6

Alcohol

SOURCE OF ALCOHOL

Alcohol is a chemical term that covers a class of substances of which only a few are ever consumed. Some members of this class are *isopropyl alcohol*, used as rubbing alcohol; *methanol* (*methyl alcohol*) or wood alcohol; and *ethanol* (*ethyl alcohol*), the alcohol we drink. The other alcohols can be consumed and have behavioral effects similar to those of ethanol, but they are rather toxic and are normally consumed only by accident. In this book, as in most others, the term *alcohol* will be used to refer to ethanol. Where other alcohols are intended, they will be mentioned by name.

Fermentation

The alcohol we drink is made largely by *fermentation*. When sugar is dissolved in water and left exposed to the air, the mixture is invaded by tiny microorganisms called *yeasts*. Yeasts thrive in this environment; they eat the sugar, and they multiply rapidly. The metabolic processes of the yeasts convert the sugar into ethanol and carbon dioxide (CO_2), which rises to the top in bubbles, and the alcohol remains. More and more yeasts produce more and more alcohol until all the sugar is used up or the yeasts are unable to continue.

The type of beverage you get from fermentation is determined by the source of the sugar. Almost any vegetable material containing sugar may be used, but the most common are grape juice, which is fermented to make wine, and grains, which are fermented to make beer. Modern fermentation is done with special yeasts rather than the wild variety. Yeasts are living organisms; They have been bred and selected over the centuries for particular types of fermentation. Because yeasts can tolerate only low levels of alcohol, fermented beverages do not have alcohol levels much above 10 to 15 percent.

Distillation

There is some debate about the discovery of *distillation*. The Chinese probably were the first to distill alcohol as long ago as 3000 B.C. For a long time the process of distillation, known only to alchemists, was a jealously guarded secret, and little was committed to writing until the Dominican scholar Albertus Magnus described the process in detail in the thirteenth century. The process of distillation is quite simple. It starts with ordinary

fermentation of a sugary substance. When fermentation is completed, the mixture is heated. Because alcohol has a lower boiling point than water, the vapor or steam given off will have a higher content of vaporized alcohol than the original product. When this vapor is condensed by cooling, the resulting fluid will also contain a higher percentage of alcohol. There is no reason why the condensed spirits cannot be redistilled again and again until the resulting fluid has the desired level of alcohol. The traditional method among moonshiners for determining whether they have distilled their product sufficiently is to take a teaspoon of the stuff and set it on fire. When the fire has burned off all the alcohol, the spoon is tipped, and if more than a drop of water remains, the liquid is distilled again.

Brandy is the result of distilling wine, and whiskey is distilled from fermented grains. Brandy and whiskey were the first popular spirits. Today, we have rum, distilled from fermented molasses, and schnapps, which traditionally is distilled from fermented potatoes. Gin and vodka are made from a mixture of water, flavoring, and pure alcohol distilled from any source. Distilled spirits, or hard liquor, usually have an alcoholic content of about 40 to 50 percent by volume. In addition to these hard liquors are the liqueurs, which are sweetened and flavored. Some well-known liqueurs are créme de menthe, which is flavored with mint; Cointreau, which has an added flavor of oranges; and the famous Greek drink ouzo, which has an anise flavor.

Midway between the distilled and fermented beverages are the fortified wines, such as sherry, port, madeira, and muscatel, which were developed during the Middle Ages. These are blends of wine with extra alcohol added to boost the alcohol content to about 20 percent. Vermouth is a flavored fortified wine developed in Turin in the eighteenth century.

MEASUREMENT OF ALCOHOL CONTENT

The description of alcohol content has always been confusing. Percentage figures may be given either by volume, as in the United States, or by weight, as in Britain. Alcohol has a specific gravity of about 0.79 (a quantity of alcohol will weigh 79 percent as much as the same volume of water), and, therefore, a ratio based on volumes will have less alcohol than the same ratio based on weight. In other words, a drink that is 50 percent alcohol by volume will be about 40 percent alcohol by weight. In Britain, alcoholic content has customarily been described in terms of *proof*. The term has its origin in the British navy, which traditionally issued all its sailors a ration of rum every day. The navy had to buy vast quantities of rum, and its purchasers developed a rather ingenious way of testing the alcohol content. They would mix the rum with gunpowder and try to light it. If it burned, this was "proof" that it was at least 50 percent alcohol by weight.

In Britain, the Customs and Excise Act of 1952 declared proof spirits (100 proof) to be those in which the weight of the spirits is 12/13 the weight of an equal volume of distilled water at 51 degrees Fahrenheit. Thus, in Britain, 100 proof spirits are 48.24 percent alcohol by weight, or 57.06 percent by volume. Other spirits are designated over or under proof; the percentage of variance is noted.

In the United States, a proof spirit (100 proof) is one containing 50 percent alcohol by volume. Thus, the U.S. proof number is twice the percentage of alcohol by volume.

All this is very confusing. Fortunately, it is becoming more common to have a beverage's percent alcohol content by volume printed clearly on the labels of bottles in unambiguous terms.

ORIGIN AND HISTORY

Alcohol has probably been a part of the human diet and that of our hominin ancestors for millions of years. Many of these ancestors, human and otherwise, were frugivores, eaters of fruit. Fruit contains a high sugar content and would have been an excellent food, but because of the sugar and the presence of yeasts, all fruit, even ripe fruit, contains a small amount of alcohol, and as it matures, the alcohol content increases. The taste and smell of alcohol then would have been

associated with food and nourishment throughout a significant proportion of our evolutionary history. As we shall see later, this long-term association has probably had a big influence on physiological and behavioral responses to alcohol (Dudley, 2000, 2002).

While people probably have been brewing alcohol since agriculture began about 10,000 years ago, it was probably small domestic brewing, and there is no record of it. The earliest evidence that humans have been fermenting alcohol are large earthenware jugs found in China that date from 9,000 years ago. There is evidence that they once stored a wine made from rice, honey, and fruit (McGovern, Zhang Tang, et al., 2004).

The earliest written set of laws, the Code of Hammurabi, written in 2225 B.C. in Assyria, sets forth some rules for the keeping of beer and wine shops and taverns. The ancient Egyptians were also known for their drinking. The Egyptian Book of the Dead, from about 3000 B.C., mentions the manufacture of a drink called "hek," a form of beer made from grain (Bickerdyke, 1971). Herodotus, the Greek historian, narrated how, at a rich man's feast in ancient Egypt, it was the custom to have a man carry around the image of a corpse in a coffin and show it to all the guests saying, "Drink and make merry, but look on this for such thou shalt be when thou are dead" (McCarthy, 1959, p. 66). The ancient Egyptians, as well as the Assyrians and the Babylonians, drank beer primarily (their climate was more suitable for the growing of grains than grapes), but they also drank a great deal of wine. The Egyptians probably taught the Israelites to make wine and beer before the Exodus to the Promised Land (Firebaugh, 1972).

There is much evidence that the Greeks, who were supposed to be "temperate in all things," may not always have been so temperate where wine was concerned. Plato had much to say about the effects of alcohol. In *The Law*, Plato said,

> When a man drinks wine he begins to be better pleased with himself, and the more he drinks the more he is filled full of brave hopes, and conceit of his powers, and at last the string of his tongue is loosened, and fancying himself wise, he is brimming over with lawlessness and has no more fear or respect and is ready to do or say anything. (Laws I, 649a–b; translation in Jowett, 1931, p. 28)

Although the early Romans had little trouble with wine, there was a great deal of insobriety and debauchery in the declining years of the Roman Empire for which the later Roman emperors, such as Nero, Claudius, and Caligula, became notorious. The fall of the Roman Empire has been blamed on the consumption of wine not so much as a result of the alcohol but because wine at the time was fermented and stored in vessels made of lead, and an additive was put in the wine to enhance the flavor and stop fermentation. This additive had a very high lead content, and it is believed that most of the Roman nobility who drank wine suffered from lead poisoning, of which mental inability is a symptom (Nriagu, 1983).

Before the Romans brought grapes and, subsequently, wine to the British Isles, the main alcoholic beverages were beer made from barley, mead made from fermented wild honey, and cider made from fermented apples. The Romans introduced grapes to Britain, but the vines never thrived in the British climate, and wine, as today, was primarily imported. After the Romans left Britain, so did the grape, but the Saxons carried on the tradition of heavy drinking with mead, ale, and cider. Taverns and alehouses were established in about the eighth century and quickly acquired such a bad reputation that priests were not allowed to enter (French, 1884).

After the Norman Conquest in 1066, drinking became more moderate, and wine was reintroduced, but the English were still heavy drinkers. "You know that the constant habit of drinking has made the English famous among all foreign nations," wrote Peter of Blois (French, 1884, p. 68).

Although distillation had been known for some time, it did not make its presence felt in England until the sixteenth century, when a number of Irish settlers started manufacturing and distributing *usquebaugh*, which became, in English, whiskey. Brandy imported from France was also becoming popular. After the restoration of the monarchy in

1660, distilleries were licensed, and the popularity of gin spread like an epidemic. (Gin is raw alcohol flavored with the juniper berry, which in Dutch is "genever." Through misunderstanding, the drink became known as Geneva dose and later as gin.)

Between 1684 and 1727, the annual consumption of distilled spirits increased from about half a million gallons to over 3.5 million gallons (French, 1884, p. 271). These figures do not include the large quantities of rum and brandy smuggled into the country to avoid paying high duties and tariffs. This epidemic raised such concern that the government passed a desperate series of laws aimed at curtailing the use of liquor, but nothing had much effect. Finally, in 1742, when consumption reached 19 million gallons, Parliament found something that worked: It banned the distillation of grain altogether for a number of years and then closely regulated the manufacture of spirits. By 1782, consumption had dropped to 4 million gallons. But these laws expired, and their enforcement was relaxed over the next 50 years. By the early part of the nineteenth century, things were almost as bad as before.

The English propensity for strong drink was transported across the Atlantic to the colonies. Colonial Americans were hearty drinkers, and alcohol played a large part in their lives.

How highly did the colonies prize booze? Their statutes regulating its sale spoke of it as "one of the good creatures of God, to be received with thanksgiving." Harvard University operated its own brewery, and commencements grew so riotous that rigid rules had to be imposed to reduce "the Excesses, Immoralities and Disorders." Workmen received part of their pay in rum, and employees would set aside certain days of the year for total inebriety (Benjamin Rush, quoted in Kobler, 1973, pp. 25–26).

Before the American Revolution, there had been some success in regulating taverns and drinking, but this control weakened after independence from England was gained.

Americans perceived liberty from the crown as somehow related to the freedom to down a few glasses of rum. Did not both freedoms give a man the right to choose for himself? As a consequence, drinking houses emerged from the war with increased vitality and independence, and the legal regulation of licensed premises waned (Rorabaugh, 1979, p. 35).

Consumption continued to increase to prodigious levels, but a precipitous decline followed between 1830 and 1860. This decline can be attributed to the singular efforts of the temperance movement.

In both England and the United States, there had always been people who openly condemned the use of alcohol, and there were organized movements against drinking and alcohol consumption. In the late 1700s in the United States, the champion of temperance was Dr. Benjamin Rush, a physician who wrote widely about the dangerous physical, social, and moral effects of alcohol. In 1785, Rush published one of the first influential temperance documents, *An Inquiry into the Effects of Ardent Spirits.*

Although Rush's writings were not heeded at the time, they inspired the American temperance movement of the early nineteenth century, which was more successful than any similar movement before or since. The temperance movement was successful because it was philosophically in tune with the moral tenor and ideals of the new republic. Socially, it filled exactly the same function as drinking. "Some men sought camaraderie at the tavern, others in their local temperance organization" (Rorabaugh, 1979, p. 189). In addition, a religious revival was sweeping the United States at the time. Total abstinence provided a symbolic way to express conversion and faith, and booze provided a target for righteous zeal.

The temperance movement was not content to rely on the force of moral persuasion to dry up the country. During this period, the movement attracted enough power to have alcohol prohibition laws enacted in 11 states and two territories. Soon a national Prohibition party was founded, and the temperance reformers set their sights on the federal government. Their vigorous campaign culminated in 1917 with the ratification of the Eighteenth

Amendment to the U.S. Constitution. This was the "noble experiment," Prohibition. It was passed, for the most part, without referendum; most legislatures were paying attention to World War I, and there was little opposition.

Because it did not have widespread public support, the law was virtually unenforceable and provided a vehicle for the rapid development and funding of mobsters and organized crime. Alcohol that was not manufactured in the United States was smuggled in from Canada and elsewhere in vast quantities.

It finally became apparent to both Herbert Hoover and Franklin Roosevelt, the Republican and Democratic candidates, respectively, in the 1932 presidential election, that Prohibition did not have popular support. One month after Roosevelt's victory, a Twenty-First Amendment to the Constitution was drafted that would void the Eighteenth Amendment. Within 2 months, it was passed by both the House and the Senate, and on December 5, 1933, the thirty-sixth state, Utah, ratified it, and it was signed into law. Prohibition had lasted almost 14 years.

After Prohibition ended, alcohol consumption rates increased steadily until they peaked in about 1979. Spurred by movements such as MADD (Mothers Against Drunk Driving), consumption has begun to decline in response to an increasing concern with health and a decreasing public tolerance of drugs in general because of the harm that they do. David Musto, a medical historian at Yale University, is among those who predict that history is likely to repeat itself and that this decline will continue into the early twenty-first century but that it will then be followed by another drinking backlash (Kolata, 1991).

