



Alcohol Withdrawal Syndrome

Dai-Jin Kim, Ph.D., M.D.

Department of Psychiatry,
The Catholic University of Korea College of Medicine,
Republic of Korea

1 Definition

- **Alcohol Withdrawal Syndrome (AWS)** defined by the manifestation of **at least 2 of the clinical signs**, which occur **within hours to a few days following cessation of heavy and prolonged alcohol consumption**, which cannot be attributed to another medical condition

2 Clinical signs

#1. Autonomic hyperactivity (i.e sweating, HR >100)

#2. Tremors

#3. Insomnia

#4. Transient visual, tactile, auditory hallucinations/illusions

#5. Nausea or vomiting

#6. Psychomotor agitation

#7. Anxiety

#8. Grand mal seizures

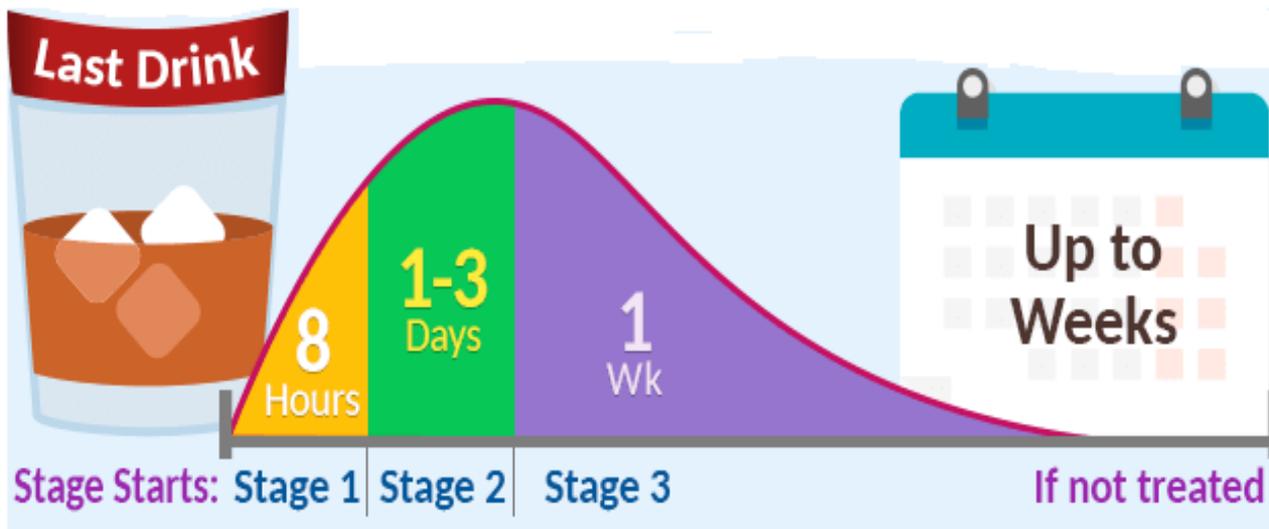
2 Clinical signs

TABLE 1 Common signs and symptoms of AWS

Autonomic symptoms	Motor symptoms	Awareness symptoms	Psychiatric symptoms
Tachycardia	Hand tremor	Insomnia	Illusions
Tachypnea	Tremulousness of body	Agitation	Delusions
Dilated pupils	Seizures	Irritability	Hallucinations
Elevated blood pressure	Ataxia	Delirium	Paranoid ideas
Elevated body temperature	Gait disturbances	Disorientation	Anxiety
Diaphoresis	Hyper-reflexia		Affective instability
Nausea/vomiting	Dysarthria		Combativeness
Diarrhea			Disinhibition

3 Stages of AWS

■ TIMELINE for AWS



6~8hrs: Shakes & Jitters

8~12hrs: Psychotic & Perceptual symptoms

~ 72hrs: Delirium Tremens

12~24hr: seizures

3 Stages of AWS

Uncomplicated AWS

Stages	Clinical Findings	Onset (Usual*)
<u>Early or Uncomplicated</u>	1) Anxiety, <i>fine</i> tremor (anxiety), tachycardia (anxiety); headache; palpitations; anorexia; GI upset; general malaise 2) May have elements of catecholamine excess (slight coarse tremor, elevated BP, elevated HR, diaphoresis, slight fever)	6-36 hrs
<u>Alcohol Withdrawal Seizure</u>	Generalized, tonic-clonic seizures, status epilepticus (rare)	6-48 hrs
<u>Alcoholic Hallucinosis</u>	Visual, auditory, and/or tactile hallucinations	12-48 hrs
<u>Alcohol Withdrawal Delirium</u> (<i>delirium tremens</i>)	Delirium, tachycardia, hypertension, agitation, fever, diaphoresis, <i>coarse</i> tremor	48-96 hrs

Autonomic hyperactivity

Complicated AWS

3 Stages of AWS

✓ Alcohol withdrawal seizure

- **Stereotyped, generalized, tonic-clonic** in character
- **Frequently occur in the absence of other signs of AWS!**
- Approx, 5% -> status epilepticus
- **Often more than one seizure 3 to 6 hrs after the first seizure**
- Anticonvulsants medications **not** required, but difficult to establish the cause in the ER -> should consider other causative factors i.e head injuries, CNS infections, cerebrovascular diseases
- Long-term severe alcohol abuse can result in **hypoglycemia, hyponatremia, hypomagnesemia** -> also associated with seizures

3 Stages of AWS

✓ Delirium Tremens (DT)

