



Episode 185 (Ch. 142 9th) – Alcohol Related Disease

Episode Overview:

- 1) Describe the EtOH pathway of metabolism. What order kinetics are involved?
- 2) Describe the AUDIT-C screening tool.
- 3) Define hazardous drinking amounts
- 4) Define substance dependence. What are signs of substance dependence?
- 5) Differential Diagnosis for acute withdrawal
- 6) Define and characterize minor + major ETOH withdrawal, and define delirium tremens (DTs)
- 7) List RF for DTs
- 8) Describe the management of severe EtOH withdrawal
- 9) List the ways EtOH precipitates or is related to Seizures; and a differential diagnosis of ETOH-related seizures
- 10) Describe the management of EtOH withdrawal seizures
- 11) Describe the pathogenesis and treatment of AKA
- 12) Describe the Wernicke's Encephalopathy triad, treatment, and prevention strategies.
- 13) List 10 complications of chronic EtOH use
- 14) List 6 contributing factor to UGI bleeding from EtOH
- 15) List 8 electrolyte/metabolic effects from chronic drinking
- 16) List 4 ways EtOH interacts with other drugs

Key Concepts:

- Moderate alcohol consumption is defined as one or two drinks/day for men and one drink/day for women.
- Benzodiazepines are the main treatment of alcohol withdrawal and alcohol withdrawal seizures. Minor alcohol withdrawal occurs as early as 6 hours and usually peaks at 24 to 36 hours after the cessation of or significant decrease in alcohol intake.
- **Major alcohol withdrawal occurs after 24 hours and usually peaks at 50 hours (but occasionally takes up to 5 days) after the decrease or termination of drinking.**
- Delirium tremens is the extreme end of the alcohol withdrawal spectrum; it consists of gross tremors, profound confusion, fever, incontinence, and frightening visual hallucinations.
- Alcohol withdrawal seizures occur 6 to 48 hours after the cessation of drinking, with 60% of patients experiencing multiple seizures within a 6-hour period.



- Alcohol withdrawal should be assessed and managed using a validated scale, such as the CIWA-Ar scale.

Rosen's in Perspective:

Anyone who works in the ER knows well the epidemic extent of alcoholism. Alcohol is the most common recreational drug taken by Americans, and per capita consumption is increasing. Alcohol is the third leading cause of preventable death in the United States; alcoholism permeates all levels of society and is a preventable cause of morbidity and mortality.

Today we'll touch on the key points for four emergent alcohol withdrawal syndromes; here's a signpost:

Syndromes

Alcohol tremulousness - occurs early, characterized by hypertension, tachycardia, tremors, and anxiety, with normal mental status

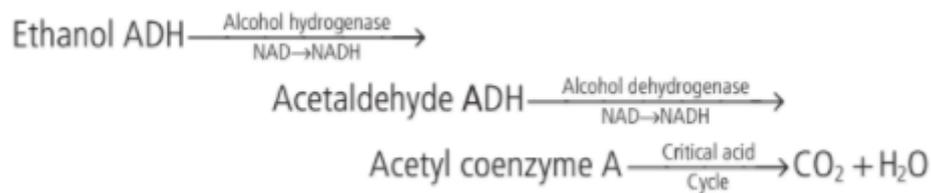
Alcohol withdrawal seizures - occurs early, usually single or brief flurry of seizures with short post-ictal period

Alcoholic hallucinosis - occurs early, no evidence of autonomic instability

Delirium tremens - occurs late, characterized by delirium and autonomic instability

[1] Describe the alcohol pathway of metabolism. What order kinetics are involved?

- **Absorption**
 - rapid
- **Distribution**
 - It is distributed uniformly to all organ systems, including the placenta.
- **Metabolism**
 - The hepatocyte: *most is metabolized to acetaldehyde, primarily by alcohol dehydrogenase (ADH). The oxidation of alcohol is a complex process involving three enzyme systems, all contained in the hepatocyte. Acetaldehyde is then quickly converted to carbon dioxide and water, primarily through aldehyde dehydrogenase (ALDH).*
 - There are genetic variations of ADH genes that affect tolerance to alcohol intake:
 - *However, about 40% of Asian people (Japanese, Chinese, and Koreans) have an inactive ALDH2 mutation that results in much higher acetaldehyde levels after drinking than normal. About 10% of people who are homozygous for this gene form cannot drink alcohol without becoming sick and have almost no risk of AUD, whereas those who are heterozygous have a relatively low rate of AUD. An alternative pathway, the microsomal ethanol-oxidizing system (MEOS), is induced by chronic alcohol exposure.*



Alcohol metabolism has two elimination rates. The alcohol elimination rate approximates zero-order kinetics (constant rate) for lower ethanol levels and first-order kinetics (amount of drug removed over time is proportional to the concentration of the drug) for higher levels, especially in chronic alcoholics; most likely, through induction of the MEOS pathway, the elimination rate is increased at higher blood levels.