Figure 6-1 shows that American consumption of alcohol appears to go through cycles. Consumption peaks every 60 to 70 years, and these peaks have been followed by declines in use. Historians have pointed out that these periods of decline were accompanied by preoccupation with health and morality and by public concern over the harm that alcohol was doing, but fairly sharp increases in consumption followed. It appears as though the United States has begun a phase of decreasing alcohol use.

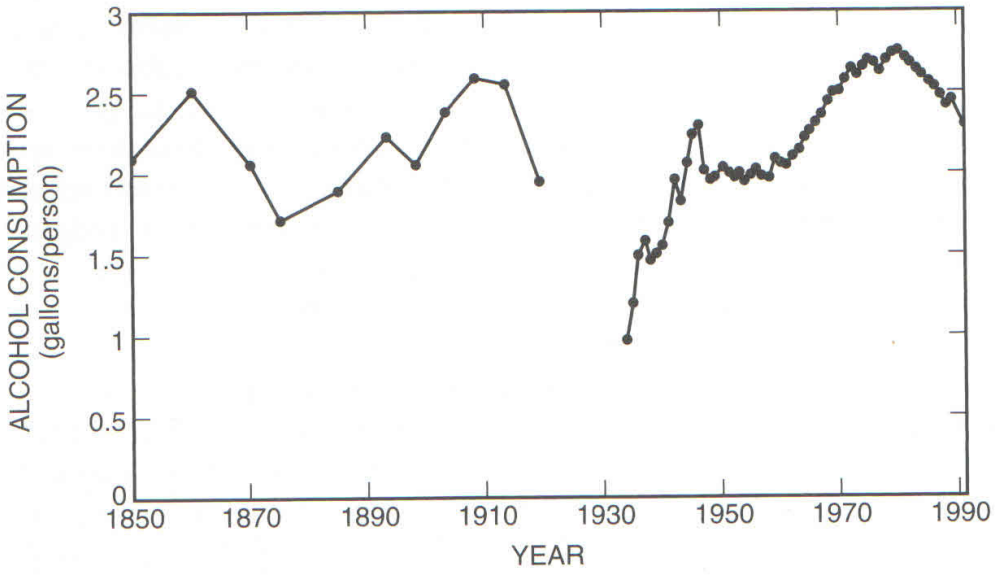

Figure 6-1 Yearly alcohol consumption, in gallons per person, of raw alcohol from 1850 to 1990 in the United States. Note that there are three peaks in consumption about 60 years apart. The gap in the early part of the twentieth century is due to Prohibition. Note the short-lived increase in consumption in the years following World War II. (G. D. Williams, Clem, & Dufour, 1993)

MEASURING ALCOHOL LEVELS IN THE BODY

Alcohol levels are usually measured in terms of the concentration of alcohol in whole blood. This is known as the *blood alcohol level* (BAL), or blood alcohol concentration. The BAL may be measured directly by taking a blood sample, but more often a breath sample is taken and analyzed using a device known as a *Breathalyzer*. It has been well established that alcohol concentration in the breath reliably reflects the concentration in the blood, and so the results of a Breathalyzer are reported as "blood alcohol level" rather than "breath alcohol level."

Metric Measurements and Percentage

The BAL is usually expressed in terms of milligrams (mg) of alcohol per 100 milliliters (ml) of whole blood. (A milligram is 1/1,000 gram; a milliliter is 1/1,000 liter; 100 ml is equal to a deciliter [dl].) The BAL may also be described as a percentage of alcohol in the blood. Conversion between these measures is not difficult; it involves only moving the decimal point three places to the left or right. For example, a BAL of 80 mg per 100 ml (or 80 mg/dl) is the same as 0.08 percent.

SI Units

There has been a recent trend toward reporting drug concentrations in *SI units* (Systéme International d'Unités), and many journals report alcohol concentrations this way. The SI unit for drugs, including alcohol, is millimoles per liter (mmol/l). To convert the metric measures to SI units, one must first convert milligrams of alcohol to millimoles and then convert deciliters of blood to liters. The first step is accomplished by dividing the milligrams by the molecular weight of alcohol, 46.07. Thus, 80 milligrams ÷ 46.07 = 1.74 millimoles. A liter is 10 deciliters; thus, 80 mg/dl is equivalent to 17.4 mmol/l. By combining these steps, milligrams per 100 ml can be converted to mmol/l simply by dividing by 4.607.

ROUTE OF ADMINISTRATION AND PHARMACOKINETICS

Figure 6-2 shows the theoretical time course for the level of alcohol in the blood after taking a single drink. This curve can be considered as being made up of several phases. The part of the curve labeled A is the absorption phase, during which absorption is taking place much more rapidly than excretion. The plateau phase, labeled B and C, is when absorption tapers off and excretion starts to lower alcohol levels. During this phase, blood levels peak. If absorption has been rapid, there may also be a brief period, immediately following the peak, when the decline in blood levels is rapid as a result of the distribution of alcohol out of the blood to other parts of the body. In the excretion phase, D, alcohol is eliminated from the body at a constant rate.

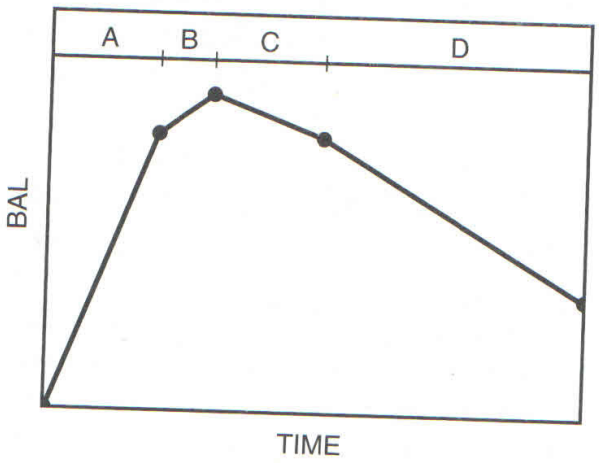

Figure 6-2 Theoretical time course for BAL after taking a single drink. Phase A is the absorption phase, in which absorption is taking place much more rapidly than excretion. Phases B and C form the plateau phase, in which absorption tapers off and excretion starts to lower alcohol levels. During this phase, blood levels peak. If absorption has been rapid, there may also be a brief period, immediately following the peak, when the decline in blood levels is rapid. This rapid decline is caused by the distribution of alcohol out of the blood to other parts of the body. During the excretion phase, D, absorption is complete, and alcohol is eliminated from the body at a constant rate.

ABSORPTION

Alcohol is normally administered orally, and absorption takes place in the digestive tract. Because the molecules of alcohol cannot be ionized, neither the pH of the digestive system nor the pH of the blood has an effect on absorption.

Alcohol readily dissolves in water, and it may pass into the blood from the stomach, intestines, or colon, but it is absorbed most rapidly from the small intestine. In addition, as long as the alcohol stays in the stomach, it is subjected to fairly high levels of alcohol dehydrogenase, the main enzyme that destroys alcohol. In the stomach, alcohol is subjected to considerable *first-pass metabolism* by *alcohol dehydrogenase*. After solid food has been eaten, the digestion process usually keeps the food in the stomach for a period of time before it is released into small quantities. Thus, the longer alcohol stays in the stomach, the more slowly it will be absorbed into the blood, and *first-pass metabolism* will cause less of it to be absorbed. In general, absorption of alcohol is faster on an empty stomach, and more will get into the body. Even though peak blood levels are higher when there is no food in the stomach, the peak will occur at about the same time, and it will take about the same time for blood levels to return to zero (Watkins & Adler, 1993).

Some medicines, such as *cimetidine* (Tagamet) and *ranitidine* (Zantac), which are commonly used to reduce stomach acidity in people who have ulcers, can increase BALs created by a given amount of alcohol. These drugs, known as H_2-receptor antagonists, are widely prescribed. Zantac 75 is ranitidine in nonprescription strength and is available over the counter. These *H_2-receptor antagonists* reduce stomach levels of alcohol dehydrogenase, and this action protects alcohol from first-pass metabolism. One study showed that the amount of alcohol that entered the blood was increased by 17 percent after ranitidine treatment for 1 week. The effect was even greater with cimetidine. The effects of cimetidine and ranitidine are greatest when alcohol is taken on a full stomach. On an empty stomach (or in the case of alcoholics), there is little first-pass metabolism in the digestive system (DiPadova, Worner, Julkunnen, & Lieber, 1987; DiPadova et al., 1992).

There also appear to be gender differences in first-pass metabolism. Compared to men, women appear to have lower levels of alcohol dehydrogenase in their stomachs; consequently, more of the alcohol a woman drinks gets into the blood, resulting in a higher BAL in a woman than the same amount of alcohol would produce in a man of similar size (Frezza et al., 1990; Whitfield & Martin, 1994). It has been speculated that this difference could be one reason why women are more vulnerable than men to the acute and chronic complications of alcoholism, including alcoholic liver disease.

Interestingly, abstainers reach lower peak BALs than moderate drinkers. The reason for this difference is not clear, but it may have to do with different degrees of first-pass metabolism in people who never drink (Whitfield & Martin, 1994).

The time to reach the maximum blood levels after drinking is highly variable between individuals and situations, but the time to reach the beginning of the plateau (B in Figure 6-2) is usually about an hour, with the peak about 15 minutes later. After a few drinks, however, absorption rates seem to increase, and the peak and plateau will be reached 20 to 25 minutes sooner (Ditmar & Dorian, 1987).

Beer appears to pass out of the stomach more slowly than other alcoholic beverages. For this reason, beer creates lower BALs than the same amount of alcohol consumed in some other beverage. The passage of alcohol through the stomach may also be facilitated by carbonation. Sparkling wines such as champagne and rosé frequently have more "kick" than still wines.

The concentration of the alcohol also contributes to the speed of absorption. Diffusion rates increase with increases in concentration; therefore, the alcohol from beverages with high alcoholic content diffuses into the blood faster than the same amount of alcohol mixed in a weaker concentration. There is, however, an upper limit to this effect. High alcohol concentrations slow

down the rate at which the stomach empties its contents into the intestine and, thus, can interfere with absorption. It is probably not a coincidence that the most rapid absorption appears to occur at about 40 percent alcohol, the concentration of most hard liquor.

INHALATION

Normally, alcohol does not evaporate fast enough to be administered by inhalation, but in 2004 a machine called AWOL (Alcohol WithOut Liquid), which vaporizes liquor in oxygen was marketed in the United States and Britain. This mixture is inhaled through a mouthpiece that looks like an asthma inhaler. The vaporized alcohol is absorbed through the lungs and goes directly to the brain, bypassing any first-pass metabolism in the stomach and the liver. These machines are calibrated to administer a shot of alcohol in about 20 minutes, about the same time it might take to drink a shot of liquor. Because of the rapid absorption and the lack of first-pass metabolism, it is likely to cause somewhat higher BALs than drinking the same amount of liquor. It is as yet unknown whether alcohol in those concentrations will cause any damage to lung tissue. This method of alcohol administration is legal in Britain and the United States but has been banned in at least one state (Colorado). Other states are also considering a ban (ABC News Online, 2004; BBC, 2004).

DISTRIBUTION

Because alcohol dissolves much more readily in water than in lipids or fat, alcohol is distributed almost entirely in body water. Therefore, individuals with different proportions of body fat, even though they may weigh exactly the same, may reach different BALs after drinking identical amounts of alcohol. Males, for example, have a lower percentage of body fat than females. Thus, if a man and a woman weigh exactly the same and drink the same amount of alcohol, the woman will have a higher BAL (assuming similar first-pass metabolism). The alcohol she drinks will be more highly concentrated in her body because her body has less water to dilute it.

Age also makes a difference, at least for males. As males age, the percentage of their body fat increases slowly. Even though their total body weight may not change, the same amount of alcohol will result in higher BALs as men get older. Women show a much smaller change in body composition with age.

It is possible to calculate the BAL for an individual after the consumption of a given amount of alcohol. Box 6-1 shows how to make these calculations for any individual.

BOX 6-1 Calculating BALs

Calculating the BAL is relatively simple. You have to know the weight and sex of the individual and the amount of alcohol consumed. To illustrate, let's calculate the BAL of a 175-pound man who has ingested 1 ounce of spirits. Because the BAL is usually given in milligrams per 100 ml of blood, it is easier to do the calculations in metric units rather than in pounds and ounces.

First, we convert the body weight (175 pounds) to kilograms by dividing by 2.2 (1 kg = 2.2 lb). This equals 80 kg. This weight must then be adjusted because not all of the body is capable of absorbing alcohol. The percentage that can absorb alcohol is estimated to be 75 percent in men and 66 percent in women. Therefore, an 80-kg man will have 60 kg to absorb alcohol ($80 \times 0.75 = 60$); 60 kg = 60,000 g or 60,000 ml of fluid because 1 ml of water weighs 1 g.

(*Continued*)

BOX 6-1

Next, we must convert alcohol to milligrams. One ounce of spirits (100 proof, or 50 percent by volume) will contain 11.2 g of alcohol (0.5 fluid ounce of water weighs 14 g), and alcohol has a specific gravity of 0.8; ($14 \times 0.8 = 11.2$); 11.2 g is 11,200 mg.

Now we can divide the 11,200 mg of alcohol by 60,000 ml of body fluid and multiply by 100. This calculation yields the BAL: 18.6 mg per 100 ml. Our 175-pound man will raise his BAL by 18.6 mg per 100 ml of blood with every ounce of spirits.

