

treatment of type 2 DM. The use of whole-grain or traditionally processed cereals and legumes has been associated with improved glycemic control in individuals with diabetes and in individuals who are insulin-resistant. Long-term studies have shown that whole-grain consumption reduces the risk of both type 2 diabetes and CVD.¹¹⁴

The combination of diet and exercise is more powerful than either one alone and may be even more effective than drugs for preventing type 2 DM. A low-fat, low-calorie diet with moderate exercise (30 minutes 5 times a week) has been shown to reduce new diabetes cases by 58% over a 3-year period. By contrast, the drug metformin, which boosts insulin sensitivity, reduced new cases by only 31%.¹²⁷ The National Institutes of Health (NIH) is conducting a 12-year, 5000 patient study to further test the additive effects of diet and exercise on diabetes.

Several types of OHDs are available, including the following:

1. OHDs used to stimulate islet cells to increase endogenous insulin secretion and enhance insulin-receptor binding (sulfonylureas).
2. OHDs that act by slowing the digestion of sugars in the intestine (acarbose).
3. OHDs referred to as *insulin-resistance reducers* or "insulin sensitizers" (thiazolidinediones such as pioglitazone [Actos] and rosiglitazone [Avandia]). Insulin sensitizers improve the action of liver, muscles, and fat tissues and do not cause liver problems as seen with troglitazone (Rezulin), which was removed from the market in March 2000.
4. OHDs used to improve hepatic and peripheral tissue sensitivity to insulin (metformin [Glucophage]), thereby increasing the effectiveness of insulin found in the body.

The advantage of this last OHD is that it does not stimulate activity with concomitant weight gain. However, diarrhea develops for 2 to 3 weeks in approximately one-third of people using this drug. One potentially serious but rare side effect is lactic acidosis, a life-threatening buildup of lactic acid in the blood. This condition can be fatal in people with kidney or liver disease or alcoholism. The main clinical feature of lactic acidosis is hyperventilation.

Treatment of Long-Term Complications. Prevention of long-term complications is the goal for all clients with DM. Risk of complications is associated independently and additively with hyperglycemia and hypertension. Intensive treatment of both these risk factors is required to prevent and minimize the incidence of most complications.²³⁷

Medical treatment of long-term diabetic complications may include dialysis or kidney transplantation for renal failure and vascular surgery for large vessel disease. Currently, the American Diabetes Association advises that people with diabetes take low-dose aspirin (75 to 162 mg) daily to help minimize risks such as heart attacks and strokes. Prophylactic aspirin therapy is recommended in both men and women with diabetes who are 40 years and older, although some diabetologists suggest that aspirin prophylaxis should begin at age 30.⁴¹

New treatment guidelines from the American College of Physicians recommend the use of statins (cholesterol-lowering drugs such as Crestor, Lipitor, Zocor, Mevacor, or Pravachol) for anyone with diabetes and diagnosed CAD—even if their cholesterol levels are normal.

Review of available data shows that statins reduced heart attacks and strokes by 22% to 44% in people with diabetes.²³¹ People with diabetes and normal cholesterol who have other cardiac risk factors, such as hypertension, obesity, smoking, age over 55, and chronic physical inactivity, may benefit from a nonstatin cholesterol medication such as gemfibrozil (Lopid).

Diabetic Ulcers. The therapist often is involved in prevention and wound care for diabetic ulcers, which may help prevent amputation. Early recognition and prompt management of wounds, ulceration, and Charcot foot can facilitate healing. For example, a CDC study showed that people with diabetes who wore proper shoe protection had only a 20% recurrence rate of ulceration compared with an 80% rate for those without offloading.²³²

Offloading or pressure reduction is a key component for healing ulcers and preventing recurrence. The normal response to damaged areas is to spare them from pressure because they are painful. However, in the insensitive foot of a person with diabetes, this normal alteration of weight-bearing surface, pressure, and duration does not take place, resulting in repetitive stress and injury with subcutaneous and cutaneous necrosis and skin breakdown.

A marked improvement in the rate of healing for plantar ulcers has been reported using a combination of total-contact cast (TCC) and tendo-Achilles lengthening (TAL; percutaneous heel cord lengthening), as opposed to TCC alone.^{10,143,172,211}

The results of at least one study show TAL should not be done in anyone with complete anesthesia of the heel pad; increased dorsiflexion can increase the risk of heel ulceration. This procedure is advised only in a multidisciplinary setting able to provide adequate nutrition, wound care, surveillance, treatment of complications and other biomechanical abnormalities and intervene early in any developing ulcerations.¹⁰⁶

Other interventions include debridement, infection control, protective dressings, revascularization, proper nutrition, and client education. Active dressings, such as growth factors and living skin, are also in use. Topical application of growth factors on wounds without infection and with at least a minimal level of vascularization was introduced in the early 1990s and has progressed to include new techniques in skin transplantation (see the section on Skin Transplantation in Chapter 21).

Infrared light therapy, such as monochromatic near-infrared photo energy (MIRE), has been applied using the anodyne therapy system (ATS) to improve sensory impairment, reduce pain, and prevent and heal ulcers. When used in conjunction with other physical therapy interventions, MIRE has been shown to improve balance in clients with diabetic peripheral neuropathy. ATS has been shown to be effective in reversing the loss of protective sensation by improving circulation. Light absorbed by hemoglobin in the blood causes the release of nitric oxide, resulting

in vasodilation and improved collateral circulation. Long-term studies are still needed to show whether the results can be sustained.^{128,129,140,198}

The use of cool laser therapy as a revascularization therapy is now available. Cool laser revascularization for peripheral artery therapy (CliRpath) uses a cool excimer laser and catheter system to vaporize arterial blockages, restoring blood flow and promoting wound healing. Reduction in pain, improved circulation, and facilitation of wound healing may help prevent limb loss in this population.

Treatment of diabetic peripheral neuropathic pain (DPNP) has not been successful using any one single intervention technique. The ideal treatment is correcting the underlying condition of chronic hyperglycemia. Many methods have been employed (e.g., capsaicin topical cream, acupuncture, and electrical stimulation) to address the painful symptoms of DPNP with limited and variable results. Medications aimed at chronic neuropathic pain have included tricyclic antidepressants (e.g., amitriptyline, nortriptyline, or imipramine), but anticholinergic effects, such as dry mouth, blurred vision, constipation, cardiac arrhythmias, and orthostatic hypotension, often limit their use.