The absorption and elimination rates of alcohol vary by individual and depend on many factors—diet, gender, body weight and habitus, speed of consumption, gastric motility, presence of food in the stomach, smoking history, age, whether the person is a chronic alcohol consumer with enzyme induction and high-activity MEOS, advanced cirrhosis, presence of ascites, and state of nourishment.

The rate of ETOH elimination varies, but in general (assuming zero order kinetics) is from 2-8 mmol/L/hr .

The exact physiologic effects of different levels are UNPREDICTABLE, some people are intolerant of levels as low as 5 mmol/L; a level of 32 mmol/L is where 50% of the adult population will be obviously intoxicated. Chronic alcoholics are tolerant of much higher levels.

- Excretion
 - Excreted through the lungs, urine, and sweat

[2] Define substance dependence. What are the signs of dependence?

This is a misleading question, because some of the current terminology has shifted based on the DSM-V. Replacing the two DSM-IV diagnoses of substance abuse and dependence is a single diagnosis, SUD, named by the type of substance involved (eg, alcohol use disorder or cannabis use disorder) and a specifier indicating severity (mild, mod, severe).

— *DSM-5 diagnostic criteria for SUD are described below .*

A problematic pattern of use leading to clinically significant impairment or distress is manifested by two or more of the following within a 12-month period:



1. *Often taken in larger amounts or over a longer period than was intended.*
2. *A persistent desire or unsuccessful efforts to cut down or control use.*
3. *A great deal of time is spent in activities necessary to obtain, use, or recover from the substance's effects.*
4. *Craving or a strong desire or urge to use the substance.*
5. *Recurrent use resulting in a failure to fulfill major role obligations at work, school, or home.*
6. *Continued use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by its effects.*
7. *Important social, occupational, or recreational activities are given up or reduced because of use.*
8. *Recurrent use in situations in which it is physically hazardous.*
9. *Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.*
10. *Tolerance.*
11. *Withdrawal.*

Preoccupation with use is often demonstrated by giving up previously important activities, increasing the time spent in activities related to substance use, and using more frequently or for longer amounts of time than planned. Consumption may continue despite the continued existence or worsening of problems caused by substance use. In applying criteria on consequences and behaviors associated with use, it is important to include alcohol-related blackouts, and impulsive sexual behavior.

Severity — Alcohol and drug symptom profiles appear to vary along a severity dimension. DSM-5 severity specifiers mild, moderate, and severe are based on the number of diagnostic criteria met by the patient at the time of diagnosis:

- **Mild – Two to three criteria**
- **Moderate – Four to five criteria**



● **Severe – Six or more criteria**

Healthcare coding and billing in the United States is based on the International Classification of Diseases (ICD). DSM-5 and ICD criteria for a substance use disorder are very similar, but ICD require a minimum of three criteria instead of two. The ICD diagnoses of “harmful use” require only substance related physical or psychological harm.

Most published clinical trials of SUD treatment studied patients diagnosed with DSM-IV disorders. Applying these results to patients diagnosed with DSM-5 SUD is imprecise, but the most closely comparable groups are:

● **Substance abuse – Mild subtype of SUD**

● **Substance dependence – Moderate to severe subtype of SUD**

Alcohol use disorder in DSM-5 replaces two psychiatric disorders in DSM-IV, alcohol abuse and alcohol dependence. Alcohol use disorder can be specified as mild, moderate, or severe (6 or more symptoms present), based on the number of DSM-5 criteria present.

