Alcohol and other drug dependencies are the major health problem among young adults and adolescents. The annual per person consumption of alcohol for Americans above the age of 15 is 2.7 gallons. This figure represents 100% pure alcohol and is equal to about 707 twelve ounce cans of beer per year. This is less than the French who consume about 6.5 gallons of alcohol a year and more than the Israeli’s at .8 gallons.

Alcohol is regularly involved in accidents, injury, death, and social problems:
- In motor vehicles deaths, 50% of drivers have been drinking
- In motor vehicle accidents in general, 30% of drivers have been drinking
- 50% of all fatal falls involve people who have been drinking
- 68% of drowning victims have been drinking

Alcohol use is involved in:
- 65% of homicides
- 75% of stabbings
- 58% of shooting
- 67% of sexually aggressive acts against children
- 56% of all assaults

BIOPHARMACEUTICS

Absorption- Alcohol is readily and passively absorbed along the entire length of the gastrointestinal system. Usually about 20% of the ingested alcohol is absorbed in the stomach; while the remaining 80% is absorbed in the small intestine. Food in the stomach can slow this absorption. Drinking carbonated drinks can speed the absorption.

Distribution- Alcohol is a very simple molecule (C₃H₇OH), small and easily absorbed (it is both water and fat soluble). Alcohol readily passes through the blood brain barrier since it is fat soluble and very small. As alcohol moves through the body via the bloodstream, it is absorbed into virtually every organ system in the body. Its distribution would be called wide.

Metabolism and Excretion- Most alcohol is metabolized in the liver; only a small amount in the stomach (<20%) and 2-3% is eliminated in breath, urine, sweat, bile or tears.

The breakdown of alcohol in the liver is as follows:

\[
\text{Alcohol} + \text{NAD}^+ \rightarrow \text{Acetaldehyde} + \text{NAD}^+ \rightarrow \text{Acetic Acid} \rightarrow \text{Water} \rightarrow \text{CO}_2
\]
Alcohol is unique in that it requires no digestion and can be absorbed unchanged from the stomach, and even more rapidly from the small intestine.

There are three basic enzyme systems involved in the metabolism of alcohol:

a) Alcohol dehydrogenase (because this enzyme is more active in men than in women, women may be more susceptible to the effects of alcohol)

b) Microsomal ethanol oxidizing system (MEOS)

c) Catalase system

The enzymatic breakdown of alcohol to water and carbon dioxide takes a lot of energy \((NAD^+)\) from the liver cells. Since the NAD energy molecules are also involved in many other of the body’s metabolic workings, the decrease of NAD robs the liver of energy it needs to do other metabolic work.

One of the more important features of alcohol metabolism in the liver is the phenomenon of \textit{enzyme induction}—the increase in numbers of enzymes (increased replication due to stimulation) in the liver result in a shorter duration of action of the alcohol, development of tolerance and reduction of action of other products that metabolize in the liver.

With most drugs a constant proportion of the drug is removed in a given amount of time, so that with a high blood level the amount metabolized is high. With alcohol though, the amount that can be metabolized is fairly constant at about .25 to .3 ounces per hour, regardless of the BAL. The major factor determining the rate of alcohol metabolism is the activity of the liver enzymes.

\textbf{PHARMACOLOGY} - Ethanol is a small molecule without protein or other components that would enable it to attach to specific receptors or membranes. In fact, there is little evidence that ethanol exerts its effects through any receptor system at all. Rather, ethanol and other primary alcohols seem to dissolve in membranes to exert their effects. Because this is such a generalized, nonspecific biophysical effect, it has a wide range of consequences within the neuron. This process of dissolving in the cell membrane and “disordering” it is called \textit{fluidization}. When the cell membrane is exposed to ethanol on a frequent basis, the lipid composition of the membrane changes creating neuroadaptations such as changes in ion channel functioning (changing the ionic balance of sodium, potassium, and calcium)–a physical basis for tolerance and dependence.

Ethanol’s effect on neurotransmitters is widespread and sometimes contradictory. Chronic ethanol consumption affects norepinephrine (small doses raise it; large doses lower it); dopamine (increasing reward center release); serotonin (mixed results in studies); acetylcholine (depressing its release); and GABA. It is important to note that little of the research in neurotransmitter metabolism shows a relationship with addictive behavior.
Alcohol has been shown to interact with several important neurohormones and receptors:

**NMDA**- Alcohol inhibits this specific form of receptor to glutamate, which is the chief excitatory neurotransmitter. By doing so, alcohol may block glutamate’s order for the cells to fire more rapidly. This may explain some of the sedative and anesthetic action on the central nervous system. The NMDA receptor is also thought to be involved in some forms of learning and memory, as well as motor control—all certainly affected by alcohol.

