Alcohol

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The Drug That Keeps Us Employed

- Statistics
- History
- Physiology
- Withdrawal
  - Treatment
I’ll Drink to That

- What’s the most common drug used in the U.S.?
- Ethanol is second
- 75% of adult Americans have used ethanol
- Third is tobacco
I’ll Drink to That, too

- $50 billion is spent on ethanol per year
- $40 – 50 billion on cocaine
- $35 billion on tobacco
- $30 billion on OTC and prescribed drugs
- $25 billion on marijuana
I Believe I’ll Have Another...

- 400,000 deaths per year from smoking tobacco
- 100,000 per year from ethanol
- 5,000 from overdoses on OTC and prescribed drugs
- 3500 from all other illegal drugs
- A few from marijuana
An’ Jush One More

- Physical dependence – physical withdrawal symptoms
- Psychological dependence – need effects for well being
- Addiction – both of the above
And One for the Road

- 50% of trauma patients are alcoholics
- 21% of all E.D. patients over 18 have been drinking
- E.D. personnel suspect drinking in only 48% of patients who are intoxicated
History

• Earliest ethanol – mead made from honey
• Beer was born when agriculture was born
• 6000 BC grape vine was domesticated
• Noah planted grape vines first when he landed on Mt. Ararat
History

• The first writing found is about fermenting grapes
• Egyptians had wine and beer
• First ban on drinking was on Egyptian soldiers – quickly repealed
• Wine gets to southern France in 600 BC
History

- Greeks had laws that doubled the punishment if person was drunk when committing the crime
- “Symposium” means “drinking together”
- Jesus drank wine regularly, turned water into wine
History

• Romans first described effects of long term drinking and withdrawal symptoms
• In the Middle Ages, wine produced by monasteries – hard to get
• Then beer came along
• The problem of addiction affecting society doesn’t emerge until “spirits” created
  – Gin in 18th century England
Not Just Humans

• Most animals get drunk and most animals like it
• Robins loaded on fermented pyracantha berries will dive bomb cats
• Durian fruit trees in Africa – animals come from miles around to eat and get drunk
• Elephants will chase a jeep carrying a drum of booze
Ethanol Kinetics

• Very small molecule, water and lipid soluble
• Doesn’t need receptor sites – goes right through lipid membranes
  – Cell membranes
  – Blood brain barrier
• Absorption begins in mouth, most is done in small intestine
• Food in stomach DOES slow absorption
Ethanol Kinetics

- 2 – 10% is excreted unchanged through lungs and kidneys
- Most is metabolized in the liver
- Yield is 7 calories per gram
- Metabolize about 10 – 20 gm/hr
  - 12 oz beer, 4 oz wine, 1.5 oz 80 proof
- Greatly variable rate of metabolism
- Alcoholics tend to metabolize more quickly
Areas of Brain Affected

- Most complex areas affected first
- Frontal lobe – controls judgment, social inhibitions is most sensitive and first affected
- Next are areas that control speech, vision, balance, coordination
- Brain stem last affected – respirations decrease
Blood Alcohol Concentration

- 50 mg/dl (0.05%) – happy, gregarious
- 100 – 250 (.1-.25%) – confusion, ataxia, nystagmus, exaggerated emotional states, incoordination
- >400 (.4%) – fatal
- Highest reported level in a survivor: 1510 mg/dl (1.5%)
Ethanol Kinetics

Ethanol

Nicotine adenine diphosphate → Acetaldehyde

Acetaldehyde → Acetic acid

Aldehyde dehydrogenase

Alcohol dehydrogenase
Factoids

• Measurable blood alcohol within 5 minutes of ingestion
• Maximum concentration between 30 and 90 minutes
• Distributed throughout all body water at same concentration as in blood
Proof

- Twice the concentration in volumes percent
- 100 proof is 50% volume
- Beer and ale: 3-6% (6–12 proof)
- Wine: 10-18% (20-36 proof)
- Brandy: 40% (80 proof)
- Spirits: 40-50% (80-100 proof)
Proof