DSM-5 diagnostic criteria for alcohol use disorder are:

- *Recurrent drinking resulting in failure to fulfill role obligations*
- *Recurrent drinking in hazardous situations*
- *Continued drinking despite alcohol-related social or interpersonal problems*
- *Evidence of tolerance*
- *Evidence of alcohol withdrawal or use of alcohol for relief or avoidance of withdrawal*
- *Drinking in larger amounts or over longer periods than intended*
- *Persistent desire or unsuccessful attempts to stop or reduce drinking*
- *Great deal of time spent obtaining, using, or recovering from alcohol*
- *Important activities given up or reduced because of drinking*
- *Continued drinking despite knowledge of physical or psychological problems caused by alcohol*



- *Alcohol craving*

-The above compiled from Uptodate 2018

[3] Describe the AUDIT-C screening test.

Some sources confirm that 25-30% patients visiting the ER meet the criteria for at risk drinking. The CAGE questionnaire is designed to assess for LIFETIME ETOH dependence and is no longer recommended as a screening tool because it is geared towards the DSM-IV diagnoses of substance abuse and dependence; plus it is not as sensitive for detecting the full spectrum of unhealthy use.

However, the Alcohol Use Disorders Identification Test (AUDIT)-C is best used for primary care settings.

AUD consist of alcohol dependence, alcohol abuse, or harmful use. These disorders are common in all developed countries and are more prevalent in men than in women, with lower but still substantial rates in developing countries.

However, most people with AUD are difficult to identify because they are likely to have jobs and families and to present with general complaints, such as malaise, insomnia, anxiety, sadness, or a range of medical problems.

In response to the high prevalence of this disease, the American Medical Association has recommended screening patients for alcohol use problems in medical and surgical settings and EDs.

AUDIT-C — The AUDIT-C is a screening test comprised of three items on excess consumption from the Alcohol Use Disorders Identification Test (AUDIT). The questions, below, have been validated primarily in male veterans but studies demonstrating validity in primary care and other populations are beginning to appear. The AUDIT-C is briefer than the original test, but still requires scoring.

- *How often do you have a drink containing alcohol?*
- *How many drinks containing alcohol do you have on a typical day when you are drinking?*
- *How often do you have six or more drinks on one occasion?*

Scores considered positive for unhealthy drinking are:

- *Three or more in women, with 73 percent sensitivity and 91 percent specificity*
- *Four or more in men, with 86 percent sensitivity and 89 percent specificity*



Although the AUDIT-C contains no items specific to disorders, the score is associated with severity; a score of 7 to 10 or greater suggests dependence

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AUDIT-C

| Question #1: How often did you have a drink containing alcohol in the past year? | |
|---|------------|
| • Never | (0 points) |
| • Monthly or less | (1 point) |
| • Two to four times a month | (2 points) |
| • Two to three times per week | (3 points) |
| • Four or more times a week | (4 points) |
| Question #2: How many drinks did you have on a typical day when you were drinking in the past year? | |
| • 1 or 2 | (0 points) |
| • 3 or 4 | (1 point) |
| • 5 or 6 | (2 points) |
| • 7 to 9 | (3 points) |
| • 10 or more | (4 points) |
| Question #3: How often did you have six or more drinks on one occasion in the past year? | |
| • Never | (0 points) |
| • Less than monthly | (1 point) |
| • Monthly | (2 points) |
| • Weekly | (3 points) |
| • Daily or almost daily | (4 points) |

The AUDIT-C is scored on a scale of 0 to 12 (scores of 0 reflect no alcohol use). In men, a score of 4 or more is considered positive; in women, a score of 3 or more is considered positive.

The goal of this test is identify people who are drinking hazardous amounts!

[4] Define hazardous drinking amounts

Alcohol contributes to 79,000 deaths and \$223.5 billion in societal costs annually in the United States. Harmful consequences and risk of disability exist on a continuum.

At-risk drinking is defined as heavy or problematic alcohol use that may lead to an array of negative consequences, including social, physical, psychological, legal, and financial problems.

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) in the United States has estimated consumption amounts of alcohol that increase health risks:

- Men under age 65
 - More than 14 standard drinks per week on average
 - More than 4 drinks on any day
- Women and adults 65 years and older
 - More than 7 standard drinks per week on average
 - More than 3 drinks on any day



Specifying these thresholds is an inexact science based on epidemiological evidence. Amounts are based on a “standard drink,” which is defined as 12 grams of ethanol, 5 ounces of wine, 12 ounces of beer, or 1.5 ounces of 80 proof spirits. The number and size of drinks that define risky amounts varies internationally.

