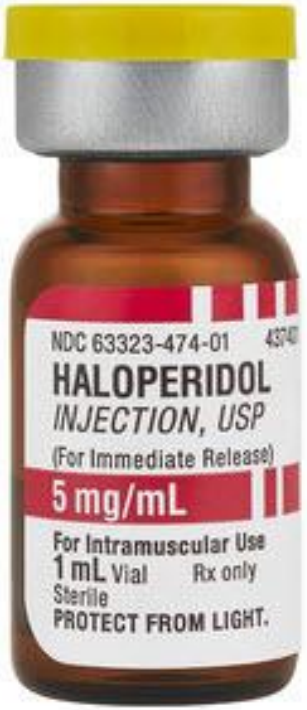
- Dissociative ketamine will achieve behavioral control for ~30 minutes
  - This is enough time to order phenobarbital and start it running in (e.g. 5-10 mg/kg depending on the context)
- As the patient is waking up from the ketamine, phenobarbital may be used to prevent re-emergence
- Phenobarbital is used here in a fashion like a benzodiazepine to prevent re-emergent agitation
- Dissociative ketamine (like dexmedetomidine) isn't a destination therapy – this simply buys time to facilitate transition to phenobarbital



Shah P, McDowell M, Ebisu R, Hanif T, Toerne T. Adjunctive Use of Ketamine for Benzodiazepine-Resistant Severe Alcohol Withdrawal: a Retrospective Evaluation. J Med Toxicol. 2018;14(3):229-236. doi:10.1007/s13181-018-0662-8.

Haloperidol for Alcohol Withdrawal Agitation (Adjunct)

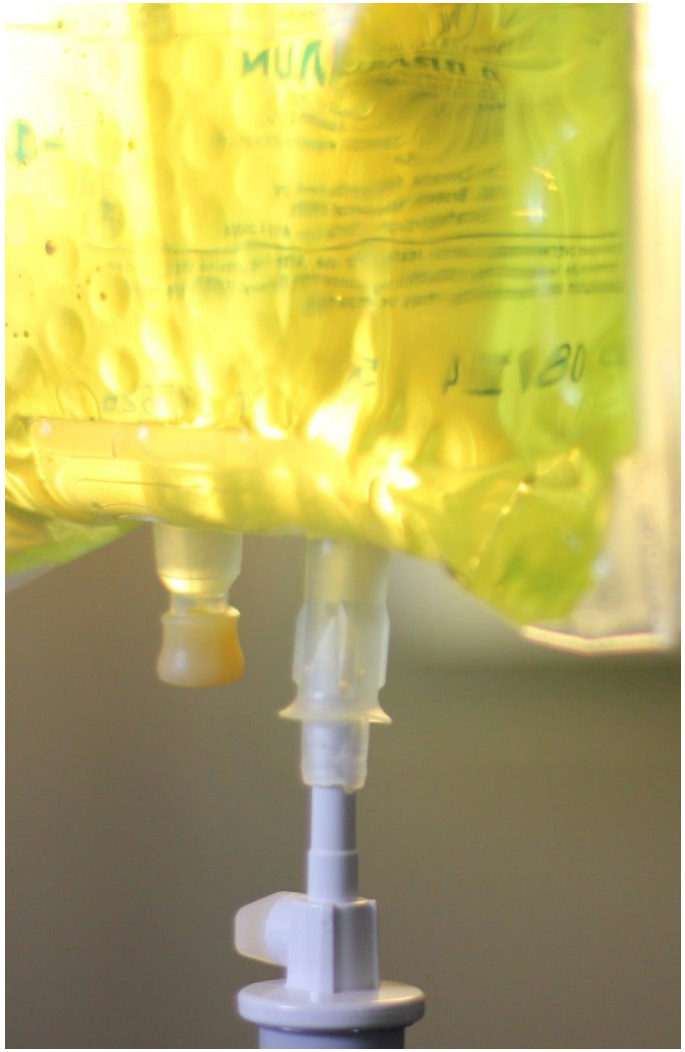
- Haloperidol (Haldol) can be used to treat agitation and hallucinations, although it can lower the seizure threshold
  - All neuroleptic agents are thought to have the potential for causing neuroleptic malignant syndrome, and cases have been reported in patients with AWD who have received neuroleptic drugs
  - No studies were identified describing the use of newer “atypical” antipsychotic agents, such as risperidone, olanzapine, and quetiapine, for AWD
  - These agents are at least as efficacious as typical antipsychotic agents for other indications and have a preferable adverse effect profile