More recently, off-label use of anticonvulsants, such as gabapentin (Neurontin) and pregabalin (Lyrica), have met with greater success. Serotonin-norepinephrine reuptake inhibitors, such as duloxetine (Cymbalta), can be used by some individuals to treat painful DPNP. By inhibiting the reuptake of these neurotransmitters, descending inhibitory pathways in the spinal cord are activated and block ascending pain signals to the brain.²³⁴

Transplantation. Research is being conducted on the use of transplanted pancreatic islet cells rather than the entire pancreas. The transplant recipient receives one or more infusions of pancreatic islet cells that include insulin-producing beta-cells. Almost 500 people with type 1 diabetes have received islet transplants at 43 institutions worldwide in the last 5 years.²²²

High rates of insulin independence have been reported at 1 year in the leading islet transplant centers. Loss of insulin independence by 5 years occurs in the majority of recipients. Life-long immunosuppression and its complications limit this treatment to candidates who have the most severe, unstable glycemic control despite optimal insulin therapy.²²²

Stem cell research may find a way for people to use their own stem cells to develop them into islet cells and allow infusions without cell-rejection complications and the need for life-long immunosuppression. In addition, artificial pancreata provide hope for future treatment without repeated injections for the person with type 1 diabetes. An artificial pancreas contains a reservoir for insulin (which must be filled by the affected individual, typically through a tube in the abdomen), and an internal glucose monitor that continuously determines the plasma glucose level, automatically releasing the appropriate amount of insulin. Such instruments are expected to reach the market shortly. The use of wireless communication between a continuous glucose sampling device and an insulin pump would give people with diabetes a

closed-loop system or electromechanical artificial pancreas.⁶³

PROGNOSIS. Diabetes control depends on the proper interaction between the following three factors: (1) food, (2) insulin or oral medication to lower blood glucose, and (3) activity (e.g., sedentary or exertional) or exercise. When diabetes is regulated successfully, complications of hyperglycemia and hypoglycemia can be avoided with minimal disruption to a normal lifestyle. However, diabetes can be fatal even with medical treatment, or it can cause major permanent disabilities and seriously impair functional abilities. Studies have shown that type 2 DM raises a person's risk of dying from heart disease by 2 to 3 times.²³⁴ In fact, about 50% of myocardial infarctions and 75% of strokes are attributable to diabetes. Diabetes is the leading cause of new blindness and is a contributory cause to renal failure and peripheral vascular disease.

Regardless of the modality of treatment used for the person with type 1 or type 2 DM, recent studies have shown clearly that tight glucose control (plasma glucose levels consistently within normal limits, approximately 100 mg/dl) delays onset and progression of diabetic complications. The only apparent danger in maintenance of tight control is the greater possibility of hypoglycemia, particularly in those people with type 1 DM who receive frequent exogenous insulin administration.⁴¹

SPECIAL IMPLICATIONS FOR THE THERAPIST 11-16

Diabetes Mellitus

PREFERRED PRACTICE PATTERNS

4C: Impaired Muscle Performance

4J: Impaired Motor Function, Muscle Performance, Range of Motion, Gait, Locomotion, and Balance Associated with Amputation

5G: Impaired Motor Function and Sensory Integrity Associated with Acute or Chronic Polyneuropathies

6A: Primary Prevention/Risk Reduction for Cardiovascular/Pulmonary Disorders

6B: Impaired Aerobic Capacity/Endurance Associated with Deconditioning

7A: Primary Prevention/Risk Reduction for Integumentary Disorders

7B: Impaired Integumentary Integrity Associated with Superficial Skin Involvement

Client education is the key to therapeutic, nonsurgical treatment of the neuromusculoskeletal complications associated with diabetes. Extensive self-management is the focus of the educational program.*

Exercise is a key component of the overall intervention plan.⁴¹ The client must be taught the importance

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Table 11-16 Clinical Signs and Symptoms of Hypoglycemia

Sympathetic Activity (Increased Epinephrine)	CNS Activity (Decreased Glucose to Brain)
Pallor	Headache
Perspiration*	Blurred vision
Piloerection (erection of the hair)	Thickened speech
Increased heart rate (tachycardia)	Numbness of the lips and tongue
Heart palpitation	Confusion
Nervousness* and irritability	Emotional lability
Weakness*	Convulsion*
Shakiness/trembling	Coma
Hunger	

From Black JM, Matassarin-Jacobs E: *Medical-surgical nursing*, ed 5, Philadelphia, 1997, WB Saunders.

CNS, Central nervous system.

*Signs most often reported by clients.

of assessing glucose levels before and after exercise and to judge what carbohydrate and insulin requirements are suitable for the activity or workout. People with diabetes and peripheral neuropathy have a high incidence of injuries (e.g., falls, fractures, sprains, cuts, and bruises) during walking or standing and a low level of perceived safety. Suggested strategies for appropriate clinical intervention to reduce these complications are available.

Complications of Insulin Therapy

HYPOGLYCEMIA

Insulin therapy can result in hypoglycemia (low blood glucose, also called an *insulin reaction*)*; tissue hypertrophy, atrophy, or both, at the site of injection; insulin allergy; erratic insulin action; and insulin resistance. Symptoms of hypoglycemia are related to two body responses: increased sympathetic activity and deprivation of CNS glucose supply (Table 11-16). The clinical picture may be varied from a report of headache and weakness to irritability and lack of muscular coordination (much like drunkenness) to apprehension, inability to respond to verbal commands, and psychosis.

Symptoms can occur when the blood glucose level drops to 70 mg/dl or less, although this value varies among those with diabetes and can be lower than 70 mg/dl before symptoms are elicited. In diabetes, an overdose of insulin, late or skipped meals, or overexertion in exercise may cause hypoglycemic reactions. Immediately provide carbohydrates in some form (e.g., fruit juice, honey, hard candy, or commercially available glucose tablets or gel); a blood glucose test should be performed as soon as the symptoms are recognized. The unconscious person needs immediate medical attention; to prevent aspiration, fluids should not be forced. Hospitalization is recommended when the following occur:

- The blood glucose is less than 50 mg/dl and/or the treatment of hypoglycemia has not resulted in prompt recovery of altered mental status.

- The individual has had seizures or is unconsciousness.
- A responsible adult cannot be with the person for the next 12 hours.
- A sulfonylurea drug causes the hypoglycemia; this type of drug reduces liver conversion of glycogen to glucose and prolongs the period of hypoglycemia.

It is important to note that clients can exhibit signs and symptoms of hypoglycemia when their elevated blood glucose level drops rapidly to a level that is still elevated (e.g., 400 to 200 mg/dl). The rapidity of the drop is the stimulus for sympathetic activity-based symptoms; even though a blood glucose level appears elevated, affected individuals may still have symptoms of hypoglycemia.

When a person with diabetes mentions the presence of nightmares, unexplained sweating, and/or headache causing sleep disturbances, hypoglycemia may be indicated during nighttime sleep (most often related to the use of intermediate and long-acting insulins given more than once a day). These symptoms should be reported to the physician.

Erratic insulin action (i.e., low blood glucose followed by high blood glucose) can occur as a result of a variety of factors such as overeating, irregular meals, irregular exercise, irregular rest periods, chronic overdosage of insulin (Somogyi effect), emotional or psychologic stress, failure to administer insulin, or intermittent use of hyperglycemic or hypoglycemic drugs (e.g., aspirin, phenylbutazone, steroids, birth control pills, or alcohol).

