

REPORT

(Case No. 106)

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Your Question

Chest pain that feels sharp (left side), fever, difficulty breathing, palpitations (heart rate) tired and lethargic, dizzy, light headed, clumsy that has lasted 4 days , not getting worse but not getting better either. 35 yrs, female non-smoker, regular exerciser with no history of medical issues other than a documented heart murmur (10 years)

Lay Summary

Many reasons can cause chest pain and the other symptoms that you described. However in your case, it was most likely an angina which was caused by a temporary lack of blood supply to the heart. The impaired heart function would lead to reduced blood supply to other part of your body particularly the brain, therefore causing a number of symptoms including difficulty breathing, palpitations, feeling tired, lethargic, dizzy, light headed, clumsy, etc. If it is mild, the damage is reversible and serves as a warning to a possible ischemic heart disease. If it repeats itself or if the pain persists, it can lead to a heart attack (myocardial infarction), which is the number one killer for both sexes in developed countries. Over 40% of people die of cardiovascular diseases in the US. Since you have had a murmur for the past ten years, one likely scenario is that you might have a mitral valve prolapse and enlarged heart. This might have led to increased demand by the heart for blood supply and caused a relative shortage of blood supply to the heart which caused damages to the heart muscle and manifested as chest pain. There are also patients suffer from heart attack without much pain or other symptoms (silent heart attack). It is very important for you to see a physician as soon as possible and get you heart checked with ECG and other tests. In this report, we have provided information about the symptoms, cause, diagnosis, prevention and management of chest pain and heart attack. Please read it carefully and seek treatment from a qualified doctor right away before it is too late.

About chest pain and Coronary Artery Disease

What Is Coronary Artery Disease?

Coronary Artery Disease

In order to perform the arduous task of pumping blood, the heart muscle needs a plentiful supply of oxygen-rich blood, which is provided through a network of coronary arteries. Coronary artery disease is the end result of a complex process called *atherosclerosis* (commonly called "hardening of the arteries"). There are many steps in this story, and some are not fully known:

- A number of environmental or physical factors are involved in triggering excess amounts of unstable particles known as *oxygen-free radicals*, which bind with and alter other molecules, a process called oxidation. (The particles are released as part of normal bodily processes, but environmental toxins, such as smoking, can produce excess amounts.)
- When free radicals are released in artery linings, they react with and oxidize *low-density lipoproteins* (LDL). (Lipoproteins are sphere-shaped bodies that carry *cholesterol*, and LDL is the well-known villain referred to as the "bad cholesterol.")
- LDL deposits mushy layers of oxidized cholesterol on the walls of the artery.
- The cholesterol accumulates.
- The injuries to the arteries during this process signal the immune system to release white blood cells (particularly those called *neutrophils* and *macrophages*) at the site. This initiates an important and damaging process called the *inflammatory response*.
- Macrophages literally "eat" foreign debris, in this case oxidized cholesterol, and become foamy cells that attach to smooth muscle cells causing them to build up.
- Over time the cholesterol hardens and forms *plaque*, which builds up on the walls of the arteries.
- The immune system, sensing further harm, releases other factors called cytokines, which attract more white blood cells and perpetuate the whole cycle, causing persistent injury to the arteries.
- Injured inner vessel walls fail to produce enough *nitric oxide*, a substance critical for maintaining blood vessel elasticity.
- Eventually these calcified (hardened) and inelastic arteries become narrower (a condition known as *stenosis*). As this process continues, blood flow slows and prevents sufficient oxygen-rich blood from reaching the heart.
- Such oxygen deprivation in vital cells is called *ischemia*. When it affects the coronary arteries, it causes injury to the tissues of the heart.
- Heart attack can occur as a result of one or two effects of atherosclerosis:

(1) If the artery becomes completely blocked and ischemia becomes so extensive that oxygen-bearing tissues around the heart die.

(2) If the plaque itself develops fissures or tears. Blood platelets adhere to the site to seal off the plaque and a blood clot (thrombus) forms. A heart attack can then occur if the blood clot formed completely blocks the passage of oxygen-rich blood to the heart.

What Is Angina?

Angina is the primary symptom of coronary artery disease and, in severe cases, of a heart attack [*see Box*]. It is typically experienced as chest pain. Angina is usually referred to as *stable* (predictable) or *unstable* (less predictable and a sign of a more serious situation.) Angina itself is not a disease. Much evidence exists, in fact, that onset of angina less than 48 hours before a heart attack may be protective, possibly by conditioning the heart to resist the damage resulting from the attack.

Angina may be experienced in different ways and can be mild, moderate, or severe:

- It is often reported as a dull, heavy pressure that may resemble a crushing object on the chest.
- Pain often radiates to the neck, jaw, or left shoulder and arm.
- Less commonly, patients report mild burning chest discomfort, sharp chest pain, or pain that radiates to the right arm or back.
- Sometimes a patient experiences shortness of breath, fatigue, or palpitations instead of pain.
- The intensity of the pain does not always relate to the severity of the medical problem. Some people may feel a crushing pain from mild ischemia, while others might experience only mild discomfort from severe ischemia.
- Some people have also reported a higher sensitivity to heat on the skin with the onset of angina.
- Angina can also be precipitated by large meals, which place an immediate demand upon the heart for more oxygen.

Stable Angina

Stable angina is predictable chest pain. Although less serious than unstable angina, it can be extremely painful. It is usually relieved by rest and responds well to medical treatment (typically nitroglycerin).

Any event that increases oxygen demand can cause an angina attack. Some typical triggers include the following:

- exercise,
- cold weather,
- emotional tension, or
- large meals.

Angina attacks can occur at any time during the day, but a high proportion seems to take place between the hours of 6:00 AM and noon.

Unstable Angina

Unstable angina is a much more serious situation and is often an intermediate stage between stable angina and a heart attack. A patient is usually diagnosed with unstable angina under one or more of the following conditions:

- Pain awakens a patient or occurs during rest.
- A patient who has never experienced angina has severe or moderate pain during mild exertion (walking two level blocks or climbing one flight of stairs).
- Stable angina has progressed in severity and frequency within a two-month period, and medications are less effective in relieving its pain.

Prinzmetal's Angina

A third type of angina, called variant or Prinzmetal's angina, is caused by a spasm of a coronary artery. It almost always occurs when the patient is at rest. Irregular heartbeats are common, but the pain is generally relieved immediately with treatment.

Silent Ischemia

Some people with severe coronary artery disease do not experience angina pain, a condition known as *silent ischemia*, which some experts attribute to abnormal processing of heart pain by the brain. This is a dangerous condition because patients have no warning signs of heart disease. In one study, people with silent ischemia experienced much higher complication and mortality rates than those with pain. (Angina pain may actually protect the heart by conditioning it before a heart attack.)

Indications of a Heart Attack

Any unusual chest pain or angina symptoms that do not clear up when medications are taken is a signal to go to the hospital.

Common Heart Attack Symptoms. Some signs to watch out for are as follows:

- Sometimes within the month before a heart attack, a patient may experience mild chest pain, unexplained fatigue and ill health, or depression.
- Right before a heart attack, many patients experience chest pain, usually precipitated by exercise or stress that does not clear up when medications are taken or when resting.
- Many patients experience the pain of a heart attack as a crushing weight against their chest accompanied by profuse sweating. The pain may radiate to the left shoulder and arm, the neck or jaw, and even infrequently to the right arm. The arm may even be numb.
- It should be noted, however, that degree of pain experienced varies greatly between individuals. Some people may feel severe pain; others might feel only a tingling sensation. Some people may only have a sense of fullness or pressure in the chest.)
- A feeling of indigestion or heartburn is common, as are nausea and vomiting.
- Some people report a great fear of impending death, a phenomena known as *angor animi*.

Atypical Symptoms in Specific Populations. It is very important to note that one-third of all heart attack patients do not have chest pain, putting them at much higher risk for a misdiagnosis.

- Women are more likely than men to be nauseous and experience pain high in the abdomen or chest. Their first symptom may be extreme fatigue after physical activity rather than chest pain. It should be noted that physicians might not be as alert to a heart problem in a woman. Symptoms of angina in women are often not typical and their complaints of chest pain are more likely to be caused by other problems. Because of these reasons, women are less likely than men to be tested aggressively for serious heart problems when they enter the emergency room. Any chest pain should always be taken seriously in anyone.
- African Americans are more likely than Caucasians to have shortness of breath and left-sided chest pain (although other symptoms are similar.) (They are also less likely than Caucasians to seek medical help quickly.)
- Symptoms in the elderly may only be shortness of breath. A 2000

study suggested that heart attacks may go undiagnosed in people over 65 who do not have a history of angina or heart failure.