- Medical emergency, which results in significant morbidity and mortality (**If untreated, mortality rate of 20%**)
- Most severe form of the withdrawal syndrome
- Characterized by fluctuating levels of psychomotor activity (hyperexcitability to lethargy), perceptual disturbances (usually visual, or tactile), **disorientation, confusion, fear and anxiety, autonomic hyperactivity** (tachycardia, diaphoresis, hypertension)
- Patients appear assaultive or suicidal or may act on hallucinations or delusional thoughts

4 Pathophysiology

✓ Ethanol = CNS depressant

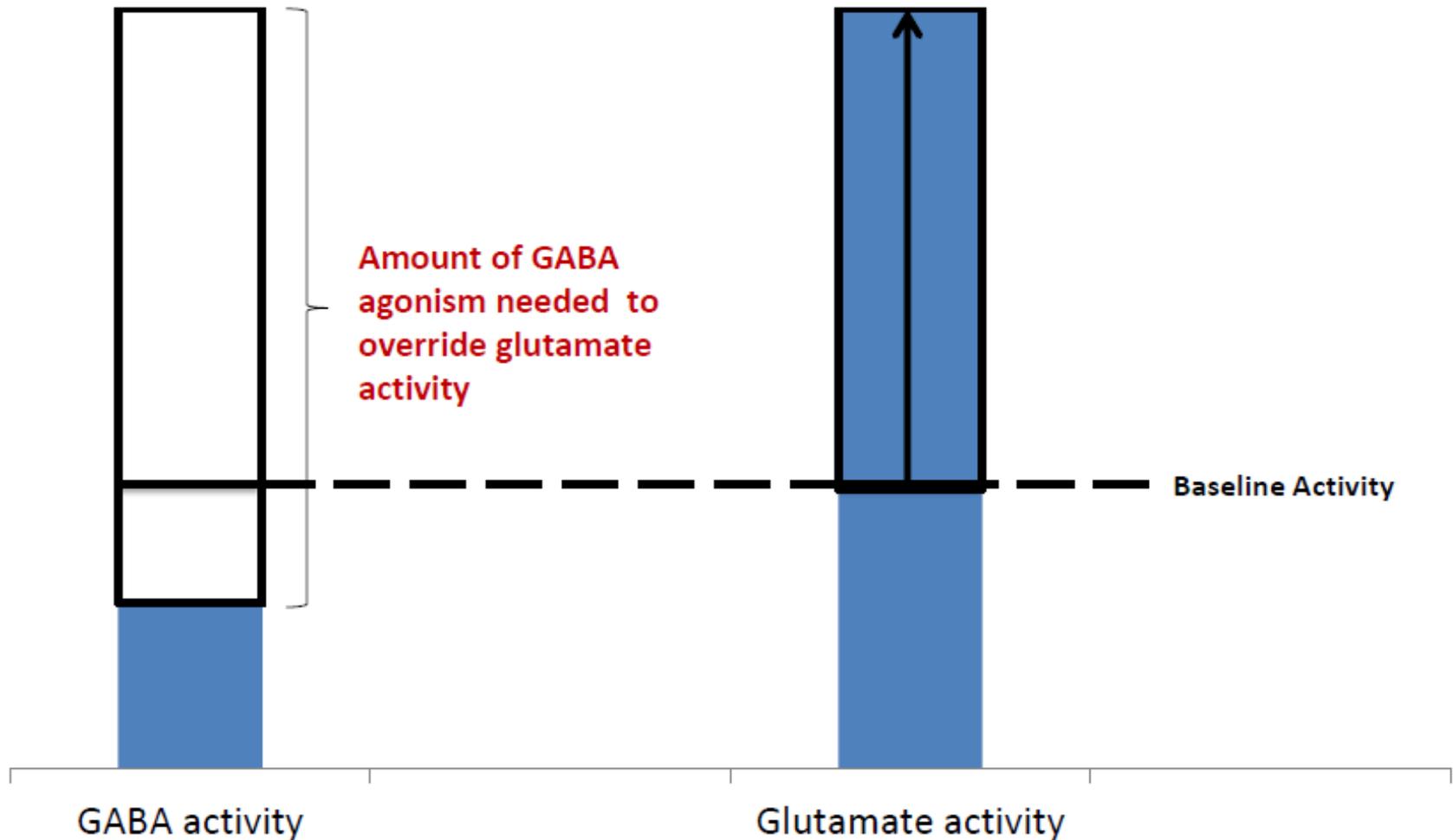
- euphoria & behavior activation at low blood concentrations d/t to increased glutamate binding to NMDA receptors
- At **higher** concentrations, acute intoxication by potentiation of GABA effects

4 Pathophysiology

- ✓ Withdrawal results from an **imbalance** in the brain of **inhibitory and excitatory neurotransmitters** : **GABA vs. Glutamate**