Beer is usually about 5 percent alcohol by volume and comes in 12-ounce bottles. One such bottle would contain 13.5 g of alcohol, or 13,500 mg. When this is spread around a 60,000-ml body, it gives a concentration of about 22.5 mg per 100 ml. Our 175-pound man would raise his BAL by 22.5 per 100 ml with each beer. The accompanying table gives the alcohol content of various common drinks so that you can do the appropriate calculations for different sources of alcohol.

To calculate how each of these drinks would affect you, take your weight in pounds and convert it to kilograms by dividing by 2.2. Next calculate the body weight (for your sex) that is capable of absorbing alcohol: male, 75 percent; female, 66 percent. This figure must then be converted to milligrams (and milliliters) by multiplying by 1,000.

Now calculate the amount of alcohol consumed in milligrams, divide it by your weight in milligrams, and multiply by 100. Remember that because the body metabolizes alcohol at a rate of about 15 mg per 100 ml per hour, you can subtract 15 mg per 100 ml for each hour that has passed since your drinking started. Caution: These estimates of your BAL using this technique are just that—estimates. Two factors in this equation are approximations: the percentage of the body that will absorb alcohol and the rate of alcohol metabolism. Both depend on many factors, such as age, health, build, experience with alcohol, and even other drugs in your system. The figures given here are population averages that might not apply to you. In general, however, this technique tends to overestimate BAL, so it should be reasonably safe for most people most of the time. It is not recommended, however, that you bet your life or your driver's license on it.

Alcohol Contents of Some Beverages

Beverage	*Alcohol Content* Percent (volume)	*Alcohol Content* (mg)
Spirits (1 fl. oz.*)		
(100 proof)	50	11,200
(89 proof)	43	9,600
(80 proof)	40	8,900
Beer (12 fl. oz.)	5	13,500
Wine (2.5 fl. oz.)	12	8,400

*A shot is 1.25 oz., so that these figures must be increased by 25 percent if "shots" are being used to mix drinks.

Alcohol is distributed rather evenly throughout body water, and it crosses the blood–brain barrier, as well as the placental barrier, without difficulty. Consequently, alcohol levels in most tissues of the body, including the brain and a fetus (if present), accurately reflect the blood alcohol content of the drinker. Alcohol in the blood circulates through the lungs and vaporizes into the air at a known rate, so it is possible to measure the alcohol level in the blood and the rest of the body by measuring the

alcohol vapor in exhaled air using a Breathalyzer, as described earlier.

EXCRETION

A small amount of alcohol may be eliminated in breath, sweat, tears, urine, and feces, but over 90 percent of all alcohol consumed is metabolized, mostly in the liver. Because humans have been consuming alcohol throughout a long period of our evolution, we have developed an efficient means of eliminating alcohol and using it as a source of energy. The usual route of metabolism is shown in Figure 1-9. It involves two steps. In the first step, the *rate-limiting step*, alcohol is converted to *acetaldehyde* by the enzyme alcohol dehydrogenase. This is the slowest step in alcohol metabolism. Consequently, the rate at which this conversion takes place limits the speed of the entire process. The conversion rate of alcohol to acetaldehyde is determined by the amount of alcohol dehydrogenase available and is relatively independent of the concentration of alcohol. The metabolism of alcohol, then, usually takes place at a steady rate throughout most BALs. (This rate may vary between individuals and from species to species.)

In the second step, the acetaldehyde is converted into *acetyl-coenzyme A* by several enzymes, the most common of which is *aldehyde dehydrogenase*. Acetyl-coenzyme A is converted mainly into water and carbon dioxide through a series of reactions known as the *citric acid cycle*, during which usable energy is released to the body. Acetyl-coenzyme A is also used in a number of bodily processes, such as the production of fatty acids and steroids. As a result, alcohol consumption and its consequent metabolism can alter a great deal of body chemistry.

Between individuals, there is considerable variability in elimination rates. The range found in one study was from 5.9 to 27.9 mg per 100 ml per hour, with a standard deviation of 4.5 (Dubowski, 1985). For the majority of individuals, the range is usually accepted to be between 10 and 20 mg per 100 ml per hour, with a mean of 15. The rate of metabolism of alcohol also seems to be influenced by drinking experience. Nondrinkers metabolize alcohol at a slightly slower rate (12–14 mg per 100 ml per hour) than light to moderate drinkers (15–17 mg per 100 ml per hour) (L. Goldberg, 1943; Whitfield & Martin, 1994).

It has also been demonstrated that food can have an effect on the rate of alcohol metabolism as well as its absorption. Ramchandani, Kwo, and Li (2001) have shown that having eaten speeds up the rate of alcohol metabolism from 25 to 45 percent. The increase did not seem to depend on the type of food eaten and is probably a result of increased blood flow to the liver caused by a food in the stomach.

Methanol is also metabolized in the liver by alcohol dehydrogenase, but the metabolic by-products are *formaldehyde* and *formic acid*, which are very toxic and metabolize very slowly. Methanol alone is not very toxic, but consumption of methanol can result in severe illness, blindness, and death as a result of accumulation of these toxins in the body. Surprisingly, these toxic effects can sometimes be avoided if a great deal of ethanol is consumed at the same time because both alcohols use the same enzyme system. Ethanol competes with methanol for the available enzymes and thereby slows down the formation of formaldehyde, so it may never reach toxic levels.

Although most alcohol is handled by the alcohol dehydrogenase system, another system appears to be in operation as well. This is known as the *microsomal ethanol-oxidizing system* (MEOS). The MEOS normally handles only 5 to 10 percent of the metabolism of alcohol, but its activity increases at higher levels of blood alcohol. The activity of the MEOS may be doubled or even tripled by continuous alcohol consumption. This increase may account for 50 to 65 percent of the increased alcohol metabolism induced by heavy drinking, a change that partly accounts for alcohol tolerance. The MEOS is important for another reason: It is also responsible for the metabolism of a number of other drugs, such as barbiturates. Therefore, if the MEOS is stimulated by continuous alcohol use, the metabolism of these other drugs will also be speeded up and vice versa

(Leiber, 1977; Leiber & De Carli, 1977). Thus, alcoholics usually have a great deal of resistance to the effects of barbiturates and other drugs.

NEUROPHARMACOLOGY

The neuropharmacology of alcohol is complex and involves a number of systems. Even though it has been studied intensively and much is now known, there are still many mysteries. Because there are a number of similarities between the effects of alcohol and the general anesthetics and solvents, it is believed that all have a similar mechanism of action and that what has been learned about anesthetics can tell us much about alcohol (see Chapter 8).

Whatever that mechanism of action might be, it is clear that neither alcohol nor the general anesthetics produce a direct effect on one specific receptor site; they have many different sites of action and mechanisms of action. The molecules of alcohol act directly on the receptor sites of a number of neurotransmitters and the ion channels they control, altering the effect of the transmitter. They may do this by interacting with a "pocket" (an alcohol-sensitive area on the receptor site) or by entering and blocking the ion channel itself (Lovinger, 1997).

One target of the alcohol molecule is glutamate transmission. It has been shown, in several parts of the brain, that acute doses of alcohol at concentrations achieved by normal drinking depress the functioning of the ion channel controlled by glutamate at the NMDA receptor for glutamate. The NMDA receptor site is in the ion channel itself, and alcohol molecules have the effect of blocking the ion channel. As a result of chronic exposure to alcohol, the brain "up-regulates" NMDA receptor-ion channel functioning; that is, the brain becomes more sensitive to glutamate to compensate for prolonged depression by alcohol. It is believed that this increase in sensitivity to the excitatory transmitter glutamate may be responsible for alcohol withdrawal symptoms that occur (Sanna & Harris, 1993) when alcohol is no longer consumed.

Alcohol is also known to stimulate the function of at least one class of serotonin (5-HT) receptor, the 5-HT_3 receptor, which opens ion channels and causes rapid-onset depolarization of the membrane. This appears to be an important step in the release of dopamine in the nucleus accumbens and, consequently, in the reinforcing effect of alcohol. It has been shown, for example, that serotonin antagonists will decrease the reinforcing effects and the discriminative stimulus effects of alcohol. Studies using photon emission tomography (PET) show that acute alcohol consumption facilitates serotonin's excitatory effects (Yoshimoto et al., 2000); however, chronic ingestion actually has the opposite effect, reducing serotonin function (Berggren, Eriksson, Fajlke, & Balldin, 2002).

The GABA-receptor-ionophore complex is also involved in the effect of alcohol, particularly ionophores controlled by the GABA_A receptor. These are inhibitory, and alcohol enhances their inhibition (see Chapter 7). PET-detected decreases in brain metabolic activity appear to be related to alcohol-induced stimulation of GABA receptors; interestingly, such stimulation is more pronounced in men than in women (Wang et al., 2003).

Alcohol also has a myriad of other neurophysiological effects. For example, it disrupts second messengers and is known to alter the functioning of monoamine oxidase, the enzyme responsible for the destruction of monoamine neurotransmitters (Tabakoff & Hoffman, 1987). It also has been shown to alter the responsiveness of the endogenous opiate system (Froehlich & Li, 1993).

Alcohol Antagonists

For thousands of years, people have been searching for a substance that would reverse the effects of alcohol. The ancient Greeks believed that the amethyst, a semiprecious stone, had this property, and the term *amethystics* has been used to describe these supposed agents.

In 1985, researchers at Hoffmann–La Roche reported that they had synthesized a substance called *RO 15-4513*, which seemed to be able to antagonize

the effects of alcohol. Careful research has shown that the drug antagonizes only some of the effects of alcohol (including self-administration; June et al., 1992), and it does so because it appears to change the effect of GABA in a manner directly opposite to the effect of alcohol. It does not, however, act as a competitive antagonist to alcohol; that is, it does not compete with alcohol for a receptor site. In addition, RO 15-4513 appears to antagonize the effects of barbiturates and benzodiazepines (see Chapter 7) by working directly on the benzodiazepine receptor site (Lister & Nutt, 1987).

There is little likelihood that RO 15-4513 could have any medical use. Although it blocks some of the effects of alcohol, it does not antagonize alcohol's lethal effects, so it cannot be used to treat alcohol overdose. In addition, it seems to possess the ability to cause convulsions, and this would make it unsuitable for treating alcoholism.

As we saw earlier, serotonin blockers are capable of partly blocking the reinforcing and the stimulus properties of alcohol. Opiate antagonists can also block some of alcohol's physiological effects and might be useful in reducing alcohol consumption and preventing relapse in alcoholics after they have received treatment (Froehlich & Li, 1993).

It has generally been widely believed that coffee will sober someone up, especially if it is black coffee. Systematic studies have done little to confirm this belief. Early studies suggested that caffeine might reverse some impairing effects of low levels of alcohol on driving (less than 100 mg alcohol/100 ml blood) but not at higher blood alcohol levels (Muskowitz & Burns, 1981). A more recent study examining the effect of 200 to 400 mg caffeine on impairment produced by alcohol at about 80 mg/100 ml blood found that caffeine was not able to alter a number of effects of alcohol, including the subjective effects. These caffeine doses were able to cause a partial reversal of a slowing of braking speed caused by alcohol but did not return braking speed to normal levels (Liguori & Robinson, 2001).

Because alcohol has so many effects on so many different sites within the body, it is unlikely that a single substance could antagonize all the effects of alcohol.

EFFECTS OF ALCOHOL

Effects on the Body

Alcohol in low and moderate doses causes a dilation of blood vessels in the skin. This is why white persons who are drinkers sometimes have a flushed face (and heavy drinkers, like W. C. Fields, have a red nose). In addition, drinking alcohol makes the skin feel warm. One of the traditional medical uses of alcohol, therefore, was as a remedy for people who had been exposed to cold. Alcoholic beverages, especially brandy, were supposed to warm the body.

By inhibiting the secretion of antidiuretic hormone, alcohol causes a loss of body water through increased urination. This occurs only while the BAL is steady or falling.

Effects on Sleep

Alcohol, like most depressant drugs, acts as a sedative and induces sleep. Studies of acute effects on normal volunteers have shown that alcohol decreases the time it takes to go to sleep, but it does not have an effect on total sleeping time.

Even at very low BALs, alcohol depresses REM sleep. At low levels, this effect is apparent during the first half of a night following drinking. In the second half, there is an increase in REM, so the total REM time during the night might be unaffected. With larger doses of alcohol, REM is depressed throughout the entire night, but after three nights of alcohol consumption, REM depression shows complete tolerance, and REM returns to normal. When alcohol is discontinued after five nights, there is a REM rebound on the sixth night. A REM rebound is a period in which the percentage of REM sleep increases above normal levels, and this causes poor sleep and unpleasant dreams.

When alcoholics stop drinking, they usually have very high percentages of REM sleep (as much as 90 percent) and other disturbances in sleep patterns that may last as long as 200 weeks (W. B. Mendelson, 1979).

EFFECTS ON HUMAN BEHAVIOR AND PERFORMANCE

Perhaps an indication of the importance of inebriation in our culture is the vast number of synonyms for being drunk. In 1737, Benjamin Franklin compiled 228 terms commonly used for being drunk. He might have missed a few, or, more likely, drinkers have continued to actively create more since his time. The *American Thesaurus of Slang*, published in 1952, lists almost 900 such terms. Most of them suggest some sort of violence or damage, such as *crashed, clobbered, bombed, swacked, plastered, tanked, ossified, looped, paralyzed*, and *wiped out*, to cite just a few. Some terms are very old. *Soused*, for example, dates back to sixteenth-century England, and *cut* was used as long ago as 1770 (Levine, 1981).

