

## CHAPTER 3

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# CARDIOVASCULAR RISK FACTORS

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## INTRODUCTION

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More than 68 million Americans currently have one or more forms of cardiovascular disease, according to the latest estimates from the federal government's National Center for Health Statistics. Many more are said to be at *risk* for developing one of these serious diseases. The concept of risk factors has evolved only over the past 45 years or so, and new factors are periodically added to the list as our comprehension of the disease process grows. To understand who is at risk and what risk actually means to an individual, one first needs to understand how diseases of the heart and circulatory system—particularly heart attacks—develop.

All heart attacks, with rare exceptions, are caused by atherosclerosis, or a narrowing and “hardening” of the coronary arteries resulting from fatty deposits called plaque. This process, by which the wall of the artery is infiltrated by deposits of cholesterol and calcium, narrows the lumen (the internal orifice) of the artery. When the degree of narrowing reaches a critical level, blood flow to the portion of the heart supplied by that artery is stopped and injury to the heart muscle—a heart attack—occurs. If the reduction in blood flow is not total and is only temporary, relative to muscle needs, permanent damage does not result but the individual may experience angina pectoris—

chest pain as a result of too little blood and oxygen to a portion of the heart in response to its needs (a process called ischemia). Atherosclerosis also occurs in other blood vessels, such as the carotid artery, which carries blood to the brain, or the arteries that provide blood to the legs, and can lead to similar problems. Significant atherosclerosis in the arteries supplying the brain may cause transient ischemic attacks (TIAs) or strokes, while peripheral arterial blood vessel disease, with intermittent claudication (pain on walking or similar activity), occurs when there is significant atherosclerosis in the arteries in the legs.

The fact that atherosclerotic plaque is largely made up of cholesterol has been known since the middle of the 19th century. Only in the 20th century, however, when general hygienic measures greatly reduced the toll from infectious diseases and allowed people to live considerably longer, did we realize the enormous impact of atherosclerosis on general health. By the 1930s and 1940s, the death rate in the United States from atherosclerotic heart disease was increasing at an alarming rate and it was clear that we were in the grips of a cardiovascular disease epidemic. The reasons for this epidemic were not entirely clear. Some scientists were convinced that there was a single cause for atherosclerosis—dietary fat and cholesterol—while others were more impressed by the association of high blood pressure or cigarette smoking with heart attacks. Most researchers fa-

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vored the theory that there had to be multiple causes for atherosclerosis, although precisely what they were was debatable.

After World War II, the first large-scale, comprehensive study to determine the causes of atherosclerotic heart disease, the Framingham Heart Study, was begun. In 1948, researchers in the town of Framingham, Massachusetts, a suburb of Boston, enrolled 5,209 local residents, ranging in age from 30 to 62, in the study. They began examining the participants every two years, and they continue to do so. In the early 1970s, 5,135 adult offspring of the original participants joined the study.

Within a short time, the Framingham investigators established that there are, indeed, many factors that predispose an individual to the development of atherosclerosis. The list of these factors, now called cardiovascular risk factors (a term coined by Dr. William Kannel, the first director of the Framingham study), continues to grow as the information from Framingham and numerous other studies becomes available and we learn more about the possible causes of atherosclerotic disease.

This chapter defines cardiovascular risk factors, classifies them, briefly describes how they interact, and discusses what individuals and their physicians can do about them.

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## HOW RISK FACTORS ARE IDENTIFIED

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A cardiovascular risk factor is a condition that is associated with an increased risk of developing cardiovascular disease. The association is almost always a statistical one, and so the fact that a particular person has a particular factor merely increases the *probability* of developing a certain type of cardiovascular disease it does not mean that he or she is certain to develop heart or blood vessel disease. Conversely, the fact that an individual does not have a particular cardiovascular risk factor (or for that matter, *any* of the known cardiovascular risk factors) does not guarantee protection against heart disease. Even today, a number of individuals who have heart attacks or strokes have none of the identified risk factors.

The box "Cardiovascular Risk Factors" lists the currently accepted cardiovascular risk factors. To understand how this list was compiled, one must know a little about epidemiology and how its techniques have been applied to identify risk factors.

### Cardiovascular Risk Factors

#### Risk Factors That Cannot Be Changed

Age  
Gender  
Heredity

#### Risk Factors That Can Be Changed

High blood pressure  
Elevated serum cholesterol  
Lipoprotein (a)  
Cigarette smoking  
Obesity  
Glucose intolerance  
Diabetes  
Fibrinogen  
Left ventricular hypertrophy  
Cocaine  
Behavioral factors (stress, Type A)

#### Protective Factors

HDL cholesterol  
Exercise  
Estrogen  
Moderate alcohol intake

The epidemiologist studies populations. He or she begins by selecting a group that is representative of the population to which the information will later be applied. To examine the cause of atherosclerosis, for example, the study group selected should be largely composed of young and middle-aged adults who have no evidence of cardiovascular disease when the study begins. Because the differences between individuals will be small, the group must be large enough to allow the relationships between the factors being studied and the disease to become evident and to enable researchers to draw conclusions about these relationships. While earlier studies were limited to much smaller groups, the advent of computers has enabled epidemiologists to collect and analyze enormous amounts of data and to study very large groups or populations, sometimes numbering hundreds of thousands.

The study group must be followed for a considerable length of time. A chronic disease such as atherosclerosis, which has many causes and usually requires years for signs or symptoms of heart disease to develop, requires multiple observations over many years to determine how each potential risk factor is changing and interacting with the others.

