Alcohol

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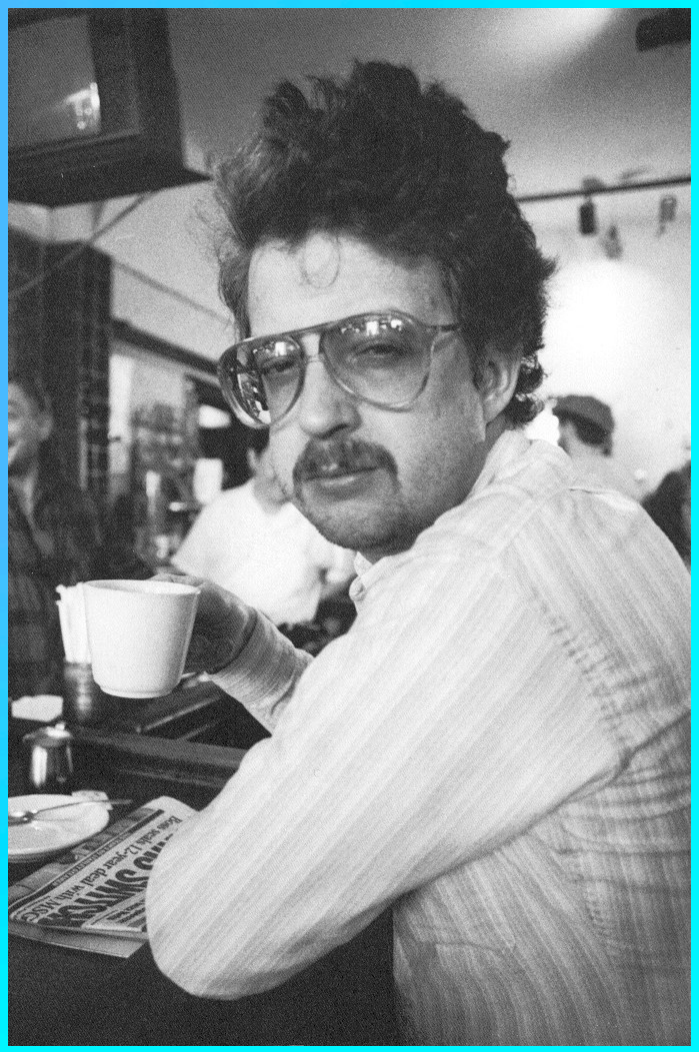
The Drug That Keeps Us Employed

- 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- First ban on drinking was on Egyptian soldiers – quickly repealed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

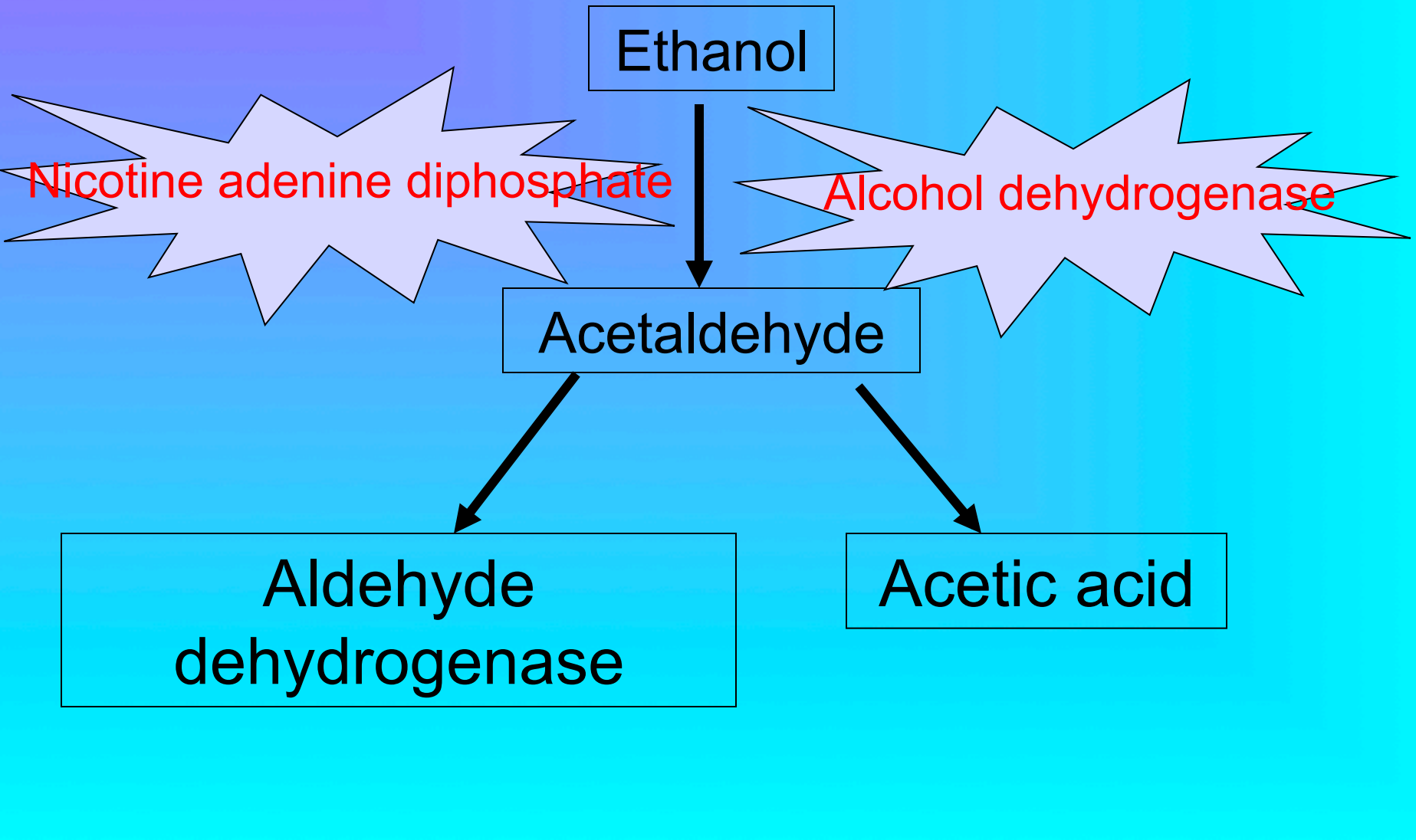
Areas of Brain Affected

- 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



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

Alcohol dehydrogenase

Acetone

Carbon Dioxide

Water

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 0ptic 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

↓

Clycolic acid

↓

Glyoylic 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

- Diazepam (Valium)
- Lorazepam (Ativan)
- Chlordiazpoxide (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 cannibanoids 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