What does it mean to be ossified or swacked? The body of literature on this subject, dating back to the time of Aristotle, is so vast that it is almost impossible to characterize it in this short space. Systematic observation of drinkers has shown that at BALs between 50 and 100 mg per 100 ml, people are more talkative, use a higher pitch of voice, and show mild excitement. At about 100 to 150 mg per 100 ml, subjects appear talkative, cheerful, and often loud and boisterous; later, they become sleepy. At BALs above 150 mg per 100 ml, subjects frequently feel nauseous and may vomit. This phase is followed by lethargy and, in some cases, stupor. At doses as high as 290 mg per 100 ml, subjects are variously sleepy, noisy, and inattentive.

The problem with dose-related descriptions such as these is that there is such variability in the responses of individuals, depending on drinking history, environment, tolerance, and motivation, that they very seldom describe the behavior of any one individual on any single drinking occasion.

Subjective Effects

Many researchers, using tests such as the POMS and the ARCI, report that alcohol has a biphasic effect with regard to time and dose. At low doses and while the alcohol blood level is rising, alcohol has a stimulant effect, and people describe elation and euphoria; but at high doses and when the blood levels are falling, subjects report primarily feelings of sedation, anger, and depression (Babor, Berglas, Mendelson, Ellingboe, & Miller, 1983). Recent research has indicated that not everyone experiences the stimulation effect; some subjects experience only the sedating effects. Interestingly, those who described stimulant-like effects also reported a greater "drug liking" for alcohol and had more impairment on the digit symbol substitution test. It has been speculated that such individuals may be at greater risk for alcohol abuse (Holdstock & de Wit, 1998).

Perception

Alcohol has a detrimental effect on vision. It increases both the absolute and the difference thresholds but usually only at high doses. A decrease in visual acuity, indicated by a lowering in the critical flicker fusion threshold, is caused by a BAL of about 70 mg per 100 ml. Decreases in peripheral vision have also been reported. Decreases in sensitivity to taste and smell occur at low doses, and a decrease in pain sensitivity is common at BALs of 80 to 100 mg per 100 ml.

Performance

Alcohol slows reaction time by about 10 percent at BALs of 80 to 100 mg per 100 ml, and large consistent deficits are evident with larger doses. Complex reaction-time tasks that require the subject to scan and integrate stimuli from several sources before responding show that at lower doses, both the speed and the accuracy of performance decrease. Deficits are also seen in hand–eye coordination tasks, for example, in which the subject is required to maintain a marker over a moving target. PET analyses show that alcohol consumption decreases blood flow to the cerebellum, a region that controls voluntary movement and coordination, which may explain impairments on tasks requiring hand–eye coordination (Volkow et al., 1988). In general, the more complex the task, the greater the impairment seen at lower doses. Small

deficits occur at doses as low as 10 to 20 mg per 100 ml. Alcohol also impairs performance on the digit symbol substitution test.

Drowsiness caused by alcohol also shows up on vigilance tasks, and impairments are noted at doses as low as 60 mg per 100 ml.

One of the most sensitive tests is the *Romberg sway test*. The subject is asked to stand with eyes closed and feet together. BALs as low as 60 mg per 100 ml can cause a 40 percent decrease in steadiness as measured by the amount of swaying. This lack of steadiness makes it difficult for a person to stand on one foot with eyes closed. Before the Breathalyzer, the police used this test to detect impairment. At higher BALs, the lack of steadiness degenerates into staggering and reeling. The increase in sway appears to be a result of the effect of alcohol on the sensitive organs of balance in the inner ear and is also responsible for the sensation that the room is spinning around, which people experience when they lie down after drinking too much. Lack of steadiness can also bring on nausea and vomiting (Money & Miles, 1974).

Many people have demonstrated the impairing effects of alcohol on many tasks, but these effects are sometimes elusive. In many cases, they depend on the expectancy and motivation of the individual. Vogel-Sprott (1992) has shown that, at low doses at least (less than 100 mg/100 ml blood), many response deficits will disappear if subjects are paid or provided with an incentive to overcome the effects of the drug. In addition, subjects who expect that the drug will have an effect are often more impaired than those who do not (Fillmore & Vogel-Sprott, 1998).

Memory and Blackouts. Alcohol is also known to have a detrimental effect on memory. Low and moderate levels of alcohol have been shown to affect both the storage and the retrieval of information, but the storage function seems to be more strongly affected (Birnbaum & Parker, 1977). Impairments in memory encoding and attention are demonstrated in the odd-ball paradigm (described in Chapter 4) using auditory evoked potentials. Ethanol administration reduced P300 amplitude and increased delay both when participants were paying complete attention to the auditory task and when attention was divided by performing the task while listening to a story (Lukas, Mendelson, Kouri, Bolduc, & Amass, 1990). In long-term alcohol abusers, PET analyses using 2-deoxy-2[^{18}F]fluoro-d-glucose show that deficits in verbal and visual memory, as well as attention, correspond with decreased metabolism in the dorsolateral prefrontal cortex and the anterior cingulate cortex (R. Z. Goldstein et al., 2004).

Heavier drinking may also cause periods of amnesia or *blackouts* where people may be unable to remember events that occurred while they were intoxicated. There are two different varieties of blackout. The first type is called a *grayout* or a *fragmentary blackout* and is the most common form of alcohol amnesia. When a grayout occurs, the drinker is able to remember only bits and pieces of events that occurred while drinking. The missing memories usually return, especially if the drinker is reminded of these events or if he or she returns to the place where they occurred. This shows that the problem is primarily one of retrieval—the memories were formed and stored in the brain, but the person has trouble accessing them later when the alcohol is gone. Grayouts are likely to result from dissociation (Overton, 1972; see also Chapter 3).

En bloc blackouts are more serious but less frequent. When this occurs, the drinker is usually able to remember events of a drinking episode up to a particular time and then remembers nothing until another well-defined point in time, usually when he or she wakes up the next morning. All events that occurred during that block of time are not remembered. In fact, there is no evidence that these memories were ever put into long-term storage because they never return, even when the person is reminded. Interestingly, during the period when a blackout is happening, the drinker may appear to behave perfectly normal. He or she can carry on a conversation and carry out many normal behaviors, such as driving a car. They can recall what happened in the past, before they began drinking, but cannot remember what happened 20 minutes ago (Ryback, 1970). They are able to hold things in

short-term storage or working memory, but they are unable to form long-term memories. There is good evidence that this is because of the effect of alcohol on the hippocampus, the part of the brain that is needed to form long-term memories (White, 2003).

Effects on Driving

Studies of the effects of alcohol on driving, in simulators and in real cars on closed tracks, have generally confirmed that alcohol begins to affect performance at about 50 to 80 mg per 100 ml (Mitchell, 1985; Starmer, 1990). At 80 mg alcohol per 100 ml blood, participants in a simulated driving study drove at higher speeds and showed a trend toward increased collisions with other cars. These performance deficits corresponded with decreases in activation of the orbitofrontal cortex and motor regions of the brain measured by functional magnetic resonance imaging (fMRI) (Calhoun, Pekar, & Pearlson, 2004).

This finding is reflected in real-life driving accident statistics. Figure 6-3 shows the relative probability of being responsible for a fatal crash at various BALs. The curve starts to rise between 50 and 100 mg per 100 ml. At 100 mg per 100 ml, the probability of being responsible for a fatal crash is seven times greater than if the BAL had been 0. After this point, the curve rises sharply. At a BAL of 200 mg per 100 ml, a driver is 100 times more likely to cause a fatal crash (Organization for Economic Cooperation and Development, 1978).

Statistics such as these establish the rationale for setting legal limits on BAL for driving. In most jurisdictions, the limit is between 80 and 100 mg per 100 ml of blood, the point at which the curve starts to rise sharply. It is important to remember, however, that these curves underestimate the risk for young, inexperienced drivers; older drivers; and people not used to drinking. Their risk of being involved in an accident is considerably elevated even at BALs below the legal limit. Figure 6-4 shows similar curves for people of different ages (Organization for Economic Cooperation and Development, 1978).

It is also interesting to note that the impairment caused by alcohol seems to last beyond the time when alcohol is gone from the body (Starmer, 1990).

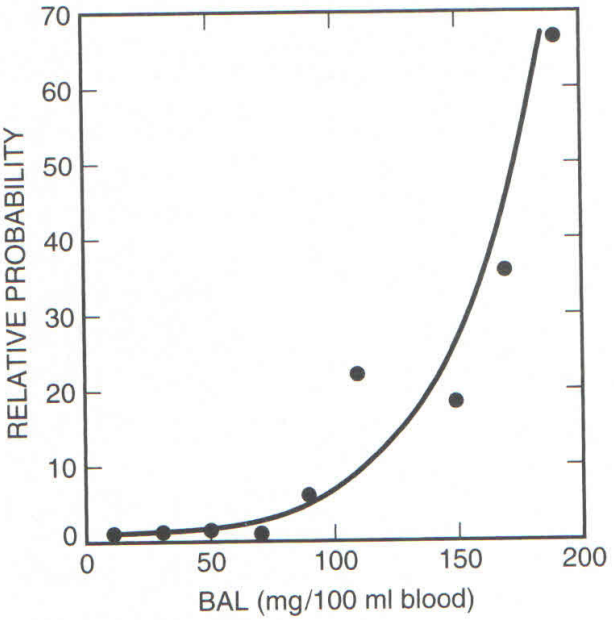

Figure 6-3 The relationship between BAL and the relative risk of being involved in a traffic accident. The risk with a BAL less than 1.0 mg per 100 ml blood is 1.0. (Organization for Economic Cooperation and Development, 1978)

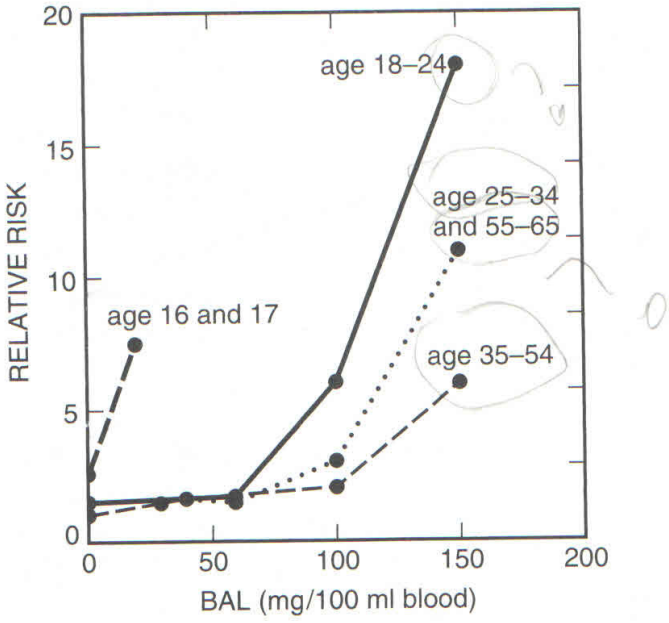

Figure 6-4 The relationship between BAL and the relative risk of being involved in a traffic accident for people of different age-groups. The risk with a BAL of 1.0 mg per 100 ml blood is 1.0. (Organization for Economic Cooperation and Development, 1978)

Disinhibition and Behavior Control

One of the frequently reported effects of alcohol is *disinhibition*, a term that is generally used to mean that under the influence of alcohol, people do things they normally would not do for fear of adverse consequences. This is most evident in conflict situations in which a certain activity has both positive and negative consequences. Alcohol reduces the influence of the negative consequences and appears to release the behavior from inhibition. This was demonstrated in an experiment by Muriel Vogel-Sprott of the University of Waterloo. Subjects made a sequence of responses for which they were given both painful electric shocks and money. The shocks severely depressed the responding of subjects who had been given a placebo but failed to suppress the responding of subjects after they had been given alcohol (BALs of 50 to 80 mg/100 ml; Vogel-Sprott, 1967).

More recent research on the effect of alcohol on behavioral control is often done using a "go–stop" task. In this task, a subject is required to make a response when a particular signal, the "go" signal, is presented but must withhold that response if the "go" signal is preceded by a "stop" signal. Studies have shown that alcohol at moderate doses does not interfere with responding to the "go" signal, but it selectively interferes with the ability of the "stop" signal to inhibit behavior. Furthermore, fMRI studies of brain activity during these tasks show that alcohol weakens the connections between the frontal areas of the cortex and the striatum, the motor area of the brain (Vogel-Sprott, Easdon, Fillmore, Finn, & Justus, 2001).

It is interesting that this disinhibition effect may actually improve performance on tasks in which anxiety or conflict is interfering with behavior. A practical example might be someone who is afraid to ask the boss for a raise. Conflict exists because the person wants the raise but is afraid of being fired or making the boss angry. After a few drinks, fear of the boss loses its control of the behavior, and the task can be performed.

In summary, perhaps the best way to characterize the effects of alcohol is to retell the old fable about Saint Martin, the monk who was reputed to have brought grapes to France. At first, the vine was hidden in the bone of a bird; then, after outgrowing the bird, it was hidden in the bone of a lion; finally, it was hidden in the bone of a donkey. Later, after the vine had grown and wine was made, the monks who drank it showed the characteristics of the animals used in its transportation. After the first bottle, they sang like birds; after the second, they had the courage of lions; but after the third, they behaved like asses.

EFFECTS ON THE BEHAVIOR OF NONHUMANS

Conditioned Behavior

For various reasons, few studies have been done on the effects of alcohol on positively reinforced behavior, but those that have been done show that the effects are dose dependent; on both fixed interval (FI)and fixed ratio (FR) schedules, alcohol increases the rate of responding at low doses and decreases the rate at higher doses.