**GABA**- Studies show that alcohol intensifies the effects of GABA, the brain’s major inhibitory neurotransmitter, by acting on one type of GABA receptor. Interestingly, popular sedatives like Valium also work on these receptors.

**Serotonin**- Perhaps the best know of the neurotransmitters, serotonin is thought to be involved with many mental states, including calmness. Studies have shown that a lack of serotonin may contribute to anxiety and depression. Also it is thought that alcohol may intensify one of these receptors, increasing the ‘reward’ response that reinforces the tendency to drink.

<table>
<thead>
<tr>
<th>Blood Alcohol Level* and Behavior</th>
</tr>
</thead>
<tbody>
<tr>
<td>.05 Lowered alertness, usually good feeling, release of inhibitions, impaired judgment</td>
</tr>
<tr>
<td>.10 Slowed reaction times and impaired motor function (fine to gross), less cautious</td>
</tr>
<tr>
<td>.15 Large and consistent increases in reaction time</td>
</tr>
<tr>
<td>.20 Marked depression in sensory and motor capability, decidedly intoxicated</td>
</tr>
<tr>
<td>.25 Severe motor disturbance, staggering, sensory perceptions greatly impaired</td>
</tr>
<tr>
<td>.30 Stuporous but conscious—little or diminished comprehension of what is going on</td>
</tr>
<tr>
<td>.35 Surgical anesthesia; about LD 1, the minimal level causing death</td>
</tr>
<tr>
<td>.40 About LD 50</td>
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</tbody>
</table>

*Blood Alcohol Levels are reported as the number of grams of alcohol in each 100 ml of blood (100 mg of alcohol in 100 ml of blood would be .10%)

**Why is "BAC" important?** For one thing, BAC levels are important because they are what law enforcement officials use to determine (based on a test or tests) whether or not you are "DUI" (driving under the influence), i.e., a "drunk" driver. For another, testing for BAC levels is done today by many employers to determine if you should be relieved from the job for a day (e.g., to sleep it off) or be immediately fired for being impaired while performing your job. Usually, the BAC levels an employer uses for those determinations are 0.020% to 0.029% (you're relieved from duty for 24 hours) and at 0.040 or higher you will be fired.
An individual's BAC level at a given moment can be determined by analyzing a sample of their blood or a sample of their breath from that moment. If you are given a "breath alcohol" test (often called a "breathalyzer" test), it is actually your blood that is being tested for its BAC level. Yes, that's correct: Even though it's a "breath" test, the Breath Alcohol Concentration (called "BrAC") reading that results from your test will scientifically relate directly to the concentration of alcohol in your blood at the time that your breath is tested. So, if you are tested and found to have a BrAC (Breath Alcohol Concentration) of 0.020% and they were to draw a sample of your blood at the very same time of your breath-test and analyze it, your BAC (Blood Alcohol Concentration) would also be at a level of 0.02%.

The chart below is only intended only as a general guide. Actual "Blood Alcohol Concentration" (BAC) values will vary by body build, sex, and current health status. Also, fatigue and other "stress factors" can temporarily lower a person's tolerance level to alcohol.

### EXPECTED BLOOD ALCOHOL CONCENTRATION ("BAC")
**BASED ON THE NUMBER OF DRINKS YOU'VE CONSUMED IN A ONE-HOUR PERIOD**

<table>
<thead>
<tr>
<th>BODY WEIGHT IN POUNDS</th>
<th>1 drink</th>
<th>2 drinks</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
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<th>8</th>
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<td>90 - 109</td>
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<td>150 - 169</td>
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<td>170 - 189</td>
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<td>190 - 209</td>
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<td>230 &amp; UP</td>
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For the purposes of this chart, “One Drink” =12 oz. Beer or 4 oz. Wine or 1 1/4 oz. 80-Proof Liquor. If you prefer 18 oz. cans of beer or 90-Proof Liquor, you need a different chart!