Mayo-Smith MF, Beecher LH, Fischer TL, et al. Management of Alcohol Withdrawal Delirium: An Evidence-Based Practice Guideline. Arch Intern Med. 2004;164(13):1405–1412. doi:10.1001/archinte.164.13.1405

Electrolyte Repletion

- IV fluids aren't going to help them sober up faster
- If symptoms are suggestive of Wernicke's Encephalopathy, be aggressive with thiamine dosing (500 mg IV infused over at least 25 minutes)
  - For prevention, a single dose of thiamine 100 mg IV over 5 minutes is a reasonable intervention
- It's likely sufficient to leave multivitamin and folate supplementation for outpatient, discharge prescriptions, as the consequences of these deficiencies don't develop overnight (and aren't likely to be fixed quickly with IV supplementation).
  - Wait until confirmed hypomagnesemia before jumping to IV magnesium supplementation



Perez S, Keijzers G, Steele M, Byrnes J, Scuffham P. Intravenous 0.9% sodium chloride therapy does not reduce length of stay of alcohol-intoxicated patients in the emergency department: a randomised controlled trial. Emerg Med Australas. 2013;25(6):527-534.

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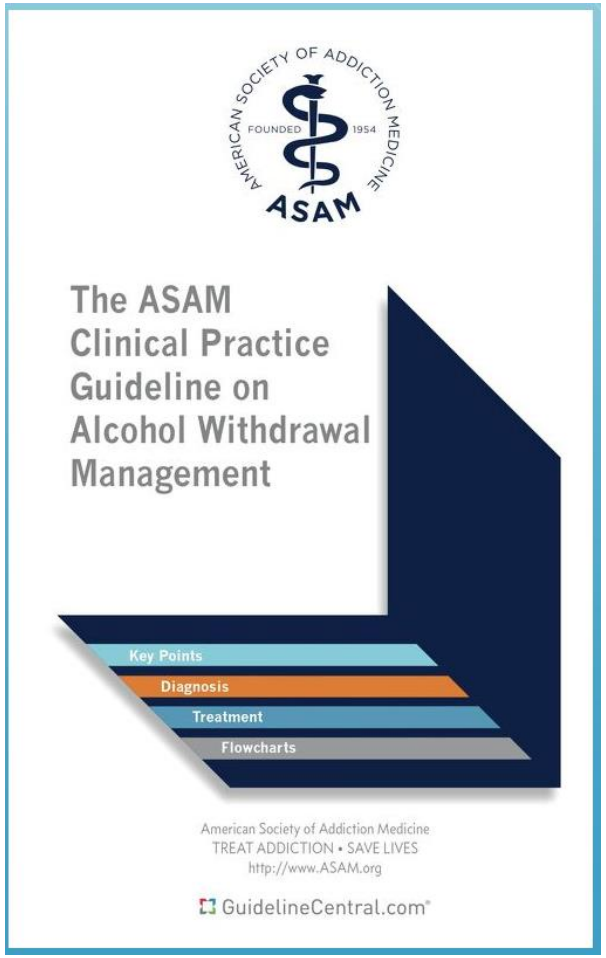