Actions taken:

Angina patients should take 1 nitroglycerine dose at the onset of symptoms and another every five minutes for three doses.

Calling 911 should be the first action taken if chest pain continues in angina patients who have taken their full three doses of nitroglycerine or in any individual with severe chest pain. Chest pain sufferers should go immediately to the nearest emergency room, preferably traveling by ambulance. They should not drive themselves.

The patient should chew an aspirin and be sure that emergency health providers are informed of this so an additional dose isn't given.

How Serious Are Angina And Coronary Artery Disease?

Coronary artery disease is the leading killer in America of both men and women, responsible for over 465,000 deaths in 1997, about 20% of all deaths. On the positive side, mortality rates from stroke and heart attack and other forms of heart disease have declined by nearly 60% in industrialized countries since their peaks in the 1960s and 1970s. (Mortality rates are on the rise in developing nations, however.) When the necessary lifestyle changes are enacted in combination with appropriate medical or surgical treatments, a person suffering angina and heart disease has a good chance of living a normal life.

What Are The Risk Factors For Angina And Coronary Artery Disease And How Can They Be Managed?

About 25% of all Americans have one or more cardiovascular disease, and about 300,000 have angina. Risk factors are not necessarily an inevitable result of aging but are primarily related to lifestyle and environmental factors. Over the past decades, heart disease declined in both men and women as they quit smoking and improved dietary habits. This rate, however, has stabilized and some studies suggest this is due to increasing obesity in the country.

Reducing Multiple Risk Factors

The risk for heart disease increases with multiple risk factors, importantly unhealthy cholesterol or lipid levels, obesity, smoking, and hypertension. (For example, a cluster of

risk factors called syndrome X poses a particularly high risk for heart and other diseases. It consists of having high blood sugar, high blood pressure, low HDL cholesterol, and high triglycerides. The syndrome, which occurs in about 3% of men and 3.4% of women, appears to be due to abnormalities in the small arteries.)

Conversely, risk plummets in the absence of multiple risk factors. For example, in a 1999 study of men and women of all ages, nonsmoking, nondiabetics who had low cholesterol levels (less than 200 mg/ml) and low blood pressure (less than 120/80) had a risk of dying from heart attack that was between 77% and 92% lower than those with risk factors. (They also had a lower risk for stroke and cancer.) Similarly, a 2000 study reported that patients who aggressively pursued a healthy lifestyle (low-fat diet, stress management, smoking cessation, moderate aerobic exercise) significantly reduced their risk for heart attack, cardiac surgery, and death.

Gender

Coronary artery disease is much more common in middle-aged men. Women have, on average, ten to fifteen more years of heart-disease free life than do men, but as women age, they catch up to men. Women, in fact, are more likely to have angina than men are. When adjusted for age, survival rates from heart attacks are similar in older men and women, but younger women are at greater risk for death from heart attack than men their own age.

The reasons for this are not clear. Estrogen, which appears to be heart protective, may play a role, and it may be that many younger women who have heart attacks have lower estrogen levels. For example, in a 2000 study, women who entered natural menopause early (age 35-40), had a higher risk for death from heart attack than did women who entered menopause later.

Many studies have reported that women are less aggressively treated than men for all phases of heart disease. More recent ones have suggested, however, that women and men are treated similarly during late stages of heart disease (such as during a heart attack), but not when they first come to the hospital with heart disease. Younger women with heart disease often do not have the same symptoms as their male counterparts and are less likely to be diagnosed correctly or aggressively. In fact, women's symptoms are less likely to appear as typical angina, and women are more often tested for gastrointestinal problems than men. (Interestingly, one 1999 study found that although, indeed, women with unstable angina were treated less aggressively than men, when their risk factors were compared head to head, men actually had a worse long-term outcome.)

Ethnicity

African Americans. In a 1998 analysis, although mortality rates from coronary artery disease declined between 1987 and 1994 in both Caucasians and African Americans, they did not decline significantly in African Americans. Of all major ethnic groups, African American women face the highest risk for death from heart disease, and their rate of heart

attacks is increasing. (Mortality rates in men do not differ much by race.) African Americans face a number of biologic and social dangers to their hearts:

- They have a higher prevalence of diabetes and hypertension than do Caucasians.
- They have poorer diets, higher stress levels, and lack of access to health care.
- All African Americans face discrimination, but women may be at particular risk for unequal treatment. In one study in which female actors portrayed heart patients, African American women were 60% less likely to receive aggressive (and expensive) diagnostic tests than African American men or any Caucasians, even though they presented with similar symptoms.
- While African Americans comprise 13% of the US population, African Americans have comprised only 2% to 9% of subjects in most of the major research trials, and so knowledge about their specific risks is limited.
- Some African Americans with coronary artery disease appear to have a genetic trait that increases the danger of triglycerides, which may be particularly hazardous in women.
- One study found that African Americans produce less nitric oxide in response to stress; this substance is critical for opening blood vessels and increasing blood flow.

Other Groups. Native Americans, particularly those in North and South Dakota, also face a much higher risk for heart disease than whites. Hispanics have a lower risk for heart disease than all these groups.

Smoking

Smokers in their thirties and forties have a heart-attack rate that is five times higher than their nonsmoking peers. Cigarette smoking may be directly responsible for at least 20% of all deaths from heart disease, or about 120,000 deaths annually. Smoking cigars may increase the risk of early death from heart disease, although evidence is much stronger for cigarette smoking.

Specific Effects on the Heart. Its damaging effects on the heart are multifold:

- Smoking lowers HDL levels (the so-called good cholesterol) even in adolescents.
- It causes deterioration of elastic properties in the aorta, the largest blood vessel in the body, and increases the risk for blood clots.
- It increases the activity of the sympathetic nervous system (which regulates the heart and blood vessels).
- Tobacco smoke may increase cardiovascular disease in women through an effect on hormones that causes estrogen deficiency.

Effects of Second-Hand Smoke. Studies continue to confirm the dangers of second-hand smoke. Regular exposure to passive smoke is now estimated to increase the risk of heart

disease in the nonsmoker by between 25% and 91%, causing 30,000 to 60,000 deaths each year. [For more information, see Smoking.]

Cholesterol and Other Lipids

A number of studies have now demonstrated that reducing LDL and total cholesterol levels and boosting HDL levels have improved survival and prevented heart attacks. Depending on risk factors, people should aim for the following cholesterol levels:

General cholesterol targets:

- Total cholesterol levels: 200 mg/dl or below.
- LDL cholesterol levels: 160 mg/dl or below. (The lower the better.)
- HDL cholesterol levels: 45 mg/dL for men and 50 mg/dL for women, with everyone aiming for about 60. (The higher the better.)
- Triglyceride levels: 200 mg/dL or lower. (Although some evidence suggests that people should aim for levels under 100 mg/dL to reduce the risk for heart disease.)

Targets for people with two or more risk factors for heart disease:

- LDL levels: 130 mg/dl or below.

Targets for people with existing heart disease:

- LDL levels of below 100 mg/dl.

Elevated levels of other lipids, including lipoprotein (a) and apolipoprotein A-1 and B are also now thought to be important indicators of heart risk. Apolipoprotein B, for example, may actually turn out to be a very accurate indicator of heart disease risk in women. [For more information, see Cholesterol and Heart Healthy Diet.]

High Blood Pressure

High blood pressure, or hypertension, has long been a proven cause of coronary artery disease. Blood pressure is categorized as:

- Optimal (below 120/80 mm Hg).
- Normal (between 120/80 and 130/85 mm Hg).
- High normal (between 130/85 and 139/89). (Some studies indicate that high normal puts one at higher risk for heart events and stroke, although others suggest this risk exists primarily in people with diabetes.)
- Hypertension, or high blood pressure (140/90).

A number of studies have now reported that an elevated *systolic* blood pressure is a significantly more accurate indicator of hypertension, particularly in the elderly. (The

systolic pressure is the higher and first number in blood pressure measurements. It measures the force that blood exerts on the artery walls as the heart contracts to pump out the blood.) [For more information, *see High Blood Pressure .*]

Sedentary Lifestyle and Exercise

People who are sedentary are almost twice as likely to suffer heart attacks as are people who exercise regularly. Regular moderate aerobic exercise benefits the heart in many ways. For instance, brisk walking has the following advantages:

- lowers the heart rate and blood pressure
- improves cholesterol
- lowers blood sugar levels
- opens up the blood vessels and, in combination with a healthy diet, may improve blood clotting factors
- reduces stress and improves mood

Some studies suggest that for the greatest heart protection, it is not the *duration* of the exercise that counts but the *total daily amount* of energy expended. Therefore, the best way to exercise may be in multiple short bouts of intense exercise. Even elderly people with unstable angina or who had a previous heart attack can benefit from a structured exercise program. Exercises that train and strengthen the chest muscles may also prove to be very important for patients with angina.

