

Elixir of life: *In vino veritas*

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The wine grape, *Vitis vinifera*, is a member of the Vitaceae, a family of vigorous, climbing, woody plants that live in the Northern Hemisphere. The plants are ill-adapted to tropical climates, and thus never crossed the equator (except those transported by humans, which are cultivated in Argentina, Chile, Australia, South Africa, and other regions in the Southern Hemisphere). The genus *Vitis* consists of some 48 species distributed between 30° and 50° latitude north throughout all continents from Japan to the western United States. Only one species, *V. vinifera*, is native to Europe and the Near East, 12 species are native to Asia, and 35 are native to North America. Two subspecies of *V. vinifera* are *V. vinifera vinifera*, the domestic table and wine grape, and its wild relative, *V. vinifera sylvestris*. Several thousands of cultivars, often known as “varieties,” of *V. v. vinifera* are known. In PNAS, Myles et al. (1) have characterized genome-wide patterns of genetic variation in several hundred cultivars of *V. v. vinifera* and 59 of *V. v. sylvestris*. They show that *V. v. vinifera* was domesticated from *V. v. sylvestris* in the Near East and have identified parent–offspring and sibling connections, most of them first-degree relationships, between some well-known varieties. The relationships are often surprising.

Wild grapes dangle in clusters that are small compared with cultivated grapes but are strikingly beautiful and must have attracted early human gatherers because they are sweeter and juicier than other fruits, and thus desirable as food and drink. Cultivation of grapes likely started in the Paleolithic before human gatherers discovered the food value of grass seeds and started cultivating cereals. A gatherer of grapes would surely preserve the surplus clusters by hanging them or storing them in a nook or vessel, where oozing juice would quickly ferment. Sooner or later, the juice would be tasted and wine discovered. This is more or less how the discovery and use of wine are recorded in early mythologies. The earliest extant work of literature, the Sumerian Epic of Gilgamesh, tells of Gilgamesh’s lover Ish-tar, a wine goddess, and of Siduri, a temple harlot who teaches civilized manners to the wild woodsman Enkidu and introduces him to wine drinking. In Persian mythology, King Jamshid loved grapes and stored them in jars to have a supply available throughout the year. He once found a jar

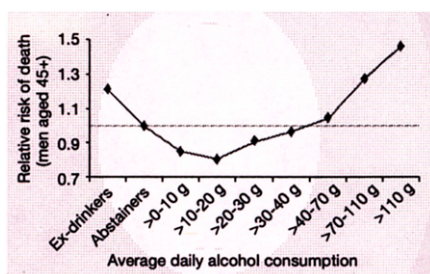


Fig. 1. The J-shaped relationship between wine drinking and risk for death (7).

in which the juice that had oozed from ripened grapes had a sour rather than sweet taste. He put the jar aside, thinking that it might be poisonous. A harem lady discovered otherwise and told her secret to the king. Cultivation of the grape and the making of wine are associated with the Syrian demigod Danel and his daughter Pagat. The snake goddess Renenutet of Egypt presides over the vintage of grapes (2). In the Bible, the earliest experience of wine is attributed to Noah. The ninth chapter of Genesis tells how, after the Flood, Noah “planted a vineyard; and he drank of the wine, and was drunken.”

The earliest archaeological evidence of cultivated grapes comes from grape pips and occasional skin and wood remains found in the southern Caucasus and dating from the Neolithic, about 9,000 y old (3). The oldest evidence of wine is from a jar dated 7,400 to 7,000 y ago, from the foothills of the Zagros Mountains near where present-day Iran meets Turkey and Iraq. The jar, located at the University of Pennsylvania Museum, has residues of tartaric acid and resin from the terebinth tree. Tartaric acid occurs in large amounts only in grapes among natural products, and terebinth resin was a wine preservative used all over the ancient Near East for millennia. Archaeological evidence indicates that wine making extended south and west from the Near East to Lower Mesopotamia and Egypt, where numerous varieties were cultivated as early as 4,500 y ago, and later to Crete, Greece, Rome, and throughout Europe all the way to Spain (3). The wild grapevine *V. v. sylvestris* ranges from Central Asia to Spain and from the Crimea to Northwest Africa. Domestication could have happened anywhere in this enormous area and more than once, but archaeological, viticultural, and genetic evidence strongly suggests that

it occurred only once, in the northern parts of the Near East (1, 3, 4).