- 5 leading mouthwashes: 28-54 proof
- Colognes and perfumes: 120 proof
- Lemon extract: 160 proof
- Nyquil: 20 proof
Making Ethanol

- Carbon, oxygen, hydrogen
- Obtained by substituting a hydroxyl group (-OH) for an –H atom on an aliphatic hydrocarbon
Making Ethanol

- Fermentation – breakdown of molecules by bacteria
  - Beer
  - Wine
  - Tequila
  - Sake
Making Ethanol

- Distillation – heating the molecules to change their structure
  - Brandy
  - Whiskey
  - Rum
Making Ethanol

• Compounding – combining elements chemically
  – Gin
  – Cordials
  – Liqueurs
Isopropyl Alcohol Kinetics

Isopropyl Alcohol

- Acetone
- Carbon Dioxide
- Water

Alcohol dehydrogenase
Isopropyl Alcohol Kinetics

- Twice a potent as ethanol
- Do not get euphoric effects
- Very irritating to stomach lining
  - N, V, D
  - Abdominal pain
  - Hematemesis, melena
- Coma at 120 mg/dl (0.12)
Isopropyl Alcohol Treatment

- Support ventilation
- Support blood pressure with volume first
- Hemodialysis if really bad
Methanol Kinetics

Methanol (wood alcohol) → Alcohol dehydrogenase → Formaldehyde → Formic acid – toxic to optic nerve.
Methanol

- Takes a lot more to feel “high”
- Fatal dose is 1 – 2 cc/kg or 80 mg/dl (.08)
- “Snowstorm” vision changes
- Anion gap acidosis
  - Acidosis caused by weird anions
- Abdominal pain
Methanol Treatment

- Ethanol drip
  - Alcohol dehydrogenase will bind preferentially to ethanol
  - Methanol excreted unchanged
- Fomepazole (4-methopyrazole) inhibits alcohol dehydrogenase
- Sodium bicarbonate – to bind with formic acid and prevent blindness
- Benzodiazepine for seizures
- Hemodialysis
Ethylene Glycol Kinetics

Ethylene Glycol → Glycoaldehyde → Glycolic acid → Glyoxylic acid → Oxalic acid (toxic to kidneys)

Alcohol dehydrogenase
Ethylene Glycol

- Anion gap acidosis
- Minimal lethal level is 21 mg/dl (.02)
- Accumulation of oxalate crystals in tissues
- Pulmonary edema
- Renal parenchyma damage from crystals
Ethylene Glycol Treatment

- Ethanol drip
  - Alcohol dehydrogenase will bind preferentially to ethanol
  - Methanol excreted unchanged
- Fomepazole (4-methopyrazole) inhibits alcohol dehydrogenase
- Sodium bicarbonate – to bind with formic acid and prevent blindness
- Diazepam for seizures
- Hemodialysis
Alcohol Dehydrogenase

- Most men have a lot more in their stomachs than most women
  - Same size male can drink same amount as same size female and have lower blood alcohol
- Aspirin deactivates the enzyme in the stomach, increasing blood alcohol concentration
Alcohol Dehydrogenase

• As much as 50% of Asians deficient; same for American Indians
• Get Antabuse reaction
  – Flushing
  – Vomiting
• Antabuse blocks alcohol dehydrogenase
• Flagyl (metronidazole) causes Antabuse reaction
Alcohol Dehydrogenase

• Two types – I and II
• Majority of population has Type 1
• Small percent have Type II
  – Process alcohol up to 40% more efficiently
  – Get only half as drunk
Neuroreceptors in the CNS

• Excitatory
  – Acetylcholine
  – Glutamate
  – Serotonin

• Inhibitory
  – Glycine
  – Gamma-aminobuteric acid (GABA)

• Causes inrush of chloride anions, hyperpolarization of neurons, less likely to fire
At the Neuron