Alcohol is similar to tranquilizers and antipsychotic drugs because it depresses shock avoidance at doses that do not interfere with escape (Heise & Boff, 1962).

The effect of alcohol on punished responding is also similar to that of the barbiturates and benzodiazepines but not quite as striking. In an early experiment, Conger (1951) trained rats to run down a runway for food and then gave their paws a shock when they began to eat. He adjusted food deprivation and shock levels carefully until the rats were willing to run partway down the runway but would not touch the food. He found that alcohol would cause the rats to approach and eat the food immediately, but rats given a placebo required many trials. Since then, several researchers have found that ethanol will increase response rates that are suppressed by contingent shock in an operant task. This result is similar to the finding in humans that alcohol tends to reduce

the control of aversive consequences on behavior, as demonstrated by Vogel-Sprott's experiment, described earlier.

DISCRIMINATIVE STIMULUS PROPERTIES

Animals can be trained very easily to discriminate alcohol from saline. In a discrimination task, Overton showed that at a dose of 3,000 mg/kg, rats will reach criterion discrimination performance in just three trials. Of the drugs tested, the only drugs that were discriminated faster were phenobarbital and pentobarbital (Overton, 1982; Overton & Batta, 1977).

Using the electrified T-maze, Overton found that rats trained to discriminate alcohol from saline generalized the alcohol response when given a barbiturate and vice versa, indicating that the two drugs produce a similar subjective state. However, in a later series of experiments, Overton (1977) was able to train rats to discriminate between alcohol and barbiturates, showing that although the effects of barbiturates and alcohol are similar, they can be discriminated by rats. It has also been shown that the alcohol response is not generalized to meprobamate (Barry, McGuire, & Krimmer, 1982), chlorpromazine, amphetamine, or atropine (Barry & Kubina, 1972). The alcohol response, however, will generalize to several anesthetics and to the solvents toluene and 1,1,1-trichloroethane (Bowen & Balster, 1997) and to isopropanol (Porcu & Grant, 2004).

The stimulus properties of alcohol can be blocked by 5-HT_3 receptor blockers but not by haloperidol, a dopamine D_2 blocker—an indication that serotonin rather than dopamine may mediate the subjective effects of alcohol (Grant & Barrett, 1991).

More recent research has shown that the alcohol stimulus is complex and made up of several elements shared with other drugs. Porcu and Grant (2004) used a three-choice discriminative task to separate these elements. They trained rats to discriminate between water ethanol and the benzodiazepine midazolam (a positive $GABA_A$ modulator). Because ethanol is also a positive $GABA_A$ modulator, this forced the rats to discriminate ethanol on the basis of some other property. In this situation, the alcohol cue generalized to dizocilpine, an NMDA receptor blocker, showing that both the effects of ethanol on GABA and the NMDA glutamate receptor have separate stimulus effects that can be separated (Porcu & Grant, 2004).

TOLERANCE

Acute Tolerance

Several studies have shown that many of the effects of alcohol are more pronounced while the BAL is rising than later when the BAL is falling. In the first study of this type, done many years ago, it was shown that while the BAL was rising, subjects first appeared intoxicated at 150 mg per 100 ml, but while the BAL was falling, they appeared sober at 200 mg per 100 ml (Mirsky, Piker, Rosebaum, & Lederer, 1945). Many other effects of alcohol also show acute tolerance (Vogel-Sprott, 1992).

Chronic Tolerance

Chronic tolerance to alcohol appears to develop rapidly in both animals and humans. The extent and speed of tolerance depend on the species studied and the alcohol effect measured. The maximal tolerance develops in a few weeks in humans and reaches a point at which doses have to be increased from 30 to 50 percent to overcome it. Tolerance disappears in rats after 2 or 3 weeks of abstinence but develops again more quickly with repeated exposure (H. Kalant, LeBlanc, & Gibbins, 1971).

Metabolic Tolerance

One effect of heavy drinking is the stimulation of both alcohol dehydrogenase, the major enzyme responsible for the destruction of alcohol, and the MEOS. As described in the section on absorption,

light to moderate drinkers are able to metabolize alcohol somewhat faster than abstainers (L. Goldberg, 1943; Whitfield & Martin, 1994). Although such changes certainly decrease the effects of alcohol, they cannot account for the extent of tolerance to alcohol described in the literature.

Behavioral Tolerance

Practice seems to be important in the development of tolerance to some of the effects of alcohol. In one experiment, a group of rats was given alcohol and placed on a treadmill. The rats quickly developed tolerance to the disruptive effects of the drug, but those that were given the same number of alcohol injections after the treadmill sessions did not show any tolerance when tested on the treadmill later under the influence of alcohol (Wenger, Tiffany, Bombardier, Nicoins, & Woods, 1981).

It has also been demonstrated that rats' tolerance to the hypothermic effect of alcohol (decrease in body temperature) is the result of a conditioned hyperthermic effect (increase in body temperature) associated with the specific environment in which the alcohol has been administered (Le, Poulos, & Cappell, 1979). Rats were given alcohol in one environment and saline in another environment. As expected, tolerance developed to the hypothermic effects of the alcohol, but when rats were given the alcohol in the environment where they had previously received only saline, the tolerance was diminished. In addition, rats that were given saline in the alcohol-related environment showed an increase in body temperature. This increase was a conditioned compensatory response to the alcohol effect (see Chapter 3).

WITHDRAWAL

As with most of the depressant drugs, chronic consumption of alcohol can cause withdrawal symptoms. Although the distinction may not always be appropriate, it is customary to think of two separate stages of withdrawal: (a) the early minor syndrome and (b) the late major syndrome, also known as *delirium tremens* or the *DTs*. The early minor symptoms usually appear about 8 to 12 hours after the end of a drinking bout, although many aspects of withdrawal may be seen during the latter part of long drinking sessions even while the drinking is still going on. Withdrawal starts in the form of agitation and tremors; other symptoms, such as muscle cramps, vomiting, nausea, sweating, vivid dreaming, and irregular heartbeats, may also be seen. This stage is usually over within 48 hours.

Fewer than 5 percent of patients hospitalized for alcohol withdrawal go on to show the late major withdrawal symptoms. After 2 days of the minor symptoms, patients show increasing agitation, disorientation, confusion, and hallucinations. Seizures may also occur (Wolfe & Victor, 1972). These major symptoms may last as long as 7 to 10 days. Alcohol withdrawal hallucinations are not usually of the proverbial pink elephant. They frequently involve smaller animals, such as rats, bats, or insects, and can be quite terrifying.

Late major withdrawal can cause death in a substantial number of cases if the symptoms are not treated. A report written at the beginning of the twentieth century, before treatment techniques had been developed, showed a 37 percent (52/140) mortality from alcohol withdrawal (Boston, 1908). Modern estimates are about 2 percent (Naranjo & Sellers, 1986).

In general, the most effective treatment of alcohol withdrawal is a combination of supportive care and the administration of another depressant drug such as diazepam, which suppresses the withdrawal symptoms and has a long duration of action. Other specific symptoms may also be treated with other drugs; for example, hallucinations can be controlled with haloperidol, an antipsychotic. Effective supportive care consists of measures such as reducing sensory stimulation by placing the patient in a dimly lit, quiet room; providing adequate food and water to prevent dehydration; keeping the patient warm and comfortable; and providing reassurance (Naranjo & Sellers, 1986).

SELF-ADMINISTRATION IN NONHUMANS

Oral Self-Administration

When alcohol is freely available to rats and monkeys in conditions in which food and water are also freely available, they will drink the alcohol but not in quantities sufficient to cause obvious intoxication or physical dependence. This type of drinking resembles typical human drinking patterns, but the thrust of this research has been to provide a model of human alcoholism, so there has been considerable research over the years to attempt to find what factors can cause this consumption to increase. Research using oral administration has been hampered because alcohol has a disagreeable taste that most nonhuman species prefer to avoid, and the effects on the central nervous system (CNS) are somewhat delayed because of slow absorption from the digestive system (Meisch, 1977).

One way to increase these low levels of intake is to subject the animal to a period of forced consumption when its only source of food or water is laced with alcohol. After a rat has been forced to consume the alcohol, its voluntary intake may increase. Depriving the animal of food or water will also induce it to consume higher levels of alcohol. Intake will sometimes remain high even after the food or water is returned (see Chapter 5). The animal will learn to press a lever on a reinforcement schedule for access to alcohol. Although some reports claim that food deprivation and other induction procedures are not necessary, they are often used.

It has been noted in these studies that physical dependence is not necessary for alcohol consumption, and when physical dependence exists, it does not increase alcohol intake. Animals that have been made physically dependent will sometimes fail to drink alcohol even while experiencing withdrawal symptoms (Hunter, Walker, & Riley, 1974).

Intravenous Self-Administration

Induction procedures are generally not necessary when alcohol is administered through a cannula implanted in the bloodstream. Giving the alcohol this way avoids the problem of bad taste and slow effect on the CNS, and most animals rapidly learn to self-administer alcohol. When alcohol infusions are freely available, the pattern of self-administration is somewhat erratic. Periods of high-level intake are followed by self-imposed abstinence lasting 2 to 4 days, when withdrawal symptoms may occur. These periods do not seem to follow any regular pattern. (Compare this with the stimulants such as cocaine; see Figure 11-2.) Figure 5-2 shows the intake of a rhesus monkey pressing a lever for intravenous alcohol over a period of 90 days in the laboratory of Jim Woods and his colleagues. The similarity of this pattern to human alcohol intake has already been noted.

SELF-ADMINISTRATION IN HUMANS

Laboratory Studies

In the laboratory, the pattern of alcohol self-administration when freely available is fairly consistent. Alcohol is consumed at high levels for several days. Then follows a self-imposed period of low consumption lasting 2 or 3 days. During this time, withdrawal symptoms may appear. Figure 5-2 shows the drinking pattern of alcoholic volunteers who worked on an operant schedule of button pushing to earn drinks. This pattern is very similar to that of a rhesus monkey under similar conditions and to the typical pattern of many chronic alcoholics under natural conditions (Griffiths, Bigelow, & Henningfield, 1980).

Factors That Affect Consumption

As we have seen in the section on the history of alcohol, its use is almost universal, but some factors are known to modify its use.

Culture. Cross-cultural studies in numerous societies in which alcohol is consumed have revealed some interesting patterns that appear to be consistent across cultures, even in our own. Alcohol consumption is generally a male activity

that is practiced socially outside the home among peer groups and not in the company of family members or people of higher status. Drinking is generally more acceptable among warriors and people who must grapple with the environment than among the members of a society who are charged with preserving tradition, such as priests, mothers, and judges (D. Robinson, 1977, p. 63).

Among individuals and cultures, many drinking patterns have been identified. The spree drinker, common in Finland, binges occasionally but stays relatively sober otherwise. A drinker common in France consumes a large fixed amount of alcohol every day steadily over the course of the day and exhibits few symptoms of intoxication. Such differences in national drinking patterns do not seem to influence certain consequences of consumption, such as rate of alcoholism or alcohol-related diseases. However, the difference may be significant when acute intoxication is important; for example, one beer a day may not ever cause a traffic accident, but the same quantity of beer, if consumed on one occasion every 2 weeks, could easily be responsible for traffic accidents.

Gender. Although heavy drinkers are more likely to be male, this fact does not mean that women drink less than men. Studies have shown that women do consume less alcohol than men, but when adjustments are made for differences in body size and ability to absorb alcohol, it turns out that women social drinkers achieve the same BALs as men (W. A. McKim & Quinlan, 1991; Vogel-Sprott, 1984).

Age. People tend to drink less when they get older. A number of studies have shown that although people drink just as frequently as they age, they tend to drink less on each occasion (Vogel-Sprott, 1984), so their total consumption declines. Unlike the difference in consumption between genders, this age-related decline in consumption per occasion cannot be explained by changes in body composition with age (W. A. McKim & Quinlan, 1991).

Behavioral Economics of Alcohol Consumption

Laboratory Studies. Numerous experiments in laboratory settings with both alcoholics and casual drinkers have shown that increases in the cost of alcohol or increases in the work required to get a drink will decrease the amount of alcohol consumed (Mello & Mendelson, 1972). For example, in an experiment by Bigelow and Liebson (1972), two skid-row alcoholics were given the opportunity to earn drinks by pulling a lever. At the lowest cost requirement, one consumed the maximum of 24 drinks a day, and the other consumed 17. At the highest work requirement, both consumed fewer than four drinks per day.

Demand Characteristics of Alcohol. It has been clearly demonstrated that consumption of alcohol is related to price (Seeley, 1960), but what is the exact relationship between price and consumption? Does the demand for alcohol show elasticity when the price changes?

There have been numerous studies of the elasticity of alcoholic beverages in populations when the price of alcohol has changed. Using many different techniques and statistics from a variety of sources, these studies show that the demand characteristics are different for different beverages in different populations. Beer, for example, has an elasticity coefficient of about −0.30 (inelasticity). This means that if the price of beer were to double, consumption would go down by only 20 percent.

Demand for spirits, on the other hand, has much higher coefficients (ranging from −0.57 to −1.95), indicating elasticity. Elasticity of wine varies, depending on the country. In France, where wine is consumed with meals and considered a necessity, it is inelastic (−0.06), but in the United States and Britain, demand appears to be elastic (−1.65 and −1.23, respectively).

