Progress against Heart Disease

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CHAPTER 1

Counting the Lives Saved

In 1978, the same year he won election to the first of his five terms as a Wyoming congressman, Dick Cheney had his first heart attack. He suffered another attack in 1984 and then a third in 1988 at age 47, but heart bypass surgery stabilized his condition until November 2000. While running for vice president, he experienced chest pains, and doctors inserted a coronary stent to prop open a narrow artery. In March 2001, now Vice President Cheney entered a Washington, D.C., hospital with chest pains and underwent a procedure to reopen the blocked artery. Just a few months later, he had a device implanted to monitor and, if necessary, slow his heart rhythm. After the surgery, the doctors said his prognosis was "terrific." Now over age 60 and with a 23-year history of heart problems, Vice President Cheney remains fully active in his duties. He sticks faithfully to his diet and exercises almost daily on his stationary bike.[1]

In January 2000, *Late Show* host David Letterman announced to guest Regis Philbin and the audience that he planned to undergo some heart tests. He said he had very high cholesterol ("Its borderline . . . 680," he joked) and a lifestyle not well suited to a healthy heart. Moreover, his father had a heart attack at age 36 and died of a coronary attack at age 57 in 1973. After the test showed blockages in his arteries, Letterman underwent emergency quintuple bypass surgery.[2] The procedure was a complete success, allowing the host to return to the show a few weeks later. Whatever problems led to the blockages, Letterman is doing well. He now jogs regularly, has lost weight, follows a low-fat diet, and continues to host his late-night show.

In 1957 at age 40, Nathan Pritikin discovered he had a seriously high

blood cholesterol level of 300. An abnormal electrocardiogram stress test later confirmed the worst—substantial coronary heart disease. To avoid drugs, surgery, or a life of inactivity, he changed his diet to eliminate nearly all fat and began walking and then jogging for an hour a day. His cholesterol plummeted to below 125, and another electrocardiogram stress test in the mid-1960s proved completely normal. His lifestyle change seemed not just to control but actually to eliminate his heart disease. Eventually, he wrote best-selling books and opened a popular California spa that promised to improve health with exercise and an extremely low fat diet. He died in 1985 at age 69, some 28 years after his first diagnosis, from causes unrelated to heart disease. An autopsy indicated he had an "absolutely remarkable" absence of cholesterol fatty deposits and calcification in his coronary arteries.[3]

These stories illustrate both the risks of heart disease and the promise in dealing with the risks. The risks of heart disease afflict the famous as well as the ordinary. The promise shows in the potential that changes in lifestyle and medical treatment have to allow people to live full lives despite having heart disease. Although people often know that heart disease is the number-one killer in the United States, they seldom realize the enormous progress made in preventing and treating the disease. The progress represents a remarkable story of scientific discovery and social change in lifestyles. To give a few examples, the lives of Americans have been extended by the

- development of machines to keep pumping blood while doing surgery on the heart,
- widespread use of emergency care to keep victims of cardiac arrest alive,
- invention of anticlotting and cholesterol drugs to prevent heart attacks,
- reliance on routine diagnostic tests to identify heart problems early,
- dramatic decline of cigarette use since the 1960s, and
- adoption of better diets and exercise activities.

As a result of this progress, the life expectancy of Americans, according to the most recently released figures, reached an all-time high in 2001 of 79.8 years for women, 74.4 years for men, and 77.2 years for men and women combined.[4] And declining mortality from diseases of the heart contributes significantly to this record-high life expectancy. Consideration of the extent of the problem of heart disease in the United States must therefore be balanced by consideration of the progress made against the problem in the last several decades.

