



Drinking heavily puts people at risk for many adverse health consequences, including alcohol use disorder, 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?

Research shows that alcohol misuse 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, and environmental factors, such as the amount of alcohol an individual consumes and his or her overall nutrition. Differences in alcohol metabolism may put some people at greater risk for alcohol problems, whereas others 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.¹ Then, acetaldehyde is further metabolized down to another, less active byproduct called acetate,¹ which then is broken down into water and carbon dioxide for easy elimination.²

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.³

The Chemical Breakdown of Alcohol



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 (CH_3CHO), a known carcinogen. However, acetaldehyde is generally short-lived; it is quickly broken down to a less toxic compound called acetate (CH_3COO^-) by another enzyme called aldehyde dehydrogenase (ALDH). Acetate then is broken down to carbon dioxide and water, mainly in tissues other than the liver.

Acetaldehyde: A toxic byproduct

Much of the research on alcohol metabolism has focused on an intermediate byproduct that occurs early in the breakdown process—acetaldehyde. 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.⁴ Some alcohol metabolism also occurs in other tissues, including the pancreas³ and the brain, causing damage to cells and tissues.¹ Additionally, small amounts of alcohol are metabolized to acetaldehyde in the gastrointestinal tract, exposing these tissues to acetaldehyde's damaging effects.⁵

In addition to acetaldehyde's toxic effects, some researchers believe that it may be responsible for some of the behavioral and physiological effects previously attributed to alcohol.⁶ For example, when acetaldehyde is administered to lab animals, it leads to incoordination, memory impairment, and sleepiness, effects often associated with alcohol.⁷

On the other hand, other researchers report that acetaldehyde concentrations in the brain are not high enough to produce these effects.⁷ This is because the brain has a unique barrier of cells (the blood–brain barrier) that help to protect it from toxic products circulating in the bloodstream. It is possible, however, that acetaldehyde may be produced in the brain itself when alcohol is metabolized by the enzymes catalase^{8,9} and CYP2E1.¹⁰

For more information, please visit: <https://www.niaaa.gov>

¹ Edenberg, H.J. The genetics of alcohol metabolism: Role of alcohol dehydrogenase and aldehyde dehydrogenase variants. *Alcohol Research & Health* 30(1):5–13, 2007. PMID: 17718394

² National Institute on Alcohol Abuse and Alcoholism. *Alcohol Alert: Alcohol Metabolism*. No. 35, PH 371. Bethesda, MD: The Institute, 1997.

³ Vonlaufen, A.; Wilson, J.S.; Pirola, R.C.; and Apte, M.V. Role of alcohol metabolism in chronic pancreatitis. *Alcohol Research & Health* 30(1):48–54, 2007. PMID: 17718401

⁴ Zakhari, S. Overview: How is alcohol metabolized by the body? *Alcohol Research & Health* 29(4):245–254, 2006. PMID: 17718403

⁵ Seitz, H.K.; and Becker, P. Alcohol metabolism and cancer risk. *Alcohol Research & Health* 30(1):38–47, 2007. PMID: 17718399

⁶ Deitrich, R.; Zimatkin, S.; and Pronko S. Oxidation of ethanol in the brain and its consequences. *Alcohol Research & Health* 29(4):266–273, 2006. PMID: 17718405

⁷ Quertemont, E.; and Didone, V. Role of acetaldehyde in mediating the pharmacological and behavioral effects of alcohol. *Alcohol Research & Health* 29(4):258–265, 2006. PMID: 17718404

⁸ Aragon, C.M.; Rogan, F.; and Amit, Z. Ethanol metabolism in rat brain homogenates by a catalase–H₂O₂ system. *Biochemical Pharmacology* 44:93–98, 1992. PMID: 1632841

⁹ Gill, K.; Menez, J.F.; Lucas, D.; and Deitrich, R.A. Enzymatic production of acetaldehyde from ethanol in rat brain tissue. *Alcoholism: Clinical and Experimental Research* 16:910–915, 1992. PMID: 1443429

¹⁰ Warner, M.; and Gustafsson, J.A. Effect of ethanol on cytochrome P450 in the rat brain. *Proceedings of the National Academy of Sciences of the United States of America* 91:1019–1023, 1994. PMID: 8302826



NIH . . . Turning Discovery Into Health®

National Institute on Alcohol Abuse and Alcoholism

<https://www.niaaa.nih.gov> • 301-443-3860

November 2021