

# **Alcoholism Lecture**

Alcohol intoxication occurs at blood levels of .050 to .080 depending on your criteria. In MO the legal definition is now a BAL of .80 - following the nationwide trend for lower levels. There is no specific treatment of intoxication. Narcotic antagonists (Naloxone, Naltrexone) can partially reverse some symptoms of intoxication (including coma). The benzodiazepine antagonists can also be useful, but carry a risk of seizures. Do not be misled by a BAL drawn when someone first walks in. If they have a stomach full of unabsorbed alcohol, their BAL can rise even though they are not continuing to drink. This is why teenagers die from drinking "contests" when drinking liquor or wine. They get drunk and pass out with a gut full of alcohol, which is then absorbed and produces a fatal CNS depression.

There is also an **immediate tolerance** to our ability to "feel" intoxicated. We feel more intoxicated when our BAL is rising than with the same BAL when it is dropping. (We then decide we are sober enough to drive, even though we are still impaired...).

**Alcohol withdrawal** occurs with a drop in BAL from the level the person's brain is accustomed to. Yes, you can be in withdrawal from alcohol and have a BAL, which would produce intoxication in many. (This is not a good prognostic sign). Most alcohol abusers can quit drinking without significant physical withdrawal symptoms. Those that do have physical withdrawal symptoms are at risk for withdrawal seizures and Delirium Tremors (DTs), (which are potentially fatal).

**The primary reason to medically treat alcohol withdrawal is to prevent seizures and DTs.** There have been, and continue to be, many "questionable" ways to treat alcohol withdrawal. The problem is that seizure and DTs occur at a low base rate and most people in withdrawal will do well even with inappropriate treatment. The result is that there are many reports in the literature showing that treatment X, Y, or Z is effective in treating withdrawal symptoms (which would have improved anyway). Many studies do not have a large enough "n" (statistical power) to show a change in the base rate of seizures and DTs. Studies done in Scandinavian countries with very large "n's" indicate that the lowest mortality rate in alcohol withdrawal occurs with treatment using a benzodiazepine.

Over the years, there have been different theories and methods used to administer benzodiazepine for alcohol withdrawal. I will discuss the preferred method and then some of the common variations.

Studies have shown the most efficient and safest treatment of alcohol withdrawal titrate the dose of the benzodiazepine to the presence or severity of symptoms of withdrawal. If there are specific symptoms, treatment occurs. If there is not a specific symptom, no medication is given. This helps eliminate both over and under treatment.

**Severity Assessment Scale** (SA Scale). This scale is administered q2h (while awake) until stable, then q6h while awake x 24 hours, then BID or up to 3 days. A score of 6 or more is considered evidence of withdrawal and triggers treatment with Librium 50 mg po or Ativan 2 mg po or IM, q2h. A score of 10 or over leads to physician notification, as it indicates a more severe withdrawal, another medical problem, or DTs.

If a patient receives consecutive prn's of Librium or Ativan and their SA scores do not decline, they should be re-evaluated and if the problem is withdrawal, the benzodiazepine dose should be doubled.

The intent is to substitute for the alcohol with a cross-tolerant drug with a half-life longer than that of alcohol. The patient is titrated out of withdrawal using prn doses. Once titrated out of withdrawal, the longer half-life allows the drug to "self taper", usually with no additional prn's being required. Studies have shown this method to be superior to both "fixed dose" and "titrate and taper" schedules. The advantage is that less benzodiazepine is used, but it is used when it is needed most.

**Fixed dose schedules** have several disadvantages. They treat every patient with the same dose, even though the individual needs vary. In essence, they treat the middle portion of the "bell-shaped curve" and ignore the extremes. Those who do not need any benzodiazepine usually do not complain about getting it. The problem is at the other end of the curve, where a higher dose is needed, but not given. These patients are a risk for seizures and DTs. The other problem with fixed dose schedules comes from pharmacokinetics. Even though the dose given is tapered, the brain levels continue to rise due to the long half-life. Patients in moderate to severe withdrawal tend to be relatively "over treated" in the middle to end portion of the taper and relatively under treated initially. The more appropriate the initial dosing, the greater the later "over dosing. Those in mild withdrawal (needing no Librium) are relatively "over" dosed initially, and even more so later.