Table 1. Alcohol Withdrawal Severity

Severity Category	Associated CIWA-Ar Range[a]	Clinical Findings
Mild	CIWA-Ar <10	Mild or moderate anxiety, sweating and insomnia, but no tremor
Moderate	CIWA-Ar 10–18	Moderate anxiety, sweating, insomnia, and mild tremor
Severe	CIWA-Ar ≥19	Severe anxiety and moderate to severe tremor, but not confusion, hallucinations, or seizure
Complicated	CIWA-Ar ≥19	Seizure or signs and symptoms indicative of delirium – such as an inability to fully comprehend instructions, clouding of the sensorium or confusion – or new onset of hallucinations

[a] Throughout this document, we provide examples for withdrawal severity using the CIWA-Ar, although other scales can be used. Regardless of the instrument used, there is a wide variety in the literature and in practice as to which scores best delineate mild, moderate and severe withdrawal. Classification of withdrawal severity is ultimately up to the judgment of clinicians and the choice of reference range may be based on their particular patient population or capabilities.

Treatment – Ambulatory

D. Pharmacotherapy

(1) Prophylaxis

→ Recommendation IV.13: Patients at risk of developing severe or complicated alcohol withdrawal or complications of alcohol withdrawal may be treated in ambulatory settings at the discretion of providers with extensive experience in management of alcohol withdrawal. Such patients should be provided with preventative pharmacotherapy. Benzodiazepines are first-line treatment because of their well-documented effectiveness in reducing the signs and symptoms of withdrawal including the incidence of seizure and delirium. Phenobarbital is an appropriate alternative in a Level 2-WM setting for providers experienced with its use. For patients with a contraindication for benzodiazepine use, phenobarbital (in Level 2-WM settings by providers experienced with its use) or transfer to a more intensive level of care are appropriate options.

→ Recommendation IV.14: A front-loading regimen is recommended for patients at high risk of severe withdrawal syndrome. Providing at least a single dose of preventative medication is appropriate for patients at lower levels of risk who have:

- A history of severe or complicated withdrawal
- An acute medical, psychiatric, or surgical illness
- Severe coronary artery disease
- Displaying signs or symptoms of withdrawal concurrent with a positive blood alcohol content