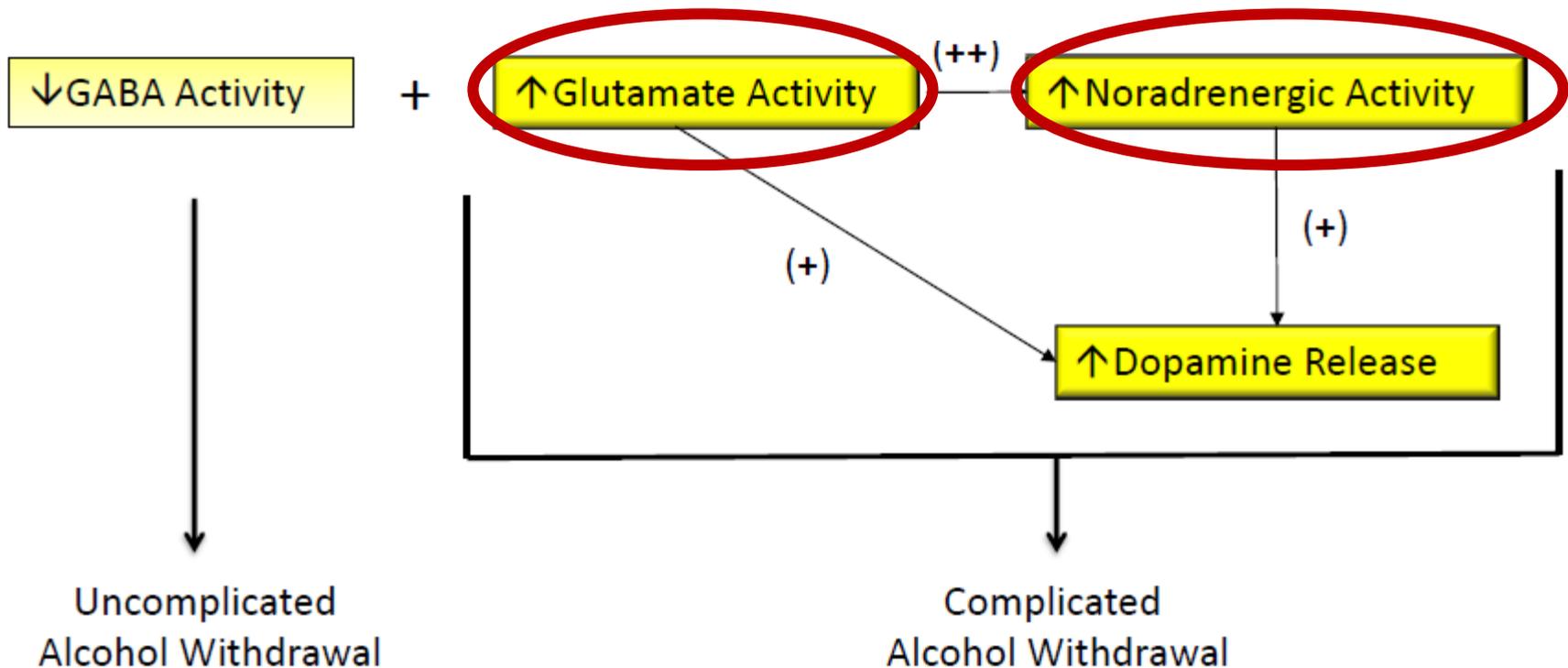
GABA	Glutamate
<ul style="list-style-type: none">▪ Alcohol increases effect of GABA, inhibitory NT▪ Results it's a decrease in overall brain excitability▪ Chronic alcohol intake -> decrease in GABA-A receptor	<ul style="list-style-type: none">▪ Alcohol inhibits NMDA receptor by preventing binding of glutamate, excitatory NT▪ Chronic alcohol intake -> up-regulation of NMDA receptor & production of more glutamate