For any epidemiological survey to be helpful, the appropriate factors must be studied. None of the risk factors on the currently accepted list got there by chance; each resulted from careful observations and

educated guesses. For example, researchers knew that men had heart attacks more often than women. Likewise, older people have more vascular disease than children, while people with high blood pressure have more strokes than those with normal pressure.

And finally, for epidemiologic surveys to be valid, each factor studied and each clinical event (an objectively defined, observable disease process, such as a heart attack) that occurs during the study must be accurately and precisely measured. Epidemiologists have learned to standardize blood pressure and various laboratory measurements, for example, to ensure that study participants are evaluated equally. Early surveys relied upon information from death certificates, which were not always accurate. Contemporary studies have access to more detailed and accurate medical records, as well as to sophisticated laboratory tests and diagnostic equipment.

For a “candidate” cardiovascular risk factor to become a permanent member of the list, it must meet several criteria:

- The statistical association between the factor and cardiovascular disease must be strong. Generally, the presence of the factor should at least double the risk of disease. Epidemiologists consider anything less than this to be a weak association.
- The association should be consistent. The risk factor should produce disease regardless of gender, age, or race, and the association should be present in all or most of the studies in which it has been evaluated.
- The association must make biological sense. A factor may appear to be related statistically to a disease, but unless such a relationship is biologically plausible, the statistical association may have little meaning.
- The impact of the proposed risk factor should be able to be demonstrated experimentally in the laboratory. (This is usually, but not always, feasible.)
- Treatment that favorably changes the risk factor should reduce the incidence of disease. This has been achieved for some, but by no means all, of the factors listed in Table 3.1.
- The factor must make an independent contribution to increasing an individual’s risk of developing disease. Some factors studied were found merely to occur together with another, genuine cardiovascular risk factor.

A statistical technique called multivariate analysis allows researchers to tease out true associations from those that appear to contribute but do not do so independently. A good example is coffee drinking, which seemed at first to be associated with an increased risk of heart disease. Multivariate analysis showed that the association was not independent, but rather due to the fact that many people smoke cigarettes when they drink coffee. When this fact was taken into account, it became clear that the real villain is the cigarette, not the caffeine.

Some cardiovascular risk factors are dichotomous; that is, they are either present or absent. Male gender and family history are two examples. Most risk factors, however, are continuous; that is, above a certain threshold level, risk rises as the strength or severity of the risk factor rises. For example, the more cigarettes smoked a day, the greater the risk of heart disease. This is also called a “dose-response.”

The risk may rise dramatically when the strength of the risk factor exceeds a certain level. Blood pressure and blood cholesterol levels are typical of such risk factors. For both of these, there is a very small increase in risk as the level rises within the range considered “normal.” This increased risk is so small that any attempt to lower it would not improve overall outlook. At the other end of the scale, there is a point (90 mm Hg for diastolic blood pressure and 240 mg/dl for serum cholesterol) above which risk increases substantially.

It is now possible to estimate quantitatively an individual’s cardiovascular risk. This technique employs data gathered from epidemiologic surveys attributing varying levels of risk to such factors as blood pressure, serum cholesterol, age, and number of cigarettes smoked per day. (See Table 3.1.) Within seconds, an individual’s probability of having a heart attack in a defined period of time can be calculated. This approach also shows that the impact of risk factors is at least additive and possibly multiplicative. What this means is that an individual’s risk is determined in part by the number of risk factors present, as well as the level of each individual factor. (See Figure 3.1.) For example, someone who has mildly elevated blood pressure *and* serum cholesterol may bear greater risk of sustaining a heart attack or stroke than would an individual with even higher blood pressure whose serum cholesterol is normal.

This compounding effect has a number of important implications for individuals. First, it is not sensible to view the risk of having heart disease as great or small on the basis of a single risk factor. Second, a treatment program for risk factor reduction must

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Table 3.1  
Coronary Heart Disease Risk Factor Prediction Chart-Framingham Heart Study

. Find Points for Each Risk Factor							
Age (if female)		Age (if male)		HDL cholesterol	Total cholesterol	systolic blood pressure	
Age Pts.	Age Pts.	Age Pts.	Age Pts.	HDL C Pts.	Total C Pts.	SBP Pts.	Other Pts.
30 -12	47-48 5	30 -2	57-59 13	25-26 7	139-151 - 3	98-104 -2	cigarettes 4
31 -11	49-50 6	31 -1	60-61 14	27-29 6	152-166 - 2	105-112 -1	Diabetic— 3
32 -9	51-52 7	32-33 0	62-64 15	30-32 5	167-182 - 1	113-120 0	male Diabetic— 6
33 -8	53-55 8	34 1	65-67 16	33-35 4	183-199 0	121-129 1	Female ECG— 9
34 -6	56-60 9	35-36 2	68-70 17	36-38 3	200-219 1	130-139 2	LVH
35 -5	N-67 10	37-38 3	71-73 18	39-42 2	220-239 2	140-149 3	0 points for each no
36 -4	68-74 11	39 4	74 19	43-46 1	240-262 3	150-160 4	
37 -3		40-41 5		47-50 0	263-288 4	161-172 5	
38 -2		42-43 6		51-55 -1	289-315 5	173-185 6	
39 -1		44-45 7		56-60 -2	316-330 6		
40 0		46-47 8		61-66 -3			
41 1		48-49 9		67-73 -4			
42-43 2		50-51 10		74-80 -5			
44 3		52-54 11		81-87 -6			
45-46 4		55-56 12		88-96 -7			

2. Sum Points For All Risk Factors-Framingham Heart Study

_____	+	_____	+	_____	+	_____	+	_____	+	_____	+	_____	=	_____
Age	"	HDL C	Total C	SBP	Smoker	Diabetes	ECG-LVH							Point total

Note: Minus points subtract from total.