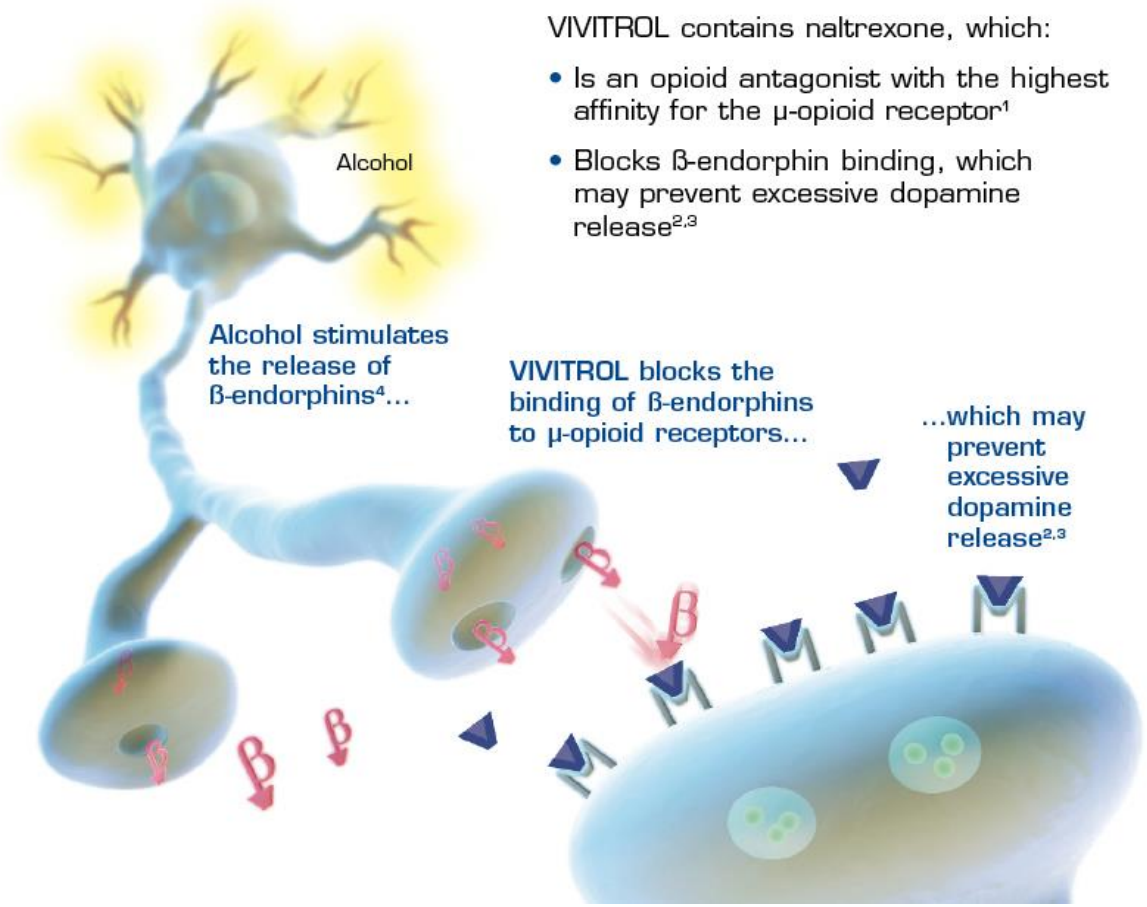
→ Recommendation IV.15: Patients at risk of developing new or worsening signs or symptoms of withdrawal while away from the ambulatory treatment setting should be provided with pharmacotherapy. Some indications of risk include a history of withdrawal episodes of at least moderate severity and being within the window for the development of symptoms in the time course of withdrawal. Benzodiazepines, carbamazepine, or gabapentin are all appropriate options for monotherapy. Providing at least a single dose of benzodiazepine followed by ongoing treatment according to symptom severity is also appropriate. If the risk of developing worse withdrawal is unknown, patients should be reassessed frequently over the next 24 hours to monitor their need for withdrawal medication.

Naltrexone (Vivitrol®)

- Naltrexone-ER is indicated for the treatment of alcohol/opioid dependence in patients who can abstain from alcohol/opioid in an outpatient setting prior to initiation of treatment with Naltrexone-ER
  - Patients should not be actively drinking at the time of initial Naltrexone-ER administration
  - Patients should be 5-7 days from last use of opioids
- Treatment with Naltrexone-ER should be part of a comprehensive management program that includes psychosocial support