4 Pathophysiology



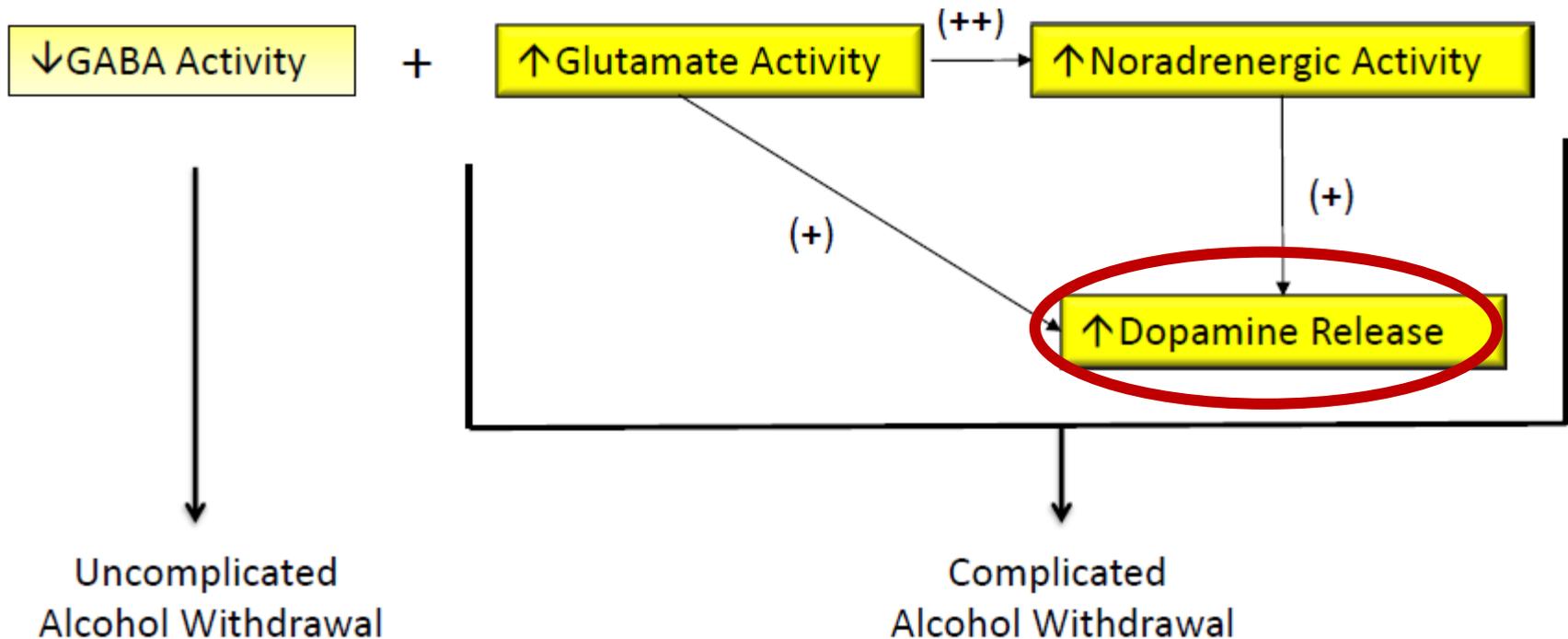
5 Pathophysiology

- ✓ Glutamate-mediated CNS excitation resulting in autonomic overactivity & neuropsychiatric complications



5 Pathophysiology

- ✓ Dopamine related potentiation of reward system thereby maintaining abuse & contributing to hyperarousal & hallucination



5 Pathophysiology

- ✓ Increased homocysteine, excitotoxic compound, through stimulation of the NMDA receptors & further raise in homocysteine via rebound activation of glutamatergic neurotransmission

5 Overview of Management

1. Evaluation of complete **clinical picture**
2. **Risk assessment** to identify patients at risk for developing alcohol withdrawal syndrome
3. Assessment and documentation of **CIWA-Ar** and **RASS** score (ICU patients) **to detect severity**
4. **Administration** of pharmacologic agent
 - **Symptom triggered therapy (STT)** with benzodiazepines
 - **Fixed dose regimens** and continuous infusion
5. Monitoring and tapering

5 Management

1. Evaluation of complete clinical picture

- Co- existing illness : trauma, infection etc
- Co-morbid medical & psychiatric diagnoses, including suicidality
- Dehydration, electrolyte, vitamin deficiencies

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

5 Management

AUDIT

PATIENT: Because alcohol use can affect your health and can interfere with certain medications and treatments, it is important that we ask some questions about your use of alcohol. Your answers will remain confidential, so please be honest.

For each question in the chart below, place an X in one box that best describes your answer.

NOTE: In the U.S., a single drink serving contains about 14 grams of ethanol or "pure" alcohol. Although the drinks below are different sizes, each one contains the same amount of pure alcohol and counts as a single drink:



2. Risk assessments

- Alcohol use history : **AU**
- Recent cessation or reduction
- Previous history of alcohol
- **History of a similar event**
- incident occurrence of DT
- **PAWSS** (Prediction of Alcohol Withdrawal Syndrome)
 - First validated tool to predict alcohol withdrawal, allow
 - Sensitivity & specificity of 100% using the threshold

Questions	0	1	2	3	4	
1. How often do you have a drink containing alcohol?	Never	Monthly or less	2 to 4 times a month	2 to 3 times a week	4 or more times a week	
2. How many drinks containing alcohol do you have on a typical day when you are drinking?	1 or 2	3 or 4	5 or 6	7 to 9	10 or more	
3. How often do you have 5 or more drinks on one occasion?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
4. How often during the last year have you found that you were not able to stop drinking once you had started?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
5. How often during the last year have you failed to do what was normally expected of you because of drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
7. How often during the last year have you had a feeling of guilt or remorse after drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
8. How often during the last year have you been unable to remember what happened the night before because of your drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
9. Have you or someone else been injured because of your drinking?	No		Yes, but not in the last year		Yes, during the last year	
10. Has a relative, friend, doctor, or other health care worker been concerned about your drinking or suggested you cut down?	No		Yes, but not in the last year		Yes, during the last year	
					Total	

Note: This questionnaire (the AUDIT) is reprinted with permission from the World Health Organization. To reflect drink serving sizes in the United States (14g of pure alcohol), the number of drinks in question 3 was changed from 6 to 5. A free AUDIT manual with guidelines for use in primary care settings is available online at www.who.org.

5 Management

Figure 3. Prediction of Alcohol Withdrawal Severity Scale (PAWSS)

PART A: THRESHOLD CRITERIA:

("Y" or "N",
no point)

Have you consumed any amount of alcohol (i.e., been drinking) within the last 30 days?
OR did the patient have a "+" blood alcohol level (BAL) on admission?

IF the answer to either is YES, proceed with test:

PART B: BASED ON PATIENT INTERVIEW:

(1 point each)

1. Have you been recently intoxicated/drunk within the last 30 days? _____
2. Have you ever undergone alcohol use disorder rehabilitation treatment or treatment for alcoholism?
(i.e., inpatient or outpatient treatment programs or AA attendance) _____
3. Have you ever experienced any previous episodes of alcohol withdrawal, regardless of severity? _____
4. Have you ever experienced blackouts? _____
5. Have you ever experienced alcohol withdrawal seizures? _____
6. Have you ever experienced delirium tremens, or DT? _____
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:

(1 point each)

9. Was the patient's BAL on presentation \geq 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 AWS. A score of \geq 4 suggests HIGH RISK for moderate to severe (complicated) AWS; prophylaxis and/or treatment may be indicated.

Source: Adapted from Maldonado JR, Sher Y, Ashouri JF, et al. 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. *Alcohol.* 2014;48(4):375-390.