EXTENT OF THE PROBLEM

Heart disease affects large parts of the population. In the United States in the year 2000, 12.6 million Americans had coronary heart disease, 4.8

million had problems of a weakened heart, and 2.0 million had faulty heart rhythms. These problems resulted in 650,000 people who had their first heart attack in 2000, 450,000 who had a recurrent heart attack, and 550,000 who experienced heart failure.[5]

Not surprisingly, heart disease is the number-one killer of Americans. In 2000, 709,894 Americans died of heart disease (29.5 percent of all deaths). The number exceeds the 551,833 deaths from cancer and the 166,028 deaths from strokes.[6] The problem similarly harms members of nearly all race and ethnic groups: heart disease tops other causes of death among whites, blacks, Hispanics, Native Americans, and Asian men. Only Asian women, who have more deaths from cancer than heart disease, deviate from the general pattern.

The problem appears most serious among men but affects millions of women as well. Men experience heart problems at younger ages than women, in large part because estrogen in premenopausal women offers some protection against heart disease. Yet, with such protection ending after menopause, heart disease becomes the number-one killer among both women and men. By age 60, for example, 25 percent of both men and women die of heart disease.[7]

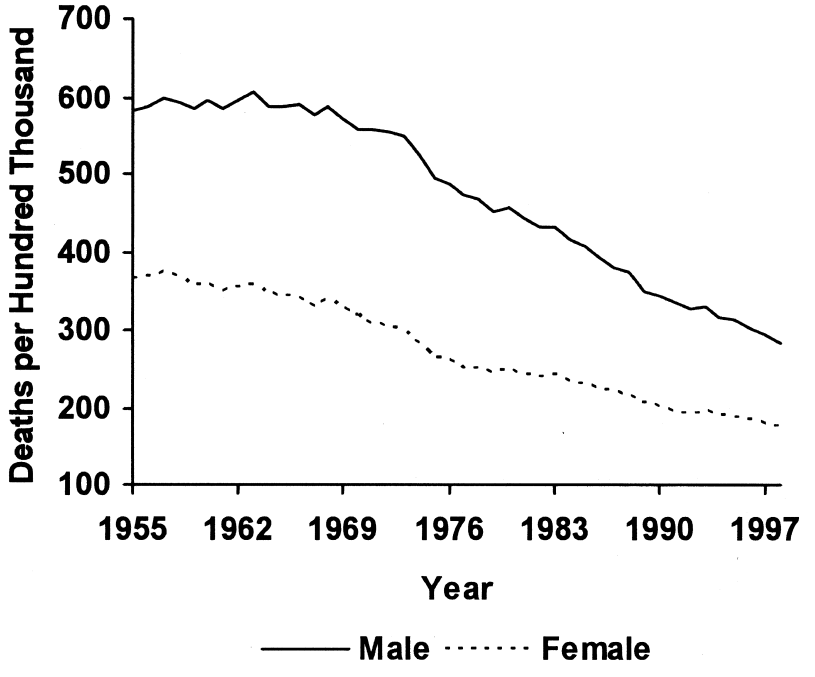
Those who live with heart problems face a serious chronic health condition that often limits daily activities. Only arthritis and back and neck conditions do more than heart disease to disrupt the ability to perform normal tasks of life. The economic costs of heart disease also illustrate the gravity of the problem. Annual expenditures for health care and for lost productivity from heart disease reached 214 billion dollars in 2002.[8] Most of the direct costs come from hospital care, but costs for nursing-home care, physician services, and prescription drugs add substantially to the total. Counting the pain and anxiety faced by those with heart disease further adds to the economic costs.

PROGRESS IN RECENT DECADES

Things look much better when viewed not in isolation but in comparison to previous decades. The trends over time reveal a substantial, persistent, and remarkable decline in deaths from heart disease. Figure 1.1 shows the age-adjusted death rates of men and women from diseases of the heart over the years 1955 to 1998. After a peak in the late 1960s, the death rates have decreased almost every year since then.