**Titrate and taper schedules** usually involve titrating the patient out of withdrawal by looking at the total amount used in the first 24 ours, and then tapering from that total at a rate of 20% per day. The titration portion is appropriate and desirable. The problem is the tapering portion, which with a longer T1/2 drug leads to relative "over" dosing in the middle to end portion of the taper (as described above). The shorter the half-life of the drug is, the greater is the desirability of tapering the dose.

**Cautions about the SA Scale:** The scale has been validated in clinical studies, but it is not perfect. It cannot know that the autonomic signs may be from another illness not responsive to benzodiazepine. (It looks bad when you use Librium to treat pneumonia, MI, hypoglycemia, etc.) It also cannot know that B-Blockers, Clonidine, and other meds can limit the autonomic symptoms and lower the score, leaving the patient at risk for seizures and DTs due to prns not being given.

The SA Scale has been validated for uncomplicated alcohol withdrawal. It was not intended for use in patients in DTs and should not be used to guide dosing with DTs.

What you find in DTs is that patients will score above 6 anytime they are awake due to the confusion, hallucination, sleeplessness, agitation, and autonomic symptoms. If SA scores are used to guide dosing, this tends to lead to q2h doses until the patient very sedated, comatose and at risk of respiratory depression.

### **Medication to use in Alcohol withdrawal**

The safest, most effective medications to use are the benzodiazepines. Within that broad class there are specific agents that are desirable for specific reasons. The 3 that are most commonly used are **Librium (Chlordiazepoxide)**, **Valium (diazepam)**, and **Ativan (Lorazepam)**. The doses cited below are equipotent for acute use. Due to T1/2 differences, they are not equivalent in chronic use.

**Librium 50 mg po.** Librium is well-absorbed po, but is less lipophilic than Valium and thus does not have the same rapid absorption "rush". (This means less abuse potential). It has a long history of use in treating withdrawal. Due to the long T1/2 of Librium and its active metabolite (96 hours), it will smoothly self-taper. It is available in parenteral form, but at a non-physiologic pH. If given IM, it precipitates in the muscle and is irregularly absorbed. **Do not give IM,** as you do not know when it will be absorbed. It can be given IV, but has no specific advantage when used this way.

**Valium 10 mg po.** Valium is rapidly absorbed po and is quite lipophilic. This gives it its well-known abuse potential. It also has a long T1/2 and will smoothly self-taper. Like Librium, the parenteral form is not at a physiologic pH. **Do not give IM,** for the same reasons as Librium. Valium is **very useful when given IV** due to its high lipophilicity. Because of the high blood flow rate through the brain, there is a strong "first pass" extraction into the brain. This produces a very rapid rise in brain levels. This is followed by a rapid redistribution to the fatty tissue elsewhere. **The effect of IV Valium is a "spike" in the brain level.** The effect of each dose occurs rapidly, but is short-lived. This allows titration with frequent doses, with lower risk of over-sedation or respiratory depression. **From the brain's point of view, Valium has a short half-life when first used, though with extended use, the fats "saturate" and the T1/2 appears to lengthen.**

**Ativan 2 mg po, IM, or IV.** Ativan has a medium rate of absorption, no active metabolites, and a short T1/2 (15 hours, which is short for the benzodiazepines). It is conjugated and excreted through the kidney, which is advantageous in the elderly or those with significant liver disease. Most importantly - **it is well absorbed when given IM.** This makes it the most versatile benzodiazepine in its administration. Do not be fooled by its shorter T1/2. Because it is relatively less lipid soluble and more protein-bound, it is less "available" to the brain than other, more lipid soluble agents. In acute dosing, it behaves as if it has a longer T1/2 (brain levels do not "spike" like they do with Valium), and thus has a greater risk of over-sedation and respiratory depression than you might anticipate.