5 Management

2. Risk assessments

■ CIWA-Ar

- ✓ To classify patients (severity of withdrawal)
- ✓ Does not predict when CIWA-Ar is elevated
- ✓ CIWA-Ar is elevated withdrawal symptom
- ✓ CIWA-Ar not appropriate for delirium due to other causes
- ✓ To guide medication
- ✓ Maximum total CIWA

Alcohol Withdrawal Assessment Scoring Guidelines (CIWA - Ar)

Nausea/Vomiting - Rate on scale 0 - 7

- 0 - None
- 1 - Mild nausea with no vomiting
- 2
- 3
- 4 - Intermittent nausea
- 5
- 6
- 7 - Constant nausea and frequent dry heaves and vomiting

Anxiety - Rate on scale 0 - 7

- 0 - no anxiety, patient at ease
- 1 - mildly anxious
- 2
- 3
- 4 - moderately anxious or guarded, so anxiety is inferred
- 5
- 6
- 7 - equivalent to acute panic states seen in severe delirium or acute schizophrenic reactions.

Paroxysmal Sweats - Rate on Scale 0 - 7.

- 0 - no sweats
- 1 - barely perceptible sweating, palms moist
- 2
- 3
- 4 - beads of sweat obvious on forehead
- 5
- 6
- 7 - drenching sweats

Tactile disturbances - Ask, "Have you experienced any itching, pins & needles sensation, burning or numbness, or a feeling of bugs crawling on or under your skin?"

- 0 - none
- 1 - very mild itching, pins & needles, burning, or numbness
- 2 - mild itching, pins & needles, burning, or numbness
- 3 - moderate itching, pins & needles, burning, or numbness
- 4 - moderate hallucinations
- 5 - severe hallucinations
- 6 - extremely severe hallucinations
- 7 - continuous hallucinations

Visual disturbances - Ask, "Does the light appear to be too bright? Is its color different than normal? Does it hurt your eyes? Are you seeing anything that disturbs you or that you know isn't there?"

- 0 - not present
- 1 - very mild sensitivity
- 2 - mild sensitivity
- 3 - moderate sensitivity
- 4 - moderate hallucinations
- 5 - severe hallucinations
- 6 - extremely severe hallucinations
- 7 - continuous hallucinations

Tremors - have patient extend arms & spread fingers. Rate on scale 0 - 7.

- 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 w/ arms not extended

Agitation - Rate on scale 0 - 7

- 0 - normal activity
- 1 - somewhat normal activity
- 2
- 3
- 4 - moderately fidgety and restless
- 5
- 6
- 7 - paces back and forth, or constantly thrashes about

Orientation and clouding of sensorium - Ask, "What day is this? Where are you? Who am I?" Rate scale 0 - 4

- 0 - Oriented
- 1 - cannot do serial additions or is uncertain about date
- 2 - disoriented to date by no more than 2 calendar days
- 3 - disoriented to date by more than 2 calendar days
- 4 - Disoriented to place and / or person

Auditory Disturbances - Ask, "Are you more aware of sounds around you? Are they harsh? Do they startle you? Do you hear anything that disturbs you or that you know isn't there?"

- 0 - not present
- 1 - Very mild harshness or ability to startle
- 2 - mild harshness or ability to startle
- 3 - moderate harshness or ability to startle
- 4 - moderate hallucinations
- 5 - severe hallucinations
- 6 - extremely severe hallucinations
- 7 - continuous hallucinations

Headache - Ask, "Does your head feel different than usual? Does it feel like there is a band around your head?" Do not rate dizziness or lightheadedness.

- 0 - not present
- 1 - very mild
- 2 - mild
- 3 - moderate
- 4 - moderately severe
- 5 - severe
- 6 - very severe
- 7 - extremely severe

5 Management

▪ RASS (The Richmond Agitation-Sedation Scale)

- ✓ Structured assessment of sedation and agitation is useful to **titrate sedative medications in *intensive care units (ICU)***
- ✓ **10-point scale, with 4 levels of anxiety or agitation, 1 level to denote a calm and alert state and 5 levels of sedation**

Richmond Sedation Agitation Sedation Scale (RASS)

Score	Term	Description	
+4	Combative	Overtly combative, violent, immediate danger to staff	
+3	Very agitated	Pulls or removes tube(s) or catheter(s); aggressive	
+2	Agitated	Frequent non-purposeful movement, fights ventilator	
+1	Restless	Anxious but movements not aggressive vigorous	
0	Alert and calm		
-1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to voice (>10 seconds)	} VERBAL STIMULATION
-2	Light sedation	Briefly awakens with eye contact to voice (<10 seconds)	
-3	Moderate sedation	Movement or eye opening to voice (but no eye contact)	
-4	Deep sedation	No response to voice, but movement or eye opening to <i>physical</i> stimulation	} PHYSICAL STIMULATION
-5	Unarousable	No response to voice or <i>physical</i> stimulation	

5 Management

■ Procedure for RASS assessment

- 1) Observe patient
 - a) Patient is alert, restless or agitated (**score 0 to +4**)