It should be noted that sudden strenuous exercise (such as snow shoveling and mowing lawns) puts such people at risk for angina and heart attack. Activities that involve raising the arms above the head may also be risky. Patients with angina should never exercise shortly after eating.

People with risk factors for heart disease should seek medical clearance and a detailed exercise prescription. And all people, including healthy individuals, should listen carefully to their bodies for signs of distress as they exercise. [*See Exercise.*]

Diabetes and Insulin Resistance

Heart attacks account for 60% and strokes for 25% of deaths in all diabetics. A 1998 study reported that people with type 2 diabetes and no history of heart disease have the same seven-year risk for a heart attack as nondiabetics with heart disease.

Long-term insulin resistance, even without type 2 diabetes, appears to have significant damaging effects on the heart. This condition occurs when insulin levels are normal to high but the body is unable to use the insulin to regulate metabolism of blood sugar and to store it for energy. In such cases, the body compensates by increasing insulin levels (hyperinsulinemia), which in turn increases triglyceride levels and reduces HDL cholesterol. Normally, insulin stimulates the release of two substances, endothelin and nitric oxide, that are important in keeping arteries elastic and open. Insulin resistance may

cause an imbalance in these substances. [For more information, *see Diabetes: Type I or Diabetes: Type II .*]

Homocysteine

Abnormally high blood levels of the amino acid homocysteine are strongly linked to an increased risk of coronary artery disease and stroke. Homocysteine may harm the lining of the arteries and contribute to blood clotting. Excessive levels occur with deficiencies of vitamins B6, B12, and folic acid. Some experts believe that high levels of homocysteine are only indicators, not causes, of heart disease. However, studies are reporting strong associations between this factor and heart disease.

Obesity

Obesity is related to hypertension, diabetes, abnormal cholesterol levels, and lack of exercise, all conditions contributing to heart attack risk. Abdominal obesity (the "beer belly") poses a particular risk. In fact, a 2000 study reported that men who have waists that measure more than 36 inches and high triglyceride levels (more than 2 mmol/L) are at high risk for developing heart disease within five years. Obesity in children is a greater risk for future heart trouble than a family history of heart disease. People who are overweight in middle age may still not completely reduce their risk for coronary artery disease later in life, even if they lose excess weight. [For more information, *see Obesity.*]

Eating Habits

Fats. Experts now believe that fats can have both harmful and beneficial effects. (Whether harmful or beneficial they are still high in calories):

Harmful fats: Everyone should limit and try to avoid the following fats:

- Saturated fats, predominantly in animal products, including meat and dairy products. (The so-called tropical oils, palm, coconut, and cocoa butter, are also high in saturated fats. Evidence is lacking, however, about their effects on the heart.)

Trans-fatty acids, which are created during a process aimed at stabilizing polyunsaturated oils to prevent them from becoming rancid and to keep them solid at room temperature. Hydrogenated fats are used in stick margarine and in many fast foods and baked goods. (Liquid margarine is not hydrogenated.)

Beneficial oils: Public attention has mainly focused on the possible benefits of monounsaturated and polyunsaturated fats found in vegetable oils. Researchers are most interested, however, in the smaller fatty-acid building blocks contained in these oils called *essential* fatty acids. Studies indicate that in a healthy balance, all of these fatty acids are essential to life:

- Omega-3 fatty acids: further categorized as:

Alpha-linolenic acid (sources include canola oil, soybeans, flaxseed, olive oil, and many nuts and seeds). Indications that it is heart protective. (Extra virgin olive oil in one study was associated with lower blood pressure. Many studies have singled out nuts, which contain omega-3 fatty acids, fiber, as being particularly beneficial for the heart by lowering LDL and total cholesterol without increasing triglycerides.) and

Docosahexaenoic and eicosapentanoic acids (sources are oily fish). May not have much effect on cholesterol but they may benefit the lining of blood vessel (the endothelium) and therefore improve blood flow.

- Omega-6 fatty acids: further categorized as linoleic, or linolic, acid (sources are flaxseed, corn, soybean, and canola oil).
- Omega-9 fatty acids: (Source is olive oil).

Some experts recommend maintaining a relatively high intake of monounsaturated and polyunsaturated fats (about 32% of calorie intake), with saturated fats representing no more than 8%. Others believe that a *very* trim diet, 20% fat with as little as 4% saturated fat, is ideal. Still others recommend fat intake somewhere in between these extremes.

Carbohydrates. Meals overly rich in carbohydrates tend to set off angina attacks, possibly because they raise insulin levels. One study suggested, in fact, that in women, sugar may pose an even higher risk for heart disease than fats do. Whole grains and fresh fruits and vegetables (particularly dark-colored ones), however, are very important. They are rich in fiber, vitamins, and other important nutrients that are heart-protective. Natural chemicals in cooked tomatoes, garlic, nuts, apples, onions, wine, and tea also appear to offer protection for the heart.

Protein. Soy is proving to be a particularly excellent source of protein. It is rich in both soluble and insoluble fiber, omega-3 fatty acids, and provides all essential proteins. It has estrogen-like compounds that might be as effective as estrogen therapy itself in slowing progression of heart disease without increasing triglycerides or the risk for breast cancer (as estrogen therapy does).

Much evidence suggests that eating fish two or three times a week, particularly oily fish (such as salmon, halibut, swordfish, and tuna) is protective.

Salt. Studies now indicate that sodium intake may be a major contributor to heart disease in overweight people. Its effect on people with normal or low weight may not be as severe, although everyone would do well to keep salt intake to a minimum. [For more information, see *Heart Healthy Diet.*]

Vitamins and Supplements

B Vitamins. Sufficient amounts of folic acid, B6, and B12 are certainly important to prevent high levels of homocysteine.

Vitamin E. A number of small studies have found an association between a lower risk for coronary artery disease with doses of vitamin E between 100 and 400 IU. One important 2000 study, however, reported that taking vitamin E in daily doses of 400 IU for over four years had no benefits for people at high risk for heart attack or other heart events. It should also be noted that in people taking medications to prevent clotting, such as aspirin or heparin, adding vitamin E could theoretically increase the risk for bleeding.

Vitamin C. Little evidence has emerged to prove any protective effects from taking vitamin C. Of interest, however, is a study suggesting that long term administration of vitamin C may improve endothelial function, a factor affecting blood flow.

Beta Carotene. Studies have reported that a high intake of beta-carotene and other carotenoids from dark colored fruits and vegetables (but not from supplements) may reduce the risk of heart attack. (Smokers who take beta carotene supplements may face a higher risk for lung cancer.)

Note: Studies are continuing to indicate that high doses of antioxidants supplements, such as vitamins C, E, and beta carotene, may have pro-oxidant effects that can harm the arteries and incur other damage. [For more information, *see Vitamins, Carotenoids, and Phytochemicals.*]

Psychologic Factors

Stress. Mental stress is as important a trigger for angina as physical stress. Incidents of acute stress have been associated with a higher risk for serious cardiac events, such as heart rhythm abnormalities and heart attacks, and even death from such events in people with heart disease. Stress may negatively affect the heart in several ways:

- Sudden stress increases the pumping action and rate of the heart and causes the arteries to constrict, thereby posing a risk for blocking blood flow to the heart.
- Emotional effects of stress alter heart rhythms and pose a risk for serious arrhythmias in people with existing heart rhythm disturbances.
- Stress causes blood to become stickier (possibly in preparation of potential injury), increasing the likelihood of an artery-clogging blood clot.
- Stress may signal the body to release fat into the bloodstream, raising blood-cholesterol levels, at least temporarily.
- Stress may lead to increased levels of homocysteine.
- In women, chronic stress may reduce estrogen levels.
- Stressful events may cause men and women who have relatively low levels of the neurotransmitter serotonin (and thus a higher risk for depression or anger) to produce more of certain immune system proteins (called *cytokines*), which in high amounts cause inflammation and damage to cells.
- Stress causes a sudden and temporary increase in blood pressure, although long-term effects are not completely known. [*See Stress.*]

Depression. Studies indicate that depression may have adverse biologic effects on the immune system, blood clotting, blood pressure, blood vessels, and heart rhythms. Depression may even impair a patient's response to medication for heart disease. In one 30-year study, men who were clinically depressed had a greater risk for heart disease and heart attack than men who were not depressed; this increased risk lasted for decades. The more severe the depression, the more dangerous to the health, although some studies have indicated that even mild depression, including feelings of hopelessness, experienced over many years, may harm the hearts in people with no early signs of heart disease . [*See Depression.*]

Alcohol

The effects of alcohol on heart disease vary depending on consumption. Evidence strongly suggests that light to moderate alcohol consumption (one or two drinks a day) protects the heart. The benefits are strongest in people at high risk for heart disease and may be fairly small in those at low risk. Light to moderate alcohol intake may even reduce the risk of sudden cardiac death and also protect against coronary heart disease in people with adult-onset diabetes. Large amounts of alcohol, however, can raise blood pressure, trigger irregular heartbeats, and damage the heart muscle. Binge drinkers have a significantly higher risk for a cardiac emergency.