The Somogyi effect occurs when the blood glucose level decreases to the point at which stress hormones (epinephrine, growth hormone, and corticosteroids) are released, causing a rebound hyperglycemia. Treatment consists of increasing the amount of food eaten and/or decreasing the insulin. The therapist may be a helpful source of education to help clients remember the many factors affecting their condition.

LIPOGENIC EFFECT OF INSULIN

Frequent injections of insulin at the same site can cause thickening of the subcutaneous tissues (hypertrophy or lipohypertrophy) and a loss of subcutaneous fat (atrophy or lipoatrophy), resulting in a dimpling of the skin that is lumpy and hard or spongy and soft. These abnormal tissue changes may cause decreased absorption of the injected insulin and poor glucose control.

The client usually is instructed to choose an injection site that is easily accessible (e.g., thighs, upper arms, abdomen, or lower back) and relatively insensitive to pain (away from the midline of the body). Sites of injection should be rotated, and rotation within each area is recommended. An individual can rotate within an area using 1 inch of the surrounding tissue at a time. The client who is going to exercise should avoid injecting sites or muscles that will be exercised heavily that day because exercise increases the rate of absorption. Following a definite injection plan can help avoid tissue damage.

Continued.

Table 11-17 Comparison of Manifestations of Hypoglycemia and Hyperglycemia		
Variable	Hypoglycemia	Hyperglycemia
Onset	Rapid (minutes)	Gradual (days)
Mood	Labile, irritable, nervous, weepy	Lethargic
Mental status	Difficulty concentrating, speaking, focusing, coordinating	Dulled sensorium, confused
Inward feeling	Shaky, hungry, headache, dizziness	Thirst, weakness, nausea/vomiting, abdominal pain
Skin	Pallor, sweating	Flushed, signs of dehydration (see Box 5-6)
Mucous membranes	Normal	Dry, crusty
Respirations	Shallow	Deep, rapid (Kussmaul's respirations)
Pulse	Tachycardia	Less rapid, weak
Breath odor	Normal	Fruity, acetone
Neurologic	Tremors; late: dilated pupils, seizures	Diminished reflexes, paresthesias
Blood Values		
Glucose	Low <50 mg/dl	High ≥250 mg/dl
Ketones	Negative	High/large
pH	Normal	Low ≤7.25
Hematocrit	Normal	High
Urine Values		
Output	Normal	Polyuria (early) to oliguria (late)
Glucose	Negative	High
Ketones	Negative/trace	High

From Ignatavicius D, Workman M, et al: *Medical-surgical nursing across the health care continuum*, ed 3, Philadelphia, 1999, WB Saunders.

Even with an insulin pump the infusion site should be changed every 2 or 3 days or whenever the client's blood glucose is above 240 mg/dl for two tests in a row. Rotating insertion sites will help prevent infection and tissue damage.

DIABETIC KETOACIDOSIS

The therapist must always be alert for signs of ketoacidosis (e.g., acetone breath, dehydration, weak and rapid pulse, and Kussmaul's respirations) progressing to hyperosmolar coma (polyuria, thirst, neurologic abnormalities, and stupor). Immediate medical care is essential. If it is not clear whether the symptoms are the result of hypoglycemia or hyperglycemia (Table 11-17), the health care worker is advised to administer fruit juice or honey. This procedure does not harm the hyperglycemic person but could potentially save the hypoglycemic person. Everyone with diabetes should wear a medical alert identification tag.

VITAMIN B DEFICIENCY

Some individuals using Metformin can develop vitamin B12 deficiency resulting in serious damage to

the nervous system. Complications can be minimized with early detection and intervention. Anyone on Metformin, especially high doses or a prolonged course of therapy, should be screened for the deficiency. The therapist can help monitor this with the client and recognize any early neurologic signs and symptoms.²⁴⁴

Diabetes and Exercise

An overwhelming body of evidence now exists that acute muscle contractile activity and chronic exercise improve skeletal muscle glucose transport and whole-body glucose homeostasis in the person with type 2 DM (Box 11-6).²²⁴ Exercise helps to increase insulin sensitivity, thus lowering blood glucose levels. Increased insulin sensitivity allows the body to utilize the available blood glucose for the person with type 2 diabetes; an increase in insulin sensitivity can last 12 to 72 hours after exercise.

There is a high prevalence of people with underlying skeletal muscle insulin resistance or impaired skeletal muscle glucose disposal such as occurs with inactivity, bed rest, limb immobilization, or denervation. Therapists must recognize, understand, and use the role of skeletal muscle in glucose homeostasis to address the needs of clients with any of these risk factors. Sinacore and Gulve published an excellent, detailed review of the pathways of glucose transport into skeletal muscle and the pathophysiology of insulin action in skeletal muscle as it contributes to disturbances of whole-body glucose metabolism.²²⁸

A program of planned exercise, including all the elements of fitness (flexibility, muscle strength, and cardiovascular endurance) can benefit persons with diabetes, especially those with type 2 DM. Exercise increases carbohydrate metabolism (which lowers the blood glucose level); aids in maintaining optimal body weight; increases high-density lipoproteins (HDLs); and decreases triglycerides, blood pressure, and stress and tension (Table 11-18).

Exercise and physical activity (even leisure-time physical activity and activity on the job) have been shown to independently reduce the risk of total and cardiovascular mortality of adults with type 2 diabetes. Exercise capacity is reduced by diabetes-related CVD, but exercise training is an excellent therapeutic adjunct in the treatment of diabetic CVD.¹⁶¹

The favorable association of physical activity with longevity occurs regardless of BMI, blood pressure, smoking habits, and total cholesterol levels.^{108,109} Once again, the therapist can be very instrumental in client education on the importance of exercise for a wide range of reasons and benefits to the individual with diabetes.

GENERAL EXERCISE CONSIDERATIONS

For anyone with diabetes, type 1 or type 2, the exercise prescription must take into account any of the complications present, especially cardiovascular changes, autonomic and sensory neuropathy, and retinopathy.²⁷¹ Muscle damage, with accompanying insulin resistance and impaired glucose uptake and disposal,