- Uptodate

[5] List the differential diagnosis for acute alcohol withdrawal

- Prescription
 - Benzodiazepines
- “Recreational”
 - ETOH

Acute intoxication of any substance during the withdrawal period:

- Cocaine
- GHB
- Amphetamines
- Any other illicit substance!

[6] Define and characterize minor and major alcohol withdrawal, and define delirium tremens (DTs)

Symptoms of alcohol withdrawal occur because alcohol is a central nervous system depressant. Alcohol simultaneously enhances inhibitory tone (via modulation of gamma-aminobutyric acid activity) and inhibits excitatory tone (via modulation of excitatory amino acid activity). Only the constant presence of ethanol preserves homeostasis. Abrupt cessation unmasks the adaptive responses to chronic ethanol use resulting in overactivity of the central nervous system.

Gamma-aminobutyric acid — Gamma-aminobutyric acid (GABA) is the major inhibitory neurotransmitter in the brain. Highly specific binding sites for ethanol are found on the GABA receptor complex. Chronic ethanol use induces an insensitivity to GABA such that more inhibitor is required to maintain a constant inhibitory tone. As alcohol tolerance develops, the individual retains arousal at alcohol concentrations which would normally produce lethargy or even coma in relatively alcohol naïve individuals. Cessation of alcohol or a reduction from chronically elevated concentrations results in decreased inhibitory tone.

Excitatory amino acids — Glutamate is one of the major excitatory amino acids. When glutamate binds to the N-methyl-D-aspartate (NMDA) receptor, calcium influx



leads to neuronal excitation by binding to the glycine receptor on the NMDA complex. Ethanol inhibits glutamate induced excitation. Adaptation occurs by increasing the number of glutamate receptors in an attempt to maintain a normal state of arousal. Cessation of alcohol or a reduction from chronically elevated concentrations results in unregulated excess excitation. - Uptodate

| Minor ETOH withdrawal | Major ETOH withdrawal | Delirium tremens (< 5%) |
|--|--|---|
| trembling, sweating, nausea, vomiting, anxiety, and agitation. | additional neuronal excitation, with epileptiform seizures and global confusion May have vital sign changes | hallucinations, disorientation, tachycardia, hypertension, hyperthermia, agitation, and diaphoresis |
| in the setting of acute reduction or abstinence from alcohol. | in the setting of acute reduction or abstinence from alcohol. | in the setting of acute reduction or abstinence from alcohol. |
| Peaks within 24 hours | Peaks within 24-48 hrs | typically begins between 48 and 96 hours after the last drink and lasts one to five days |

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Timing of alcohol withdrawal syndromes

| Syndrome | Clinical findings | Onset after last drink |
|------------------------|--|------------------------|
| Minor withdrawal | Tremulousness, mild anxiety, headache, diaphoresis, palpitations, anorexia, GI upset; Normal mental status | 6 to 36 hours |
| Seizures | Single or brief flurry of generalized, tonic-clonic seizures, short post-ictal period; Status epilepticus rare | 6 to 48 hours |
| Alcoholic hallucinosis | Visual, auditory, and/or tactile hallucinations with intact orientation and normal vital signs | 12 to 48 hours |
| Delirium tremens | Delirium, agitation, tachycardia, hypertension, fever, diaphoresis | 48 to 96 hours |

Graphic 75499 Version 1.0

[7] List risk factors for delirium tremens

- A history of sustained drinking
- A history of previous DT
- Age greater than 30
- The presence of a concurrent illness
- The presence of significant alcohol withdrawal in the presence of an elevated alcohol level



- A longer period since the last drink (ie. patients who present with alcohol withdrawal more than two days after their last drink are more likely to experience DT than those who present within two days)

[8] Describe the management of severe alcohol withdrawal

Alcohol withdrawal remains a clinical diagnosis. It may be necessary to perform extensive testing, including lumbar puncture and cranial CT, to rule out other diagnostic considerations with confidence. This is particularly true when the presentation includes altered mental status and fever.