A simple calculation gives a sense of the enormous change implied by the rates shown in figure 1.1. The major type of heart disease—coronary artery disease—accounted for 514,000 deaths in 2000. However, it would have caused 1,329,000 deaths if the rate had remained at its 1968 peak.[9] We tend to take this progress for granted, but if put in the form of a headline—815,000 LIVES SAVED!—it would rightly gain much more at-

Figure 1.1
Heart Disease Mortality Rates, 1955–1998



Source: World Health Organization, *World Health Statistics Annual* (Geneva, Switzerland: World Health Organization, 1996 and earlier years), http://www.who.int/whosis. (Age-adjusted rates.)

tention. Summing the lives saved for each year since 1968 makes the figure even larger. Based on a projection from zero lives saved in 1968 to the 815,000 lives saved in 1998, the full 31-year time span shows more than *13 million lives saved* due to the lower mortality rates from heart disease.

These lives saved are not limited to the very old, who would die soon of other causes anyway. To the contrary, heart disease mortality has fallen faster among the young and middle-aged than the old.[10] Lowering premature mortality has shifted death from heart disease to the older ages. With family members, friends, coworkers, and neighbors living longer, few of us have not benefited in some way from these trends.

In historical perspective, this is a stunning change. In 1900, heart disease was the fourth most common cause of death in the United States, after pneumonia, tuberculosis, and diarrheal disease. By 1910, it had reached first place in large part because of the decline in deaths from the other

infectious diseases. But beginning in 1920, the rate of heart disease mortality began a 30- to 40-year climb. By midcentury, heart disease accounted for more than a third of all deaths. After World War II, the nation addressed this epidemic with major research and public health efforts. The National Heart Institute was created to fund research, the American Heart Association aided with a national campaign to reduce risk factors, and the surgeon general's report warned the public of the risks of cigarette smoking for heart disease (as well as lung cancer, respiratory disease, and a variety of other problems). By the end of the 1960s, heart disease mortality began to fall and has continued the downward trajectory since then.

The decline of heart disease represents one of the most important public health achievements of the twentieth century. As Professor Eugene Braunwald stated in the prestigious *New England Journal of Medicine,* "Since the battle against cardiovascular disease was joined in mid-century, the news from the cardiovascular front has been almost uniformly positive. . . . An almost unbroken series of positive developments has encouraged the perception that the war against cardiovascular disease has been won or is well on its way to being won."[11]

In a 1996 editorial in *Science* magazine, Professors Michael S. Brown and Joseph L. Goldstein, winners of the Nobel Prize in Medicine in 1985, argue that progress against heart attacks will continue: "Heart attacks were recognized as a public health problem only in this century. They are likely to lose this notoriety in the next. The reason? Four decades of progress in understanding cholesterol and the lipoproteins that carry it in blood plasma."[12] Reviewing evidence from a variety of studies of animals, human populations, and clinical experiences, Brown and Goldstein suggest that even in the presence of other risk factors, lowering cholesterol with lifestyle changes and new drugs can do much to reduce heart disease.

The major goal now is to develop a noninvasive screening method to detect coronary artery disease in its early stages. Then, "exploitation of recent breakthroughs . . . may well end coronary heart disease as a major public health problem early in the next century."[13] Others second these optimistic predictions. Two other leading medical researchers state that "[t]he past decade has seen remarkable progress in clinical and basic research and many areas of opportunity are promising. The pace of current progress in clinical and basic research is such that remarkable improvement in the quality and length of life for those at risk for cardiovascular disease is likely."[14] Future advances involving a variety of new diagnostic techniques, medications, treatment procedures, and understandings of the sources of heart disease will no doubt help maintain the positive momentum. These advances may even make it possible to predict and treat the disease long before it occurs.[15]

We often hear the opposite: poor diet and limitations of modern medicine threaten our health and well-being. Although room for improvement

always remains, the facts concerning heart disease demonstrate enormous progress rather than failure.