Studies on Laboratory Animals. Most studies with laboratory animals have shown that the demand for alcohol is elastic. In an experiment by Carroll, Rodefer, and Rawleigh (1995), rhesus

monkeys responding for oral ethanol on FRs ranging from 4 to 128 showed a coefficient of −2.3, indicating elasticity. Heyman (1996), however, in a study with rats with a long history of alcohol consumption, found a coefficient of 0.09, indicating inelasticity. His rats responded on a variable ratio (VR) schedule that ranged from VR 4 to VR 20, and he found inelasticity even though a sucrose substitute was available. His findings suggest that elasticity may vary, depending on the extent of experience with alcohol.

Availability. Changes in price can alter the consumption of alcohol, and it appears that changes in availability can as well. Governments have considerable means of control over the availability of alcoholic beverages: enforcing a legal drinking age, licensing drinking establishments and liquor stores, and regulating the days and/or hours permitted for operation and sale. Considerable research has shown that alcohol consumption increases as alcohol becomes easier to obtain, and it decreases when it is more difficult to get (Single, 1988); that is, it behaves like any other commodity in the marketplace (Babor, 1985; Österberg, 1992; Popham, Schmidt, & de Lint, 1976).

Here are some examples:

- In 1989, when Iceland ended a 75-year prohibition on beer, the consumption of wine and liquor declined by 25 and 18 percent, respectively, but total alcohol consumption from all sources increased by 23 percent (Österberg, 1992).
- Studies of the effects of permitting wine to be sold in grocery stores in four states—Idaho, Maine, Virginia, and Washington—showed that in three of the four states, the change in law resulted in an overall increase in total alcohol consumption (Macdonald, 1986).
- For 8 months, 10 of Finland's liquor monopoly stores were closed on Saturdays on a trial basis. This experiment resulted in a total decrease in alcohol consumption of 3.2 percent and, also decreased public drunkenness and alcohol-related violence (Säilä, as cited in Österberg, 1992).

ALCOHOLISM

When the social reform movement of the nineteenth century was campaigning for better treatment of people who drank too much, they adopted the position that excessive drinking was a disease. Previously drunkenness was known by such terms as *inebriety* or *intemperance*, but more medical-sounding terms were developed, including *alcoholism*, *dipsomania*, and *narcomania*. *Alcoholism* survived and is now the commonly accepted term (Barrows & Room, 1991).

Like the term *dependence*, *alcoholism* may be used in two different ways: (a) as an explanation or (b) as a description of behavior. Many definitions are purely descriptive; they describe a pattern of behavior and then label it alcoholism. What is confusing is that many descriptions are used as though they were explanations. For example, the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV*) defines substance dependence (see Box 5-1). (The *DSM* defines substance dependence and abuse; this is generally taken to mean alcoholism if the substance is alcohol.) The *DSM-IV* definition is a description of a state of affairs; it is not an explanation. Unfortunately, many writers use such descriptions as though they were explanations. For example, it could be said that an individual is an alcoholic because he or she fits the *DSM-IV* description. This statement is fair enough, but it cannot be said that this individual drinks excessively because he or she is an alcoholic. (This would be a circular argument; we know that person X is an alcoholic because he or she drinks too much, and we know that person X drinks too much because he or she is an alcoholic.) The only way around this circularity is to define the condition of alcoholism in terms other than the behavior of drinking; then the term can legitimately be used as an explanation of the behavior.

Explaining something is considerably more complicated than describing it. Explanations take the form of theories, and good theories must withstand the test of scientific investigation. Over the years, a great number of theories have been proposed to explain alcoholism. In Chapter 4, there

was a discussion of several theories of addiction that could be applied to alcoholism, but alcoholism had its own disease theory that has been widely accepted for many years since Jellinek proposed it in 1960. It is a disease theory, and it suffers from the general problems that all disease theories have, but it is so widely accepted that it is worth discussing.

The Disease Explanation

In the 1950s, E. M. Jellinek first clearly proposed that alcoholism was a disease. His arguments were published in his book *The Disease Concept of Alcoholism* (Jellinek, 1960). Jellinek was associated with the *Alcoholics Anonymous* movement, and the increasing prominence of this movement and Jellinek's arguments were effective in convincing both the American Medical Association and the World Health Organization to declare alcoholism a disease. In spite of this, its status as a disease is still the subject of considerable heated debate.

One of the more important assumptions of this disease theory is that alcoholism is not caused by alcohol. Alcoholism is a genetic disease, and people are alcoholics from the time they are born. Everyone, both alcoholic and nonalcoholic, starts drinking in the same way, in a moderate, social manner, but there are some who progress to drink more and more heavily, and eventually they enter the *prodromal phase* of alcoholism, which is characterized by frequent blackouts. Many such people are not "alcoholics." They are "problem drinkers" who either stay that way or eventually stop drinking. Some individuals progress to become *gamma alcoholics* (Jellinek's term). The change from being a problem drinker to a gamma alcoholic is marked by two symptoms: (a) a loss of control over drinking, and (b) physical dependence indicated by high levels of tolerance and withdrawal symptoms such as seizures, hallucinations, and the delirium tremens. It is worth noting that the distinction between problem drinkers and alcoholics is the presence or absence of physical dependence and loss of control, not the amount consumed. Problem drinkers may actually consume more than alcoholics, but they are not considered alcoholics, and they do not have the disease. Any research on the disease of alcoholism, therefore, must be done on alcoholics, not on problem drinkers. This distinction is responsible for many arguments over data between supporters and opponents of the disease model.

We have already considered the role of physical dependence in alcoholism, so we will now look at some of its other assumptions.

Genetics of Alcoholism. Evidence is clear that the risk of becoming an alcoholic is increased as much as fourfold if a close relative (mother, father, or sibling) is an alcoholic. Families, however, share both genetics and environment, and the challenge to researchers has been to separate these factors.

It is known, for example, that the amount of drinking of identical twins (who have exactly the same genes) is more similar than the drinking behavior of fraternal twins (who have the same genetic similarity as normal siblings). Thus, the closer the genetic makeup, the more similar the drinking pattern. It has also been shown that an adopted person with a biological parent who is an alcoholic has an increased risk of alcoholism, but having an adoptive parent who is alcoholic does not increase the risk of becoming alcoholic (Schuckit, 1992). Unfortunately, twin studies cannot completely disentangle genetics from environment, and adoption studies have serious conceptual and methodological flaws that make it difficult to draw firm conclusions (Searles, 1988). Nevertheless, there is an overwhelming volume of data supporting the heritability of alcoholism. It seems, though, that heritability varies considerably, depending on factors such as gender, the measure of drinking behavior, the definition of alcoholism, and the population studied (Goldman, 1993).

There is no single alcoholism gene, and the influence of genetics is modified by environment. A person with an identical twin who is alcoholic has only a 60 percent chance of being alcoholic, so something more than genetics must be involved. Genetics probably controls some aspects of body chemistry, personality, or brain function that

increase the probability that a person will drink in an alcoholic manner in a particular environment. A variety of genetic susceptibilities to alcohol may cause problems only in particular environments. The right combination of environment and genetics may be necessary to make a person drink in an alcoholic manner.

FHP Versus FHN. One method that could be useful in understanding the nature of the disease of alcoholism might be to compare alcoholics with nonalcoholics on a number of measures; any consistent difference in the physiology, biochemistry, personality, or response to alcohol could give a clue as to the nature of alcoholism. A problem with this approach is that it is quite likely that any differences found might be caused by the alcohol consumed, not the alcoholism.

One way to avoid this difficulty is to compare people who are likely to become alcoholics before they start drinking with those who are less likely and to note the differences (remember that according to this theory, an alcoholic is an alcoholic before he or she starts drinking). We know that people who come from families in which there is a history of alcohol problems (*family history positive* [FHP]) are at a greater risk of becoming alcoholic than those who have a family history without alcohol problems (*family history negative* [FHN]). One interesting line of research has attempted to compare high-risk (FHP) and low-risk (FHN) individuals to see whether it is possible to detect markers that might be able to identify potential alcoholics or shed some light on the disease of alcoholism.

Although early studies were encouraging, there do not appear to be any consistent differences between FHP and FHN individuals in terms of pharmacokinetics and metabolism of alcohol, and no clear-cut differences have been established in cognitive and neuropsychological measures of personality (Searles, 1988) or in alcohol preference, alcohol-liking scores, BALs, or alcohol-induced impairment (de Wit & McCracken, 1990).

Some studies, however, have detected differences between FHN and FHP subjects in electroencephalographic responses, and in some experiments, FHP subjects may show a greater sensitivity to the subjective and motor-impairing effects of alcohol than FHN subjects (Porjesz & Begleiter, 1987; Schuckit, 1987, p. 1531; Schuckit, 1992).

If alcoholics are really different from nonalcoholics, these differences are rather difficult to establish. They appear to be limited to subtle changes (in the electroencephalogram, hormone levels, and subjective sensitivity) that require large-scale, carefully controlled experiments to detect. It is still not clear how any of these differences contribute to the development of alcoholic drinking, if they do at all.

Loss of Control

According to the disease model, one of the defining characteristics of alcoholism is *loss of control*. It is assumed that exposure to even one or two drinks of alcohol will cause, in the alcoholic, an uncontrollable craving to drink more and more. In other words, the alcoholic will lose control of alcohol consumption; one drink develops into one drunk.

Since the time it was proposed, the loss-of-control theory has never received significant experimental support. In fact, most research has disconfirmed the basic notion (Finagrette, 1988). A number of studies in England (D. L. Davis, 1962) and the United States (Armor, Polach, & Stambul, 1978) have found many cases of alcoholics who have reverted from excess drinking to moderate social drinking and have maintained that level for years. These studies caused a storm of controversy, and many alcoholism experts denounced them as dangerous and unscientific and attacked them on various grounds (Pendrey, Maltzman, & West, 1982).

Some have argued that most of these studies were done with problem drinkers, not with populations of gamma alcoholics, as defined by other characteristics such as physical dependence. In addition, it has been argued that most studies purporting to show that alcoholics can return to controlled drinking do not allow a sufficiently long time frame to detect whether controlled drinking is possible (Maltzman, 1994).

In addition to the research with alcoholics in treatment, laboratory studies have repeatedly shown that alcoholics are perfectly capable of moderating their alcohol intake in response to such manipulations as increased cost, and they virtually never lose control (Mello & Mendelson, 1972). Such laboratory studies are also challenged on the grounds that the laboratory is too artificial to be relevant to alcohol use in a natural setting (Maltzman, 1994).

Perhaps related to the concept of loss of control is the phenomenon of priming (see Chapter 5). It was shown some time ago that noncontingent infusion of the drug would reinstate drug self-administration in laboratory animals that had stopped pressing a lever. De Wit and Chutuape (1993) have shown that social drinkers are much more likely to choose an alcoholic drink and report an increased craving for alcohol after they have been given a priming dose of alcohol. This study was later replicated (Chutuape, Mitchell, & de Wit, 1994), but a more recent study was able to show only an increased desire for alcohol, not an increased choice of alcohol among primed social drinkers (Kirk & de Wit, 2000). Priming has also been demonstrated in laboratory animals. While priming looks like loss of control, it is not clear whether it is analogous to loss of control. Priming is a fairly universal phenomenon that can be seen in many species with many different reinforcers, while loss of control as described by Jellinek is seen only for alcohol and only in alcoholics.

HARMFUL EFFECTS OF AN ACUTE ADMINISTRATION

Alcohol Poisoning

A single dose of alcohol, if large enough, can be lethal. A blood alcohol level of about 300 to 400 mg per 100 ml of blood will usually cause loss of consciousness. In a study of alcohol poisonings, Kaye and Haag (1957) reported that without therapy, people whose BALs reached 500 mg per 100 ml of blood died within an hour or two. The world record for high BAL is probably 1,500 mg per 100 ml, reported in a 30-year-old man whose life was saved by vigorous medical intervention. Later he reported that he had drunk 4.23 liters of beer and an undetermined number of bottles of liquor in the space of 3 hours (O'Neil, Tipton, Prichard, & Quinlan, 1984).

As with most depressant drugs, death by alcohol usually results from respiratory failure. Alcohol is a rather toxic substance, and the lethal dose is uncomfortably close to the usual social dose. A 150-pound male would have to drink 7.5 ounces of liquor to have a BAL of 150 mg per 100 ml of blood. These numbers are at the upper levels of an acceptable social high. Around 25 ounces of liquor would produce a BAL of 500 mg per 100 ml of blood, probably a lethal dose for most people. Thus, the therapeutic index for alcohol is about 3.5 (25/7.5).

Fortunately, alcohol has a built-in safety feature: People vomit or pass out before they can kill themselves. People who die from alcohol poisoning usually drink a large amount quickly and in high concentrations. They are able to get a lethal dose into their bodies before they lose consciousness.

Hangover

The problem of how to avoid a hangover from alcohol has occupied some of history's best minds, as this passage from Plato's *The Dialogues* illustrates:

> They were about to commence drinking, when Pausanias said, "And now, my friends, how can we drink with the least injury to ourselves?" I can assure you that I feel severely the effect of yesterday's potations, and must have time to recover; and I suspect that most of you are in the same predicament, for you were of the party yesterday. Consider then: "How can the drinking be made easiest?" (Symposium 176a–b, translation in Jowett, 1931)

Like the ancient Greeks, most drinkers have, at some time, suffered the next day for having had too much the night before. Apart from the puritanical notion that we are getting just what we deserve, there are several explanations for a hangover. These explanations suggest that hangover results

from alcohol-produced effects, such as low blood sugar levels, dehydration, and irritation of the lining of the digestive system. There is no doubt that most effects of alcohol contribute to discomfort the next day, but it is probably best to think of a hangover as a miniwithdrawal from alcohol, a rebound excitation of an alcohol-depressed nervous system, that is, a miniwithdrawal symptom. This rebound makes the brain more sensitive to seizures.