Conditions, such as infection (eg, meningitis), trauma (eg, intracranial hemorrhage), metabolic derangements, drug overdose, hepatic failure, and gastrointestinal bleeding, can mimic or coexist with alcohol withdrawal

| Treatment |
|--|
| Benzodiazepines |
| First line therapy for ALL alcohol withdrawal syndromes |
| Most patients with symptoms require IV therapy initially |
| Give: |
| Diazepam, 5 to 10 mg IV, repeat every 5 to 10 minutes, OR |
| Lorazepam, 2 to 4 mg IV, repeat every 15 to 20 minutes |
| Massive doses (>2000 mg diazepam in 48 hours) may be required |
| Clinically stable patients with minimal symptoms may be treated with oral medications |
| Barbiturates |
| Synergistic with benzodiazepines; give if patient refractory to high-dose benzodiazepines |
| Phenobarbital 130 to 260 mg IV, repeat every 15 to 20 minutes |
| Intubation frequently required with concurrent benzodiazepine and barbiturate use |
| ALL patients requiring barbiturates are monitored in an intensive care unit |
| Propofol |
| Excellent agent if patient refractory to benzodiazepines and barbiturates |
| Intubation almost always required |
| 1 mg/kg IV push as induction agent for intubation; titrate continuous infusion for sedation |



| |
|--|
| Supportive care |
| Assure adequate fluid and electrolyte replacement |
| Give parenteral thiamine 100 mg and glucose daily |
| Give multivitamin supplements |
| Ensure adequate caloric support |

Patients should be placed in a quiet, protective environment. Mechanical restraint may be necessary temporarily for patients suffering from delirium tremens (DT) in order to protect both the patient and caretakers.

**[9] List the ways that alcohol precipitates or is related to seizures.
List a differential for alcohol withdrawal seizures.**

See Box 142.2 in the 9th edition.

We already know that the abrupt withdrawal of ETOH leads to an imbalance of glutamate in the CNS. But there are at least 6 ways that ETOH may act to produce seizures:

1. by its partial or absolute withdrawal after a period of chronic intake,
2. by an acute alcohol-related metabolic disorder (eg, hypoglycemia, hyponatremia),
3. creation of a situation leading to cerebral trauma,
4. precipitation of seizures in patients with idiopathic or post-traumatic epilepsy,
5. or lowering of the seizure threshold in patients with prior existing intracerebral disease states.
6. Increasing susceptibility to other disorders associated with seizures, including neurosyphilis, acquired immunodeficiency syndrome (AIDS), brain abscess, and meningitis.

[10] Describe the management of alcohol withdrawal seizures.

In general: only supportive care!

Withdrawal-associated seizures are generalized tonic-clonic convulsions that usually occur within 12 to 48 hours after the last alcoholic drink, but may occur after only two hours of abstinence. The seizures occur predominantly in patients with a long history of chronic alcoholism, as evidenced by their typical onset during the fourth and fifth decades of life.



****Withdrawal seizures are usually singular or occur as a brief flurry of seizures over a short period. Recurrent or prolonged seizures or status epilepticus are not consistent with withdrawal-associated seizures and should prompt an investigation into possible structural or infectious etiologies, generally guided by the findings of cranial computed tomography (CT) and/or lumbar puncture. *****

Benzodiazepines, [phenobarbital](#), and [propofol](#) can be used to treat status epilepticus while investigations proceed. Several studies have demonstrated that [phenytoin](#) is ineffective in the treatment of alcohol withdrawal seizures and the drug should not be used for this purpose. Although seemingly benign, alcohol withdrawal seizures left untreated progress to delirium tremens in nearly one-third of patients

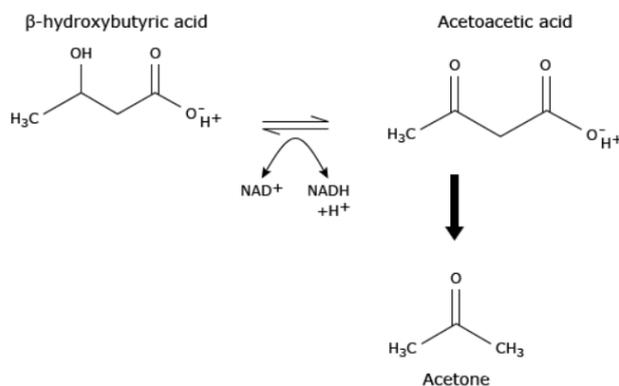
[11] Describe the pathogenesis and treatment of alcoholic ketoacidosis.

Ketoacidosis is the term used for metabolic acidosis associated with an accumulation of ketone bodies. The most common cause of ketoacidosis is diabetic ketoacidosis. Two other causes are fasting ketosis and alcoholic ketoacidosis.

