

## WEEK #1 Appendix – “THE DOCTOR’S OPINION”

**[Optional Reading: Additional Information from “Wikipedia” and the “National Institute on Alcohol Abuse and Alcoholism”]**

Metabolism is the body's process of converting ingested substances to other compounds. Metabolism results in some substances becoming more, and some less, toxic than those originally ingested. Metabolism involves a number of processes, one of which is referred to as oxidation.

Through oxidation, alcohol is detoxified and removed from the blood, preventing the alcohol from accumulating and destroying cells and organs. A tiny amount of alcohol escapes metabolism and is excreted unchanged in the breath and in urine. Until all the alcohol consumed has been metabolized, it is distributed throughout the body, affecting the brain and other tissues.

When alcohol is consumed, it passes from the stomach and intestines into the blood, a process referred to as absorption. Alcohol is then metabolized by enzymes, which are body chemicals that break down other chemicals. In the liver, an enzyme called alcohol dehydrogenase (ADH) controls the conversion of alcohol to acetaldehyde. Acetaldehyde is rapidly converted to acetate by other enzymes and is eventually metabolized to carbon dioxide and water.

Alcohol also is metabolized in the liver by the enzyme cytochrome P450IIE1 (CYP2E1), which may be increased after chronic drinking. Most of the alcohol consumed is metabolized in the liver, but the small quantity that remains un-metabolized permits alcohol concentration to be measured in breath and urine. The liver can metabolize only a certain amount of alcohol per hour, regardless of the amount that has been consumed. The rate of alcohol metabolism depends, in part, on the amount of metabolizing enzymes in the liver, which varies among individuals, especially in heavy drinkers and alcoholics.

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### The Chemical Breakdown of Alcohol

$$\text{CH}_3\text{CH}_2\text{OH} \xrightarrow{\text{ADH}} \underset{\text{Acetaldehyde}}{\text{CH}_3\text{CHO}} \xrightarrow{\text{ALDH}} \underset{\text{Acetate}}{\text{CH}_3\text{COO}^-}$$

The chemical name for alcohol is ethanol ( $\text{CH}_3\text{CH}_2\text{OH}$ ). The body processes and eliminates ethanol in separate steps. Chemicals called enzymes help to break apart the ethanol molecule into other compounds (or metabolites), which can be processed more easily by the body. Some of these intermediate metabolites can have harmful effects on the body.

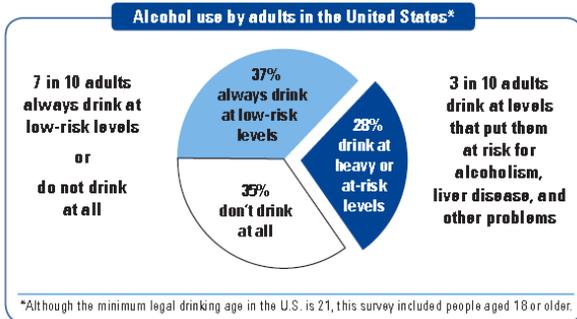
Most of the ethanol in the body is broken down in the liver by an enzyme called alcohol dehydrogenase (ADH), which transforms ethanol into a toxic compound called acetaldehyde ( $\text{CH}_3\text{CHO}$ ), a known carcinogen. However, acetaldehyde is generally short-lived; it is quickly broken down to a less toxic compound called acetate ( $\text{CH}_3\text{COO}^-$ ) by another enzyme called aldehyde dehydrogenase (ALDH). Acetate then is broken down to carbon dioxide and water, mainly in tissues other than the liver.

Reference: <http://pubs.niaaa.nih.gov/publications/AA72/AA72.htm>

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Drinking heavily puts people at risk for many adverse health consequences, including alcoholism, liver damage, and various cancers. But some people appear to be at greater risk than others for developing these problems. Why do some people drink more than others? And why do some people who drink develop problems, whereas others do not?

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Research shows that alcohol use and alcohol-related problems are influenced by individual variations in alcohol metabolism, or the way in which alcohol is broken down and eliminated by the body. Alcohol metabolism is controlled by genetic factors, such as variations in the enzymes that break down alcohol; environmental factors, such as the amount of alcohol an individual consumes and his or her overall nutrition; a person's age; and for alcoholics how long their disease has progressed.

Differences in alcohol metabolism may put some people (especially alcoholics) at greater risk for alcohol problems, whereas others ("normies") may be at least somewhat protected from alcohol's harmful effects.

**The Chemical Breakdown of Alcohol:** Alcohol is metabolized by several processes or pathways. The most common of these pathways involves two enzymes—alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH). These enzymes help break apart the alcohol molecule, making it possible to eliminate it from the body. First, ADH metabolizes alcohol to acetaldehyde, a highly toxic substance and known carcinogen (causes cancer). Then, in a second step, acetaldehyde is further metabolized down to another, less active byproduct called acetate (acetone), which then is broken down into water and carbon dioxide for easy elimination from the body.

**Other enzymes:** The enzymes cytochrome P450 2E1 (CYP2E1) and catalase also break down alcohol to acetaldehyde. However, CYP2E1 only is active after a person has consumed large amounts of alcohol, and catalase metabolizes only a small fraction of alcohol in the body [1] Small amounts of alcohol also are removed by interacting with fatty acids to form compounds called fatty acid ethyl esters (FAEEs). These compounds have been shown to contribute to damage to the liver and pancreas.

**Acetaldehyde:** a toxic byproduct — Although acetaldehyde is short lived, usually existing in the body only for a brief time before it is further broken down into acetate, it has the potential to cause significant damage. This is particularly evident in the liver, where the bulk of alcohol metabolism takes place. Some alcohol metabolism also occurs in other tissues, including the pancreas and the brain, causing damage to cells and tissues. Additionally, small amounts of alcohol are metabolized to acetaldehyde in the stomach and intestines, exposing these tissues to acetaldehyde causes damaging effects.

In addition, **alcohol directly contributes to malnutrition** since a pint of 86-proof alcohol (not an unusual daily intake for an alcoholic) represents about half of the daily energy requirement. However, ethanol does not have any minerals, vitamins, carbohydrates, fats or protein associated with it. Alcohol causes inflammation of the stomach, pancreas, and intestines which impairs the digestion of food and absorption into blood. Moreover, the acetaldehyde (the oxidation product) can interfere with the activation of vitamins.