Estrogen

Benefits of Estrogen. Estrogen appears to have many benefits for the heart:

- It protects against unhealthy cholesterol, triglyceride, and other lipid levels.
- It may have direct actions on blood vessels, relaxing, and opening them and keeping their lining smooth.
- Estrogen is also an antioxidant. It helps neutralize oxygen free radicals.
- The effects of estrogen on blood pressure are not clear; oral contraceptives, for instance, appear to increase pressure slightly. Two 1999 studies reported, however, that supplementary estrogen reduced night-time blood pressure in women with normal pressure.
- Estrogen also affects many blood clotting factors in the liver; it reduces blood viscosity (stickiness) and may enhance fibrinolysis, the natural process for breaking down blood clots. (Estrogen's effects on clotting, however, are complex, since there is also a well-known increased risk for thromboembolism (blood clots that blocks a vessel) in women taking estrogen.

Hormone Replacement Therapy. After menopause, estrogen levels decline dramatically. Hormone replacement therapy for postmenopausal women is problematic, however. A number of studies have reported that unopposed estrogen helps prevent heart disease from developing in the first place. Neither unopposed estrogen therapy nor estrogen combined with progestins, however, appears to stop progression of heart disease in

women who already have evidence of it. In fact, studies have also reported that the risk for heart attack and stroke is slightly higher in the first two years of treatment. The risk declines afterward, however, and in one study by the fourth and fifth year, HRT-users had fewer heart events. The reasons for the higher risk may be due to estrogen's actions on increasing the risk for blood clots and possible pro-inflammatory effects in certain women. [*See also Estrogen Therapy* .]

Genetic Factors

Genetics are involved in increasing the likelihood of developing important risk factors (eg, diabetes, obesity, and high blood pressure). One genetic variant called apolipoprotein E4 (ApoE4) affects cholesterol levels, particularly those associated with heart disease. A 1999 study suggests that it may be a significant risk factor for coronary artery disease in early middle age. (This variant also increases the risk for Alzheimer's disease.)

Infectious Agents

Some microorganisms and viruses have been under suspicion for triggering inflammation in the arteries and contributing to heart disease risk. The primary suspects have been *Chlamydia pneumoniae* (a non-bacterial organism that causes mild pneumonia in young adults), *H. pylori* (bacteria responsible for peptic ulcers), and the viruses herpesvirus and *cytomegalovirus*. Animal studies have reported strong associations between some of these microorganisms and future heart disease, but recent studies have suggested that any causal role in people is likely to be weak. Nevertheless, research does suggest that inflammation after infection may injure the cells lining blood vessels. And, in a 1999 study, researchers did report that patients who had high levels of a byproduct of bacterial infection called endotoxin had three times the normal risk for heart disease. This study still does not prove that bacteria actually cause heart disease.

Other Factors

Factors before Birth and In Infancy. Low weight at birth and in the womb has been associated with later heart disease in a few studies. Some suggest, however, that this may just reflect poor nutrition in the mother, which appears to affect life-long risk. A 2000 British study reinforced the idea that pre-birth or other early events have little significant effect on heart disease risk in later life.

Seasonal Differences. More deaths from heart disease occur in December and January and fewest in the summertime. Although lower temperatures and snow shoveling may play a role in some cases, more winter deaths have been reported even in warm regions. Holiday stress or fewer daylight hours have been suggested as other reasons for these higher winter rates.

Iron. High dietary intake of iron may be an important factor in the process of atherosclerosis.

Physical Characteristics. Male pattern baldness, hair in the ear canals, and creased earlobes are associated with a higher risk for heart disease in white males. (Interestingly, in African American men, of these factors, only creased earlobes were associated with a higher risk in one study.)

Snoring and Sleep Apnea. A 2000 study reported a modest increase in heart disease in women who snore regularly, regardless of whether they were overweight or had other heart risk factors. Snoring is a common symptom of obstructive sleep apnea. In this condition, tissues in the upper throat collapse at intervals during sleep, thereby blocking the passage of air. Sleep apnea is a known risk factor for high blood pressure and is highly associated with obesity. But it may contribute to heart disease through other actions as well. For example, during the night, apnea has been associated with a higher incidence of ischemia (reduced supply of oxygen rich blood) and in the morning with "stickier" blood (increasing the risk for blood clots).

What Are Tests For Stable Angina And For An Initial Diagnosis Of Coronary Artery Disease?

Blood and Urine Tests

Blood and urine tests that indicate a risk for coronary artery disease and heart attack include those for cholesterol, homocysteine, the protein albumin, and blood clotting factors, especially fibrinogen.

Electrocardiograms

An electrocardiogram (ECG) measures and records the electrical activity of the heart during an angina attack. Between 25% and 50% of people who suffer from angina or have silent ischemia, however, have normal ECG readings.

Echocardiograms

An echocardiogram uses ultrasound images of the heart. This test is more expensive than an ECG, but it can detect muscle weakness from a prior heart attack or motion abnormalities. Echocardiograms may be more useful for women than ECGs.

Stress Test

Basic Procedure. A stress test (exercise tolerance test) monitors the patient's heart rhythms, blood pressure, and clinical status. Because stress tests can *precipitate* angina, irregular heart rhythms, or, rarely, even heart attacks, they must be performed under careful supervision. A typical stress test involves the following:

- The patient walks on a treadmill or rides a stationary bicycle. (For patients who cannot exercise, the drug dobutamine may be given, which simulates the stress of exercise.)
- Exercise continues until the heart is beating at least 85% of its maximum rate or until heart rhythm abnormalities, angina, fatigue, or other symptoms of heart trouble occur.
- An ECG is usually used to monitor heart rhythms during a stress test, although an echocardiogram may be used.
- Failure to reach the target heart rate may be a sign of a risk for heart attack and angina in people with coronary artery disease or even a predictor for coronary artery disease in people without a current problem.

Unfortunately, only about 65% of patients are diagnosed correctly using an ECG with the test, and the accuracy is even worse for women. (Using an echocardiogram instead of an ECG may be a more accurate procedure for women.) About 10% of healthy patients, particularly younger people, will have abnormal test results (false positive).

Stress-Thallium Test. The stress-thallium test may be used with the exercise stress test. It is a reliable measure of severe heart events:

- Before starting to exercise, the patient receives an injection of thallium 201, a radioactive chemical, which is taken up by normal heart muscle cells.
- Immediately after exercise, heart scans are performed.
- If muscle tissue is damaged by ischemia (oxygen deprivation), it will fail to take up thallium and will be detected on the scanned image.
- If the scan detects damage, it is repeated two or three hours after exercise.
- Damage due to a *prior* heart attack will persist when the heart scan is repeated. Injury caused by angina, however, will have resolved by that time.

Electron Beam Computed Tomography

Electron beam computed tomography (EBCT) scans (also called ultrafast computed tomography (CT) scans) are so fast that they can freeze the motion of the heart. Scans from EBCT reveal deposits of calcium on the arterial walls, indicators of current and future coronary artery disease. This is the only technique that can detect coronary artery disease in all stages of development from asymptomatic heart disease to conditions severe enough to produce heart attacks. The test is expensive, however, and there is much controversy over whether EBCT should be used as a widespread screening tool to detect early coronary artery disease.

What Are The Tests Used To Determine A Heart Attack?

Electrocardiogram

The electrocardiogram (ECG) measures the wave patterns of the heart. It is the critical first diagnostic step and when a heart attack is suspected, a patient is monitored continuously with an ECG. It is used to both determine the severity of the condition and the optimal immediate treatment. It is also extremely important to rule out other dangerous conditions. The most important wave patterns in diagnosing and determining treatment for a heart attack are called *ST elevations and Q waves* .