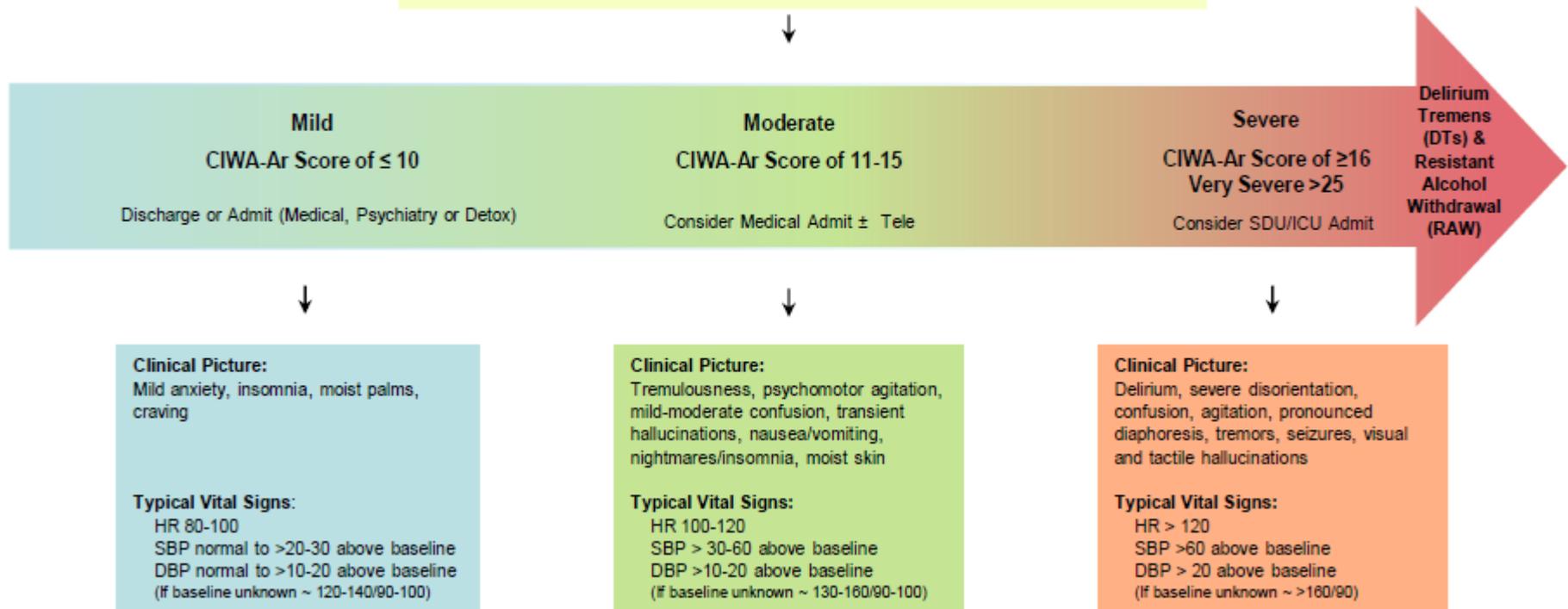
- 2) If **not alert, state patient's name** and **say to open eyes and look at speaker**
 - a) Patient awakes with sustained eye opening and eye contact (**score -1**)
 - b) Patient awakes with eye opening and eye contact, but not sustained (**score -2**)
 - c) Patient has any movement in response to voice but no eye contact (**score -3**)

- 3) When **no response to verbal stimulation, physically stimulate** patient by shaking shoulder and/or rubbing sternum
 - a) Patient has any movement to physical stimulation (**score -4**)
 - b) Patient has no response to any stimulation (**score -5**)

5 Management

3. Administration of pharmacologic agent

Use CIWA-Ar score and clinical picture to guide medication dosing
Dosing may need to be customized to meet each patients needs



5 Management

- ✓ **Benzodiazepine : first-line treatment for AWS**
 - Modulation of GABA binding to the GABA-A receptor, providing an inhibitory effect which is similar to that of ethanol
 - Rapid penetration of the BBB & hepatic metabolism
 - Recommended for both primary & secondary seizure prophylaxis in AWS - within the first 2 days of withdrawal, BZDs reduce the incidence of seizures by up to 84% and prevent the development of DT

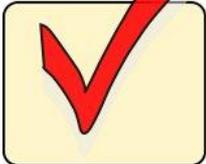
5 Management

✓ Then, which Benzodiazepine ??

- The current literature **does not** suggest on BZD to be more efficacious than another
- Factors to consider
 - 1) With rapid onset to control agitation symptom
 - 2) With long action to avoid breakthrough symptoms
 - 3) With less dependence on hepatic metabolism to lower the risk of oversedation
- Diazepam : fulfills the first two aspects & represents the primary choice
however, 4~9 fold increase in terminal half-life in the elderly
and patients with liver disease → side-effect !!
- **Lorazepam : preferred choice for the elderly and patients with cirrhosis or severe liver dysfunction**

5 Management

Symptom triggered therapy (STT)
with benzodiazepine



STT decreases length of stay,
total BDZ dose, incidence of
intubation

- Not applicable in non-verbal patients
- Not safe in patients with a past history of withdrawal seizures because they can occur without AWS symptoms

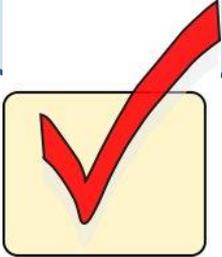
**Fixed dose regimen &
continuous infusions**



- Patients who need medication regardless of symptoms
i.e those with a **history of seizures or DT**
- Patients with comorbid medical illness who **cannot be evaluated on withdrawal symptoms**
i.e intubated state

5 Management

Symptom triggered therapy (STT)
with benzodiazepine



- **Regular assessment of patient's withdrawal symptoms using CIWA-Ar scale**
- **5~10mg of diazepam or 25~100mg chlordiazepoxie initially**
- **Repeated assessment 1h later**
 - **If symptoms (+), doses repeated hourly until the score is below 8**
 - **Once stable, assessed every 4~8hrs for additional therapy**

Fixed dose regimen & continuous infusions



- **Fixed amount** of medication is administered at regular intervals
- **Dizepam or chlordiazepoxie**
- A ceiling dose of **60mg of diazepam** or **125mg of chlordiazeposide**
- Following 2~3days of stabilization of the withdrawal syndrome, BZD gradually tapered off over a period of 7-10days