3. Look Up Risk Corresponding to Point Total										4. Compare to Average 10-Year Risk				
Probability of CHD			Probability of CHD			Probability of CHD			Probability of CHD			Probability		
Pts.	5 Yr.	10 Yr.	Pts.	5 Yr.	10 Yr.	Pts.	5 Yr.	10 Yr.	1%.	5 Yr.	10 Yr.	Age	Women	Men
<1	<1%	<2%	10	2 %	6%	19	8%	16%	28	19%	33%	30-34	<1%	3%
2	1%	2%	11	3%	6%	20	8%	18%	29	20%	36%	35-39	<1%	5%
3	1%	2%	12	3%	7%	21	9%	19%	30	22%	38%	40-44	2%	6%
4	1%	2%	13	3%	8%	22	11%	21%	31	24%	40%	45-49	5%	10%
5	1%	3%	14	4%	9%	23	12%	23%	32	25%	42%	50-54	8%	14%
6	1%	3%	15	5%	10%	24	13%	25%				55-59	12%	16%
7	1%	4%	16	5%	12%	25	14%	27%				60-64	13%	21%
8	2%	4%	17	6%	13%	26	16%	29%				65-69	9%	30%
9	2%	5%	18	7%	14%	27	17%	31%				70-74	12%	24%

## Using Table 3.1

Table 3.1 was created using data from the Framingham Heart Study to help individuals determine their risk of developing coronary heart disease in five or ten years. It represents a first attempt at developing a data-based tool that patients and their physicians can use as a starting point for a discussion of modifying behavior.

Although the Framingham database is one of the most comprehensive available, it has some limitations. For example, it may be less accurate for African-Americans than for whites. The table has been criticized by some for its inclusion of both total cholesterol and HDL cholesterol, thereby perhaps giving extra weight to cholesterol as a risk factor. The table also indicates that an electrocardiogram is necessary to determine if left ventricular hypertrophy is present.

Nevertheless, the table is useful as a general tool for individuals to use in estimating their risk of developing coronary heart disease and comparing their risk to the average. They can also use it to see how changing a modifiable risk factor may affect their total risk. For example, a person who is a smoker can look at the difference in risk if smoking is stopped. Likewise, someone with elevated cholesterol can look at the effect of lowering it. Modifying a single risk factor may affect life expectancy by as much as eight years; when there are strong and multiple risk factors the effect can be substantial. Life expectancy is not the only reason to consider changing risk-prone behavior. Behavioral changes can also have a very positive effect on the quality of life.

be comprehensive. Third, it is likely that measures to prevent atherosclerotic heart disease and stroke will be most beneficial in those with the highest risk, and difficult to prove in those with only a minimally increased chance of developing these diseases.

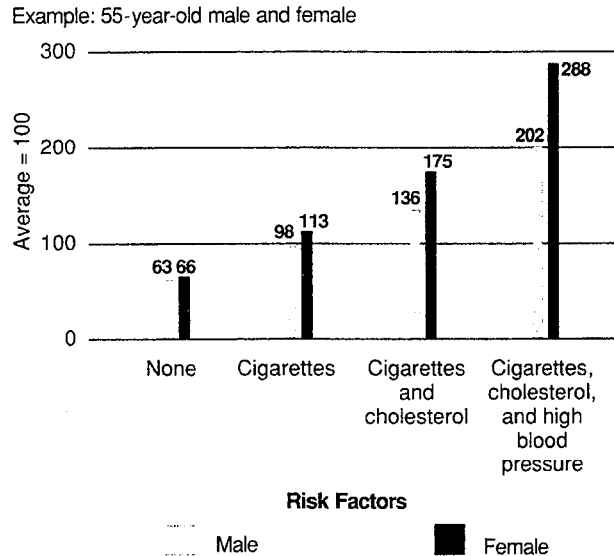
## THE EFFECT OF MODIFYING RISK FACTORS

Taking action that modifies a risk factor does not necessarily imply that the probability of a heart disease or stroke will be eliminated. Furthermore, when a strong risk factor is present, treating it—even if the treatment is very effective—does not necessarily mean that the risk is reduced. Fortunately, treatment

Figure 3.1

### Danger of Heart Attack By Risk Factors Present

This chart shows how a combination of three major risk factors can increase the likelihood of heart attack. For purposes of illustration, this chart uses an abnormal blood pressure level of 150 systolic and a cholesterol level of 260 in a 55-year-old male and female.



Source: Framingham Heart Study, Section 37: The Probability of Developing Certain Cardiovascular Diseases in Eight Years at Specified Values of Some Characteristics (Aug. 1987).

of the major risk factors—smoking, high blood pressure, and elevated cholesterol levels—has been shown to reduce the possibility of a heart attack.

In general, it is a monumental scientific undertaking to demonstrate that treatment or modification of a risk factor reduces the number of heart attacks, strokes, or other cardiovascular diseases. Because atherosclerosis has many causes and is almost always present in some degree in all of us, studies to show that a specific treatment works are difficult to design. Furthermore, the results may be hard to interpret and apply to the general population.