There are three ketone bodies

- Beta-hydroxybutyric acid
- Acetoacetic acid
 - The only TRUE KETOACID
- Acetone
 - True ketone, but NOT an acid

Ketone bodies



Graphic 87660 Version 1.0

Pathogenesis:

- Think about this in the malnourished patients with chronic alcoholism who have a history of binge alcohol ingestion. Active drinking has often stopped because of the development of abdominal pain, nausea, and vomiting. Blood ethanol levels at this time may be low or not detectable.
- Hepatic generation of ketone bodies is usually stimulated by the combination of low insulin levels and high glucagon levels (ie, a low insulin/glucagon ratio that can result, for example, from fasting).



- ETOH withdrawal amplifies the response to fasting and increases fatty acid breakdown
 - As ethanol levels begin to fall, increased levels of catecholamines (particularly norepinephrine) and cortisol resulting from ethanol withdrawal amplify the hormonal responses to fasting (low insulin levels, high glucagon), causing a marked increase in lipolysis and fatty acid delivery to the liver.
 - Patients with alcoholic ketoacidosis typically present with a history of chronic alcohol abuse, malnutrition, and a recent episode of binge drinking.

Presentation:

- Nausea, vomiting, and abdominal pain
- Generalized abdominal tenderness, hepatomegaly, and laboratory evidence of alcoholic hepatitis and/or pancreatitis
- Hypovolemia and/or potassium depletion
- Tachycardia and hypertension due to alcohol withdrawal, pancreatitis, and/or volume depletion, as outlined above
- Increased respiratory rate, due to alcohol withdrawal, pain, and/or respiratory compensation for the metabolic acidosis
- Plasma alcohol levels may be low or undetectable at presentation in patients with alcoholic ketoacidosis. In addition, such patients may have hypoglycemia or hyperglycemia, hypokalemia, hypophosphatemia, hypomagnesemia, an elevated serum osmolal gap, and mixed acid-base disorders.

Diagnosis of AKA:

- Suspicion or clinical history and a low glucose level (90% with a glucose <13 mmol/L)
- Elevated anion gap
- Ketonuria (*) or ketonemia (serum beta-hydroxybutyrate much superior)

Keep that ddx broad! Don't forget other life threats: diabetic ketoacidosis, lactic acidosis, poisoning due to methanol or ethylene glycol (which is more common in alcoholics), and, in patients with advanced, usually chronic kidney disease, uremic acidosis

Management:

- Correct the underlying cause behind the acidemic state
- Supportive!
 - Correct hypovolemia with dextrose and saline solutions
 - Dextrose will help reduce ketone production, and help the body produce more bicarbonate to reverse the metabolic acidosis
 - Simultaneously administer at least 100 mg Thiamine IV or IM
 - Correct hypokalemia (especially important in people who are severely hypoK before giving dextrose!)
 - IV or PO
 - Correct phosphate depletion
 - Typically potassium phosphate given PO (unless extremely low)
 - K-Phos 500 mg PO four times a day with meals
 - IV magnesium salts



* **Nitroprusside** reacts with acetoacetate and, to a much lesser degree, acetone (which is not an acid). However, nitroprusside does not react with beta-hydroxybutyrate. This is an important limitation since beta-hydroxybutyrate is usually present at higher concentrations than acetoacetate. The ratio of beta-hydroxybutyrate to acetoacetate is normally 1:1, increases to 3:1 in diabetic ketoacidosis, and may increase to 10:1 in alcoholic ketoacidosis. The higher beta-hydroxybutyrate-to-acetoacetate ratio in alcoholic patients is due to a higher NAD⁺/NADH ratio generated by alcohol metabolism. Thus, in most patients with alcoholic ketoacidosis, nitroprusside tests underestimate the degree of ketone bodies in plasma, and some patients may have negative tests

- Compiled from Uptodate “Fasting ketosis and alcoholic ketoacidosis”

[12] Describe the Wernicke’s Encephalopathy triad, treatment and prevent strategies.

Wernicke encephalopathy is an acute neurologic disorder caused by **thiamine** deficiency and manifested by a clinical triad of encephalopathy, oculomotor dysfunction, and gait ataxia.

Wernicke’s DATE. diplopia, ataxia, thiamine, encephalopathy

Wernicke encephalopathy produces petechial hemorrhagic necrosis in midline brain structures and corresponding deficits in mentation, oculomotor function, and gait ataxia.