CONTINUING CHALLENGES

Success in dealing with heart disease has in some ways resulted in a sense of complacency.[16] Less common, but more intractable diseases of cancer and AIDS have grabbed the most attention and garnered the most research funding in recent years. Despite progress, however, heart disease remains a crucial public health problem that requires continued vigilance. Jan I. Breslow, a former president of the American Heart Association, notes that lack of funding for cardiovascular research can slow progress toward the goal of eliminating heart disease as a major public health problem.[17]

Challenges certainly remain in the battle against heart disease. With the aging of the population, the numbers of persons with heart disease at older ages will increase despite progress in preventing and treating the problem among the young and middle-aged. Even at younger ages, blacks and females have not enjoyed the same decline in heart disease as white males. Those with low socioeconomic status and in southern regions of the country continue to have particularly high rates of heart disease. Worldwide, the growth of heart disease in developing nations can counter improvements in more developed nations. Surprisingly, coronary heart disease is expected to become the leading cause of death among residents of developing nations by 2020 and contribute substantially to the worldwide burden of disease.[18]

Some worry that trends toward healthier lifestyles may not continue. Although the typical diet today contains less fat than decades ago, the downward trend appears to have stalled. Diabetes and obesity are rising, and improvements made in reducing hypertension in recent decades appear to have ended. Declining rates of smoking have also slowed, particularly among young men and women. These changes may have already slowed the decline in heart disease and suggest that room for continued improvement remains.[19]

Recognizing new challenges in dealing with heart disease, however, does not negate what has been accomplished. The progress has been substantial. Along with lower death rates from heart disease, the past several decades have brought increased knowledge about the causes and treatment of the disease. Some background on how the heart works and what happens when it does not work can help to understand the growth of this knowledge.

HOW THE HEART WORKS

The heart is a pump with four chambers that work in amazing harmony. First, blood filled with carbon dioxide and waste products of cell metab-

olism returns from the body in veins to the upper-right chamber (or right atrium) of the heart. Second, the blood enters through a valve into the lower-right chamber (or right ventricle). From the right ventricle, the blood is pumped under low pressure through the pulmonary artery to the lungs, where it releases the carbon dioxide and absorbs oxygen. Third, the oxygenated blood returns through the pulmonary vein to the heart in the upper-left chamber (or left atrium). Fourth, the blood then enters through a valve into the lower-left chamber (or left ventricle). From the left ventricle, the blood is pumped under high pressure through the aorta into arteries that will carry it throughout the body. During this process, heart valves control the movement of blood across the chambers. Much like one-way doors, they let blood into a chamber but not back out.

The process repeats on average 72 times a minute, over 100,000 times a day, over 37 million times a year, and nearly 3 billion times in a life. It pumps around 4,000 gallons of blood a day. For a muscle that is only a bit larger than the size of one's fist and weighs only 10 to 20 ounces, or about the same as a can of soda, the heart shows exceptional strength and endurance. The left side of the heart is particularly thick and strong because it has to contract enough to send the blood throughout the body (rather than to the nearby lungs).

Unlike other muscles, the heart never rests and proves essential to the functioning of all parts of the body. Like the rest of the body, the heart needs oxygenated blood. Since it cannot absorb blood directly through its walls, it depends on three important coronary arteries to nourish the muscle (*coronary* comes from a Greek word meaning "like a crown" and reflects the fact the coronary arteries fit over the heart like a crown). In fact, 10 percent of the blood pumped by the heart goes through these arteries.

To start the pumping action, the heart generates electrical signals from its own bioelectrical system rather than receiving impulses from the brain. The signals trigger the heart muscle to contract, but the contractions must be synchronized among the four chambers to make the pumping of the heart efficient. We speak of a heartbeat, but the heart contraction actually involves two closely spaced movements stimulated by the electrical system. The two upper chambers contract first, and then the two lower chambers follow an instant later. We refer to the heart as systolic when it is contracted and pumping blood out and diastolic when it is relaxed and filling with blood. These terms correspond to the components of blood pressure, or the force exerted against the arteries, with systolic the upper number and diastolic the lower number.