• Gets into ALL synapses in the CNS
• Has greatest effect in the GABA receptor
• GABA is the most common inhibitory neurotransmitter
• GABA slows things down
• The GABA receptor has specific sites for benzodiazepines and barbiturates
• No site for alcohol, but greatest effect
GABA Receptors

• All vertebrates have benzo sites in GABA receptors
• Exceptions: squid, lobsters, earthworms, woodlouse, hagfish
• Benzos and barbiturates control seizures; withdrawing ethanol causes seizures
• In some animal studies, effects of ETOH have been blocked by flumazenil
GABA Receptors

• Get constantly stimulated by alcohol
• Naturally down-regulate (tolerance)
• When alcohol withdrawn, not enough GABA receptors to keep things calm in the brain
• Get sympathetic over-stimulation
Alcohol Withdrawal
Sympathetic Over-Stimulation

- Tremulousness
- Anxiety
- Tachycardia
- Hypertension
- Psychomotor agitation

- Diaphoresis
- Dilated pupils
- Hallucinations
  - Auditory
  - Visual
- Generalized Tonic-Clonic Seizures
Onset of Symptoms

• Do not have to have zero blood alcohol level; just lower than usual functioning level
• 8 – 12 hrs – craving and tremors
• 24 hrs to 5 days – severe withdrawal to delirium tremens
When Does Withdrawal Become Delirium Tremens?

• When the patient can not tell hallucinations from reality
• Severe confusion
• Uncontrollable agitation
• FEVER
Alcohol Withdrawal Treatment

- Drugs
- Ralley bag
Drugs

Benzodiazepines

• Diazepam (Valium)
• Lorazepam (Ativan)
• Chlordiazepoxide (Librium)
Benzos

• Start with a solid dose
  – 20 mg diazepam PO or 5 – 10 mg IV
• Repeat every 1.5 to 2 hours prn
• Diazepam 20 mg PO = lorazepam 4 mg PO = chlordiazepoxide 100 mg PO
• Diazepam 5-10 mg IV = lorazepam 1-2 mg IV = chlordiazepoxide 100 mg IV
Other drugs

• Clonidine – central alpha agonist
  – Lowers BP
  – Lessens tremor, sweating, anxiety
  – May lessen craving

• Beta Blockers
  – Mixed reviews
  – Beware contraindications – asthma, CHF
  – Atenolol 50 – 100 mg qd
  – Propanolol 40 mg q 6 hrs
Withdrawal Seizures

• Within first 48 hours, up to 96 hrs
• Peak incidence between 13 and 24 hours
• Up to 15% of alcoholics get withdrawal seizures
• Most common in binge drinkers
• Most often classic generalized tonic-clonic. Can be focal
Withdrawal Seizures

- Seizures do not predict severity of withdrawal symptoms
- 75% more likely to get withdrawal seizures again
- Not to be confused with alcoholic epilepsy:
  - Seizure threshold is LOW, even with high ethanol levels
  - Seizures occur at random, not associated with withdrawal
Withdrawal Seizures

• Treat with benzos
  – I.V. midazolam most common
  – Then PO benzos

• NOT phenytoin
  – Phenytoin does not prevent further withdrawal seizures
  – Has lots of bad side effects
Ralley Bag

• The alcoholic MAY be deficient in
  – Thiamine
  – Folate
  – Other B vitamins
  – Vitamins C and E
  – Magnesium

• One oral multivitamin works just as well
Reasons for Deficiencies

- Inadequate diet
- Malabsorption
- Interruption of transport and storage
- Altered metabolism
- Increased excretion
Effects of Deficiencies

- Neurologic disorders
  - Altered mental status
  - Ataxia
  - Peripheral neuropathies
  - Weakness
  - Coma
The Usual Ralley Bag

- D5 LR or NS
- Thiamine 100 mg
- Folic acid 5 mg
- Multivitamins
- Magnesium 1 gm
Thiamine Deficiency