If I had to choose one benzodiazepine to use it would be Valium, due to its rapid first pass effect and usefulness in dose titration.

**Liver dysfunction** is a well known effect of chronic alcohol dependence. It is important to differentiate liver enzyme elevation due to an acute chemical hepatitis from actual liver dysfunction resulting from liver damage and cirrhosis. Enzyme elevation does not mean liver damage, and lack of elevation does not mean the person does not have liver damage. If liver damage is suspected you should look for evidence of this in clotting dysfunction, bilirubin, varices etc. I do not hesitate to use Librium or valium in patients with enzyme elevations but not evidence of cirrhosis. If the drug metabolism is slower and the half life is longer it is an advantage- assuming you are using the Severity Assessment scale and do not give them excessive doses .

If they have known liver damage or cirrhosis, I would use Ativan or use the others with caution to avoid over-treating them.

### **Medications not to use for Alcohol withdrawal**

**Thorazine** was a great advance in the treatment of schizophrenia. It is a poor choice to use in alcohol withdrawal. It is not cross tolerant with alcohol, lowers the seizure threshold, is anticholinergic, and has an alpha blockade effect. There is no reason to believe it will decrease the rate of DTs and it increases the risk of seizures and orthostatic BP changes. The only advantage is that it is usually sedating and has anti-emetic effect.

**Beta-blockers** will block the autonomic manifestations of the withdrawal by decreasing BP and pulse rate. They are not cross-tolerant with alcohol and there is no reason to believe they reduce the rate of seizures or DTs. They will lower the SA score through their effect on pulse, BP, and tremor. This can lead to under-treatment and an increased risk of seizures and DTs. **Benign Familial Tremor** can look very much like the tremor from alcohol withdrawal. It also is very responsive to alcohol. This can lead to errors in diagnosis when the patient indicates they can stop the "shakes" by drinking. If you determine that the patient has a familial tremor, try treating it with propranolol, which is often effective at low doses.

**Clonidine** is an alpha agonist to inhibitory neurons and decreases autonomic stimulation. It is quite useful in controlling most of the autonomic symptoms of opiate withdrawal. As with the B-blocker, there is no reason to believe it will prevent seizures or DTs, and it will lower the SA score (leading to under treatment).

**Tegretol** should increase the seizure threshold and this may be of some benefit. There are no studies indicating it decreases the rate of DTs. On a more practical level, it has a risk of toxicity and a low therapeutic index. It can produce side effects (esp. nausea and vomiting), which will increase the SA score. This could lead to dose increases when decreases would be appropriate. Because of its anticonvulsant and anti-

Kindling effect, there may be a role for the use of Tegretol, but the studies to define this role are pending.

**Alcohol** has long been used to try and manage withdrawal, though it has many disadvantages. The primary disadvantages are the relatively short half-life, potential for "toxicity", and side effects, low therapeutic index, interactions with other medications, and re-enforcement of drinking. The above, combined with no evidence of superiority in efficacy, leave you at risk of a malpractice suit, should any of the well-known "adverse events" occur. The most common use is PO. If you consider the amount consumed by most alcoholics compared to the amounts typically prescribed for withdrawal you would anticipate little pharmacologic effect. IV alcohol is more problematic. If given peripherally, the concentration limits its use secondary to pain and vein sclerosis. To give a significant amount requires a significant fluid load and expense. If given by central line, the fluid volume can be restricted, but you are still left with the low therapeutic index, short half-life, drug interactions, and risk of toxicity to various organs. Given the lack of documentation of efficacy and distinct disadvantages, I recommend avoiding its use.

**Antihistaminic sedatives** are another group that are not truly cross-tolerant and have a potential for anticholinergic side effects.

**Dilantin** has been advocated to prevent withdrawal seizures. Its ability to do this is questionable, as it has not been found consistently effective when studied. The best insurance against seizures is to vigorously treat with benzodiazepines and give magnesium, if they are deficient.