5 Management

USE LOWEST EFFECTIVE DOSES TO MAINTAIN DESIRED DEGREE OF SEDATION, TITRATE UP AS NEEDED TO GAIN INITIAL CONTROL

Re-dose medications according to symptoms to achieve CIWA scores \leq 8-10 or to achieve light sedation

Chlordiazepoxide prophylaxis 100mg PO x1 is indicated when CIWA-Ar $<$ 8 if history of severe AWD/DT's or RAW **AND** if ED work-up/observation or inpatient admission is anticipated

CIWA-Ar score $<$ 8

No treatment, reassess every 4 hr is stable, earlier if clinical picture changes

If CIWA-Ar $<$ 8 & if patient is eligible for discharge, may discharge

CIWA-Ar score \geq 8-10

Chlordiazepoxide 50 mg PO x1

Then, reassess CIWA score 1 hr after medication dose and redose if CIWA $>$ 8

If CIWA remains $<$ 8-10 may reassess every 4 hrs then redose prn

Goal = CIWA-Ar score \leq 8-10

If CIWA-Ar 8-10 **AND** medically stable x 4 hrs may admit to psychiatry and/or "Detox", unless history of severe AWD/DT's/RAW

If $>$ 300 mg used in 4 hrs **OR** CIWA-Ar \geq 11 for 4 hrs (despite treatment) **anticipate using IV medications AND upgrade to moderate or severe scale**

In patients with a co-morbid psychiatric diagnosis, CIWA-Ar scores must be combined with the clinical picture to attempt to differentiate acute psychiatric symptoms from acute AWD

If CIWA-Ar scores $<$ 8 x 24 hrs **AND** patient is eligible for discharge, may discontinue treatment or discharge

Chlordiazepoxide 100 mg PO X1

Reassess CIWA-Ar score 1 hr after medication and redose if CIWA $>$ 8. May re-dose every 1 hr

If $>$ 300 mg used in 4 hrs **OR** CIWA-Ar \geq 11 for 4 hrs (despite treatment), **anticipate using IV medications**

Diazepam 5 mg IV x1 (preferred)

Reassess in 10 min and redose if CIWA-Ar \geq 8. If 5 mg not effective, increase to 10 mg every 10 min for subsequent doses **OR**

Lorazepam 1 mg IV x1

Reassess in 20 min and redose if CIWA-Ar \geq 8. If 1 mg not effective, increase to 2 mg every 20 min for subsequent doses

If \geq 40 mg diazepam or \geq 6 mg lorazepam used in 1 hr, consider possibility of severe withdrawal

If \geq 100 mg diazepam or \geq 10 mg lorazepam used in 4 hrs **OR** if CIWA-Ar \geq 16 for 4 hrs, upgrade to severe **AND** consider alternate diagnosis **AND consult Pulmonary Triage**

Goal = CIWA-Ar score \leq 8-10

Reassess Clinical Picture, CIWA-Ar score & VS at minimum of every 4 hrs once symptoms are stable

If CIWA-Ar increases to \geq 11, re-dose at last effective dose (not cumulative)

If CIWA-Ar remains \leq 8-10 may reassess every 4 hrs then redose prn

Once CIWA-Ar stable between 8-12 for 24-48 hrs, taper doses by 20% per day

CIWA-Ar Score of \geq 16 or high benzodiazepine doses used **Consult Pulmonary Triage** & consider Psychiatry

Consult Lesion service

Diazepam 10 mg IV x1 (preferred)

Reassess in 10 min and redose if CIWA-Ar $>$ 10. If 10 mg not effective, increase to 20 mg every 10 min for subsequent doses

OR

Lorazepam 2 mg IV x1

Reassess in 20 min and redose if CIWA-Ar $>$ 10. If 2 mg not effective, increase to 4mg every 20 min for subsequent doses

If \geq 200 mg in the initial 3 hrs or \geq 400 mg in the first 8 hrs of diazepam **OR** \geq 30 mg in the initial 3 hrs or \geq 60mg in the initial 8 hrs of lorazepam **OR** CIWA-Ar $>$ 25 **OR** frank delirium, assume DT's or RAW **AND** consider alternate diagnosis **AND**

CONSULT PULMONARY TRIAGE

Floor Goal= CIWA-Ar \leq 10, light sedation

ICU Goal= CIWA-Ar \leq 10, RASS 0 to -3

Reassess Clinical Picture, CIWA-Ar score & VS at minimum of every 2 hrs once symptoms are stable

If CIWA-Ar increases to \geq 13, redose medication at last effective dose (not cumulative)