- Coenzyme in several reactions
- Essential for conversion of CHOs, fat, proteins
- Beri-beri
  - Polyneuritis
  - Cardiac pathology
  - Peripheral edema
Thiamine Deficiency

• Associated with Wernicke’s encephalopathy and Kosakov’s Syndrome
Wernicke’s Encephalopathy

- About 12% of chronic alcoholics
- Ophthalmoplegia
- Ataxia
- Abnormal mentation
Korsakov’s Syndrome

- A part of Wernicke’s
- Confabulation – invents information to cover memory deficits
- Retrograde amnesia – poor short term memory
- Anterograde amnesia – can’t learn or retain new information
Thiamine and Wernicke’s

- 100 mg of thiamine can improve symptoms for a little while
- One dose of thiamine doesn’t change anything in the long run
- It’s never been shown that an episode of Wernicke’s has been precipitated by giving a single dose of glucose in thiamine deficiency
- Thiamine is indicated ONLY for pts showing Wernicke’s/Korsakov’s
Folate or Folic Acid Deficiency

- Affects cells that divide rapidly
  - Bone marrow
  - Gut mucosa
- Macrocytic anemia
- Even if you give folate, pt still has macrocytic anemia until he/she stops drinking
- One dose of folate doesn’t do a thing
Multivitamins

• Standard multivits
  – A, D, E, B1, B2, B3, B5, B6, B12, C, biotin, and folic acid
• Oral bioavailability is 100%, even in chronic drinkers
• Nobody has been able to demonstrate these vitamin deficiencies in alcoholics
• A single dose does nothing
Magnesium

- Serum magnesium level is meaningless
  - Total body store of Mg is 24 grams
  - 50 –60% in bone
  - 40 – 50% intracellular
  - Less than 1% in serum
    - Half of that is bound to protein or complexed to ions
- Serum Mg is less than ½ of 1% of body Mg
Magnesium Deficiency

- Alcohol ingestion causes urinary loss of Mg
- 25 – 30% of alcoholics are seriously hypomagnesemic
- Usually down about 9 grams
- Contributes to withdrawal symptoms
- Not the cause of DTs
- Authors suggest oral magnesium replacement; I.V. only if severe symptoms
Magnesium Deficiency

• Neuromuscular hyperactivity
  – Tremors
  – Vertical nystagmus
  – Weakness

• Psychiatric disturbances

• Calcium and potassium abnormalities
The Real Purpose of the Ralley Bag

• The alcoholic can look up and think we are doing something to fix him/her

• My suggestion:
  – Mg 2 gms
  – Yellow food coloring
  – Maybe a different color each time the patient comes in (blue is for the very serious)
Addiction

- All habit forming drugs affect the mesotelencephalic dopamine system.
- This system is a major mediator of reward-reinforcing mechanisms in the brain.
- Uses dopamine as its neurotransmitter.
Addiction

• Cocaine blocks reuptake of dopamine
• Amphetamines trigger release of dopamine
• Barbiturates, benzodiazepines, opiates lower the threshold of dopamine activation
• Nicotine, alcohol, caffeine, PCP and cannabinoids indirectly activate the mesotelencephalic dopamine system
Genetic Propensity for Alcoholism

• Aristotle and Plutarch both wrote that alcoholics bring forth alcoholic children
• Close relatives of alcoholics are 4 times more at risk of becoming alcoholic, even if raised in totally different environment
• Identical twins show a higher rate of alcoholism than fraternal twins
Genetic Propensity for Alcoholism

• Some people have a different dopamine receptor, called D2
• 69% of alcoholics found to have allelic gene for this receptor
• 20% of non-alcoholics have it
• This dopamine receptor is strongly associated with “reward” behavior
Genetic Propensity for Alcoholism

- Predictors of future alcoholism
  - Lowered response to alcohol
  - Lowered EEG response to alcohol
  - Enhanced release of beta-endorphin in response to alcohol
What Makes a Hangover?