Box 11-6**DIABETES MELLITUS: KEY POINTS TO REMEMBER****General Guidelines**

- Although "safe" blood glucose levels are between 100 and 250 mg/dl (i.e., the person is not likely to experience DKA), the goal of therapy may be toward tighter control (e.g., in a young person with type 1 DM, 90 to 130 mg/dl) or moderate control (e.g., in an adult with type 2 DM, up to 150 mg/dl). A measurement more than 120 mg/dl should still be monitored closely in any age group
- If the blood glucose level is ≤ 100 mg/dl, a carbohydrate snack should be given and the glucose retested in 15 min to ensure an appropriate level. Food eaten in response to blood glucose levels between 70 and 100 mg/dl is symptom dependent (i.e., if a person's blood glucose is 80 mg/dl but no signs or symptoms of hypoglycemia are present, no snack is necessary)
- Observe carefully for signs or symptoms of DKA: acetone breath, dehydration, weak and rapid pulse, Kussmaul's respirations
- Avoid exercise if blood glucose ≥ 250 mg/dl with evidence of ketosis
- Administer fruit juice or honey to anyone with diabetes who is in a hypoglycemic state. If uncertain whether the person is hypoglycemic or hyperglycemic, provide juice or honey anyway
- Exercise must be carefully planned in conjunction with food intake and administration of insulin or oral hyperglycemic agents
- Do not exercise during peak insulin times. The peak activity of insulin occurs at different times depending on the type, dose, and time of the insulin injection (see explanation in text)
- When under stress, the person with diabetes has increased insulin requirements and may become symptomatic even though the disease is usually well-controlled in normal circumstances
- Avoid exercising late at night if this has not been gradually and consistently incorporated into the overall lifestyle. Delayed hypoglycemic reactions can occur during sleep hours after heavy, unaccustomed exercise late in the evening

Before Exercise

- Take at least 17 oz of fluid before exercise (approximately two 8 oz glasses).
- Glucose levels must be monitored immediately before exercise.
- Do not exercise when blood glucose levels are at or near 250 mg/dl with urinary ketones and use caution if glucose level is > 300 mg/dl and no ketosis is present.²⁷¹

DKA, Diabetic ketoacidosis; DM, diabetes mellitus.

can occur when untrained individuals begin to exercise.²²⁸ For this reason, clients with diabetes must start any new activity at a well-tolerated intensity level and duration, gradually increasing over a period of weeks or even months.²⁷¹

Some thought should be given to the specific type of exercise selected. The young individual, in good metabolic control, can safely participate in most activities. The therapist should always be aware of and screen for clients who may have eating disorders, espe-

- Do not exercise without eating at least 2 hr before exercise (exercise about 1 hr after a meal is best, but individual variations must be determined).
- Do not inject short-acting insulin in muscles or sites close to areas involved in exercise within 1 hr of exercise because insulin is absorbed much more quickly in an active extremity.
- Clients with type 1 DM may have to reduce the insulin dose or increase food intake when initiating an exercise program.
- Ketosis can be checked by means of a urine test before exercise (e.g., if the blood glucose is close to 250 mg/dl). If the test is positive (i.e., showing large numbers of ketones in the urine), exercise should be delayed until the urine test shows negative or low numbers of ketones. The person should administer insulin. Delay exercise until glucose and ketones are under control.
- Do not use drugs that may contribute to exercise-induced hypoglycemia (e.g., β -blockers, alcoholic beverages, diuretics, estrogens, phenytoin).
- Menstruating women need to increase their insulin during menses, especially those who are inactive or who do not exercise on a regular basis

During Exercise

- It is best to exercise regularly (5 times/wk or at least every other day) and consistently at the same time each day.
- Duration of exercise is optimal at 40 to 60 min, although as little as 20 to 30 min of continuous aerobic exercise is beneficial in improving glucose homeostasis.
- During prolonged activities, a readily absorbable carbohydrate snack (e.g., fruit) is recommended for each 30 minutes of activity. After exercise, a more slowly absorbed carbohydrate snack (e.g., bread, pasta, crackers) helps prevent delayed-onset hypoglycemia. Activities should be stopped with the development of any symptoms of hypoglycemia, and blood glucose tested.
- Replace fluid losses adequately.
- Monitor blood glucose every 30 min during prolonged exercise.
- Anyone with diabetes should not exercise alone. Health care workers, partners, teammates, and coaches must understand the possibility of hypoglycemia and how to manage it.

After Exercise

- Glucose levels must be monitored 15 min after exercise, especially if exercise is not consistent.
- Increase caloric intake for 12 to 24 hr after activity, according to intensity and duration of exercise.
- Reduce insulin, which peaks in the evening or night, according to intensity and duration of exercise.

dally those who engage in excessive, intense exercise as a means of controlling their weight. Specific screening methods and questions are available for the therapist.⁹⁰

The middle-aged and older person with diabetes should be encouraged to be physically active, but because the aging process leads to degeneration of musculoskeletal structures, exercise can exacerbate these problems.⁴¹

Continued.

Table 11-18 Benefits and Potential Risks of Exercise in People with Diabetes Mellitus

Benefits	Potential Risks*
Improves cardiovascular function	Hypoglycemia in people taking oral hypoglycemics or insulin
Improves maximum oxygen uptake	Worsening of hyperglycemia
Improves insulin binding and sensitivity	Cardiovascular disease, such as myocardial infarction, arrhythmias, excessive increases in blood pressure during exercise, postexercise orthostatic hypotension, or sudden death
Lowers insulin requirements (type 2 DM)	Microvascular disease, such as retinal hemorrhage or increased proteinuria
Improves sense of well-being and quality of life	Degenerative joint disease
Promotes other healthy lifestyle activities	Orthopedic injury related to neuropathy
Increases carbohydrate metabolism	
Improves blood glucose control†	
Reduces hypertension	
May help with weight reduction	
Improves lipid profile	
Reduces stress	

DM, Diabetes mellitus.

*These are potential risks over the long term. In general, the benefits of regular exercise outweigh the risks.

†Not confirmed for insulin-dependent diabetes mellitus (type 1 DM).

However, even for the person with type 1 DM in good control, sports in which hypoglycemia may be life-threatening (e.g., scuba diving, rock climbing, or parachuting) should be discouraged. Walking necessitates care toward proper footwear for the person who does not already have evidence of peripheral neuropathy.

Intermittent, high intensity activities (e.g., racquetball, baseball) or contact sports (e.g., basketball or soccer) should be avoided to prevent trauma (especially to the feet or eyes). High resistance strength-training programs should be limited to the young person with diabetes who has no diabetic complications. More specific recommendations for the long-distance runner and other athletes are available.^{4,15,144,159,243}

Low-resistance strength training programs should be encouraged unless retinopathy is present (weight-lifting is contraindicated in anyone with proliferative retinopathy; see Box 11-7). Exercise involving jarring or rapid head motion may precipitate hemorrhage or retinal detachment. Outdoor activities must be evaluated carefully, taking into consideration the weather extremes (hot or cold) and the person's ability to maintain distal circulation. Stationary indoor equipment (many types are now available) may be the best overall choice.