For a study of a proposed treatment (usually called a clinical trial) to be valid, it must have a control: The treatment must be tested against another treatment or against no treatment at all. (“Treatment” in a clinical trial might mean a drug or a modification in behavior such as exercising more or eating less saturated fat.) Volunteers enrolled in such a study must be representative of the patients in whom the treatment will be used. For example, if the subjects already have advanced atherosclerosis, the treatment used may appear ineffective, when in fact it might have been successful if started earlier in the course of the disease. If the subjects are at very low risk, the treatment may not appear to work because the like-

likelihood that disease would develop is so small. It would be hard in this case to show a difference between the treatment and the control groups.

Investigators who conduct clinical trials must carefully define the population to be studied and the particular cardiovascular benefit they hope to achieve. Some treatments studied have mistakenly been judged ineffective when, in fact, the trial was simply too small or did not last long enough to show the benefit expected.

Unfortunately, too, clinical trials designed to evaluate the benefits or risks of therapy with respect to clinical events take a long time to complete. Because of the enormous effort and cost, it is impossible to devise ideal tests for every new and allegedly better approach to therapy. Physicians must analyze the findings from both epidemiologic surveys and clinical trials, synthesize the data, incorporate new information, and then apply it to individual patients. That is a difficult task.

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## RISK FACTORS THAT CANNOT BE CHANGED

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### AGE

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**The** risk of cardiovascular events increases as we get older. In many epidemiologic surveys, age remains one of the strongest predictors of disease. More than half of those who have heart attacks are 65 or older, and about four out of five who die of such attacks are over age 65.

Of course, nothing can be done to reduce age. However, careful attention to diet and maintaining fitness may delay the degenerative changes associated with aging.

### GENDER

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Men are more likely than women to develop coronary heart disease, stroke, and other cardiovascular diseases that are manifestations of atherosclerosis. Whether this is because male hormones—*androgens*—increase risk or because female hormones—*estrogens*—protect against atherosclerosis is not completely understood. It is likely that both play a role, but that the protective role of estrogens is the predominant factor. This seems to be supported by the fact that heart disease risk for women rises dra-

matically after menopause, when their bodies stop producing estrogen. Nevertheless, coronary heart disease is the number one cause of death among American women.

Women in the United States currently live an average of six years longer than men. Recently, some studies have suggested that much of the difference in life expectancy can be explained by the fact that more men than women smoke cigarettes. As more teenage girls are starting to smoke than are teenage boys, this advantage may disappear. Should this trend go unchecked, women may soon have as much coronary heart disease and other complications of cigarette smoking as do men, or more.

### HEREDITY

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There is no question that some people have a significantly greater likelihood of having a heart attack or stroke because they have inherited a tendency from their parents. In some instances, such as familial hypercholesterolemia (very high levels of cholesterol in the blood), the pattern of inheritance is well understood and the specific biochemical defects are well characterized. For most cardiovascular risk factors, however, the specific way in which inheritance plays a role is not at all clear. As in almost all situations in medicine, both heredity and environment play a role and it is often difficult to know where one stops and the other begins. Prior generations did not have the level of medical care we now enjoy, nor the general awareness about health; the details of the illness that one's grandparents or even parents had may not be precise. Prior to the 1960s, many more people smoked and little attention, if any, was paid to diet and fitness. So it **is** possible that environmental factors, not genes, were responsible for Grandpa's heart attack or stroke.

In practical terms, anyone who has a family history of heart disease that occurred at an early age (below 55) should be especially careful to reduce the impact of any risk that can be controlled. Even if one can successfully control known risk factors, there are, unfortunately, a number of inherited characteristics that we have not yet identified and so cannot favorably affect. Individuals with a history of atherosclerotic cardiovascular disease in the family simply have to be more vigilant if they wish to avoid heart attacks and strokes. We should remember, however, that almost every family has some member who died of a heart or blood vessel disease, since about half of all deaths are attributable to these diseases. If these ep-

isodes occurred in relatives who were 75 or 80, it may not be a major cause for concern.

Heredity also includes race. For reasons that are not completely understood, African-Americans have considerably higher rates of diabetes and both moderate and severe high blood pressure, adding to their overall risk of heart disease. (For more information, see below and Chapter 22.)

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## RISK FACTORS THAT CAN BE CHANGED

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### HIGH BLOOD PRESSURE

High blood pressure, or hypertension, is the risk factor that affects the greatest number of Americans and the one we know the most about. Estimates vary according to the source, but anywhere from 35 million to more than 60 million Americans have elevated blood pressure.

There are several ways to classify hypertension. It is generally agreed that high blood pressure is defined as readings that consistently exceed 140/90 mm Hg, when measured over a period of time with a blood pressure cuff (sphygmomanometer). Experts focused on diastolic blood pressure, the lower of the two numbers, which represents the resting pressure between heartbeats. Anyone with a reading equal to or greater than 90 mm Hg has diastolic hypertension, regardless of the level of the higher number, which represents the systolic, or pumping, pressure.

Some individuals, particularly those over 65 or 70 years of age, have what is called isolated *systolic* hypertension. The most recent expert committee defines this as a systolic blood pressure of 160 mm Hg or more, when the diastolic blood pressure is less than 90 mm Hg.

Actually, the levels of both systolic and diastolic blood pressures determine an individual's risk. In fact, of the two readings, the systolic blood pressure may be the superior predictor of all the complications we attribute to hypertension.