MISCONCEPTIONS ABOUT THE HEART

Knowledge about how the heart works has emerged slowly throughout human history, and misunderstandings have lasted for thousands of years.

Primitive peoples had a good sense of the importance of the heart and blood: the beat of the heart matched the pulse of blood vessels, death ended the flow of blood, and a wound to the heart area—the center of the body—produced much blood. However, they had little understanding of the structure and function of the heart and circulation. The first systematic study of the heart came from the Greeks about 400 B.C. An unknown author described the two great vessels leading to the heart and the valves between the vessels and the heart chambers but identified only two rather than four chambers.[20] Not for another 130 years, in 270 B.C., was it discovered that the heart works as a pump and contains four chambers. A physician in Alexandria, Egypt, correctly concluded that blood enters the heart through the veins, and that the veins and arteries were connected, but he believed that air, rather than blood, flowed through the arteries.

A major—yet still incomplete—advance in the understanding of the workings of the heart came from the greatest of Greek physicians, Galen (A.D. 129–ca. 199). Galen recognized that the heart pumped blood rather than air through the arteries, saw the importance of the heart valves in preventing the blood from flowing backwards, and made several other important discoveries. Although human dissection was outlawed, Galen discovered much from experiments on live farm animals. After learning how to cut animals open without killing them, he could observe a beating heart.[21] Based on his experiments and the four hundred books he wrote on physiology, Galen's fame spread, and scholars and physicians accepted his word without question for the next 1,300 years.

However, Galen made mistakes that others continued to repeat. For example, he thought that invisible openings existed between the right and left sides of the heart that allowed blood to pass directly across chambers (when, in fact, blood goes to the lungs from the right side and returns from the lungs to the left side). He also thought that air and blood flowed separately to the heart chamber where they mixed. The errors of Galen and other physicians at the time likely resulted from their study of animal hearts, which differ in important ways from human hearts. In addition, the hearts moved so quickly, and so much was hidden behind the heart walls and within the vessels, that it was easy to make mistakes.

Physicians in Italy in the sixteenth century made the first efforts to correct the long-standing misconceptions about how the heart works.[22] Despite facing intense criticism, even hatred, for challenging the long-accepted beliefs of the Greeks and Romans, brave scholars demonstrated that no opening existed between the left and right sides of the heart. They further realized that blood exited from the right side of the heart, filtered through the lungs, mixed with air, turned bright red in color, and returned to the left side of the heart. The right and left side of the heart thus beat simultaneously, although for different purposes—one to send blood to the lungs and one to send the blood recently returned from the lungs to the rest of the body. Much remained to be learned about the heart and circulation, but progress toward a modern understanding had begun.

WHAT CAN GO WRONG

Heart disease is more than a single ailment but includes a variety of problems in the functioning of the many parts of the heart. Indeed, one major problem originates from disease of the blood vessels that feed the heart rather than from the heart itself. Much can go wrong with the operation of the heart and its blood vessels. Corresponding to the structure of the heart, the problems can be divided into several groups.

Coronary Heart Disease

The primary cause of heart disease and death from heart disease in modern societies is the inability of the coronary arteries to deliver the blood and oxygen needed by the heart muscle. Since the heart requires a continuous supply of blood, any blockage of the coronary arteries threatens the ability of the heart to operate. The most common cause of coronary heart or artery disease is atherosclerosis—a progressive development of material that becomes attached to the walls of the coronary arteries and restricts the flow of blood. The material or "plaque" consists of cholesterol deposits, calcium, and abnormal cells, and its buildup reflects blood vessel disease more generally.

Plaque serves to progressively narrow the artery and makes it difficult for blood to flow through to the heart muscle. The coronary arteries also become less flexible when filled with plaque (*sclerosis* means hardness) and help less in propelling the blood through the vessel. More seriously, even if a small plaque ruptures, it can trigger clotting of the blood within the artery that seriously obstructs the blood flow. This is the major cause of a coronary "event" or "acute coronary syndrome."