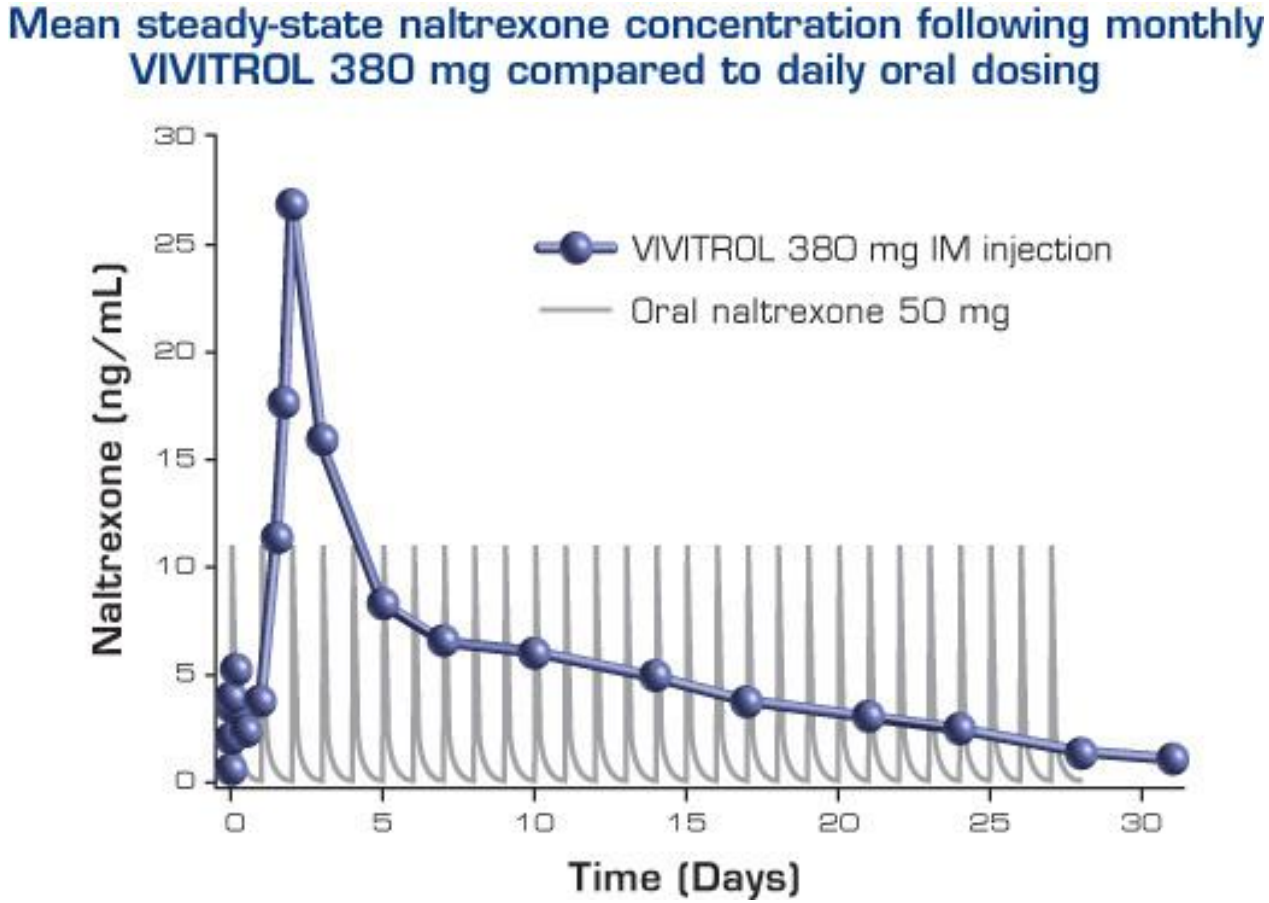
VIVITROL full Prescribing Information. Alkermes, Inc.

Naltrexone (Vivitrol®)



VIVITROL contains naltrexone, which:

- Is an opioid antagonist with the highest affinity for the μ-opioid receptor[1]
- Blocks ß-endorphin binding, which may prevent excessive dopamine release[2,3]



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Naltrexone

- Signs or symptoms of opioid withdrawal, particularly in patients requiring a more rapid transition from agonist to antagonist therapy
- Liver function tests, baseline and subsequent monitoring
- Clinical studies indicate that 50 mg of Naltrexone hydrochloride will block the pharmacologic effects of 25 mg of intravenously administered heroin for periods of 24 hours
  - Other data suggest that doubling the dose of Naltrexone hydrochloride provides blockade for 48 hours, and tripling the dose of Naltrexone hydrochloride provides blockade for about 72 hours

Ling W. (2012). Buprenorphine implant for opioid addiction. Pain management, 2(4), 345–350. https://doi.org/10.2217/pmt.12.26.

Knowledge Check #4

- What is an absolute contraindication to Vivitrol?


thank you

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Thank you.