The most reliable early information on high blood pressure comes from the Framingham Heart Study, which showed early on that as both the systolic and diastolic blood pressure levels rise, the likelihood that an individual might develop coronary heart disease, stroke, congestive heart failure, peripheral vascular disease, and kidney problems rises as well. The association is strongest for stroke, although it is highly

significant for other cardiovascular diseases, too. The Framingham Heart Study also showed that people with hypertension had a higher death rate, when all causes were added together, than did those with normal readings. All of these findings have been amply confirmed by many other studies and apply to both men and women, as well as to people in their 60s and 70s and beyond.

Hypertension is a special problem for African-Americans. Overall, the percentage of blacks in the United States with hypertension is 50 percent greater than that of whites or Asians. Black men under the age of 45 are particularly prone to developing kidney failure from hypertension, eventually requiring dialysis or a kidney transplant. Blacks are also more likely than whites to have heart enlargement as a result of hypertension and ultimately to have congestive heart failure.

Hypertension often occurs together with other cardiovascular risk factors, particularly obesity, elevated levels of cholesterol and triglycerides, and diabetes mellitus. This suggests that there may be a common cause for these conditions, but it may simply be that an environmental factor, such as overeating, may lead to some or all of these problems.

There is a wealth of studies to show that successfully treating hypertension will substantially reduce the increased risk associated with it. Fortunately, too, we now have many well-tolerated antihypertensive medications that lower blood pressure and can be taken indefinitely. Although most of the treatment data are based on drugs, such measures as weight loss, salt restriction, and exercise may also lower blood pressure. As yet, however, no long-term studies have shown convincingly that these life-style changes are as successful as drugs in preventing strokes and other complications of hypertension. (For more information, see Chapter 12.)

### HIGH BLOOD CHOLESTEROL AND RELATED LIPID PROBLEMS

Elevated levels of serum lipids (cholesterol and triglycerides) are extremely common and are one of the most important of the heart disease risk factors that can be changed. Yet, there is considerable confusion about the role of cholesterol as a cardiovascular risk factor. (See Chapter 4.)

Epidemiologic studies have shown that the level of total cholesterol in the blood is a strong predictor of the likelihood that an individual will develop coronary heart disease and, to a much lesser degree, a stroke. Most experts consider levels under 200 mg/dl

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to be normal and those between 200 and 239 mg/dl to be borderline high. Levels above 240 mg/dl present an increased risk for a heart attack—more than double the risk of levels below 200 mg/dl. About one out of four Americans falls into this latter category.

Total cholesterol levels are made up of several fractions. The most important and best studied are high-density lipoproteins (HDL cholesterol, or HDL-C) and low-density lipoproteins (LDL-C). These levels and their relationship to each other maybe more important than total cholesterol levels in predicting heart disease risk. LDL levels over 160 mg/dl are definitely associated with increased risk, while values from 130 to 159 mg/dl are borderline. In contrast, HDL cholesterol is the fraction of cholesterol that appears to protect against coronary heart disease. The higher the level of HDL, the lower the risk. Ideally, it should be at least 35 mg/dl. A ratio of LDL to HDL greater than 3.5 or 4:1 is generally agreed to increase risk.

Many studies have failed to show an independent contribution to coronary heart disease risk from an elevation of triglycerides, another fatty component in the blood. Recent data, however, suggest that triglycerides may be an important predictor of risk, especially in women and those with diabetes mellitus.

While an individual's lipid profile is affected by age (total cholesterol rises with the years), gender (women tend to have higher levels of HDL), and heredity (elevated cholesterol and triglycerides tend to run in families, and certain families have extremely high levels), the picture can be significantly changed by life-style modifications. A diet low in saturated fat and cholesterol will lower serum cholesterol an average of 5 percent, but this diet maybe more effective in some people. The general rule of thumb is that risk of coronary heart disease decreases by 2 percent for every 1 percent drop in total serum cholesterol.

Reducing alcohol intake in heavy drinkers and (for those who are overweight) body weight can significantly reduce triglyceride levels. Regular exercise will lower triglycerides and increase HDL cholesterol, and stopping smoking will also raise HDL cholesterol. For people with very high total cholesterol and LDL cholesterol levels, diet and exercise alone may not result in a great enough reduction, and these life-style measures may need to be combined with cholesterol-lowering drugs. (See Chapter 23.)

### Lp(a)

Lipoprotein (a) or "Lp little a" was discovered in 1963, but its importance was not appreciated until recently.

Lp(a) is a molecule composed of the protein portion of low-density lipoprotein (LDL), which is called apoB<sub>100</sub>, and another protein called ape(a). Ape(a) is very similar chemically to plasminogen, a naturally occurring substance that participates in dissolving clots that form in the bloodstream. Lp(a) has the opposite effect, however. It interferes with the normal process of clot lysis (dissolving) and thus may increase the likelihood that once a clot forms, a heart attack or stroke will occur.

Recent epidemiologic studies have shown that increased Lp(a) levels are associated with a greater frequency of coronary artery disease, increased clogging (stenosis) of coronary artery bypass grafts, and stroke (cerebrovascular disease). The impact of Lp(a) levels on the risk of coronary heart disease is as strong as that seen with total cholesterol levels or reduced high-density lipoprotein (HDL) levels, and the increase in risk attributable to high Lp(a) levels is independent of other risk factors. At this time, of the drugs available, only nicotinic acid seems to lower Lp(a) levels. Whether this reduction decreases the risk of developing disease is still unclear.