## **DELIRIUM TREMENS**

Delirium Tremors (DTs) is a delirium resulting from withdrawal from alcohol. It is relatively uncommon (<5%), but has a significant mortality rate (2-5%) with treatment. Before treatment with benzodiazepines was available, the mortality rate was much higher. **The major reason to medically treat alcohol withdrawal is to prevent DTs and seizures.**

As you would anticipate from the name, people in DTs have a tremor and a delirium. The tremor is coarse and irregular. It can involve the tongue and eyelids, as well as the hands. It does not stop with intentional activity and may make eating and drinking fluids difficult. The delirium classically includes vivid hallucination, which can be visual, auditory, or tactile (often reported as bugs on or in the skin). The patient is usually agitated and aroused when awake. They will often respond to hallucinations and may be combative. Autonomic hyperactivity is common, with elevated BP, tachycardia, sweating, and mild fever. Other features of delirium are present, but tend to be overshadowed by the more obvious symptoms above. These features would include memory disturbance manifested by disorientation and difficulty learning new material, difficulties with concentration and focusing attention, disorganized thinking and

disturbed sleep/arousal pattern. There may be lucid intervals (or at least intervals of significant improvement).

The first episode of DTs usually occurs after 10 to 15 year history of heavy drinking (meaning it is rare in 20s and early 30s). Having had one episode is a risk factor for subsequent episodes - though this may be a "marker" for increased risk in general. The onset of DTs usually occurs within 2-3 days following a significant reduction or cessation of drinking. It is preceded by the usual symptoms of alcohol withdrawal - though these may not be obvious. It also may be preceded by withdrawal seizures (rum fits). The duration is usually 2-7 days. There is often a concurrent medical illness, which increased the risk of DTs and will often prolong the course. **It is essential to look for other illness and conditions contributing to the delirium.**

The risk of DTs is increased by duration and severity of drinking, a history of past severe withdrawal or prior DTs, and the number and severity of concomitant medical problems and conditions. Presumably the abruptness of the reductions or cessation in drinking is also a factor. Abuse and abrupt reduction in the intake of short half-life benzodiazepines or barbiturates will increase the risk of DTs as they have an independent risk of withdrawal, seizures, and delirium.

The differential diagnosis of DTs includes a "simple" delirium from any of its other multiple etiologies. A nearly identical picture can occur from withdrawal delirium from short half-life benzodiazepines, barbiturates, and various other "sedative hypnotics". Hallucinosis can result from chronic alcohol use. This usually has predominantly auditory hallucinations and is not accompanied by the memory disruption and other cognitive dysfunction seen with a delirium. Tremor can occur from multiple etiologies. A tremor coincidental with delirium, dementia, severe infection, or a psychotic disorder can be mistaken for DTs.

There are a variety of rating scales to monitor alcohol withdrawal and to guide treatment with regard to dosing of benzodiazepines. These scales are not appropriate for guiding dosing in treating DTs, as they will lead to excessive doses. To my knowledge there are no rating scales specifically for DTs. I suspect this is because DTs is often complicated by other concurrent illness, and its response to treatment is subtle.

**The goal of treatment in DTs is to reduce the morbidity and the mortality. There is not a "cure".** Studies have shown that appropriate treatment with benzodiazepines will provide some behavioral control, reduce complications, and reduce the mortality rate. There is no clear-cut evidence that the duration of the episode is lessened (no cure).

**Once a patient is in DTs, there is no way to end the episode.** This has 2 implications: (1) you must try and prevent the onset of DTs, (2) when a patient is in DTs, you must recognize that the continuation of the delirium does not indicate inadequate treatment. Failure to recognize the later leads people to give a prn every time the

patient is awake (which is when they are inappropriate). This leads to patients who are comatose or in respiratory depression.