Individuals may experience symptoms from not getting enough blood through the coronary arteries. The lack of blood and oxygen to the heart muscle creates a pressure-like warning pain in or around the chest, shoulders, neck, or arms termed *angina pectoris.* The connection of the nerves around the heart to other parts of the body results in a diffuse pain. The symptoms usually subside with rest or medication but nonetheless indicate that the muscle is lacking oxygen. In other cases, the lack of oxygen to the heart muscle does not cause clear warning signals of pain. Ischemia or the lack of oxygen to the heart muscle can be all the more serious when it involves no angina or warning pain.

A myocardial infarction or heart attack occurs when a coronary artery becomes completely blocked, and the heart muscle supplied by that artery dies. *Myocardial* comes from *myocardium,* the technical term for the heart (in Greek, *myo* means muscle, and *kardia* means heart); the term *infarction* means death of the muscle cells. The seriousness of the heart attack depends on the amount of the heart muscle that dies. A myocardial infarc-

tion usually stems from the sudden rupture of an atherosclerotic plaque and subsequent clotting and blocking of the artery. The victim feels a squeezing pain in the chest that spreads to other parts of the upper body and is accompanied by sweating, nausea, or fainting; the pain may also simulate severe indigestion or heartburn. Not all chest pain results from a heart attack—similar feelings can come from indigestion, anxiety, or benign heart conditions. However, if the pain and symptoms are severe or last for more than 15 minutes, they probably require immediate medical attention.

Cardiac Arrhythmia

Irregular heartbeats, or cardiac arrhythmia, can be too slow or too fast. When the heart rhythm is too slow (bradycardia), the part of the heart that generates electrical impulses becomes damaged, and the impulses may become weak or insufficient. Another form of bradycardia involves a condition called heart block, which prevents the electrical impulses from reaching the two lower chambers of the heart or the ventricles. When the heart rhythm is too fast (tachycardia), the disorderly contraction can limit the ability of the heart to pump blood to the body. Most seriously, ventricular fibrillation involves chaotic electrical impulses and the independent contraction of muscle fibers that halt meaningful contraction of the ventricles. This results in the stoppage of blood flow to the body, the loss of consciousness in a few seconds, and, without intervention, death in a few minutes.

Other types of arrhythmia include premature ventricular contractions that produce an "extra heartbeat" in the lower chambers. Premature ventricular contractions are generally benign unless they reflect other underlying heart problems. Atrial fibrillation (also known as flutter) occurs when the upper chambers beat irregularly and rapidly. Although not as serious a problem as ventricular fibrillation, atrial fibrillation causes the upper and lower chambers to beat irregularly, leads to clotting inside the heart and can result in a stroke if a clot breaks off and travels to the brain.

Valvular Heart Disease

There are several causes of valvular heart disease, or the inadequate operation of the heart valves, such as rheumatic fever, congenital heart disease, cardiac dilation, and age-related calcification of the valves. However, the condition usually shows in one of two ways. First, the valve openings become too narrow and make it difficult for the blood to move from one chamber to the next. This is called valvular stenosis and leads to increased pressure in the heart chamber behind the valve. Second, the

valves become incompetent so that blood leaks back across the valves when they are supposed to be closed. This is called valvular regurgitation and causes the heart chambers to dilate with extra blood.

In more extreme cases, both types of valvular problems can lead to congestive heart failure. Unlike the death of heart tissue from a heart attack, heart failure refers to the improper pumping of the heart, and congestive refers to the resulting buildup of fluids in the body. For example, if valvular problems affect the right atrium of the heart, blood is not properly absorbed from the veins, and edema or swelling of the liver, abdomen, and legs can result. If valvular problems affect the left atrium, then fluids accumulate in the lungs and make breathing difficult.