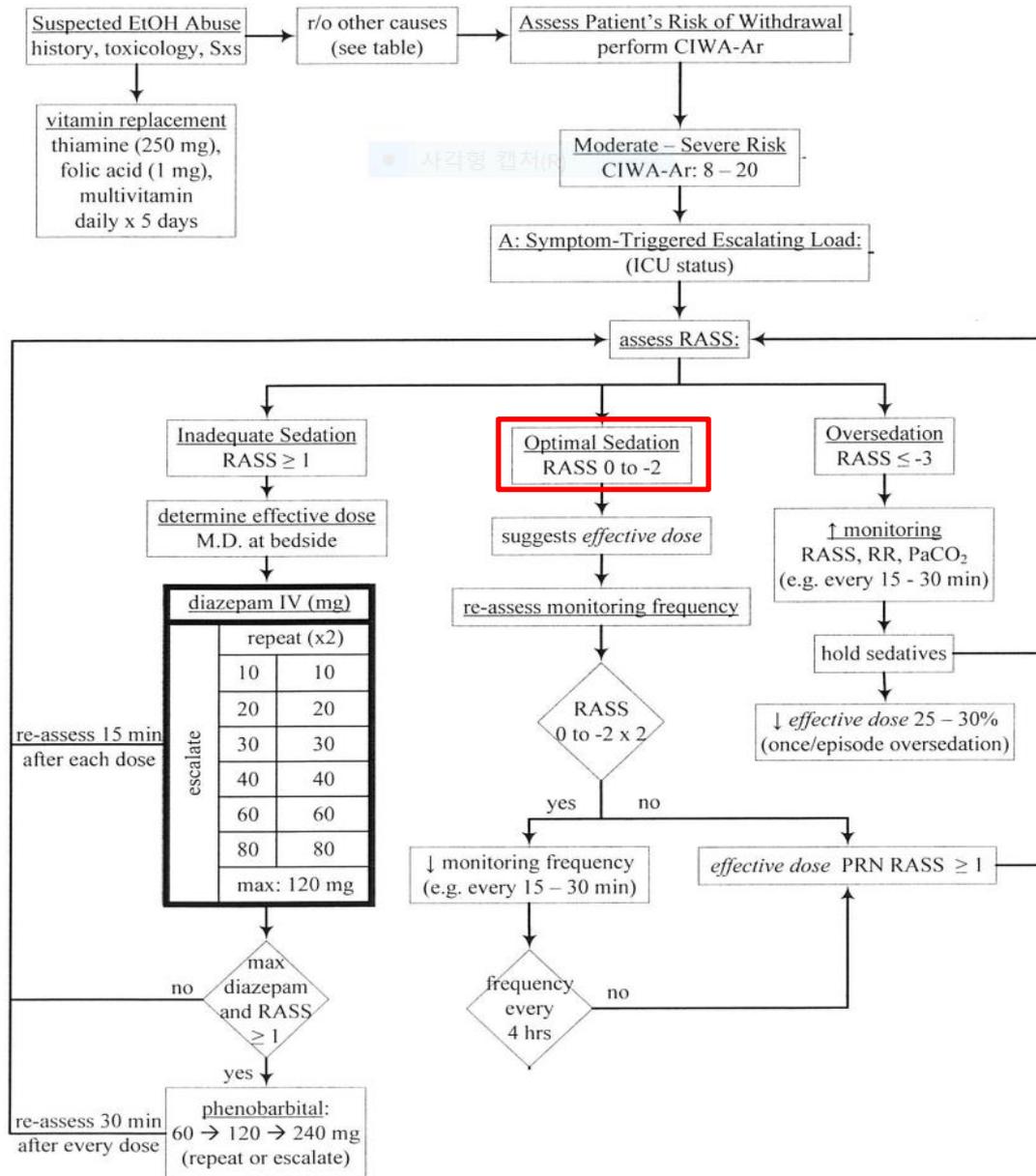
If CIWA-Ar increases to \leq 12, redose at half the last effective dose (not cumulative)

If CIWA-Ar 10-15 for 12 hrs, then downgrade to moderate dosing regimen (tapering per moderate scale)

5 Management

✓ AWS protocol in ICU based on a Sx-triggered approach

- BZD every 15 to 30 min until target sedation level (RASS : 0 to -2)
- Escalating diazepam doses up to a max. of 120mg (lorazepam 24mg)
- Effective dose every 4hrs



Alcohol withdrawal protocol based on a symptom-triggered, dose-escalation approach using BZDs and phenobarbital
Duby JJ et al.(2014) Alcohol withdrawal syndrome in critically ill patients

5 Management

✓ Nonbenzodiazepines

1) Antipsychotics (i.e haloperidol)

- Associated with higher mortality due to **cardiac arrhythmia** by prolongation of the QT interval
- Associated with the **lower seizure threshold**
- Should be used **cautiously in AWS**, particularly in its early stage (<48h)
- Nevertheless, may be considered as **adjunctive therapy to BDZ in the late stage of AWS, when agitation, delirium, and hallucinations are not controlled with BZD alone**

2) Antiepileptic agents (i.e carbamazepine)

- In summary, Cochrane review investigating 56 studies with a total of 4076 patients found **no sufficient evidence in favor of any antiepileptic agent for therapy of AWS**

5 Management

✓ Nonbenzodiazepines

3) Alpha-2 agonistic agent

- Can be used to decrease sympathetic outflow leading to reduction in autonomic hyperreflexia

✓ Adjunctive therapeutic agents

■ Magnesium

- Mg : inhibitor of neurotransmitter NMDA-driven hyperexcitability
- Chronic alcohol use is associated with magnesium deficiency

■ Thiamine

- Parenteral thiamine should be given in carbohydrate-containing fluids
- Prevention of Wernicke's encephalopathy

Medication	Dose and Frequency	Comments
Folic acid	1mg PO/IV daily.	<ul style="list-style-type: none"> Folate deficient anemia associated with alcohol abuse.
Magnesium	Treat IV/PO as needed to reach appropriate serum levels.	
Multivitamin	1 dose daily PO/IV.	<ul style="list-style-type: none"> Not needed if patient is receiving tube feeds.
Thiamine*	100mg PO/IV/IM Q8H/TID during acute alcohol withdrawal, then reduce dose 100 mg daily thereafter.	<ul style="list-style-type: none"> Administer before IV dextrose or glucose derivative to prevent Wernicke's encephalopathy (see below for signs, symptoms, and treatment).

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Thank You for your attention