The appropriate endpoint in dosing is a patient who is somewhat sedated or mildly intoxicated when awake and not being stimulated. They will continue to demonstrate the delirium though confusion, disorientation, poor memory, hallucinations, delusions, etc. They may require soft restraints for their own safety. When stimulated, they may become uncooperative, irritable or combative, but this will dissipate when the stimulation ends.

When the diagnosis of DTs is made or strongly suspected, **treatment** should be initiated with benzodiazepines. The preferred drug is **Valium**, given IV (see the comments about Valium on page 4 for why it is preferred). Treatment should be initiated with 10 mg given IV and followed with 5 mg every 5 minutes until the patient is somewhat sedated or mildly intoxicated. After that, additional 5 mg doses should be used to maintain this state. Because Valium has a long T<sub>1/2</sub> after fatty tissues are saturated, it is better to use liberal dosing initially (first 24-36 hours), and then use occasional prn doses. This will avoid excess sedation later on. An alternative to IV Valium is IV Ativan in doses of 4 mg IV initially, followed by 2 mg IV q 5 min. Ativan is advantageous with those with severe liver disease, as it is conjugated and excreted through the kidneys. It also can be given IM if necessary (example: an agitated patient who does not currently have IV and will not tolerate one).

The above recommendation is analogous to the one made earlier for treating alcohol withdrawal. The same comments about fixed dose schedules and titrate and taper dosing apply. The difference is that **in treating DTs, you cannot use SA scales to guide resolution of the delirium**. This means you must recognize what your endpoint is so you avoid over-sedation.

Things to avoid in treating DTs:

- (1) Assuming alcohol alone is producing the delirium
- (2) IM Valium and Librium
- (3) IV alcohol

## **Substance Abuse Detox Orders:**

1. Admit to 2C – SATU
2. Diagnosis:
3. Allergies:
4. Diet:
5. Severity Assessment q 2 hrs. until stable, while awake, then q 6 hrs. while awake X 24 hrs., then BID X 3 days, then DC.
6. Notify physician of severity assessment  $\geq 10$ .
7. EKG
8. Alcometer on admission.
9. AA/Narcotics Anonymous pass prn after Librium/Ativan discontinued. Alcometer and/or urine drug screen on return.
10. Labs:
11. Urine drug screen
12. Librium 50 mg po (or Ativan 2 mg po or IM) q 2 hrs. prn severity assessment  $\geq 6$ . DC after 4 days.
13. Thiamine 100 mg IM X 1 on admission.
14. Stuartnatal 1+1 po q AM.
15. Tylenol 650 mg po q 4 hrs. prn headache/pain.
16. Maalox Plus 15 cc or Alternagel 30 cc po q 2 hrs. prn dyspepsia.

## **Scoring Criteria: Alcohol or Sedative Withdrawal Severity Assessment**

### Tremor:

1. Tremor felt by examiner but not visible
2. Mild, visible tremor
3. Marked visible tremor

### Tachycardia:

1. 90-110 beats/min.
2. 110-130 beat/min.
3. 130 beats/min.