Elevated ST-segments indicate that the artery to an area of the heart is blocked, and that the full thickness of the heart muscle is damaged. In most cases patients go on to develop a full-blown heart attack, medically referred to as a Q-wave myocardial infarction. ST-elevations are good indicators for aggressive treatments (thrombolytic drugs or angioplasty) to reopen blood vessels. In some cases, however, the patient's status drops to a non-Q-wave myocardial infarction, a less serious condition. [*See below* .]

Non-elevated ST segments indicate a normal heart beat and occur in about half of patients with other signs of a heart event. In such cases, laboratory tests are needed to determine the extent, if any, of heart damage. In general, one of three following conditions may be present:

- Angina (blood test results or other tests show no serious problems and chest pain resolves). Most patients with angina can go home.
- Unstable angina (blood tests do not show markers for heart attack but chest pain is persistent). Unstable angina is potentially serious.
- Non Q-wave myocardial infarction (blood tests suggest a developing heart attack but most likely injury in the arteries is less serious than with a full-blown heart attack).

Depressed ST-segments represent a potentially very serious problem.

Blood and Urine Markers

When heart cells become damaged, they release different enzymes and other molecules into the blood stream. Elevated levels of such *markers* of heart damage in the blood or urine may help predict a heart attack in patients with severe chest pain. Some of these factors include the following:

- Troponins. The enzymes cardiac troponin T and I are released when the heart muscle is damaged. Both are proving to be among the best markers for a high risk for heart attacks in patients with non-elevated ST segments.
- Creatine kinase myocardial band (CK-MB). CK-MB has been a standard marker but it is not very accurate since elevated levels can appear in people without heart injury. Certain forms of CK-MB may improve its ability to specifically target heart injury.
- Myoglobin. Myoglobin is a protein found in heart muscles. It is released early in the injured heart and it may be useful in combination with CK-MB and the troponins.

- Fibrinogen is a protein involved in blood clotting.
- C-reactive protein is a product of the inflammatory process. Markers that show a very strong inflammatory response in patients with unstable angina may be important indicators for aggressive treatment.

Angiography

Angiography is an invasive test that may be performed on patients who have very incapacitating angina that does not respond to medical therapy.

- A narrow tube is inserted into an artery, usually in the leg or arm, and then threaded up through the body to the coronary arteries.
- A dye is injected into the tube and an x-ray records the flow of dye through the arteries.
- This process provides a map of the coronary circulation, revealing any blocked areas.

Of some importance is a study reporting that women with chest pain may have a normal angiogram but still have evidence of heart disease from tests. Major complications include stroke, heart attacks, and kidney damage. These risks are very low (about 0.1%), however, if the procedure is done in an experienced medical center (one that performs at least 300 of these operations every year). Allergic reactions can also occur. The procedure is expensive, and between 10% to 30% of patients who have this procedure have normal results. Many experts believe, therefore, that this procedure is overused.

Imaging Tests

Echocardiograms. Echocardiograms are useful in patients who are suspected of having a heart attack caused by a rupture in the aortic artery.

Magnetic Resonance Imaging. Enhanced software for magnetic resonance imaging (MRI) techniques, which are nonradioactive, are providing accurate information on arterial blood flow, including that in very small vessels not visible using angiography.

Ruling out Other Causes of Symptoms

Other Conditions that Cause Chest Pain. Many conditions may cause chest pain. High on the list are the following:

- Dangerous conditions that must be ruled out include rupture of the aorta, collapsed lung, acute inflammation of the heart, or a blood clot in the lung.
- Anxiety attacks.
- Gastrointestinal disorders (gallstone attacks, peptic ulcer disease, hiatal hernia, heartburn).
- Asthma.

- Problems affecting the ribs and chest muscles (injured muscles, fractures, arthritis, spasms, infections).
- Spasm in the coronary artery.
- Abnormalities of the heart muscle itself.
- Hyperthyroidism.
- Anemia.
- Vasculitis (a group of disorders that cause inflammation of the blood vessels).
- Exposure to high altitudes (rare).

What Are The General Guidelines For Managing Angina And Coronary Artery Disease?

Determining Treatments and Severity

Patients with chest pain and ECG showing elevated ST segments or other obvious signs of dangerous blockage have heart attacks and are immediately treated accordingly. [See Heart Attack.] Patients with chest pain and an ECG reading showing *non-elevated* ST-segments, however, have possible angina, unstable angina, or pending heart attack. [See *Electrocardiogram above.*] Experts must be able to predict which of these patients are most at risk for developing a serious condition with two weeks of admission. They define this risk as three end points: death from any cause, nonfatal heart attack, and arteries that are so blocked that they require an urgent operation to open them within two weeks.

To determine who is most or least at risk for this so-called triple-end point, some experts developed a very promising and easy scoring system based on the following criteria:

- Age 65 years or older.
- Three or more risk factors for heart disease (family history, hypertension, diabetes, current smoking, or unhealthy cholesterol levels).
- Previous blockage of an artery of at least 50%.
- ST-segment deviation.
- Severe angina symptoms.
- Aspirin use within the previous week.
- Elevated creatine kinase or its MB fraction. [See Blood and Urine Tests above.]

In one 2000 study the lowest score (having 1 or none of these risk factors) suggested a 5% risk for the triple-end point, while the highest score (6 or 7) suggested a 40% risk.

Guidelines for Managing Angina and Coronary Artery Disease

Drug therapy is effective for the treatment of stable angina and for slowing progression of coronary artery disease. Unstable angina may require surgical intervention in addition to the therapies given for stable angina. Lifestyle changes are essential for improving outcome in anyone with heart disease. Experts have come up with a mnemonic device

(ABCDE) for remembering ten factors that are fundamental for angina management:

- A. Aspirin and antianginal drugs
- B. Blood pressure and beta-blockers
- C. Cholesterol and cigarettes;
- D. Diet and diabetes;
- E. Exercise and education.

What Are The Drugs Used For Angina And Coronary Artery Disease?

Nitrates

Nitrates have been used in the treatment of angina for over a hundred years. These drugs release nitric oxide, thereby relaxing the smooth muscles in blood vessels. Many nitrate preparations are available; the most commonly used are nitroglycerin, isosorbide dinitrate, and isosorbide mononitrate. Erythrityl is popular overseas but is prescribed less in the US. Nitrates can be absorbed from the gastrointestinal tract (oral tablet), skin (ointment or patch), and from under the tongue (sublingual tablet or spray).

Rapid Acting Nitrates. Rapid-acting nitrates are used to treat acute attacks. Nitroglycerin is the most widely agent for this purpose. It can be administered under the tongue (sublingually or as a spray) or pocketed between the upper lip and gum (buccally) and can relieve angina within minutes. The procedure for taking nitroglycerine during an attack is as follows:

- At the onset of an angina attack, the patient administers one sublingual or buccal tablet or one metered dose of the spray.
- If the pain is not relieved within five minutes the patient takes a second dose; a third can be taken after another five minutes if symptoms persist.
- If pain continues after a total of three doses in 15 minutes, the patient should go to the nearest emergency room at once.

Nitroglycerin is very volatile so its potency can be easily lost. A patient should take the follow precautions:

- Keep no more than 100 tablets on hand stored in their original container.
- When first opened, the cotton filler should be discarded, and the cap screwed on tightly immediately after each use.
- A supply should always be kept close at hand in case of an attack, with the rest kept in a cool dry place.

Intermediate to Long-Term Nitrates. Sublingual tablets of isosorbide dinitrate and erythrityl have a somewhat slower onset of action than nitroglycerin and are useful for preventing exercise angina. They are recommended for angina attacks only in patients who do not respond to nitroglycerin.

Ointments, patches, and oral tablets are used for longer-term prevention of angina attacks:

- Transdermal patches are applied in the morning to any hair- or injury-free area on the chest, back, stomach, thigh, or upper arm. Hands should be washed after each patch or ointment application and sites of application should be rotated to avoid skin irritation.
- Nitroglycerin ointment is applied by measuring out an even amount on an applicator paper and then placing, not rubbing or massaging, it on the chest, stomach, or thigh. Any ointment that remains from the previous application should be removed.