EXERCISE PRECAUTIONS

As positive as exercise is in the prevention and control of diabetes, the therapist must keep in mind that diabetes is a metabolic disorder with cardiovascular and

Box 11-7

CONTRAINDICATIONS TO EXERCISE IN DIABETES MELLITUS

- Poor control of blood glucose levels
- Unevaluated or poorly controlled associated conditions:
 - Retinopathy
 - Hypertension
 - Neuropathy (autonomic or peripheral)
 - Nephropathy
- Recent photocoagulation or surgery for retinopathy
- Dehydration
- Extreme environmental temperatures (hot or cold)

circulatory implications. Reduced blood flow to the skin and skeletal muscle can be further compromised by intense exercise, and recovery time is longer. All possible effects of exercise must be kept in mind when designing an exercise program. Strenuous exercise can have some serious side effects and is not recommended for most people with diabetes.¹⁹⁰

Before beginning any exercise program, the person with diabetes should undergo a detailed medical evaluation with appropriate diagnostic studies. Screening should be done for the presence of macrovascular and microvascular complications that may be worsened by the exercise program. A careful history and physical examination should be done by the physician and should focus on the signs and symptoms of disease affecting the heart, blood vessels, eyes, kidneys, and nervous system.^{41,271}

The therapist can help by designing an exercise program that suits the individual's needs. Low-impact activities, such as walking, bicycling, and swimming, are good choices for anyone who has a loss of sensation in the feet. Strength training, especially upper body work, puts no additional strain on the feet. Resistance exercise training may help avoid insulin therapy, especially for overweight women with gestational DM.²⁵ Moderate intensity resistive training also can improve mobility and strength in older adults with diabetes, potentially reducing the rate of mobility loss during aging.²⁴

DIABETIC AUTONOMIC NEUROPATHY

Many people with diabetes may not be able to exercise intensely to a calculated heart rate because of preexisting heart conditions, deconditioning, age, neuropathies, arthritis, or other joint problems. Exercise may be contraindicated in anyone with a severe form of autonomic neuropathy (Box 11-7), especially anyone with vasomotor instability, angina, and a history of myocardial infarction.⁴¹ The therapist is advised to communicate and collaborate with the client and physician when considering an exercise program for anyone with this problem.

Generally, individuals with autonomic neuropathy have a poor ability to perform aerobic exercise because of decreased maximal heart rate and increased resting heart rate. Persons with a generalized form of autonomic neuropathy may have hypotensive episodes

after exercising, especially those who are deconditioned. They also demonstrate a predisposition toward dehydration in the heat and poor exercise tolerance in cold environments.

People with diabetic autonomic neuropathy may have a higher resting heart rate but lower maximal heart rate, making exercise at safe levels more difficult. It may be better to use the percent of heart rate reserve (% HRR), which is the difference between resting heart rate and maximum heart rate, as a valid measure in prescribing exercise intensity instead of the rating of perceived exertion (RPE) scale, which relies on self-assessment of exertion.⁴² The American College of Sports Medicine (ACSM) recommends exercise intensity levels for clients with diabetic autonomic neuropathy should remain in the 40% to 75% HRR span.³

Some people with autonomic neuropathy may have silent myocardial infarctions without angina. The first symptom may be shortness of breath resulting from congestive heart failure. Decrease in nerve innervation to the heart associated with this type of neuropathy may prevent a normal increase in heart rate with stress or exercise, requiring careful observation and monitoring of vital signs during exercise. Blood pressure regulation is altered with autonomic neuropathy; exercise can further stress the impaired system. Clients with autonomic neuropathy are prone to hypothermia, dehydration, and hypotension or hypertension.

Diabetes is associated with reduced tolerance to heat. Autonomic neuropathy may also include changes in thermoregulation with a decreased or altered ability to perspire. Exercise with a concomitant increase in core body temperature can lead to heat stroke.¹⁹² Impairment of sweating has been demonstrated even with isometric exercise.¹⁹⁴ Proper hydration is essential, and precautions should be taken to avoid heat stroke. The Valsalva maneuver should be avoided.

EXERCISE IN TYPE 1 DIABETES MELLITUS

The person with type 1 DM tends to be thin, may be poorly nourished, and because of the islet cell deficiency, always needs exogenous insulin for adequate control of blood glucose. Exercise can increase strength and facilitate maintenance of weight and provide other important benefits (see Table 11-18), but unfortunately exercise has not been proven to provide increased glycemic control for the person with type 1 DM.

During exercise in individuals without diabetes, blood glucose levels remain normal, largely as a result of hormonal mediation with an increase in glucagon and catecholamines, which supply the necessary glucose for use by muscles and other body tissues. In a person with type 1 DM, these hormonal adaptations are lost and as a consequence, when too little insulin is available, the cells are sensing starvation so an excessive release of glucagon and catecholamines occurs.

These hormones further increase glucose mobilization into the bloodstream and significantly increase an already high level of glucose and ketones. If the hyperglycemia and ketosis is high enough and/or if the person is dehydrated, DKA can be precipitated.⁴¹

The person with well-controlled type 1 DM may commonly work out for approximately 30 to 45 minutes of sustained intense aerobic exercise without problems. Lack of adequate glycogen stores (i.e., decreased glycogen stores in the liver and to a lesser extent, in skeletal muscle) leads to impaired aerobic exercise endurance when compared with the nondiabetic person.

Hypoglycemia is a common occurrence in persons with type 1 DM who are exercising. In those who do not have diabetes, plasma insulin levels decrease during exercise and insulin counterregulatory hormones (glucagon and epinephrine) promote increased hepatic glucose production, which matches the amount of glucose used during exercise.

For the person with type 1 DM, who is not insulin deficient (because of exogenous administration of insulin), plasma insulin concentrations may not fall during exercise and may even increase if exercise occurs within 1 hour of insulin injection. These sustained insulin levels during exercise enhance peripheral glucose uptake and stimulate glucose oxidation by exercising muscle. For this reason, insulin should not be injected into muscles or at sites close to areas involved in exercise within 1 hour of exercise. Insulin pump infusion sites must be subcutaneous and not intramuscular.

Moderate periods of exercise provide beneficial effects, but longer periods may result in hypoglycemia. Watch for symptoms such as sweating, shakiness, nausea, headache, and difficulty concentrating. The greatest risk of severe hypoglycemia occurs 6 to 14 hours after strenuous exercise. Muscle and hepatic glycogen must be restored during periods of rest. Insulin and caloric intake must be adjusted after strenuous exercise to avoid severe nocturnal hypoglycemia.

EXERCISE IN TYPE 2 DIABETES MELLITUS

In contrast, people with type 2 DM are often obese, and exercise is a major contributor in controlling hyperglycemia. Exercise can improve short-term insulin sensitivity and reduce insulin resistance, making it possible to prevent type 2 DM in those persons at risk and to improve glycemic control in those with diabetes.²²⁴ These effects disappear a few days after exercise is discontinued. Long-term higher intensity exercise training (80% peak aerobic capacity) provides more enduring benefits to insulin action compared to low or moderate intensity exercise.⁵⁷

Hypoglycemia is not as common a problem for the person with type 2 DM because endogenous insulin levels usually can be maintained. Control of blood glucose levels by lowering the medication dose or increasing carbohydrate intake (or both) before exercise can prevent hypoglycemia. However, individuals with type 2 diabetes who receive insulin or sulfonylureas may have a risk for hypoglycemia similar to that of people with type 1 DM.^{41,224}

For anyone with diabetes, exercise should not be initiated if the blood glucose is 70 or less. Since one

Continued.