Cardiomyopathy

Cardiomyopathy refers to diseases of the heart muscle. If the muscle of the left ventricle becomes weak, the amount of blood pumped in each heart beat drops, and the body does not receive its full quotient of blood. Called dilated cardiomyopathy, this problem results in shortness of breath, weakness, fatigue, and leg swelling and can produce life-threatening arrhythmia.

Hypertension or high blood pressure weakens the heart by making the vessels less elastic and the muscle walls thick and stiff. The inelasticity then requires the heart to pump harder to send the blood through the body. With the increased strain, the heart can become enlarged, and the enlargement can produce heart failure. Hypertrophic cardiomyopathy involves an inherited tendency of the ventricular muscle to thicken. This weakens the efficiency of the heart pumping and can cause sudden death in young athletes.

Heart Failure

Heart failure is not a specific disease. Rather, it describes a group of symptoms involving the inability of the heart to pump enough blood to meet the body's needs. Heart failure results from several underlying problems, including valve problems, cardiomyopathy, high blood pressure, and damaged heart tissue from a heart attack. These underlying problems weaken the heart enough that the blood does not properly circulate. Consequently, the body tissue does not get the nutrients and oxygen it needs and does not get its waste materials removed. Shortness of breath and fatigue result, as does the accumulation of fluids in the lungs, feet, legs, and trunk. Because heart failure often involves the congestion of the tissues and lungs with fluid, it is often called congestive heart failure.[23]

WILLIAM HARVEY: THE HEART AND BLOOD CIRCULATION

In 1628, William Harvey published *An Anatomical Treatise on the Motion of the Heart and Blood in Animals.* Historians of medicine consider it one of the most important books ever published on physiology, one similar in significance to Newton's work nearly 50 years later on gravity and the movement of the planets for modern physics. A serious and studious young man, Harvey went to study medicine in Italy, where he observed his professors dissecting human corpses. He returned to England to obtain a doctorate in medicine from Cambridge University, joined the teaching staff at St. Bartholomew's Hospital at London, and lectured at the Royal College of Physicians. He later served as the royal physician for King James I and King Charles I of England.

Harvey was the first to recognize that blood circulates through the body as a result of the pumping action of the heart. Although such an assertion seems obvious now, it represented a major change in the understanding of the time. Since Galen, physicians had thought that the body continuously created blood from food and "consumed" the blood as it moved to muscles and organs. By measuring the amount of blood pumped by the heart, Harvey revealed the fallacy of this assertion. His calculations demonstrated that the blood pumped by the heart in 30 minutes far exceeded the weight of the body. This much blood could not possibly be created anew but must instead recirculate through the body, each time transferring nutrients rather than being used directly. Harvey further demonstrated that blood moves away from the heart in the arteries to the veins and returns to the heart through the veins. Without a microscope, he could not see the tiny capillaries that connect the arteries to the veins, but his reasoning correctly led to the inference that such connections must exist.

In straightforward and logical wording, Harvey revolutionized thinking about the heart and circulation of the blood: "It is absolutely necessary to conclude that the blood in the animal body is impelled in a circle, and is in a state of ceaseless movement; that this is the act or function which the heart performs by means of its pulse, and that it is the sole and only end of the movement and contradiction of the heart."[24] Although his claims proved accurate, the criticism of his work by those unwilling to accept new truths damaged Harvey's reputation. He suspected as much would happen: "But what remains to be said upon the quantity and source of blood which thus passes, is of so novel and unheard of character, that I not only fear injury to myself from the envy of a few, but tremble lest I have mankind at large for my enemies."[25] Despite such criticism, history soon proved Harvey's work to be correct, and his insights created a basis on which medical science and cardiology could build.

CORONARY ATHEROSCLEROSIS

Coronary artery or heart disease is by far the major cause of death in the United States—comprising about 63 percent of all heart disease deaths

in 1998. Since it results from the buildup of plaque in the coronary arteries, it is a blood vessel disease as well as a form of heart disease. Coronary heart disease is not an event but a condition that progresses from mild to severe. The progression is complex and not fully understood, but it involves multiple factors.