Long-acting forms may lose their effectiveness over time, so physicians generally schedule nitrate-free breaks to prevent tolerance. Some concern exists that nitrate-free periods might increase the risk for angina and adverse heart events. One large study, however, found no increased danger when patients used a nitroglycerine patch with scheduled breaks. The use of drugs known as ACE inhibitors, normally used for high blood pressure, may help prevent tolerance to nitrates. (Some studies suggest that vitamin C or E might also may help.)

Side Effects. Side effects of nitrates include headaches, dizziness, nausea, blurred vision, fast heartbeat, and sweating. Low blood pressure and dizziness can be relieved by lying down with the legs elevated. *Note:* These effects can be significantly worsened by alcohol, beta-blockers, calcium channel blockers, sildenafil (Viagra), and certain antidepressants.

Withdrawal. Withdrawal from nitrates should be gradual. Abrupt termination may cause angina attacks.

Beta-Blockers

Beta-blockers reduce the oxygen demand of the heart by slowing the heart rate and lowering arterial pressure. They are now well known for reducing deaths from heart disease. Beta-blockers do not stop angina attacks, but used preventively, they reduce their frequency and the dependency on nitrates. They may also be beneficial for people with silent ischemia. (Beta-blockers are less useful for the treatment of Prinzmetal's angina.)

Specific Beta-blockers. Beta-blockers include propranolol (Inderal), labetalol (Normodyne, Trandate), acebutolol (Sectral), atenolol (Tenormin), metoprolol (Toprol), and bisoprolol (Zebeta). Carvedilol (Coreg), a newer agent known as a nonselective beta-blocker, appears to be as safe as the older beta-blockers and may prove to have additional

advantages. A nasal spray form of propranolol appears to be very beneficial in helping to reduce exercise-induced angina attacks.

Side Effects. Some beta-blockers tend to lower HDL cholesterol (the beneficial cholesterol) by about 10%; the effect is most marked in smokers. Fatigue and lethargy are the most common psychologic side effects. Some people experience vivid dreams and nightmares, depression, and memory loss. Exercise capacity may be reduced. Other side effects may include cold extremities, asthma, decreased heart function, gastrointestinal problems, and sexual dysfunction. If side effects occur, the patient should call a physician, but it is extremely important not to stop the drug abruptly. Angina, heart attack, and even sudden death have occurred in patients who discontinued treatment without gradual withdrawal.

Aspirin and Other Anti-Clotting Agents for Unstable Angina

Anti-clotting agents, either anticoagulants (eg, heparin, warfarin) or anti-platelet drugs (aspirin, glycoprotein IIb/IIIa receptor antagonists, clopidogrel), are being used to treat unstable angina, to protect against heart attacks, and prevent blood clots during heart surgeries. Oral anticoagulants, such as warfarin, are showing promise. They may be used alone or in combinations, depending on the severity of the condition. Aspirin alone has been reported to reduce risk of death from heart attack or stroke by 25% to 50% and to cut risk of non-fatal heart attacks by 34 percent. All anti-clotting therapies carry the risk of bleeding, which can lead to dangerous situations, including stroke.

Aspirin. Aspirin inhibits blood platelets (major clotting factors). Low-dose aspirin is usually the first choice for preventing heart attacks in people with stable angina or those with risk factors for a first heart attack. Aspirin is more effective in reducing pain from unstable than stable angina. Of concern, however, is a 2000 study suggesting that low-dose aspirin may provide primary prevention only for patients with low-normal blood pressure. Prolonged use may produce gastrointestinal ulcers and bleeding.

Of further concern are reports suggesting an association between recent use of aspirin or similar drugs called NSAIDs and a higher incidence of hospitalization in heart failure patients, particularly if they are also taking diuretics or ACE inhibitors. In fact, one study suggested that anyone with a history of heart disease who is taking NSAIDs may be at higher risk for heart failure. (Low dose aspirin may not pose this danger.) Studies are needed on these important questions.

Heparin. The anticoagulant heparin, used alone or in combination with aspirin, is another standard blood-thinning drug, but it must be intravenously administered and monitored carefully for signs of bleeding. (A 1999 study indicated that adjusting the heparin dose according to the patient's weight when it is administered during acute conditions can reduce the risk for hemorrhage.)

Enoxaparin (Lovenox), dalteparin (Fragmin), or reviparin are drugs known as low-molecular weight heparins (LMWHs). They require injections but do not need continuous

monitoring, as heparin does. Studies are finding that they are very effective for unstable angina and are outperforming standard heparin in patients with severe conditions. Patients may even be able to self-administer LMWHs as people with diabetes do insulin.

Warfarin. Warfarin (Coumadin) is an oral anticoagulant. It prevents clots by inhibiting vitamin K and can be taken orally. It is particularly beneficial for patients with atrial fibrillation. It, too, must be monitored. In one 1999 study, the most successful regimens in reducing risk for heart attack and stroke were moderate-to high-intensity oral anticoagulants in combination with low-dose aspirin. Low-intensity warfarin had about the same effectiveness as aspirin. Further trials are needed.

Glycoprotein IIb/IIIa Receptor Antagonists. Glycoprotein IIb/IIIa receptor antagonists thin blood by blocking platelets. Examples of these drugs include abciximab (ReoPro, Centocor), eptifibatide (Integrelin), lamifiban, and tirofiban (Aggrastat). Early studies suggested that they reduced the risk for heart attack or death in many patients with unstable angina when combined with low-weight heparin or other agents. A major 2000 study on abciximab, however, reported that it offered no additional protection. In fact, patients who took it had poorer results than those on placebo, particularly after taking it for a long time. More research is needed to determine the implications of this study. Glycoprotein IIb/IIIa receptor antagonists are still helpful in relieving anginal pain in angioplasty patients, and a number of studies report significant benefits with the use of intravenous administration for unstable angina.

Certain patients (eg, thin, elderly, nonwhite, with more than one heart risk factor) may be at high risk for thrombocytopenia, a drastic reduction in platelets that can cause severe bleeding, after taking these drugs.

Platelet Inhibitors. Clopidogrel (Plavix) and ticlopidine (Ticlid) are platelet inhibitors. Studies indicate that clopidogrel is more effective than either aspirin or ticlopidine for reducing the incidence of a heart attack. Ticlopidine has been associated with dangerous blood disorders, particularly thrombocytopenia, and is used only in certain circumstances. Although clopidogrel has largely replaced ticlopidine because it had a better early safety profile, reports of thrombocytopenia in patients taking clopidogrel have created some concern. More research is needed to determine if the risk is as high as in ticlopidine. Platelet inhibitors may be particularly useful in preventing blood clots after angioplasty. [See Angioplasty and Coronary Stents, below.]

Hirudin. Hirudin is a substance derived from the saliva of leeches. Bivalirudin (Hirulog) is the standard drug derived from hirudin. Studies are suggesting that hirudin agents may be more effective and safer than heparin. (Hirudin, however, can cause major bleeding episodes.)

Other Anti-Clotting Agents. Other promising anti-clotting drugs include the anticoagulant argatroban (Novastan) and danaparoid (Orgaran).

Statins

Cholesterol-lowering drugs commonly known as the statins may improve blood flow through the arteries, even after being taken for only a few months. In a 1999 review of major clinical trials of the drugs, researchers found that statins effectively reduce not only levels of LDL cholesterol but also the risk of major coronary events, including first and second heart attacks, in both women and men and in people older than sixty-five. They are even proving to reduce the risk for heart attacks in people with normal or below-normal cholesterol. [For more information *see Cholesterol.*]

Angiotensin Converting Enzyme Inhibitors

Angiotensin converting enzyme (ACE) inhibitors are important agents. They are used in hypertension and currently recommended as first-line treatment for people with diabetes and kidney damage, for some heart attack survivors, and for patients with heart failure. Now, an important 2000 study that tested ramipril (Altace), has suggested that other patients might benefit from it. In the study, high-risk patients who took ramipril significantly lowered their risk for heart attack, stroke, complications of diabetes, and death. Such patients had either coronary artery disease, a history of stroke, or diabetes plus at least one other heart risk factor, such as high blood pressure, unhealthy cholesterol levels, or smoking. (Ramipril had no effect on angina, however.) It is not yet known if these benefits apply to other ACE inhibitors, such as captopril (Capoten), enalapril (Vasotec), lisinopril (Prinivil, Zestril), and fosinopril.

Side Effects. Side effects of ACE inhibitors are uncommon but may include an irritating cough, excessive drops in blood pressure, and allergic reactions. Of great concern is research suggesting that aspirin (and other so-called NSAIDs) increases the risk for heart failure in patients taking ACE inhibitors [see *Anti-Clotting Agents* below].