Table 11-19 Making Food Adjustments for Exercise: General Guidelines

Type of Exercise and Examples	If Blood Glucose Is*:	Increase Food Intake By:	Suggestions of Food to Use
Exercise of short duration and low-to-moderate intensity (walking half mile or leisurely bicycling for <30 min)	<100 mg/dl ≥100 mg/dl	10-15 g carbohydrate/hr of exercise not necessary to increase food.	1 fruit or 1 starch/bread exchange
Exercise of moderate intensity (1 hr of tennis, swimming, jogging, leisurely bicycling, golfing)	<100 mg/dl 100-180 mg/dl 180-300 mg/dl ≥300 mg/dl	25-50 g carbohydrate before exercise, then 10-15 g/hr of exercise. 10-15 g/hr of exercise. Not necessary to increase food. Do not begin exercise until blood glucose is under better control. 50 g carbohydrate; monitor blood glucose carefully.	½ meat sandwich with a milk or fruit exchange 1 fruit or 1 starch/bread exchange
Strenuous activity or exercise (about 1-2 hr of football, hockey, racquetball, or baseball games; strenuous bicycling or swimming; shoveling heavy snow)	<100 mg/dl 100-180 mg/dl 180-300 mg/dl ≥300 mg/dl	25-50 g carbohydrate, depending on intensity and duration. 10-15 g carbohydrate. Do not begin exercise until blood glucose is under control.	1 meat sandwich (2 slices bread) with a milk and fruit exchange ½ meat sandwich with a milk or fruit exchange 1 fruit or starch/bread exchange

* 100 mg/dl = 100 ml. The 100 mg/dl is a general guideline. Wide individual variations occur in this area. The timing of food intake may be symptom-dependent. Some individuals may experience symptoms of hypoglycemia when the blood glucose is 150 mg/dl, others not until the level is below 80 mg/dl and so on.

effect of exercise is the transfer of glucose in the cells, glucose levels should be checked again 2 hours after exercise. Vigorous exercise should not be undertaken within 2 hours before going to sleep at night because this is when exercise-induced hypoglycemia can occur with potentially fatal consequences.

Unplanned exercise can be dangerous for people taking insulin or oral hypoglycemic agents. During periods of exercise, muscles are stimulated to take up glucose to supply the fuel to the working muscles, causing blood glucose levels to fall abruptly. However, anyone with blood glucose levels at or near 300 mg/dl should *NOT* exercise because vigorous activity also can raise the blood glucose level by releasing stored glycogen. Exercise or therapy sessions should be scheduled to avoid peak insulin times (see Table 11-15) and to avoid periods of fasting (e.g., missed meal or just before the next meal).

Exercise in the morning is recommended to avoid hypoglycemia resulting from fluctuations in insulin sensitivity caused by factors such as diurnal variations in growth hormone. Growth hormone levels remain low in the afternoon, and less gluconeogenesis occurs. Vigorous or intense exercise late in the day or evening can lead to delayed hypoglycemia during sleep, which is dangerous.

BALANCING INSULIN, FOOD, AND EXERCISE

As mentioned, insulin should be injected in sites away from the part of the body involved in exercising. Because glucose can enter the cells without insulin during exercise, food should be eaten if the person is exercising more than usual. Conversely, when exercis-

ing less often, a lighter diet or more insulin is required.

Glucose levels should be monitored before and after exercise (or therapy activities), remembering that the effect of exercise can be felt up to 12 to 24 hours later. Those clients taking insulin should have their own glucose monitoring devices (fingerstick or laser punctures).

After exercise, available glucose is important for the replenishment of muscle glycogen stores. Bouts of hypoglycemia can be delayed until hours after completion of exercise. The insulin-dependent person must regulate activity so that the rate of energy expenditure balances the amount and type of insulin and food intake (Table 11-19). Women who are menstruating may need to increase their insulin during menses.

EXERCISE AND THE INSULIN PUMP

The normal metabolic response to exercise in a person who does not have diabetes is to decrease the release of insulin as muscles contract, causing the transport of more blood glucose into cells without insulin. A small amount of circulating insulin remains available during exercise to counterbalance the release of glucose-raising hormones (e.g., catecholamines, glucagon, growth hormone, and Cortisol).

CSII therapy brings the exercising individual with diabetes a response as close to normal as possible. But anyone with diabetes who uses an insulin pump must make frequent insulin adjustments to mimic the normal metabolic response, thereby maintaining a more normal glycemic control, especially during

periods of higher intensity or longer duration exercise.⁴³ Most people using an insulin pump have type 1 (insulin-dependent) DM, although anyone with type 2 DM who uses insulin can also wear a pump.

Time of day, exercise intensity, and elevated starting blood glucose levels appear to affect the metabolic response and can result in hyperglycemia instead of the more usual hypoglycemia for several hours after exercise. Metabolic control can deteriorate with intense exercise even in people who have tightly controlled blood glucose levels. It is suggested that 30 minutes of mild-to-moderate exercise is possible 2 or 3 hours after breakfast when using insulin pumps. The insulin level can be adjusted to minimize circulating free insulin levels and the risk of hypoglycemia during and after activity.^{43,235}

One of the disadvantages of an insulin pump is that it can malfunction or become displaced without the person knowing it. Exercise can exacerbate the situation when insulin delivery has been unknowingly disrupted and hypoinsulinemia is developing. The therapist should always be alert to any signs of DKA in clients using an insulin pump. Teach the client to be vigilant during exercise to maintain the integrity of the infusion site and to pay attention to any symptoms of impending DKA (e.g., thirst, nausea, weakness, or excessive urination).

Before the advent of the insulin pump, anyone with type 1 diabetes whose blood glucose was less than 100 mg/dl was instructed to consume a carbohydrate snack before starting or continuing the activity. With CSII, pump users can simply reduce or suspend insulin during the activity. Insulin reduction and carbohydrate intake are determined by the intensity and duration of the exercise activity. For example, a change in either insulin or carbohydrate intake may compensate for shorter, less intense activities but not in the case of intense, aerobic exercise.⁴³

Diabetes and Neuromusculoskeletal Complications

The treatment of musculoskeletal problems does not differ from treatment for these same conditions in the nondiabetic population. Early aggressive therapy for the adhesive capsulitis usually results in restoration of functional motion, even though full range of motion may not be achieved.

Hand function can be maintained and disease progression delayed with hand therapy, especially for the stiff hand syndrome. SLJM does not always benefit from therapy, but treatment intervention should be tried. For either of these conditions, the client must understand the importance of a self-directed exercise program established by the therapist to prevent recurrence of symptoms and to maintain functional outcomes.

Intervention for CTS must take into account the neuropathic and the entrapment components in the person with diabetes; surgical decompression may not be beneficial because of the neuropathic component. Nonsurgical efforts should be the focus of treatment. In conditions such as adhesive capsulitis and CRPS a

successful outcome is more likely with early medical and therapeutic intervention.