All three of these classic symptoms are present in only one-third of patients. Any one of these, most often encephalopathy, may be seen in isolation. WE should be considered when one or more occur in at-risk patients.

There is no diagnostic test that confirms the diagnosis, so whenever you suspect it, give thiamine!

A suggested treatment regimen is 500 mg intravenous (IV), infused over 30 minutes, repeated three times daily for two consecutive days and 250 mg IV or IM once daily for an additional five days. Oral thiamine and multivitamin supplementation are recommended thereafter as long as the patient remains at risk.

- Wernicke encephalopathy may be precipitated by administration of intravenous glucose solutions to individuals with **thiamine** deficiency. In susceptible



individuals glucose administration should be preceded or accompanied by thiamine 100 mg IV.

-uptodate

Korsakoff amnestic syndrome is the CHRONIC form of thiamine deficiency.

[13] List 10 complications of chronic alcohol use

ETOH negatively impacts every organ system.

Here are just a few effects:

- CV
 - Dysrhythmia formation - A fib, VTach.
 - Worsen CAD
 - HTN
 - Cardiomyopathy
 - Increased risk of sudden death
- Resp
 - Increased risk of aspiration and pneumonia
 - Increased risk of bronchospasm and sleep apnea
- Neuro
 - Peripheral polyneuropathy (probably in conjunction with thiamine and B12 deficiency)
 - Wernicke's encephalopathy
 - Korsakoff's psychosis or amnesic state, also called alcohol induced persisting amnestic disorder
 - Cerebellar degeneration
- GI
 - GI bleeding
 - Hepatic damage
- Infectious disease
 - Chronic immunosuppression
- Oncologic effects
- Psychiatric disease and social isolation
- Metabolic - endocrine (see question below)

[14] List 6 contributing factors to upper GI bleeding from alcohol

- Development of portal hypertension and varices from cirrhosis
- ETOH induced gastritis / esophagitis
- ETOH related GI cancers
- ETOH related hemostasis disorders
 - *thrombocytopenia, qualitative platelet disorders, deficient production of hepatic clotting factors, GI variceal formation, and vitamin K deficiency*



- Comorbid substance use disorders:
 - Smoking, cocaine, NSAIDs
- Increased risk for dieulafoy's lesions
- GI trauma from withdrawal or intake leading to mallory-weiss syndrome (or another cause of vomiting such as pancreatitis)

[15] List 8 metabolic/electrolyte effects from chronic alcohol use

Poor oral intake; intestinal pathology: Diarrhea and impaired intestinal absorption are common problems of the chronic alcoholic. Alcohol increases small intestine transit time and decreases brush border enzyme activity.

Thiamine, vitamin B12, amino acids, folic acid, and glucose have impaired absorption in alcoholics. Dietary deficiencies in folic acid and protein, pancreatic insufficiency, abnormal biliary secretion, and direct toxic effects of ethanol on the GI tract contribute to malabsorption. Abstinence and adequate nutrition reverse the diarrhea and much of the malabsorption.

- Hypoglycemia (glycogen deplete liver! Glucagon won't help!)
 - Inhibited gluconeogenesis
- Hypokalemia
- Hypomagnesemia
- Hypophosphatemia
- Hyponatremia
- Hypocalcemia
- Low testosterone (and increased estrogen = decreased libido, feminization, and gynecomastia)
- Low cortisol
- Low growth hormone
- Insulin resistance
- Hypertriglyceridemia
- Hypoparathyroidism
- Hypoalbuminemia
- Hypovitaminosis D
- depressed hypothalamic thermoregulation, peripheral vasodilation producing heat loss
- Heme effects
 - Anemia
 - Low platelets
 - Poor hemostasis
 - Leukopenia

See Table 142.3 in 9th Edition

[16] List 4 ways alcohol interacts with other drugs



- Increased toxic effects of acetaminophen
- Further lower the seizure threshold with bupropion
- Enhances the depressant effect of cannabis, benzodiazepines and most other sedatives
- Prolongs the severity and duration of intoxication with cocaine
- Increases risk for lactic acidosis with metformin
- Disulfiram-like reaction when metronidazole and ETOH are consumed
- Enhances the hypotensive effects of medications like PDE5 inhibitors and nitrates

And many others....!