Calcium Channel Blockers

Calcium channel blockers reduce heart rate and slightly dilate the blood vessels of the heart, thereby decreasing oxygen demand and increasing oxygen supply. Those approved for angina include verapamil (Calan, Isoptin), nifedipine (Adalat, Procardia), nicardipine (Cardene), amlodipine (Norvasc), diltiazem (Cardizem, Tiazac), and bepridil (Vascor). Combinations with other agents may be beneficial. (Single use of agents, in any case, is not helpful for patients with unstable angina.) There is no evidence, in any case, that calcium channel blockers increase survival rates, and their safety in some cases is being questioned. A major 2000 study now suggests that they are inferior to other drugs (including diuretics, beta-blockers, and ACE inhibitors) in treating high blood pressure. Severe and even dangerous side effects, including an increase in heart attacks and sudden death, have occurred with short-acting forms, including short-acting nifedipine and bepridil. (A 1999 study found no worse survival rates in heart attack patients who took diltiazem, nifedipine, amlodipine, or verapamil. Bepridil, however, posed some risk and, in any case, is not recommended unless patients do not respond to other calcium blockers.) Currently the National Heart, Lung, and Blood Institute warns that short-acting nifedipine should be used with great caution (if at all), especially at higher doses, in patients with angina. No one currently taking any calcium channel blocker should stop

taking it abruptly, because such action could dangerously increase the risk of high blood pressure. Overdose can cause dangerously low blood pressure and slow heart beats. It should be noted that drinking grapefruit juice with these drugs could increase their effects, sometimes to toxic levels.

Experimental Drugs

Ranolazine. Ranolazine is a unique drug under investigation that reduces the work of the cells in the heart without damaging them. Early studies are showing success in improving short-term exercise tolerance.

Nicorandil. Nicorandil, known as a potassium channel activator, has anti-ischemic and antiarrhythmic properties and may be a useful add-on for patients who need aggressive treatment. Severe mouth sores have been reported in some patients with long-term use.

Antibiotics. The antibiotics tetracyclines and quinolones, which are prescribed for *Chlamydia pneumoniae* and *H. pylori*, have been associated with a lower risk for heart attacks.

What Are The Surgical Treatments For Angina And Coronary Artery Disease?

Candidates for Surgery

Conditions Warranting Surgery. To date, surgery is usually recommended for patients who have the following conditions:

- Unstable angina that does not respond promptly to medical treatment.
- Severe recurrent episodes of angina that last more than 20 minutes.
- Severe coronary artery disease (eg, severe angina, multi-artery involvement, evidence of ischemia), particularly if abnormalities are evident in the left ventricle of the heart, the main pumping chamber. Whether surgery should be used as early treatment for mild angina is controversial. Studies have been mixed on the long-term survival rates in patients who had drug versus surgical treatments. In general, experts believe there is no harm in choosing drug treatments first and angioplasty if symptoms persist.

Choosing a Procedure

A number of invasive techniques are available for treating coronary artery disease. The two standard surgical procedures are *coronary artery bypass grafting* (commonly called bypass) and *percutaneous transluminal coronary angioplasty* (commonly called angioplasty). Studies have generally reported similar effectiveness in the two procedures, although one or the other may be preferable for specific patients.

Advantages with Angioplasty. Angioplasty has the following advantages for most patients:

- It is less invasive than bypass.
- It is initially less expensive. (Although the postoperative need for more medications and the high risk for repeat procedures to reopen the artery reduce the long-term difference in cost between the two procedures.)

Advantages of Bypass. Bypass is usually the appropriate procedure, however, in patients with the following conditions:

- Three or more blocked arteries.
- A left main artery narrowed by 50% or more.
- A very long diseased portion of the artery.
- Diabetes. (In fact, some experts believe angioplasty should rarely, if ever, be used for these patients.)
- The elderly. (Although angioplasty rates are improving in this group, and in one study such patients had a long-term survival rate equal to others.)

Considerations for Women. Women have higher mortality rates than men after surgery no matter what procedure, perhaps because they tend to be older and sicker when they have a heart operation. One study of bypass patients, however, indicated that simply being female was a risk factor for higher mortality regardless of age or health status.

Patients considering surgery should discuss all options and risks with their physician. No surgical procedure cures coronary artery disease, and patients must continue to rigorously maintain a healthy life-style and continue any necessary medications.

Coronary Artery Bypass Graft Surgery (CABG)

The Standard Procedure. Coronary artery bypass graft surgery (CABG) is very invasive and involves the following processes:

- The chest is opened and the blood is rerouted through a lung-heart machine.
- The heart is stopped during the procedure.
- Large blood vessels are taken from the patient's chest, stomach, or leg (a long vessel called the saphenous vein). Grafts taken from three arteries (two in the chest wall plus one from the abdomen) may prove to be more successful than the more traditional approach, taking grafts from two arteries in the chest and the saphenous vein from the leg. Bypass operations that use the three arterial grafts are very complicated, however, and only skilled surgeons should undertake them.
- The blood vessel grafts are transplanted in front of and beyond the blocked arteries, so the blood flows through the new vessels around the blockage.
- Most people are hospitalized for at least a week and do not return to full activity for at least two months.

Complications. Under the best circumstances, bypass surgery carries about a 1% operative mortality rate and the average is 3%. Complications include the following:

- Atrial fibrillation (very fast and irregular heart beats).
- Blood clots that form in the new graft, closing it up. (Therapy with anti-clotting drugs help keep the graft open and working properly. For long-term prevention of closure as well as slowing progression of atherosclerosis, aggressive use of cholesterol-lowering drugs may be more beneficial than the standard anti-clotting drugs.)
- Of some concern was one study reporting that 23% of patients experienced some mental impairment five years after bypass surgery; this warrants further investigation.

Angioplasty and Coronary Stents

Percutaneous transluminal coronary angioplasty (PTCA), usually simply called angioplasty, involved opening the blocked artery. A typical angioplasty procedure involves the following steps:

- The surgeon threads a narrow catheter (a tube) containing a fiber optic camera directly to the blocked vessel.
- The physician opens the blocked vessel using *balloon angioplasty*, in which the surgeon passes a tiny deflated balloon through the catheter to the vessel.
- The balloon is inflated to compress the plaque against the walls of the artery, flattening it out so that blood can once again flow through the blood vessel freely.
- In order to keep the artery open afterwards, surgeons now commonly employ a device called a *coronary stent*, which is an expandable metal mesh tube that is implanted during angioplasty at the site of the blockage.
- Once in place, the stent pushes against the wall of the artery to keep it open. (A number of studies are reporting fewer future heart attacks and restenosis in patients who receive stents compared with those who had angioplasty alone.)

Stenting is now used in about 60% of angioplasty procedures. Studies report high survival rates with the use of stents, including their use with multiple blood vessels and as the *initial* device after a heart attack instead of balloon angioplasty. Recently, however, this widespread use is being questioned. In one study, there was no difference in outcome between balloon angioplasty and coronary stents, except in certain cases. Of additional concern was a 1999 study reporting more injury to the walls of the artery after six months in patients with coronary stents compared to angioplasty or atherectomy (see below). Research is needed to determine which individuals would benefit most from stents. Some experts now recommend they be used only to prevent restenosis in patients with large blood vessels (greater than 3 mm).

Recuperation. Angioplasty is less invasive than bypass surgery, requiring only one night in the hospital. Recuperation takes about a week. It should be pointed out the chest pain

after the procedure is very common and usually due to problems other than ischemia. Chest pain is even more common when a stent is used, possibly because the artery is stretched.

Short-Term Complications: Reclosure During or Shortly after Angioplasty. Reclosure of the artery during or shortly after angioplasty is often but not always due to blood clots. Aspirin, heparin, coumarin, or combinations of anti-clotting drugs are generally used during and after the operation. Aspirin is more effective than heparin. New anti-clotting agents (tirofiban, abciximab, argatroban, **clopidogrel**, or bivalirudin) may be more effective for preventing reclosure, often when administered in combination with heparin or aspirin. Anti-clotting drugs are not wholly protective, in any case, because reclosure in some cases is due to other, unknown causes. [See also *Anti-Clotting Agents under What Are the Drug Treatments for Angina and Coronary Artery Disease?*, above.]