For most drinkers, hangovers are not physiologically serious, but for persons with epilepsy, heart disease, or diabetes, hangovers could have serious medical consequences (Gauvin, Cheng, & Holloway, 1993).

The Greeks never did answer Pausanias's question "How can the drinking be made easiest?" apart from concluding that "drinking deep is a bad practice," but over the centuries, a number of cures have been suggested, including eating a spoonful of sugar or drinking lots of water. To the extent that a hangover can be thought of as a withdrawal from alcohol, one cure is to take a "hair of the dog that bit you." Consuming more alcohol relieves the hangover by depressing this rebound excitability in the same way that other depressant drugs are used to treat withdrawal. If the alcohol is taken in small quantities, it might work, but if too much is consumed, it will only postpone withdrawal.

Alcohol-Induced Behavior

Apart from the self-inflicted physical harm that can be done by an acute administration of alcohol, the drug can be responsible for changes in behavior that cause untold social, psychological, financial, and physical harm to the drinker and others. It is not possible to catalog all the manifestations of harm, but most people have been made aware of them in some form. They include accidents caused while drunk or hung over not only while driving but also in industry and at home (Gutjahr, Gmel, & Rehm, 2001), crimes committed under the influence of alcohol, and damage done to families and social relationships. All these effects are difficult to quantify, and some may not be a direct result of alcohol. They are nonetheless real and must be included in any assessment of the harmful effects of alcohol.

Reproduction

A well-known quote from Shakespeare's *Macbeth* states that drink "provokes the desire, but takes away the performance" in matters sexual. The bard's analysis is essentially correct. Acute alcohol consumption may increase interest by diminishing inhibitions, but, at least in higher doses, it reduces sexual arousal in both males and females. In males, alcohol at lower doses (BAL less than 100 mg/100 ml) may increase the duration of erections and, thus, provide increased opportunities for fulfillment of the partner. This fact may explain why alcohol is often perceived as enhancing sexual performance (Mello, 1978; Rubin & Henson, 1976).

A study with rats showed that increasing doses of alcohol caused increasing disruptions of copulation of male rats with receptive females. In addition, low doses of alcohol that disrupted copulation with receptive females caused male rats to attempt to copulate with unreceptive females, something they would normally not attempt. These findings support the speculation that low doses of alcohol adversely affect uninhibited sexual performance but can stimulate sexual behavior that is normally inhibited (Pfaus & Pinel, 1988).

HARMFUL EFFECTS OF CHRONIC CONSUMPTION

The Liver

Prolonged drinking of alcohol damages the liver. The damage usually starts with a buildup of fat in the liver. Alcoholics also frequently contract alcoholic hepatitis, which usually develops into *cirrhosis*, which means "scarring." The liver becomes filled with scar tissue and is no longer able to function, and the condition is frequently fatal, especially if alcohol consumption is not stopped.

Cirrhosis is present in 8 percent of chronic alcoholics; among nonalcoholics, the condition affects only 1 percent. Alcohol consumption

accounts for 40 to 90 percent of liver cirrhosis deaths in the United States. Generally, alcohol consumption of over five drinks a day for at least 5 years is necessary for the development of cirrhosis

The Nervous System

Some alcoholics and heavy drinkers may show a cluster of symptoms that includes a loss of memory for past events, an inability to remember new material, and disorientation and confusion. These symptoms are collectively known as *Korsakoff's psychosis*. They are a result of damage in certain parts of the brain first noted by Wernicke and called *Wernicke's disease*. The condition seems to result from deficiency of thiamin (vitamin B1), which is common among many alcoholics (Victor, Adams, & Collins, 1971). Many of the conditions suffered by alcoholics can be traced to vitamin deficiencies, chiefly because people who drink large quantities of alcohol do not normally have a balanced diet. In addition, alcohol can damage the digestive system and interfere with the normal absorption of some nutrients.

The Wernicke–Korsakoff syndrome is not the only neurological damage associated with heavy drinking. A number of other disorders of both the central and the peripheral nervous system, such as epilepsy, cerebellar syndrome, and alcoholic dementia, are attributable either directly or indirectly to excessive alcohol use (Marsden, 1977, p. 189). Individuals with a chronic history of alcohol consumption exhibit global demyelination of neurons, glial cell loss, loss of neuronal dendrites, neuronal death, and neuronal shrinkage in many different brain regions (Mann et al., 2001). Consistent with this, MRI analysis of chronic alcohol users shows widespread brain tissue loss (Gazdzinski, Durazzo, & Meyerhoff, 2005) and decreases in cerebral blood flow (Demir, Ulug, Lay Ergun, & Erbas, 2002). These effects are partially reversed with prolonged abstinence from alcohol, with the greatest increases in brain volume noted within the first month of withdrawal (Gazdzinski et al., 2005).

Cancer

The use of alcohol is directly related to cancers of the mouth, throat, and liver—the parts of the body that are directly exposed to high alcohol concentrations and susceptible to alcohol damage. This may be a result of the first metabolite of alcohol, acetaldehyde, which is a known *carcinogen*. Acetaldehyde is created in the upper digestive tract by alcohol dehydrogenase, which is present there and is responsible for first-pass metabolism of alcohol.

There is conflicting evidence relating alcohol consumption with breast cancer. In general, there appears to be a weak association in the general population, but alcohol does increase breast cancer in populations that are otherwise at risk, that is, those who have a family history of breast cancer or those postmenopausal women taking estrogen replacement therapy (Gunzerath, Faden, Zakhari, & Warren, 2004).

Reproduction

In males, chronic alcohol consumption is known to cause impotence, shrinking of the testicles, and a loss of sexual interest. Although there have been few studies of the effects of chronic alcohol consumption in females, there is evidence that it can cause menstrual dysfunctions, such as amenorrhea, dysmenorrhea, and premenstrual discomfort (Mello, 1987, p. 1517).

There are ancient beliefs that alcohol might be teratogenic (responsible for birth defects). In ancient Carthage, drinking on wedding days was forbidden; it was believed that it might cause an abnormal child to be born (K. L. Jones & Smith, 1975). Aristotle warned against drinking during pregnancy, and later, at the time of the gin epidemic in England, it was noted that there was an increase in infant deaths. Similar effects associated with alcohol consumption have been reported in the medical literature, and the extent of the problem is now fully appreciated. It is now recognized that the use of alcohol during pregnancy can harm the developing fetus and may

result in a number of behavioral, anatomical, and physiological irregularities, which are known as *fetal alcohol syndrome* (FAS) in their more severe form or *fetal alcohol effects* (FAE) or *alcohol-related birth defects* or *alcohol-related neurobehavioral disorder* if only a few behavioral or neurological symptoms are present.

The manifestations of FAS are mental retardation, poor coordination, loss of muscle tone, low birth weight, slow growth, malformation of organ systems, and peculiar facial characteristics, such as small eyes, drooping eyelids, and a misshapen mouth that looks like the mouth of a fish. These symptoms do not always appear together, but the chances for development of any or all of these effects increase according to the amount of alcohol drunk during pregnancy.

The mechanism by which alcohol affects the developing fetus is not known. Many normal, healthy children are born to women who have drunk heavily during pregnancy, so alcohol alone cannot be entirely responsible. As Abel and Sokol (1989) suggest, alcohol is a necessary but not a sufficient condition for FAS or FAE. Other factors that may be involved include (a) having previous children, (b) being black, (c) having a high score on an alcohol screening test, and (d) having a high percentage of drinking days. It also seems clear that occasional high levels of consumption do more damage than the same amount of alcohol consumed at chronic low levels (Abel & Sokol, 1989; Maier & West, 2001). It has also been suggested that high levels of acetaldehyde may be a factor (Hard, Einarson, & Koren, 2001).

Functional disruption neural of organization may occur in the formation of the cortex. It appears that alcohol is responsible for a disruption of cell migration in the cortex; only four layers, rather than the normal six layers, are formed. In addition, these cells may end up migrating to the wrong layer (Abel, 1989).

Apart from FAS, maternal alcohol consumption can affect growth. At ages 10 and 14, children of women who drank an average of one drink a day during the first 3 months of pregnancy were 4 pounds lighter than children born to nondrinking mothers. (Day et al., 2002).

There does not appear to be any time during pregnancy when it is safe to drink, but it seems clear from both human and nonhuman studies that drinking during early stages of pregnancy is most likely to be harmful. In fact, considerable harm can be done to the fetus before a woman even recognizes that she could be pregnant (Maier & West, 2001).

The only way to be certain of avoiding all these effects is to avoid alcohol completely during pregnancy (and during times when becoming pregnant is possible). If there is any drinking at all, high BALs should be avoided.

Heart Disease

Degeneration of the heart muscle, known as *alcoholic cardiomyopathy*, results directly from the chronic consumption of alcohol. This condition most likely arises from the effect alcohol has on the metabolism of the membrane of the cells of the heart muscle. The result is very similar to cirrhosis of the liver and was once described as "cirrhosis of the heart" (Myerson, 1971, p. 183).

Other Effects

Chronic use of alcohol may also be responsible for a number of other pathologies. These include diseases of the digestive system such as ulcers and cancer, inflammation and other disorders of the pancreas, pneumonia and other diseases of the lungs and respiratory system, abnormalities of the blood, and malnutrition.

It has been observed for some time that alcoholics are more susceptible to many infectious diseases and less responsive to treatment. The reasons for this susceptibility include differences in lifestyle, nutrition, and liver functioning, but it has become clear recently that alcohol has an adverse effect on all aspects of the functioning of the immune system, thus impairing the body's ability to resist and fight infections (Baker & Jerrells, 1993).

BENEFITS OF ALCOHOL CONSUMPTION

It is not unusual for substances that are physiologically stressful and toxic at high doses to be beneficial at low doses. This effect is called *hormesis* (Dudley, 2002). It may reflect an evolutionary adaptation to substances that an organism is naturally exposed to at low doses. The sort of exposure to alcohol experienced by our frugivore ancestors may have favored the evolution of metabolic adaptations to alcohol that maximize its benefits and minimize its harm.

Historically, alcohol has been used as a medicine. Avicenna, the tenth-century Persian physician, recommended wine for his older patients, although he cautioned his younger patients to drink it in moderation. Arnaud de Villeneuve, who reputedly invented brandy in the thirteenth century, hailed it as the water of immortality and called it *aqua vitae*, "water of life." He was convinced that it would increase longevity and maintain youth (W. A. McKim & Mishara, 1987).

There has been a great number of epidemiological studies that have plotted daily dose of alcohol against the relative risk of some or another health problem. Relative risk is calculated by dividing the incidence of a disease in people who use a given amount of alcohol by the incidence of that disease in people who do not consume any alcohol at all. Thus, if 5 percent of alcohol abstainers get cancer and 10 percent of heavy drinkers get cancer, then the relative risk of heavy drinkers is 2.0; that is, they are twice as likely to get cancer than abstainers. The relative risk of abstainers is always 1.0, and numbers less than 1 indicate a reduced risk of the disease. Figure 6-3 shows a plot of the relative risk of having an automobile accident against BALs.

When alcohol consumption is plotted against relative risk of coronary heart disease, the result is in the form of a "J" curve or a "U" curve, depending on the range of doses reported; that is, relative risk drops to numbers less than 1 for moderate consumption (usually defined as one or two drinks a day) but increases to higher numbers as daily consumption increases (Gunzerath et al., 2004). The relative risk of myocardial infarction (heart attack) is reduced by 25 percent in men who consume up to two drinks a day. In fact, it has been suggested that if all drinking of alcohol ceased, there would be about 80,000 more deaths from coronary heart disease each year in the United States (Pearson & Terry, 1994). This protective effect of alcohol is likely a result of the ability of alcohol to lower levels of low-density cholesterol and increase high-density cholesterol.

Another J-shaped risk curve with alcohol consumption has been reported for diabetes; moderate drinking reduces the incidence of type 2 diabetes. One study showed a 60 percent reduction associated with two drinks a day, but at three drinks a day this protective effect disappeared. And the incidence of diabetes increased as alcohol consumption increased above that level (Gunzerath et al., 2004).

Finally, because alcohol reduces blood clotting and reduces levels of low-density cholesterol that can clog arteries, it might be expected that alcohol would be able to increase blood flow to the brain and reduce the risk of ischemic strokes (caused by clots blocking arteries in the brain). In fact, there appears to be some beneficial effect of alcohol on dementia caused by diminished blood flow to the brain in older people but not on dementia caused by Alzheimer's disease. A J curve also has been shown for risk of ischemic strokes in the elderly, with two drinks a day giving the best protection but seven drinks a day increasing relative risk to 3.0 (Gunzerath et al., 2004).

In general, it appears that there are some beneficial effects to low and moderate alcohol consumption, but it seems that most of the conditions where alcohol is beneficial are those associated with aging. Young people are at relatively low risk of coronary heart disease, ischemic stroke, and diabetes. Therefore, they are not likely to benefit from any of the beneficial effects of alcohol but are exposed to all the risks of alcohol consumption, whereas older people are more likely to get some

benefit. Research has shown that for those under 60, increased alcohol consumption is related to increased risk of dying from any cause (no J curve), but for those over 60, the relative risk of dying was less for light and moderate drinkers than for heavy drinkers and abstainers. This relationship was the same for both sexes (Rehm & Sempos, 1995). It is possible that all this was foreseen a thousand years ago by Avicenna when he recommended wine for his older patients.