• Dehydration
• Migraine response to additives
  – Red wine
• Hypokalemia, hypomagnesemia
• “Rebound” of stimuli sensitivity
• Alcohol irritates gastric lining – vomiting, abdominal pain
Effects on Organs

- Brain
- Stomach
- Heart
- Liver
- Immunity
- Pancreas
Brain

• Thiamine deficit – Wernicke’s
• Black out
  – 30–40% of men in late teens, early 20’s
  – Not a precursor to alcoholism
• Fragmented sleep
• Peripheral neuropathy
• Cerebellar degeneration – unsteady gait
• Alcoholic dementia
Stomach and Esophagus

- Stomach
  - Gastritis
    - Hematemesis
    - Abdominal pain
- Esophagus
  - Esophagitis
  - Esophageal varices from portal hypertension
Effect on Heliobacter Pylori

- Red wine significantly decreases levels of *H. pylori* in the stomach
- It’s not the alcohols
- It’s the phenol molecules
Cardiovascular

• Ethanol enters cardiac cells
• Dilated Cardiomyopathy
• Systolic pump failure
• Hypertension
• Can be more or less reversible if stop drinking
• Moderate amounts can be beneficial
Liver

- Alcoholic fatty liver
- Alcoholic hepatitis
- Alcoholic cirrhosis
- Alcoholic ketoacidosis
- Alcoholic hypoglycemia
Alcoholic fatty liver

- Lipid metabolism all messed up
- Accumulate LDL in blood and liver
- Liver gets large, full of fat
- Totally reversible when stop drinking
Alcoholic Hepatitis

• Next phase of liver damage
• Anorexia, nausea, vomiting
• Jaundice
• Fever, malaise
• Start getting portal hypertension
  – Esophageal varices
  – Ascites
• Slow recovery when stop drinking
Alcoholic cirrhosis

- Takes years and years to develop
- Only 10 – 15% of alcoholics get it
- Liver doesn’t function well
- Can’t metabolize well
- Can’t synthesize proteins correctly
- Stop making several clotting factors
- can
Alcoholic Ketoacidosis

- When chronic alcoholic stops eating or drinking
- With or without vomiting
- Low or zero blood alcohol
- Large serum ketones
- Large anion gap
- Frequently hypokalemic
- Normal or high serum glucose
Alcoholic Ketoacidosis

• Treatment
  – Lots of D5LR or D5NS
  – Potassium if hypokalemic
  – Magnesium for good luck
Alcoholic Hypoglycemia

- Gluconeogenesis in liver is impaired
- Every alcoholic should be hypoglycemic, but few of them are
- Hypoglycemia common in pediatric ethanol ingestions
Immunity

• Cellular immunity
• Humoral immunity
• Cancer
Cellular immunity

- Don’t kick out white blood cells as well in response to invasion
- Can’t fight infection as well
- Small wounds become large, weeping sores
- Catch every respiratory infection that comes along
Humoral Immunity

- Do not form antibodies as well to tetanus toxoid and hepatitis B vaccines
- Probably don’t form other antibodies as well, either
Cancer

• Cancer rate is 10 times that of general population
• Common sites
  – Head
  – Neck
  – Esophagus
  – Stomach
  – Liver
  – Pancreas
Pancreas

- Unknown why heavy drinking causes pancreatitis
- Possibly autodigestion
- Chronic pancreatitis can’t absorb Vitamin B12
- Get impaired glucose tolerance
- Jaundice from head of pancreas obstructing hepatic ducts
Sex

- Men
  - Concentrations of <.1% can increase sexual drive in men
  - > .1% causes impotence
  - Occasional testicular atrophy

- Women
  - Amenorrhea
  - Smaller ovaries
  - Infertility
  - Spontaneous abortion
Recognition and Treatment

- Most E.D.s do no routine screening
- It has been shown that just bringing up the subject and offering help does have an effect
- More patients will access resources if the problem is discussed