## CIGARETTE SMOKING

Cigarette smoking is a major contributor to coronary heart disease, stroke, and peripheral vascular disease—even though smokers tend to be thinner and to have lower blood pressure than nonsmokers. Overall, it has been estimated that 30 to 40 percent of the approximately 500,000 deaths from coronary heart disease each year can be attributed to smoking. Individuals who smoke, regardless of their level of other risk factors or family history, are at significant risk of premature coronary disease and death. Smokers, for example, have less of a chance of surviving a heart attack than nonsmokers. Evidence from the Framingham Heart Study shows that the risk of sudden death increases more than tenfold in men and almost fivefold in women who smoke. Smoking is the number one risk factor for sudden cardiac death and for peripheral vascular disease.

Smoking cigarettes that are low in nicotine and tar does not decrease the risk of heart disease, which is increased by the effect of smoke on blood vessel walls. In fact, some people tend to smoke more and inhale deeply when they switch to this type of cigarette, increasing their exposure to the carbon monoxide in the smoke itself.

Fortunately, the risk of heart disease begins to de-

cline rapidly as soon as smokers—even heavy, long-time smokers—stop. Ultimately, their level of risk is almost the same as that of people who have never smoked. (See Chapter 6.)

### OBESITY

Any level of overweight appears to increase heart disease risk. Obesity can predispose the development of other risk factors, and the greater the degree of overweight, the greater the likelihood of developing other antecedents of atherosclerosis (such as high blood pressure and diabetes) that will increase the probability that heart disease will develop. Those who are obese (more than 30 percent over their ideal body weight) are the most likely to develop heart disease, even if they have no other risk factors. One recent study that examined more than 100,000 women age 30 to 55 showed that the risk for heart disease was more than three times higher among the most obese group than among the leanest group.

It also appears that how our weight is distributed may be even more important than exactly how much we weigh. There are two basic patterns of obesity one in which excess fat is found primarily in the abdominal area (the “beer belly” or apple shape) and one in which excess fat deposits form around the hips and buttocks (the pear shape). The former type is called male-pattern obesity or android obesity; the latter, female-pattern or gynecoid obesity. Android obesity, which is also found in some women (especially after menopause), is associated with an increased risk of cardiovascular disease, specifically, coronary heart disease and stroke. A general rule of thumb is that a man’s waist measurement should not exceed 90 percent of his hip measurement and that a woman’s waist measurement should be no more than 80 percent of her hip measurement.

Android obesity appears to be most closely related not only to risk but also to other cardiovascular risk factors—namely hypertension, elevated triglycerides, low HDL cholesterol, elevated blood sugar levels, and diabetes mellitus. The common feature of all these conditions is an elevation in the level of insulin (the hormone that regulates the metabolism of sugar in the body) in the blood and a condition called insulin resistance, in which body tissues (especially the large muscles) do not respond normally to insulin. The likelihood that fat distribution and insulin resistance are related to genetics again points to the pivotal role of heredity in disease risk.

### DIABETES MELLITUS AND INSULIN RESISTANCE

Individuals with diabetes mellitus, especially those whose diabetes occurs in adult life, have an increased incidence of coronary heart disease and stroke. Those who have slightly elevated blood sugar levels but do not have detectable diabetes also have an increased risk of developing these problems. Many individuals whose diabetes begins after age 40 or 50 (so-called adult-onset or Type II diabetes) often have higher than normal levels of circulating insulin. The primary role of insulin, a hormone produced by the pancreas, is to maintain blood sugar at normal levels and to assist this body fuel in entering each of the body’s cells. For some reason, some individuals do not respond as readily to insulin, and more is required to do the job; they have insulin resistance. Elevated levels of insulin can raise blood pressure and assist in the deposition of and reduce the removal of cholesterol from plaques in the arteries. Both these actions increase the likelihood that atherosclerosis and its complications will develop.

Fortunately, weight reduction and exercise can improve the burning up of blood sugar (glucose) and prevent or slow down the onset of diabetes.

Individuals who develop diabetes in childhood (so-called juvenile-onset or Type I diabetes) are more likely to develop kidney and eye problems than coronary heart disease or strokes. In this type of diabetes, insulin is absent due to disease in the pancreas.

### FIBRINOGEN

Serum fibrinogen is a component of the blood that plays a central role in the clotting process. Recent results from the Framingham Heart Study and elsewhere have shown that the level of fibrinogen is an independent cardiovascular factor. Why higher levels of this clotting factor increase risk is not yet known, but it is likely that individuals with higher levels may be more prone to develop clots in their arteries, thereby increasing the risk of a heart attack or stroke. Fibrinogen levels rise with age, and in that sense are not a risk factor that can be modified. However, fibrinogen levels are also adversely affected by cigarette smoking, which can be controlled.

### BEHAVIORAL FACTORS

Coronary-prone behavior, sometimes referred to as “Type A behavior, is felt by some, but not all, experts to be an important risk factor for coronary heart dis-

ease. Current definitions of Type A personality include a sense of time pressure and chronic impatience as well as excessive hostility. Contrary to popular belief, working hard or long hours is not necessarily a feature of the Type A or coronary-prone personality. Type A individuals tend to become upset easily, often for little cause, and are always in a hurry. They are constantly trying to do yet one more thing. Though many individuals who have heart attacks fit this personality description, current studies have not conclusively proved that a Type A personality is a true cardiovascular risk factor. (See Chapter 8.)

#### LEFT VENTRICULAR HYPERTROPHY (LVH)

The left ventricle is the chamber of the heart that pumps blood to all parts of the body except the lungs. Numerous studies show that individuals with left ventricular hypertrophy—an enlarged left ventricle in which the heart muscle has thickened—are prone to develop heart failure and are at greater risk of heart rhythm disturbances (arrhythmias) and sudden death. The majority of persons with an enlarged left ventricle either have hypertension or have already had a heart attack. Fortunately, we now know that successful treatment of hypertension will not only reduce blood pressure but will also reduce the size of the left ventricle and probably lower the risk associated with ventricular enlargement.

