After swallowing wine, approximately 20% is absorbed in the stomach and 80% is absorbed into the duodenum (first part of the small intestine) and the small intestine wall. Things that affect the rate of absorption include time of day, activity level, type of alcohol consumed, i.e. concentration, bubbles, speed of consumption, fasting or non-fasting state, and whether or not one is consuming alcohol with food.

After oral absorption of a moderate amount of alcohol, the gut and to a larger part, liver remove 95-98% of ethanol through metabolism before it reaches other organs systemically. This is known as “first pass metabolism” and represents the difference between the amount of drug consumed and the amount that reaches the systemic circulation.

The rest of the ethanol is eliminated through breathing, sweating, and urinating.
Rates of ethanol elimination vary by ethnicity with the highest rates exhibited by Native Americans > Caucasians > African Americans. Differences in liver mass incompletely explain variance in gender and ethnic differences in ethanol clearance. Metabolic interindividual variability may explain the rest.

A simple pathway of ethanol metabolism is the following:

\[
\text{CH}_2\text{CO}_2\text{H (ethanol)} \rightarrow \text{CH}_3\text{COH (acetaldehyde)} \rightarrow \text{CH}_3\text{COO}^- \text{(Acetate)}
\]

The enzymes that catalyze this reaction are polymorphic and mutations for some of the genes that encode for these enzymes have been identified.

Alcohol dehydrogenase (ADH) metabolizes ethanol to acetaldehyde. There are many subtypes of ADH. ADH-7 is mainly found in the stomach lining and there, is the subtype responsible for metabolizing ethanol to acetaldehyde. However, it is absent in Asians and found at low levels in Caucasian women. Studies on relatively small numbers of patients undergoing obesity surgery show that ethanol metabolism is slowed and the maximum blood alcohol content is higher and the time to clear ethanol from the bloodstream longer compared to obese controls. One mechanism of action may be shrinking of the surface area of the stomach lining and decreasing ADH-7 stores.

Acetaldehyde is a toxic metabolite. Aldehyde dehydrogenase (ALDH), the enzyme that catalyzes the breakdown of acetaldehyde to acetate, comes in multiple molecular forms. Specific enzymes that are encoded by ALDH1 and ALDH2 genes are thought to be involved in acetaldehyde oxidation. The ALDH2 gene and its mutated enzymes are the most important genetic factors associated with reduced ethanol consumption and alcoholism incidence. Forty percent of East Asians, i.e., 1 billion people of the world’s population either lack or have
an inactive form of ALDH2. A modest amount of ethanol consumption in these individuals causes intense facial flushing due to accumulation of acetaldehyde. This leads to an aversion to drinking (thought to be more biochemical than culturally influenced) thus protection against alcoholism. ALDH2 deficiency is also associated with alcohol-induced asthma, increased risk of esophageal and oropharyngeal cancers, increased cardiac damage due to heart attack or certain surgical procedures, reduction in effectiveness of nitroglycerin in treating angina or chest pain, increased risk of Alzheimer’s and other neurodegenerative diseases.

Dr. Thomas Hurley and his group from the University of Indiana recently identified a molecule, Alda-1, that activates wild-type ALDH2 and restores near-wild-type activity to ALDH2*2. Translating this basic science discovery into clinical practice may lead to possible treatments of the above diseases. Parenthetically, as emphasized in the Wine Spectator’s report of this finding, a drug facilitating metabolism of acetaldehyde and avoiding the “flushing syndrome” would lead to more alcohol consumption in this population which spells profit for the beer, wine, and spirits industry but also will contribute to the risk of alcoholism.

What about “le nez rouge”, the red nose and its association with alcohol consumption? The medical term is, “rhinophyma” and the cause is unknown. It is mistakenly associated with excess ethanol consumption. Rhinophyma is an irregular and progressive nasal hypertrophy, due to hyperplasia and fibrosis of the sebaceous glands and surrounding soft tissues.

Samantha Perez-Miller, Hina Younus, Ram Vanam, Che-Hong Chen, Daria Mochly-Rosen & Thomas D Hurley.


Chen CH, Budas GR, Churchill EN, Disatnik MH, Hurley TD, Mochly-Rosen D. Activation of aldehyde dehydrogenase-2 reduces ischemic damage to the heart.