Wine and table grape varieties are propagated by cuttings or buds from pre-existing vines. The first vine of a given variety is the only one that grew from a seed, the outcome of a cross between two parents. All vines of a given variety are clones, genetically identical except for occasional somatic mutations that may have occurred since the variety was isolated.

Over the past 200 y, grape breeders have performed cross-pollinations between selected parents to develop different varieties. All classic wine varieties predate deliberate cross-pollination, however, and none originated from a controlled cross.

The charters of the American colonies of Virginia and the Carolinas specify the goal of making wine, taking advantage of the abundance of grapevines. The settlers soon discovered that native grapes gave wines with foxy or other unlikable tastes, however. Plantings of *V. vinifera* as early as 1619 failed because of vine disease. Thomas Jefferson lived in France in 1784–1789 as resident US minister to the French government and became a wine connoisseur, particularly of Bordeaux vintages. As an enthusiastic practitioner of scientific farming, he embarked in 1807 on an ambitious planting program of some 300 vines from 24 European varieties. He anticipated that grapevines, like so many other crops, would flourish in the fertile soil and climate of Virginia. Jefferson’s vineyard experiment failed spectacularly at first. It failed again each of the six times he tried it. He never learned that what killed his vines was black rot and the *Phylloxera* root louse. Junipero Serra and his Franciscan missionaries were somewhat more successful in the drier California climate. *V. vinifera* was planted in 1769 near San Diego and then further north, all the way to Sonoma, where the first vineyard was planted in 1805.

Wine-making in California was revolutionized in the early 1850s by the Hungarian Agoston Haraszthy. Haraszthy had the wisdom or good luck to plant dry slopes, with no possibility of irrigation, on 560 acres that he had acquired in 1857, not far from San Francisco. He wrote a manual on planting and wine making; in 1861,

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the governor of California commissioned him to visit Europe's best wine areas and bring back vines. Six months later, he was back in Sonoma awaiting the arrival of 100,000 vines of 30 different varieties, which arrived in January 1862. In the mid-1860s, vines of superior quality were planted in California in substantial numbers. By 1868, there were 29 substantial grape farmers in Sonoma and Napa. By the 1880s, numerous vineyards had been planted in Napa Valley with many of the best French white and red varieties.

In 1866, the grapevines of a vineyard in the Rhône Valley sickened and soon died of unknown causes. Over the next 2 y, the dying vineyards rapidly spread first in the Rhône Valley, then to other regions of France, and eventually to other countries. The cause was discovered by 1868 to be "a plant louse of yellowish color" (5), which completely destroyed the root system. The infamous *Phylloxera* had destroyed most vineyards throughout the world by 1900, including most in California. Among the cures proposed, one proved to be successful: to use American species as rootstock and graft onto them scions of desirable premium varieties. Initially, *Vitis labrusca* was used as rootstock, including the Concord and Clinton varieties, which are the main sources of grape juice and jelly in the United States. It was soon found that *V. labrusca* provides insufficient resistance. Double (and even triple) hybrids of varieties of *Vitis riparia* and *Vitis rupestris* have proved more effective and are used widely throughout the world.

The top country producers and consumers of wine are Italy, France, and Spain. The United States is fourth in production but largest in total consumption because of its large population. The average consumption per person in the United States, although it is gradually increasing, is about one glass per week compared with nearly one glass per day in the three Mediterranean countries, where it is slowly decreasing. In wine consumption per person, the United States ranks 57th in the world.