Diabetes and Foot Care

Disorders of the feet constitute a source of increasing morbidity associated with diabetes. Foot problems are a leading cause of hospital admission in people with diabetes, and diabetes is the most common reason for lower limb amputation. Half of those cases are preventable with proper foot care.^{229,256} Treatment of the underlying diabetes has little effect on any joint disease already present. The most beneficial intervention includes stabilizing the joint, minimizing trauma, maintaining muscular strength, and performing daily foot care.

The therapist must teach each person with diabetes proper foot and skin care (see Box 12-14). Regular foot checks after exercise using a mirror to inspect all surface areas and between the toes is advised. Having the therapist demonstrate and consistently carry this out with the client is a helpful educational tool. Any areas of warmth, erythema, swelling, or skin changes must be evaluated carefully and immediately. The therapist is advised to reinforce client education at each and every session.

DIABETIC PERIPHERAL NEUROPATHY

Assess for risk factors for amputation (e.g., previous ulcer or amputation) and for signs of diabetic neuropathy (e.g., numbness or pain in hands or feet or footdrop; see Table 12-21 and discussion of neuropathic [diabetic] ulcers). Scarborough²¹⁴ includes an excellent summary of assessment (tests and measures) for the foot and lower extremity. Vinik and Mehrabyan also offer an excellent review of diabetic neuropathies that will be of interest to any clinician working with this problem.²⁵⁶

Keep in mind that ankle-brachial index (ABI) measurements used to assess arterial circulation may have limited value in anyone with diabetes because calcification of the tibial and peroneal arteries may render them noncompressible.³⁰

Provide clients with a monofilament for self-testing (Fig. 11-15). For a description of an easy and reliable method to test for protective sensation using the Semmes-Weinstein monofilaments, see the reference section.^{54,173} This test is an easily used clinical indicator for identifying people who are at risk for developing foot ulcers and requiring subsequent amputations. It can clearly demonstrate physiologic changes in peripheral nerve function. If the person cannot feel the monofilament when applied with slight pressure against the skin, there is an increased risk of ulceration. The results of this test provide a definitive idea of who can benefit most from preventive care, education, and prescription of appropriate therapeutic footwear.¹⁷³

Decreased sensation in the feet associated with diabetic neuropathy can affect both the timing and quality of gait, requiring retraining of the somatosensory and vestibular systems to help compensate for the somatosensory deficit.^{101,193} Gait and strength training are

Continued.

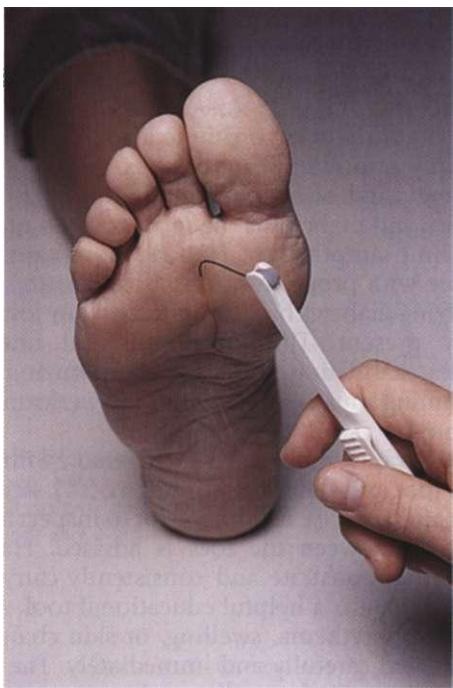


Figure 11-15

Semmes-Weinstein monofilament testing for protective sensation. Performed if the client is suspected of having peripheral neuropathy or known diabetes with possible peripheral neuropathy. The 5.07 monofilament (calibrated to apply 10 grams of force) has been adopted for screening in the diabetic population. The monofilament is applied perpendicular to the test site with enough pressure to bend the monofilament for 1 second. Abnormal response: client does not perceive the monofilament. Do not test over calloused areas. An initial foot screen should be performed on anyone with diabetes and at least annually thereafter. Anyone who is at risk should be seen at least four times a year to check their feet and shoes to help prevent foot problems from occurring. (From Seidel HM: *Mosby's physical examination handbook*, ed 6, St Louis, 2006, Mosby.)

important in the management of large-fiber neuropathies when impaired vibration, depressed tendon reflexes, and shortening of the Achilles tendon occur.²⁵⁶ Diabetes gait may occur independent of sensory impairment. Increased joint movement, wider stance, and slower pace demonstrated in some individuals with type 2 diabetes may be neurologic in origin and not related to muscle weakness or loss of sensation in the feet.¹⁹¹

Anyone with peripheral neuropathy is advised to avoid soaking the feet. There is a danger of burns, and prolonged exposure to warm water leaves the skin susceptible to fungal infections. Whirlpools are contraindicated and baths are not advised (showering may be best). Bathing and soaking remove the protective barrier from the skin and can lead to other infections, especially if there are fissures from dry skin caused by decreased circulation.

The first Consensus Guidelines for DPNP developed by the American Society of Pain Educators (ASPE) are now available.⁷ Having a standard of care is important in the treatment of pain associated with DPNP. Improved safety and quality of care may result in fewer

amputations and potentially better compliance with recommendations for physical activity and exercise with subsequent decreased secondary complications associated with poor glycemic control.

NEUROPATHIC (DIABETIC) ULCERS

The most common cause for neuropathic (diabetic) ulcers is excessive plantar pressure in the presence of sensory neuropathy and foot deformity. Neuropathic foot ulcers can occur anywhere pressure or shear force is applied to the foot (top, sides, or bottom). Many occur beneath the metatarsal heads and are the result of painless trauma caused by excessive plantar pressures during walking.¹⁷⁴

The presence of corns or calluses is an indication that footwear fits poorly and should be carefully evaluated by the therapist. Additionally, cartilage requires insulin for glucose uptake, metabolism of carbon dioxide, and collagen synthesis. Lacking an adequate supply, the articular cartilage in the person with diabetes does not tolerate repetitive trauma, compression, and motion, making proper footwear all the more important.¹⁹⁷

Note the location of any foot ulcerations for possible causes that can be corrected. For example, ill-fitting shoes may cause ulcers on the medial or lateral borders of the feet, whereas ulcers on top of the foot may be caused by deformities such as hammer (claw) toes.

The risk of ulceration and poor wound healing in the diabetic population underscores the importance of therapists providing nonsurgical alternatives for these problems. Although the management of the diabetic foot (Charcot joint) sometimes requires surgery, most people can be treated with appropriate cast, shoe, orthotic devices, or other therapeutic footwear. When a neuropathic joint is detected early, offloading the joint and avoiding weight bearing for 8 weeks may prevent progression of disease.