Cholesterol

Cholesterol is a fatty substance that the body uses to help form cell membranes and manufacture vitamin D and certain hormones such as estrogen. We ingest cholesterol in our food, but in the absence of such food, the liver can manufacture all the cholesterol the body needs. Cholesterol is one type of blood lipid (triglycerides are another). More important than cholesterol alone are lipoproteins that combine protein and lipids and transport cholesterol to cells. Low-density lipoproteins (LDL) enclose and transport cholesterol to cells and can accumulate in artery walls. Called the bad cholesterol, LDL contributes to heart disease. High-density lipoprotein (HDL) carries cholesterol back to the liver for processing and disposal and may even remove cholesterol from the artery walls. In contrast to bad cholesterol, this good cholesterol protects against heart disease. Common blood lipid tests now compare the level of total cholesterol (low- and high-density lipoproteins) to the level of high-density lipoproteins.

Evidence that elevated levels of cholesterol increase the risk of a heart attack by contributing to the buildup of plaque along the walls of the coronary arteries comes from three sources.[26] First, animals with low levels of LDL have no atherosclerosis, and raising LDL in animals universally causes the disease. Second, human populations with low LDL have little atherosclerosis, and the disease increases in proportion to LDL in all populations studied. Third, trials of drugs called statins that lower LDL also reduce heart attacks. However, elevated cholesterol represents just one of numerous risk factors. Many people with high LDL cholesterol (or high ratios of total cholesterol to HDL) do not have heart attacks, and many who have heart attacks do not have high cholesterol.

Blood Clots

When a blood clot (or thrombus) lodges in a major artery (called atherothrombosis), it can become part of the plaque and narrow the artery. Blood clots protect and repair an injured part of a blood vessel but at the same time can grow so large as to block the flow of blood. Ideally, anti-clotting elements in the blood balance clotting elements, but under some circumstances, the clot does not get dissolved and accumulates LDL cholesterol and immune cells that contribute to plaque buildup. Certain kinds

of cholesterol may reduce the ability of the body to naturally dissolve blood clots in blood vessels. In addition, high levels of a molecule called fibrinogen that forms the strands of the blood clot can exacerbate clotting problems.

Insulin

The pancreas releases insulin into the bloodstream to help bring sugar and fat to the body's cells, but elevated levels can lead to a faster heart rate and to high blood pressure. High sugar levels and high insulin can also damage the lining of the arteries and raise LDL cholesterol.

The Immune System

When immune cells called macrophages take residence just inside the artery wall, they can attract LDL cholesterol—particularly the damaged or oxidized LDL cholesterol. The uptake of cholesterol can then transform the immune cells into foam cells, which in turn accumulate into fatty streaks and contribute to the buildup of plaque. In addition, the immune cells release a substance that can inflame the artery wall, much as an allergic substance might inflame the sinus lining. This inflammation also promotes the development of fatty streaks and plaque buildup. Children as young as age 10 have fatty streaks in their arteries that may later develop into artery-clogging plaques, which highlights the fact that the development of atherosclerosis is a lifelong process rather than a sudden event.

Lipoprotein(a)

Beginning in the 1990s, a possible explanation of heart disease based on the action of a particle in the blood called lipoprotein(a) emerged.[27] The particle helps repair torn blood vessels but may have the side effect of promoting blood clots in the coronary arteries. It does so by inhibiting the effectiveness of a similar protein that dissolves blood clots. When in excess, lipoprotein(a) thus promotes atherosclerosis. Since the level of lipoprotein(a) in the blood correlates with heart disease, varies greatly across individuals, and is stable over time, it may serve as a useful indicator of the risk of a heart attack.

INJURIES TO THE ARTERY WALL

Elevated cholesterol, blood clotting, high insulin, and immune response all contribute to the buildup of plaque, but the process may begin with an injury to the artery wall. The initial injury may come from a disturbance