Grapes are the most valuable agricultural crop in the United States, which produced 6.88 million tons of grapes in 2009, with California accounting for 89% of the total. California's wine grape production was 3.30 million tons, 54% of total

grape production. The United States exported 15.8% of its wine production and imported 29.2% of its wine consumption. The economic impact of California's wine production was \$30 billion, with wine sales of \$19 billion. The California wine industry provides 145,000 full-time equivalent jobs in the state.

Two events of major consequence for the wine industry are known as "The Judgment of Paris" and "The French Paradox." In 1976, Steven Spurrier, a wine merchant in the heart of Paris, organized a blind wine-tasting event, with leading French sommeliers and other experts, where 10 red and 10 white wines from France and California were evaluated. The French reds were icons, such as Châteauneuf-Haut-Brion and Château Mouton Rothschild; the whites included Bâtard-Montrachet Ramonet-Prudhon and Puligny-Montrachet Les Pucelles Domain Leflaive. The winners in both categories were California wines: Stag's Leap for red and Château Montelena for white. There was shock on both sides of the Atlantic. California wines were not just satisfactory but deserved attention from global wine enthusiasts. An "explanation" advanced by French critics was that California reds are made to be drunk when still young, whereas Bordeaux grand crus are made to last much longer. Spurrier organized two retastings of the same red wines, one in 1986, with only French judges, and one in 2006, on the 30th anniversary of the original event, with a mixture of American, British, and French wine experts. On both occasions the California wines were rated overwhelmingly better than in 1976: in 2006, all the top five reds were from California. Ridge Monte Bello came in first, followed by Stag's Leap, Heitz Martha's, Clos du Val, and Mayacamas.

In 1991, the CBS television program *60 Minutes* aired what became known as the "French Paradox." The French, as well as men in other Mediterranean countries, experience comparatively low mortality from coronary heart disease in spite of high exposure to coronary risk factors, such as smoking, cholesterol, high fat consumption, obesity, and high blood pressure. This was explained as likely attributable to a diet high in wine, particularly red wine. The *60 Minutes* program received much attention. Consumption of

wine in the United States increased by 44% the following year.

In 1819, an Irish physician, Dr. Samuel Black, attributed the much lower prevalence of angina pectoris in France than in Ireland to the "French habits and modes of living" (6). There is now a wealth of evidence that moderate drinking of wine, particularly red, decreases the risk for mortality. A plot of risk for dying against alcohol consumption yields a J-shaped curve, showing that moderate drinkers outlive both teetotalers and heavy drinkers and that teetotalers outlive heavy drinkers (Fig. 1). The beneficial effects of moderate red wine drinking are often attributed to resveratrol and other polyphenols, antioxidants derived from the skins, seeds, and stems of grapes. Beneficial health effects include, first and foremost, lowered risk for cardiovascular disease but also for some forms of cancer, stroke and other cerebrovascular accidents, type 2 diabetes, macular degeneration, Alzheimer's disease, vascular dementia, kidney stones and gallstones, bone density, hip fracture, and other diseases (8).

The origins of cultivated grape varieties, including the best known and premium ones, were shrouded in unreliable narratives until the advent of molecular genetics. Carole Meredith, at the University of California, Davis, pioneered early research showing first that Cabernet Sauvignon is the offspring of Sauvignon Blanc and Cabernet Franc, probably as an accidental cross-pollination several centuries ago (9); that Chardonnay, Gamay Noir, and other varieties of northeastern France are the offspring of Pinot (Pinot Noir in several cases) and Gouais Blanc (10); that California's Zinfandel is the same as southern Italy's Primitivo (11), which, in turn, matches Croatia's Crljenak Kastelanski; and other parental and sibling relationships. Myles et al. (1) have now revealed parent-offspring and sibling relationships for many other varieties. What is surprising is that so many well-known varieties are related by only one step. Less surprising now, because of Meredith's work, is that white grapes often are ancestral to red, or vice versa, such as the mentioned instances of Cabernet Sauvignon and Sauvignon Blanc as well as Chardonnay, Gamay, and Pinot Noir.

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