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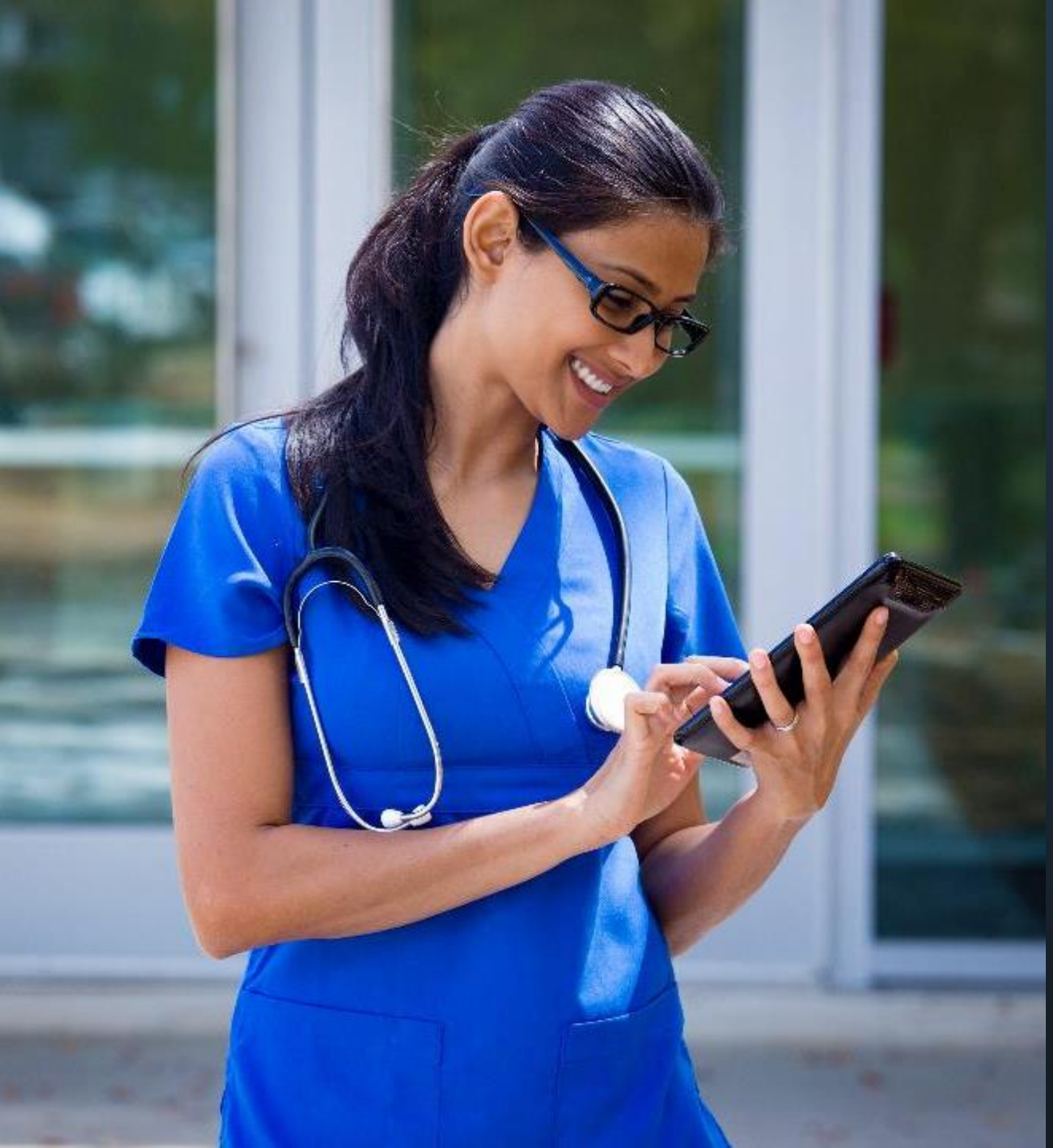

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