<table>
<thead>
<tr>
<th>BAC of .01% to .05%</th>
<th>NOTE THAT FOR MANY PEOPLE, ONLY “ONE” DRINK WILL TAKE THEM TO THIS LEVEL OF DECREASED COORDINATION.</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAC of .05% to .08%</td>
<td>NOTE THAT EVERYONE HAS REACHED THIS POINT AFTER JUST THEIR 1\textsuperscript{ST} OR 2\textsuperscript{ND} DRINK!</td>
</tr>
<tr>
<td>BAC of .08% and over</td>
<td>NOTE THAT SOME PEOPLE REACH THIS POINT BY THEIR 2\textsuperscript{ND} DRINK AND ALL HAVE BY THEIR 3\textsuperscript{RD} OR 4\textsuperscript{TH}.</td>
</tr>
</tbody>
</table>

**Some-to-great loss of judgment and coordination, thinking dulled, changes in mood and behavior.** A BAC of 0.02% at many U.S. companies will require that an employee be relieved of duty for 24 hours and at 0.04 they will be fired. In an organization with a "zero-tolerance" policy as regards alcohol use, you will be fired if you test at 0.01% (which is less than 0.010%)

**Functioning ability definitely impaired.** Walking, speech, and hand movements clumsy. Blurred, split, or tunnel vision may occur. Judgment and equipment operating ability impaired. Chance of accident is greatly increased by up to 300% or more.

**Functioning and judgment very seriously affected.** Responses greatly slowed. Behavior greatly affected. Very high risk of accident. In most U.S. States, with a BAC of .08% or higher, you will be arrested if driving a car.
Brain- Owing to its high solubility, ethanol distributes quickly into the Central Nervous System. While the effects are modulated by the rate of increase in the blood alcohol level, hereditary predisposition and tolerance of the individual, and the “mind set” or environment of the individual, the effects are most noticed with rising blood levels.

One of the first parts of the brain that alcohol affects is the reticular activating system (RAS) and cerebellum near the brain stem. The RAS is a portion of the brain stem which takes incoming peripheral nervous messages and sorts them for passage to other parts of the brain. The RAS can be divided into two parts—the stimulating part and the depressant part. Then the stimulating part is dominant the message flow is good and the person is alert. If the depressive side is dominant, the message flow is poor and the person may fall asleep. The body has five basic chemicals (NEUROTRANSMITTERS) for controlling this (they control other functions too!!!): dopamine, acetylcholine, serotonin, glutamate, and GABA.

Alcohol causes the depressant part of the RAS to dominate by:
   a) inhibiting the glutamate receptors (depressing their response)
   b) glutamate receptors up-regulate in response to chronic inhibition from alcohol
   c) activating the GABA-mediated increase in chloride ion flows (helping GABA to be more effective as a neuron action inhibitor. It acts as a GABA agonist!
   d) By altering neuronal cell wall permeability, alcohol interferes with transport and conduction systems, increasing their fluidity, and changing ionic balances of sodium, potassium and calcium.

In the CNS, alcohol stimulates the release of dopamine and acetylcholine resulting in CNS depression. (THERE IS AN INTERESTING THEORY ABOUT HOW THESE BRAIN AMINES WORK WITH ACETALDEHYDE TO PRODUCE AN OPIATE LIKE SUBSTANCE IN THE BRAIN). There is also the fact that the stimulation of dopamine release in the nucleus accumbens and other limbic system areas (VTA) is very rewarding.

Alcohol also seems to increase the presynaptic action of serotonin transporters and disrupts the effectiveness of serotonin in the brain system.

Acute ethanol intoxication manifests with:
   • General disinhibition with increased confidence, impaired judgment and insight, slurred and generous speech, decreased concentration, altered motor skills and memory, poor sensory perception, and mood swings.
   • Facial flushing
   • Mydriatic pupils
   • Nystagmus
   • Increased heart and respiration
   • Progression to a stupor can occur followed by coma and death
Nervous system diseases in chronic alcoholics are varied. The most common are related to compromised protein synthesis and malnutrition. Wernicke-Korsakoff syndrome is caused by an alcohol induced deficiency of thamine (B1).

**Gastrointestinal Effects**- Alcohol is frequently substituted for food by many alcoholics. Ethanol exerts its effects on nutritional status both directly and indirectly. By interfering with gastrointestinal (GI) functioning, alcohol causes direct injury to tissue and promotes malabsorption. Inhibition of esophageal peristalsis contributes to an increased incidence of reflux and possibly cancer.

Concentrations of ethanol greater than 10% in the stomach increases gastric secretions with greater hydrochloric acid and lowered pepsin content. Greater than 20% concentrations of ethanol further induces pyloric spasm with delay in emptying contents of stomach. Still higher concentrations (greater than 40%) damage mucosal surfaces. Alcoholics are prone to gastritis, gastrointestinal bleeding, and tears in the gastroesophageal junction. Impaired absorption occurs in the small intestine.

Nutritional disturbances are a result of poor absorption, metabolism, and the basic fact that alcoholics may substitute up to 50% of their caloric intake with alcohol. Deficiencies worth noting include:

**Thiamine**- Also know as vitamin B1, thiamine deficiencies contribute to central nervous system problems such as Wernicke-Korsakoff syndrome (marked by confusion, stupor, memory impairment, and poor balance and gait) and thiamine-responsive cardiomyopathy.