Long-Term Complications: Reclosure (Restenosis) Within a Year of Angioplasty. Narrowing or reclosing of the artery (restenosis) occurs within a year of angioplasty in nearly half of angioplasty patients, often requiring a repeat operation. Reclosure, in this case is not due to blood clots and so anti-clotting agents are not useful. Theories for the cause of restenosis include the following:

- The release of large amounts of oxidants (damaging unstable particles) at the surgical site may activate damage in certain white blood cells that causes overgrowth in smooth muscles in the blood vessels. With this theory in mind, researchers have tested an antioxidant drug, probucol (Lorelco), with some success. Other drugs that are being investigated for their ability to limit smooth muscle growth include verapamil, a calcium channel blocker, and a protein called angiopeptin.
- Some experts argue that other activities, such as scarring, may remodel and narrow the blood vessels.

A number of approaches, including coronary stents, have been developed to prevent restenosis.

- Radiation treatment of the site is used to prevent reclosure, although some experts are concerned about its long-term safety. Studies suggest, however, a high rate of late blockage occurring after angioplasty within two to 15 months in patients who receive radiation treatments.
- Directional atherectomy has been another attempt to solve the problem of reocclusion of the blood vessels. A balloon catheter is inserted for determining position; then, a tiny cutter spinning at 2,500 rpm removes plaque fragments from the arterial walls. The use of angioplasty with the coronary artery stent, however, is proving to be safer and more effective.

Minimally Invasive Bypass

Minimally invasive bypass (also called buttonhole or keyhole bypass) surgeries are exciting advances in basic bypass surgery that are currently being tested with good success for patients with disease in single vessels.

- One uses a four-inch incision, and the surgeon works on the front of the heart while it is beating slowly.
- In another, the heart is stopped; fiberoptic scopes and instruments are passed through a number of finger-sized incisions and the surgeon works on all sides of the heart guided by a video image from a tiny camera inserted through a four-inch incision.

Early results show that minimally invasive bypass procedures will be less expensive, require a shorter hospital stay, and be a significant improvement over conventional coronary artery bypass surgery. To date, they are performed only in a few medical centers for select candidates.

Transmyocardial Revascularization

Lasers have been used with both angioplasty and bypass procedures, but the risks have been high and the treatment is expensive. One laser procedure called transmyocardial laser revascularization (TMLR) applies laser energy directly to areas in the heart where blockage has occurred and creates 10 to 50 tiny channels.

It has been approved for patients with severe angina who do not respond to other treatments. A number of studies are showing that the procedure improves quality of life and reduces anginal pain. One reported, however, that improvements were insignificant for patients with severe angina and after a year, survival rates were lower in those who had TMLR (89%) compared to patients taking medications (96%).

Experience with this procedure is still limited, and more studies are required to determine if TMLR is any more effective than medications. The procedure itself carries some risks for complications, including some that can be life-threatening. New laser techniques may help reduce these problems.

Enhanced External Counterpulsation (EECP)

A noninvasive technique called enhanced external counterpulsation (EECP) has been used successfully by over a million people in China and is currently in trials in the US. The technique uses an air pump that inflates and deflates pressurized cuffs around the legs, causing blood to be pushed into the heart. In different studies, it has relieved angina in over 75% of patients who used it. The benefits persist, and there is some evidence that it produces actual cellular changes that benefit the heart. Those with three diseased vessels, however, do less well, and the procedure is not appropriate for those with heart failure or blood clots in the legs. EECP will not be likely to replace angioplasty or bypass, but it may reduce the need for nitrates.

Experimental Procedures

Endoscopic Transthoracic Sympathicotomy. A last resort for people with severe untreatable angina is a procedure known as endoscopic transthoracic sympathectomy. This operation blocks the nerves that cause chest pain and, in one European study, proved to be very beneficial in relieving angina. Because such patients no longer experience any chest pain, however, they may not experience important symptoms of heart attack if they occur.

Ultrasound Thrombolysis. As a potential alternative to angioplasty, researchers have developed an ultrasound thrombolysis device that uses high frequency sound waves to dislodge and dissolve the fatty plaques on the walls of coronary arteries. A long probe with three wires at the tip that transmit the ultrasound waves is inserted into the artery through a standard angioplasty catheter. High-power pulses of high frequency ultrasound waves are delivered three times at one-minute intervals. Initial experiments have found that this treatment effectively reopens clogged arteries with a relatively low restenosis rate.

Where Else Can Information Be Obtained About Angina And Coronary Artery Disease?

National Heart, Lung, and Blood Institute Information Center, P.O. Box 10305, Bethesda, MD 20824-0105. Call (301-592-8573) or on the Internet (<http://www.nhlbi.nih.gov/>)

American Heart Association, 7272 Greenville Ave., Dallas, Texas 75231-4596. Call (214-373-6300) or (call 800-242-8721) or on the Internet (<http://www.americanheart.org/>)

American College of Cardiology, Heart House, 9111 Old Georgetown Rd., Bethesda, MD 20814-1699. Call (800-253-4636) or (301-897-540) or on the Internet (<http://www.acc.org/>)

Aspirin Foundation of American. Call (800-432-3247) or on the internet (<http://www.aspirin.org>)

A very useful web site (<http://www.heartinfo.org/>).

Find Clinical Trials at <http://apps.nhlbi.nih.gov/clinicaltrials/>

Find a Heart Specialist at <http://www.certifieddoctor.org/search.asp>

Important Notes About the Significance and Limitations of This Report

- 1. It is very important for patients to understand their own medical problems and have a healthy and positive attitude toward their illness. It has been proven that active patients' participation is an integral and vital part for most effective therapies. Often times, the patients have an instinct or feeling about their own problems that is better than the judgment of anyone else including their physicians'. Therefore, you should read the information carefully and try to have a correct and objective assessment of your condition. This will help you to ask the most relevant questions to your doctors and avoid any possible mistakes in diagnosis and management of your disease. Information of the latest understanding and discoveries about your condition will empower you and your physicians to make the most sensible decision about your health and disease.**
- 2. It is also very important for you to fully understand the limitations about the information that we provide in this report. Please note that without examining the patient and knowing the complete details of the patient's history, family history, test results, complete symptoms, treatments, medication, etc, it is impossible for us to make any diagnosis of the specific condition that the patient may suffer. Please do not take this report as the definitive answer to your specific medical problem. The information provided is merely for you to gain a better understanding of the diseases and conditions that may be relevant to your unique situation. Always consult with your qualified physicians before taking any actions about your illness.**
- 3. You should also be aware that the available knowledge about our body and diseases are limited and are rapidly changing. There are many unknowns about the abnormal states and even the normal functions of the human body. Many diseases and symptoms are listed as cause-unknown in the most up-to-date and authoritative text books of medicine, but in fact, most of them are caused by some factors that the medical community has not yet discovered. Even though medical research has accumulated a tremendous amount of knowledge about the thousands of diseases, it is safe to say that there are much more waiting to be discovered than those we already know. Every year, month or even week, there are many medical research findings published in the literature that advance our knowledge about how our body functions and dysfunctions and how to manage and treat different diseases.**

Therefore, on the one hand, you should accept the limitation of our current knowledge and appreciate that you and your physicians may have known all there is to know about your disease. On the other hand, you should always strive to know more and find out the latest advances about the understanding and treatment of your condition.

4. You should also have a realistic grasp of the many names, procedures and diagnoses that the medical doctors use in describing your disease. The medical names and terms are simply ways for the doctors to define and label a set of conditions that may have a common cause or common pathological changes. But in reality, there are many diseases and conditions of the patients that are not clear-cut, and cannot be fit into a certain name or definition. Many patients suffer from a combination of abnormalities or borderline lesions that cannot be clearly defined or diagnosed with a simple term. Each patient is different and unique. Each illness is a result of the unique body condition and circumstance the particular patient has encountered and reacted. Every patient should be evaluated and treated individually. Please do not be disappointed if there is no specific medical term associated with your specific case or more than one possibility exists for your condition. This is probably the norm rather than the exception. Your goal is not to find a disease name that has a perfect fit to your condition, but to understand the complexity of your situation and make your body return to the broad normal range that you can function and live normally.
5. Even though we are trying our best in finding the most relevant and accurate information about your condition, we cannot guarantee the completeness and accuracy of the research that we performed a on your question. It is possible that we may have missed some important information in our report. We also cannot verify the accuracy of all the information that are published in text books, journals and literatures from which we obtained our information and prepared the report. The patients are advised to consult with their physicians and make their own judgment of the knowledge that we provide. You may check with us periodically to follow the most recent advances in your field of interest.
6. We emphatically state that we cannot be held responsible for any actions the patients or their physicians take upon reviewing our reports and any consequences that may be derived thereafter. We should not be held responsible for any damages that may be caused by interpreting or misinterpreting the reports provided thereof. We hope that our service is helpful to you and your physicians.

The End