If alcohol has so many health benefits, should it be "prescribed" to abstainers? One article summed up the dilemma this way: "Nowhere in medicine is the double edged sword so sharp on both sides" (Sandridge, Zylstra, & Adams, 2004, p. 670). These authors believe that the beneficial effects could be offset by the risks of addiction, especially in people with a family history of alcoholism. They believe that patients should be informed of all the pros and cons and then be allowed to make a truly informed decision.

It must also be remembered that all this research is correlational, not experimental. It is possible that there is some third factor, such as general health, that correlates with alcohol consumption; for example, people who are generally healthy are less likely to get sick and are also more likely to be moderate alcohol consumers. Timothy Naimi and his colleagues at the Centers for Disease Control and Prevention in Atlanta, Georgia, analyzed the findings of a large-scale population health study and found many factors that correlated with both moderate alcohol consumption and reduced risk of cardiovascular disease. They point out that many of these factors are not measured in those studies that show that moderate alcohol consumption is associated with a lowered risk of cardiovascular disease, so there is no way of assessing their involvement in the relationship (Naimi et al., 2005).

TREATMENTS

Because there has been little agreement over the years about what alcoholism really is and why people drink, many types of treatments have been developed to help those who want to reduce their alcohol intake. It is usually agreed that the first step must be to eliminate physical dependence if it is present. This is usually done in a hospital or a detoxification center where the alcoholic goes through withdrawal under medical supervision until all withdrawal symptoms are over. Following detoxification, an active treatment phase may or may not be followed by a long-term program to prevent the recurrence of drinking (a *relapse*, in the language of physicians).

The nature of the therapy and its outcome goal are determined by how the therapist defines alcoholism. If alcoholism is considered a disease, theoretically it should be possible to cure the underlying disorder. The excessive drinking, which is a symptom, will then disappear. As mentioned earlier, there is little agreement on the nature of the underlying disorder, so this method of cure is not currently possible.

The reinforcement approach described earlier presumes that excessive drinking is a result of normal behavioral processes interacting in a maladaptive way with the environment. Treatments then aim to reestablish acceptable behavior patterns by using the behavioral principles of conditioning and instrumental learning that have been developed to change other abnormal or undesirable behavior patterns.

In practical terms, there is little difference between the disease model approach and the reinforcement approach. Both are aimed at changing the behavior of alcoholics. The disease approach differs from the reinforcement approach in one basic way: The disease approach insists that because the disease cannot be cured, the aim of all therapy must be total abstinence from alcohol.

Alcoholics Anonymous

Alcoholics Anonymous (AA) was founded in 1935. It grew out of the Oxford Movement, a popular Protestant religious movement in which small groups met weekly for prayer, worship, and discussion, with the aim of self-improvement. One Oxford group meeting in Akron, Ohio, was

attended by an alcoholic stockbroker and an alcoholic physician, both of whom were seriously but unsuccessfully trying to stop drinking. They found that their fellowship and that of the group helped them to stop drinking. They brought other alcoholics into the group, and many had similar success. In fact, helping other alcoholics to stay sober seemed to be making an important contribution to the maintenance of their own sobriety. As the meetings got bigger, new groups were formed, and eventually they broke away from the Oxford Movement and became AA (Alcoholics Anonymous, 1980).

The organization has grown rapidly and spread around the world. In 1982 there were 20,000 groups in 100 countries, and the estimated world membership was well over 1 million (Maxwell, 1984, p. 2). As of January 1, 2005, AA estimates that there are almost 105,000 groups and a membership of 2 million (Alcoholics Anonymous, 2005).

Although AA broke away from the Oxford Movement, it has retained many of the elements that seemed to be responsible for its effectiveness, including religion, although this aspect can be moderated to suit each individual.

At every meeting of AA, someone reads the 12 steps and the 12 traditions that explain the basic principles and processes the organization has found to be effective over the years (Alcoholics Anonymous, 1998). The AA approach, also known as the 12-steps approach, has been adapted to many other support groups for people who have problems controlling gambling, overeating, and the use of other drugs.

AA is not a temperance organization. The temperance movement is religion based and made up largely of individuals who are not alcoholics and have never had a drinking problem but wish to impose their views about alcohol on others. AA is made up of alcoholics. AA members are not antiliquor and do not seek to impose their views on anyone else. The organization exists only to help alcoholics who want to achieve sobriety.

The AA approach to alcoholism coincides with the disease model discussed earlier. Most AA members believe that to control drinking, the individual must first admit to being "powerless over alcohol" and unable to control drinking without help. AA members believe that drinking can be controlled only by relying on a greater power, often identified as "God," or "God as we have come to understand Him" (or Her) for people who are uncomfortable with the concept. They feel that there is no cure; there are only alcoholics who drink and alcoholics who do not drink. For this reason, members are expected to attend regular meetings for extended periods of time. It is not unusual for new members to attend more than six meetings a week. (In fact, there is a tradition of new members doing "90 meetings in 90 days.") In addition to attending meetings, members often see each other socially outside of meetings and frequently talk on the phone, especially if stress or desire for alcohol is threatening a member's resolve (Maxwell, 1984). For many people, AA is not a treatment at all; it is a long-term commitment and a way of life. It has been estimated that AA is currently helping as many alcoholics in the United States as all medical facilities combined. It has been estimated that about 5 percent of all alcoholics are affiliated with AA (Finagrette, 1988, p. 89).

There can be no doubt that AA is very effective for many drinkers. In fact, it has been claimed that participation in AA is the most effective treatment, but this is a difficult claim to test, largely because AA does not permit itself to be subjected to the same close scientific evaluation that other treatment techniques must undergo. In addition, the persons who try and stick with AA are most likely to have a high socioeconomic status and a stable social situation, are highly motivated to quit, are between ages 40 and 45, and have spouses who help with the treatment (Baekeland, 1977). These are the best candidates for help, no matter what the treatment (Ogbourne & Glaser, 1981).

Vaillant has suggested that one reason why AA works is that it provides alternative sources of reinforcement and keeps the alcoholic busily engaged in activities that are incompatible with drinking alcohol. AA provides a busy schedule of social and

service activities with supportive former drinkers, especially at times of high risk (e.g., holidays). AA requires members to "work the program" and encourages returning again and again to group meetings and to sponsors who provide an external conscience (Vaillant, 1992, p. 52).

Treatment with Other Drugs

Antabuse. Antabuse (disulfiram) blocks the action acetaldehyde dehydrogenase. Drinking alcohol with this enzyme out of commission will cause a buildup of acetaldehyde in the body, which makes a person feel very sick. If alcohol is not consumed, the drug has little effect. Therefore, a person taking the enzyme blocker cannot drink without getting sick. It is frequently prescribed for alcoholics as an adjunct to other therapies, but it can work only if the alcoholic takes it regularly. Some studies with disulfiram show fairly high alcohol abstinence rates among those who take the drug regularly, but properly controlled clinical trials with random assignment to groups have failed to show that disulfiram is superior to a placebo (Gorelick, 1993). Antabuse offers some protection from unplanned or spontaneous drinking, but a patient who wants to drink can simply stop taking the drug. Antabuse, however, has proven effective when used in conjunction with treatment programs such as the Community Reinforcement Approach (discussed later in this chapter).

There have been encouraging results from using drugs that specifically operate on the serotonin system. The most studied drugs in this regard are selective serotonin reuptake inhibitors (SSRIs; see Chapter 14), which increase levels of serotonin in the synapse. A series of studies at the Addiction Research Foundation in Toronto found that fluoxetine and sertraline, drugs normally used as antidepressants, reduced alcohol intake by 9 to 14 percent and increased the number of abstinent days in volunteer subjects who were described as heavy social drinkers or early problem drinkers. The result has been replicated with alcoholics (Gorelick, 1993).

A number of other drugs have also been shown to reduce alcohol consumption in both humans and laboratory animals, including drugs that stimulate 5-HT_{1A} receptors (buspirone) and drugs that block either 5-HT_2 (ritanserin) or 5-H_3 receptors (ondansetron). It seems that the SSRIs reduce all consummatory behavior, but the effect of these drugs seems to be more specific in reducing alcohol consumption (Litten & Allen, 1993).

Why do both agonists and antagonists of serotonin receptors show this effect? Many of these drugs are also used clinically as antidepressants, and alcohol abusers are frequently found to be clinically depressed. Interestingly, the alcohol-suppressing effect is evident as soon as the drug is taken, but the antidepressant effects usually do not show up for several weeks (see Chapter 14). Serotonin is involved in a complex way with the neurophysiology of alcohol consumption. In particular, serotonin is involved in the release of dopamine in the mesolimbic dopamine system.

Other Drugs. There is also evidence that the dopamine D_2 receptor agonist (bromocriptine) and the opiate receptor blocker (naltrexone) are effective in reducing alcohol consumption in laboratory animals and in human alcoholics (Litten & Allen, 1993).

Behavior Therapy

Behavior therapists treat alcohol drinking like any other positively reinforced response and try to stop drinking by reinforcing behaviors that are not compatible with drinking (Caddy & Block, 1983).

Community Reinforcement Approach. If competing sources of reinforcement can reduce the use of alcohol, as discussed in Chapter 5, might it be possible to teach people to take advantage of other sources of reinforcement and reduce their dependence on alcohol? Training in social skills (such as how to get and hold a job) or more effective ways of relating to people, teaching and encouraging recreational activities, and improving family relations are often incorporated into

treatment programs. Because interpersonal relationships and social support are also seen as important, it is becoming more common to incorporate the entire family of the alcoholic into the therapeutic process (Higgins, 1997).

Relapse Prevention. It is also known that relapse to drinking is more likely to occur in circumstances in which a person (a) feels angry or frustrated with a personal or social situation or (b) is under social pressure to drink. One approach, developed by G. A. Marlatt and his associates (W. H. George & Marlatt, 1983), stresses identification of situations that cause a high risk of relapse to excessive drinking and training of coping responses to each situation so that the individual will feel in control and will not need to resort to alcohol.

CHAPTER SUMMARY

- Ethyl alcohol is created during the fermentation of the sugar contained in fruits and grains. Fermented beverages, such as wine and beer, have a low alcohol content (10 to 15 percent). The concentration of alcohol can be increased by distillation. The result is hard liquor, which usually has an alcohol content of 40 to 50 percent.
- Alcohol content can be given as a percent by weight or volume. Because the specific gravity of alcohol is .79, there is more alcohol in a percent by weight than the same percent by volume.
- Alcohol has been consumed in fermented fruit by our fruit-eating ancestors for millions of years but has been deliberately made for only about the past 10,000 years.
- Alcohol consumption in the United States has cycled through highs and lows. Currently, its use is declining.
- Alcohol levels in the blood can be measured with a Breathalyzer and are usually reported in terms of percentage, or milligrams of alcohol in 100 milliliters of blood, or in SI units.
- Alcohol is consumed orally. It is absorbed quickly and distributed evenly in body water. It easily crosses the blood–brain barrier and the placental barrier.
- Most of the alcohol consumed is metabolized by the enzyme alcohol dehydrogenase at a constant rate, which averages about 15 mg per 100 ml of blood per hour.
- Alcohol does not have a specific receptor site but is known to alter the functioning of neurotransmitters, including glutamate, by blocking the NMDA receptor. GABA and serotonin are also altered by alcohol.
- Even at low levels, alcohol disrupts performance and can interfere with complex activities. It generally causes feelings of happiness and reduces the ability of aversive events to control behavior. Higher doses cause loud, vigorous behavior, and even higher doses cause loss of consciousness and, finally, death.
- Alcohol can cause memory disruption in the form of either a grayout (fragmentary memory loss due to dissociation) or an en bloc blackout (complete loss of the ability to form new memories while intoxicated).
- Increasing BAL is associated with an increased risk of being involved in an automobile accident, and the risk is much higher in young and inexperienced drivers.
- The discriminative stimulus effects are similar to the barbiturates and can be blocked by a serotonin receptor blocker.
- Tolerance develops to the effects of alcohol through many different processes. Alcohol causes physical dependence, and the withdrawal symptoms of the late major type (delirium tremens) can be quite severe and may even cause death if not treated.
- Both humans and nonhumans self-administer alcohol in a similar pattern involving binges and erratic periods of abstinence. Consumption is influenced by culture, gender, age, and availability.
- There are many explanations of excessive drinking or alcoholism. The disease model claims that alcoholism is a disease and that alcoholics are different from nonalcoholics even before they start drinking. In addition, because of "loss of control," alcoholics can never drink in moderation and are unable to control their drinking.
- There is little evidence to support alcohol loss of control in alcoholics, and only small differences have been found between those with a positive family history of alcoholism and those with a negative family history.

- Alcohol can cause physical dependence. It also causes a hangover.
- Alcohol has many harmful effects, including death by respiratory suppression in high doses. Acute effects can cause both industrial and automobile accidents, and continuous use can cause cirrhosis of the liver, Wernicke–Korsakoff syndrome, and various types of cancer and heart disease. In addition, if taken during pregnancy, alcohol can cause various malformations of the fetus known as fetal alcohol syndrome (FAS) or alcohol-related neurobehavioral disorder (ARND).
- Low to moderate levels of alcohol consumption can have health benefits, including reduction in the risk of cardiac disease and stroke.
- Excessive alcohol use, or alcoholism, can be treated, but success rates are low.
- There are numerous treatments for alcoholism, including Alcoholics Anonymous, treatment with other drugs including disulfiram and SSRIs, community reinforcement, and relapse prevention training.