#### COCAINE

The escalating use of cocaine in the United States has resulted in angina, abnormal heart rhythms, high blood pressure, heart attacks, and death—even in healthy young adults. Cocaine constricts the coronary arteries, decreasing blood flow to the arteries of the heart, and reduces the amount of oxygen available to the heart while increasing the heart rate and its demand for oxygen. This combination of effects can precipitate a cardiac crisis and sometimes death, even upon the first use of the drug.

Cocaine is also a risk factor for congenital heart disease. Babies born to women who took cocaine during pregnancy are at increased risk of atrial-septal and ventricular-septal defects, as well as other congenital anomalies and adverse effects, such as low birth weight, that are directly related to the drug's action on the mother's cardiovascular system. (See Chapter 6.)

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## PROTECTIVE FACTORS

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#### EXERCISE

While it is not clear that a sedentary life-style is a cardiovascular risk factor, the evidence is convincing that regular exercise will reduce the likelihood of a heart attack and may improve the chances of survival if one does occur. Exercise also seems to have a positive effect on a number of other risk factors. Whether its benefit lies in the fact that it helps control weight, improves the body's ability to use insulin, conditions the heart muscle, increases levels of protective HDL cholesterol, moderates stress, or lowers blood pressure—or a combination of these effects—is not clear. Whatever the reason, regular exercise can lower cardiovascular risk and it should be encouraged for everyone within the limits of each individual. (See Chapter 7.)

#### ESTROGEN

Estrogen (the major female sex hormone) protects against heart attacks and other forms of cardiovascular disease. Estrogen increases HDL cholesterol, which may explain how the hormone reduces the incidence of heart attacks in premenopausal women. It is now clear that once menopause occurs, women are at the same risk for heart attacks as are men. Thus, it is reasonable to advise that postmenopausal women receive estrogen replacement therapy unless it is medically contraindicated. Although it is likely that estrogen replacement therapy reduces the frequency of heart attacks, such therapy may increase the risk of cancer of the uterus. This risk can be reduced or eliminated by combining estrogen with progesterone, another female sex hormone. In fact, recent studies indicate that combined hormone therapy may actually reduce the possible risk of breast or uterine cancer. As an added advantage, postmenopausal estrogen replacement reduces the severity of osteoporosis—the bone thinning that is a leading cause of death and disability in older women. (See Chapter 19.)

#### ALCOHOL

In moderation—that is, no more than one or two drinks a day—alcohol may protect against coronary heart disease and atherosclerosis. Although the exact

mechanism is not understood, it appears that alcohol raises HDL cholesterol. The association is certainly not strong enough to recommend that nondrinkers take up alcohol consumption. Furthermore, drinking four or more drinks per day can have deleterious effects. It raises blood pressure and puts the individual at significant risk of liver damage, central nervous system complications, and a number of other serious problems, some of which are cardiovascular. (See Chapter 6.)

## A PROGRAM FOR CARDIOVASCULAR RISK FACTOR MODIFICATION

How should you use the information presented in this chapter to make certain that you are doing everything possible to avoid a heart attack, stroke, or other complication of atherosclerosis? The first step is to assess, with the help of a physician, whether or not you are a high- or low-risk individual.

For some answers, you do not need a doctor. Do you smoke cigarettes? Are you overweight? Do you drink too much? Is there heart disease or high blood pressure in the family? To fully assess risk, however, a physician is needed. He or she will measure blood pressure, send blood for serum cholesterol, triglyceride, and glucose measurements, and perform a his-

tory and physical examination. An electrocardiogram or more specialized procedures can be done to determine if the heart is enlarged. With this information, a table such as Table 3.1 may be helpful in assessing the interaction of various factors to determine total risk.

Once all of this information is collected and evaluated, a treatment program, directed at modifying risk factors, can be started. For those who are free of cardiovascular risk factors or clinical vascular disease, certain simple steps can always help, and will do little if any harm:

- *Eat a heart-healthy diet*—one low in saturated fats and cholesterol. Use monosaturated or polyunsaturated fat.
- *Reduce weight if it is elevated.* Even a small amount of weight loss can be helpful if you are overweight.
- *Moderate your salt intake.* Many people are not sensitive to salt and their blood pressure will not rise even if their intake of table salt and other forms of sodium is high. The problem is, we cannot distinguish who is and is not salt-sensitive without complex testing. Most of us eat more salt than we need. Many foods are naturally high in sodium and others have salt added in processing. Simple measures such as not adding salt to the food as it is cooked or at the table will reduce sodium intake to a reasonable amount. This degree of salt restriction

Table 3.2  
The American Heart Association’s Recommendations for Periodic Health Examinations

A (x) indicates this test or medical procedure should occur at this age.							
Age	Medical history	Physical exam	Blood pressure <sup>1</sup>	Plasma lipids <sup>2</sup>	Body weight	Fasting glucose	Baseline ECG chest X-ray
20	x	x	x	x	x	x	x
25,30,35	x	x	x	x	x	x	
40	x	x	x	x	x	x	x
45,50,55	x	x	x	x	x	x	
60	x	x	x	x	x	x	x
61-75 (every 2½ years)	x	x	x	Optional <sup>3</sup>	x	x	
75 and over (every year)	x	x	x	Optional <sup>3</sup>	x	Optional <sup>3</sup>	

<sup>1</sup>Blood pressure should be taken every 2½ years in normal patients.