**Niacin**- Lack of niacin contributes to the development of a disease called pellagra. It is marked by the 4D’s—dermatitis, diarrhea, dementia, with progression to death.

**Folate**- A persistent folate deficiency is associated with peripheral neuropathy, poor absorption of vital nutrients in the organ systems, anemia, and a painful inflammation of the tongue (loss of vitamin B6, Pyridoxine Hydrochloride, also contributes to anemia and neuropathy in alcoholics).

**Zinc and Magnesium**- Zinc and magnesium are the most frequently seen mineral deficiencies in alcoholics. These minerals are vital for many cellular functions and their decrease contributes to CNS and muscular irritability and possibly seizures.

**Vitamins A, D, and K**- Inadequate amounts of fat-soluble vitamins A, D, and K accompany poor diet, malabsorption, and alcohol induced organ damage. Aggressive therapy must be cautious because an overdose of vitamins can be toxic to an already compromised liver.
**Hepatic Effects**- Ethanol oxidation in the liver generates an increase in acetaldehyde, hydrogen ions, and an increase in energy shift (NADH/NAD ratio). This disrupts the normal functioning of the liver and leads to a fatty infiltration of the liver. Over time organ damage including fatty liver, hepatitis, and cirrhosis occur. Laboratory evaluations reveal elevated SGOT, SGPT, LDH, and prothrombin time. Cirrhosis occurs in 5-10% of alcoholics with, at first, enlargement of the liver then a shrinking as the liver becomes scarred and hardened. Patients may present with anorexia, weight loss and fatigability.

**Pancreatic Effects**- Problems with the pancreas follow a stimulation to release enzymes and “autodigestion” results. With nutritional abnormalities, fat accumulation, loss of vitamins, iron and calcium accumulation, there is an overall state of inflammation. Alcoholics are at risk for acute pancreatitis (most frequent in males 30-40 years of age) and pancreatic cancer.

**Cardiovascular**- Initial physiological effects of alcohol on the cardiovascular system are an elevation in blood pressure and heart rate. These effects are evident in the acute intoxication state, can persist with chronic drinking, and are evident during withdrawal. Peripheral blood flow is increased in low doses and yields some benefit from drinking. Blood flow in the brain increases with severe intoxication in response to oxygen depletion. Lethal doses of alcohol depress respiration and cause cardiovascular collapse.

Alcohol can have multiple consequences on the heart—disturbances in rhythm and cardiomyopathy (Cardiomyopathy is a type of heart disease in which the heart becomes abnormally enlarged, thickened and/or stiffened. As a result, the heart muscle’s ability to pump and/or receive blood is usually weakened. This condition is generally progressive and may lead to heart failure).

**Endocrine or Hormone Effects**- Multiple hormone systems are affected by alcohol, most notably those in the hypothalamic-pituitary-adrenal axis producing high amounts of stress hormone (hyperaroused state) and disruption in the production of sex hormones. Also, alcohol can affect insulin levels and stimulate hyperglycemia (high blood sugar levels resulting from the defective secretion or action of the hormone insulin) followed by states of hypoglycemia. Alcohol also decreases the output of antidiuretic hormone responsible for retaining fluid in the body—this increases urine flow and adds to dehydration.

**Musculoskeletal**- As with other organ systems, there exists a spectrum of muscular and skeletal effects due to alcohol—decreased contractility, inflammation, necrosis (death) of tissue, electromyographic changes, and nerve damage.

**Hematic or Blood System**- Alcohol interferes with pathways for Iron metabolism and blood synthesis. Anemia results as do problems for patients with sickle cell trait or disease.
**Alcohol Withdrawal** - The abstinence syndrome that develops with alcohol and other depressant category drug withdrawal is medically more severe and more likely to cause death than withdrawal from any other drug. For that reason, it is highly recommended that a medical review or clearance be obtained prior to initiating the detoxification process. Stages of withdrawal are generally:

Stage 1- Tremors, excessively rapid heart rate, hypertension, heavy sweating, loss of appetite and insomnia

Stage 2- Hallucinations (auditory, visual, and/or tactile)

Stage 3- Delusions, disorientation, delirium, sometimes intermittent in nature and usually followed by amnesia

Stage 4- Seizure activity

These symptoms usually begin somewhere between 3 and 10 hours after the last drink and usually resolve in 2 to 5 days. In a chronic drinker with high alcohol intake or one who is in poor physical condition, the minor symptoms may progress to and overlap with the major symptoms. Major withdrawal symptoms usually will resolve within 3 to 6 days.