### Hypertension:

1. Systolic 150-175 MM.
2. Systolic 175-200 MM.
3. Systolic over 200 MM.

### Sweating:

1. Mild barely visible
2. Moderate
3. Marked, clothes or bedding soaked

### Fever:

1. Up to 100 F (38C)
2. 100-101 F (38 – 38.5 C)
3. Over 101 F (38.5 C)

### Agitation:

1. Activity increased above normal
2. Restless “Fidgety”
3. Restless, pacing or thrashing about in bed

### Sleeplessness:

1. Up or awake frequently at night, for brief intervals only
2. Awake half the night
3. Awake all night.

### Hallucinations:

1. Misperception of environmental stimuli
2. Auditory only or visual only
3. Auditory and visual hallucinations

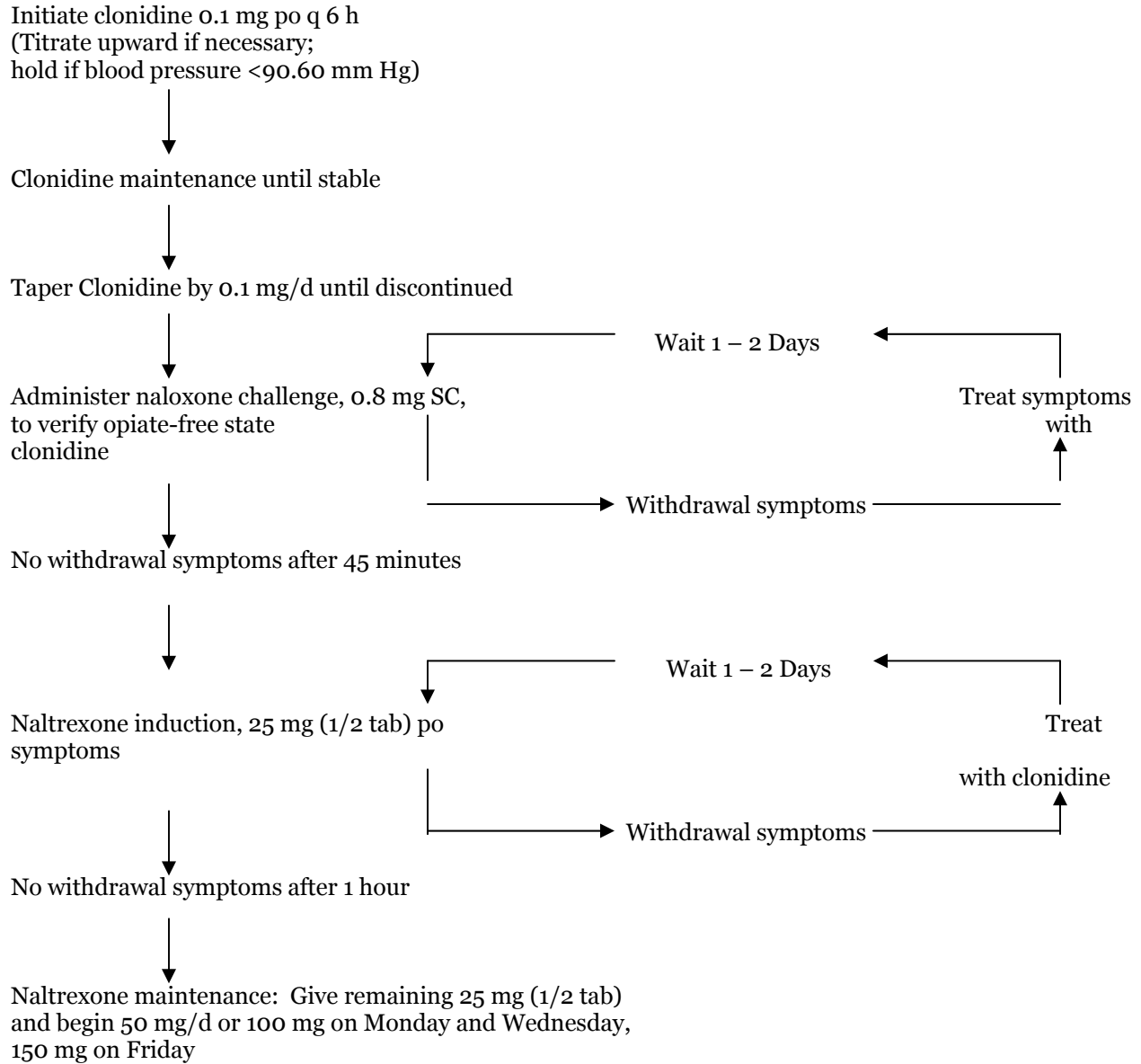
### Confusion:

1. Partially aware of examiner and surroundings
2. Sometimes out of contact with staff and situation
3. Detached, no contact with staff, disoriented

### Convulsions:

Notify the physician at once.

## Steps in the pharmacologic treatment of opiate withdrawal



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Read Article:

Cusaak JR, Anderson TW: Physical Signs of Addiction. Federal Practitioner, August 1998.