<sup>2</sup>Plasma lipids include fasting cholesterol and triglycerides.

<sup>3</sup>Optional if baseline levels are well documented.

*Note:* These recommendations are reviewed periodically and are subject to change. They can, however, be used as a general guideline.

## HOW TO LOWER YOUR RISK OF HEART DISEASE

is absolutely safe and does not rob food of its taste, especially if herbs and spices are used as alternative flavorings.

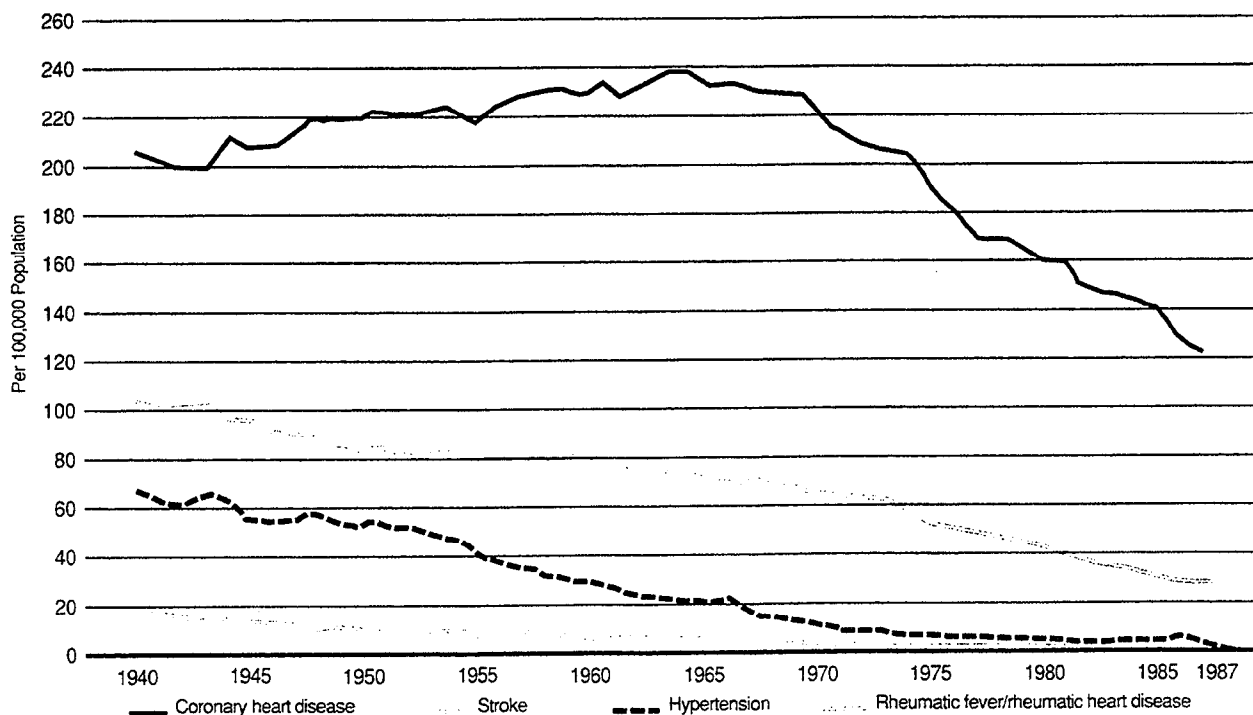
- **Start a regular exercise program.** Virtually everyone can benefit from regular exercise. To be helpful, the program need not be too strenuous and can be tailored to an individual's preferences, schedule, and physical capabilities. Regular walking may be all that is necessary.
- **If you smoke, stop.** Nothing will be more beneficial!
- **If you drink alcohol, do so in moderation.**
- **Learn stress-reduction techniques** and avoid reacting to stressful situations in ways that will only serve to aggravate the problem.
- **Have your risk factor status assessed on a regular basis.** A clean bill of health on one occasion does not guarantee a lifetime of protection. Blood pressure, if normal, should be checked every two years or so, and cholesterol, if normal, should be checked every five years. (These recommendations are reviewed periodically as

more is learned about risk. See Table 3.2 for current recommendations from the American Heart Association.)

What about individuals with definite hypertension or elevated cholesterol levels? The time to initiate therapy and the choice of therapy should be left to the physician, but always in consultation with the patient. In general, those who are at high risk because of very high blood pressure or cholesterol level or who have multiple risk factors require *drug* treatment, although a brief trial of diet, exercise, or other life-style changes may be appropriate first.

It is crucial to understand that treatment of cardiovascular risk factors is preventive medicine at its most challenging. After all, the physician is asked to select an effective and affordable regimen that does not make the patient sick and that can be useful for life. The irony is that in their early stages, neither hypertension nor high blood cholesterol produces symptoms, yet therapy for these conditions may interfere with enjoyment of life or, in some cases, actually cause symptoms.

Figure 3.2  
Age-Adjusted *Death Rates for Major Cardiovascular Diseases*



Nevertheless, dietary or behavioral changes and drug therapy have proved worthwhile. It is clear that modifying cardiovascular risk factors is remarkably successful preventive medicine. In the United States, we have made considerable inroads against the epidemic of cardiovascular disease. Since 1972, we have reduced the death rate from strokes by more than 50

percent and deaths from coronary heart disease by more than 40 percent. (See Figure 3.2.) Other countries that have followed our lead are beginning to do as well. It is likely that with increased understanding and application of the principles discussed here, we can do even better.