The presence of a previous history of plantar ulceration may alert the therapist to the need to teach the client how to control activity levels to lessen shear forces on scars from previous ulcers.²⁷ Orthoses are often used to redistribute or move pressure away from a blister or other area of pressure. Soft, moldable orthoses are preferred to the rigid orthoses used by clients with other types of foot problems. An excellent review of various offloading techniques for the treatment of neuropathic ulcers is available.²²¹

TCC is an effective intervention for neuropathic plantar ulcers. Monitoring of foot problems through the use of skin temperature changes using dermal thermography may provide valuable information to the clinician in the detection, treatment, and prevention of neuropathic foot problems.¹¹

Total contact inserts (TCI) and metatarsal pads can be used to reduce excessive plantar stresses, thereby preventing skin breakdown and ulceration. The TCI reduces excessive pressures at the metatarsal heads by increasing the contact area of weight-bearing forces. Metatarsal pads act by compressing the soft tissues proximal to the metatarsal heads and relieving compression at the metatarsal heads.¹⁷⁴

The prevention of foot problems before they begin is always the most effective method in offsetting the development of foot ulceration and infection and their potentially devastating effects. The use of proper footwear, proper cleaning and lubrication of the feet, safe removal of corns or calluses, and the removal of mechanical sources of foot pressure are critical components in the prevention of foot problems. Client education is a key component in the monitoring and detection of potential difficulties.¹⁹⁷

DELAYED WOUND HEALING

Because wound healing (surgical and nonsurgical) is impaired in the diabetic foot, surgery can be accompanied by increased risks of poor healing and infection. Sympathectomy, arthrodesis, and joint immobilization have not been proved helpful. Organ transplantation in someone with diabetes is also a risk factor for delayed wound healing because of the chronic immunosuppression required.²²⁷

The detrimental effects of cigarette smoking on wound healing and peripheral circulation are well documented (see the section on Substance Abuse in Chapter 3). Smoking increases insulin resistance, worsens diabetes complications, and has a negative effect on prognosis. People with diabetes who smoke have a higher all-cause mortality rate than those who do not smoke.²³³

Smoking cessation is one of the two most important ways to reduce macrovascular complications in adults with diabetes. Control of hypertension is the other. The American Diabetes Association recommends that all health care providers routinely identify the smoking (tobacco use) status of clients with diabetes and offer cessation support and education.⁶

Substance abuse of any kind can impair or slow the rehabilitation process, especially delaying wound healing. Client education in this area is an important aspect of treatment. Despite strong evidence that clinician support of smoking cessation is effective for smokers who have diabetes, only about half report that their physician ever advised them to stop or cut down on their smoking (or substance use).¹⁵²

The U.S. Public Health Service Clinical Guideline²⁴⁵ suggests health care providers use the 5 As: ask, assess, advise, assist, and arrange. A brief nonconfrontational discussion of smoking cessation may help move the smoker to the next level of readiness. The clinician can help clients think about what will be better if they quit; moving the person to the contemplation stage (ready to quit in the next 6 months) doubles the chance of quitting during that time.¹⁹⁹

Diabetes and Physical Agents

Numerous studies from the 1980s and continued ongoing research have documented the large interindividual and intraindividual variability in subcutaneous insulin absorption, a major contributing factor in the variability of blood glucose. The therapist must be aware of these factors and plan intervention accordingly. Specifically, insulin absorption is impaired or altered by smoking, injection site, thickness of skin-

fold (adipose tissue), exercise, subcutaneous edema, local subcutaneous blood flow, ambient and skin temperature, and local massage.^{9,103}

The application of heat causes local vasodilation and hyperemia (excess blood to an area), necessitating burn precautions in this population. In a therapy practice, heat application may take the form of hot packs, paraffin, hydrotherapy, fluidotherapy, infrared radiation, ultrasound, or aquatic (pool) physical therapy.

Heat from the use of hot baths, whirlpools, saunas, or sun beds has been shown to accelerate the absorption of subcutaneous injections of insulin, by increasing skin blood flow. To reduce the risk of hypoglycemia, local application of heat to the site of a recent insulin injection should be avoided. The use of cryotherapy (cold) with its effects of vasoconstriction and decreased skin blood flow would be expected to slow or delay insulin absorption from the injection site.

Diabetes and Menopause

As life expectancy increases, women are living a greater proportion of their lives in the postmenopausal phase, a time when the prevalence of type 2 diabetes also increases. The therapist should be aware that the consequences of CVD, osteoporosis, and cancer are more pronounced in women who have type 1 or type 2 diabetes, especially in women who have metabolic syndrome followed by the development of type 2 diabetes.

The transition from premenopause to postmenopause estrogen-deficient status is associated with the emergence of many features of the metabolic syndrome, such as central obesity (intraabdominal body fat), insulin resistance, and dyslipidemia, which are also known to be risk factors for CVD. The prevalence of the metabolic syndrome increases with menopause and may partially explain the apparent acceleration of heart disease after menopause.³⁵

Women with type 1 diabetes frequently go through menopause at an earlier age than women who do not have diabetes. Premature or early menopause may be considered an unstudied complication of type 1 diabetes.⁵⁸ Risk factor assessment for any of these comorbidities throughout the life cycle is especially important for any woman who has diabetes.

As the woman with diabetes approaches menopause, changes in estrogen and progesterone affect how cells respond to insulin and therefore blood glucose levels. Menopause symptoms can mimic low blood glucose levels (e.g., moodiness or short-term memory loss).

Sleep disturbance and weight gain associated with menopause make it harder to control blood glucose levels. There is an increased risk of urinary tract infection, especially for the menopausal/postmenopausal woman on insulin and/or who has had diabetes for 10 or more years.²³ During the postmenopause years when female hormone levels remain low, insulin sensitivity may increase with a drop in the expected blood glucose levels.²⁰⁶

Continued.

There are conflicting reports on the role of hormone replacement therapy (HRT) for postmenopausal women who have type 2 DM. Whether HRT improves glycemic control or worsens insulin sensitivity remains unproved. Results may vary according to the type of HRT, age of the woman, and route of administration.^{9,122}

Diabetes and Psychosocial Behavior

The therapist should keep in mind the psychologic and behavioral aspects of diabetes with regard to improving clinical outcomes. Common psychologic problems known to complicate diabetes management include poor self-esteem, impact on the family dynamics, family and social support, compliance and motivation, eating disorders, quality of life, and so on. A team approach that includes close collaboration between diabetologists, psychologists, and physical therapists is important.¹

Diabetes and Aquatic Physical Therapy¹⁷

See also Appendix B: Guidelines for Aquatic Physical Therapy.

The Aquatics Section of the American Physical Therapy Association (APTA) has an annotated bibliography with relevant articles related to pool therapy, including the use of aquatics with medical conditions such as diabetes mellitus. This document is available through the Aquatics Section of the APTA.

Swimming may be a good choice to offer the individual with diabetes, once again taking care to provide meticulous foot care. Wearing boat shoes (specially designed shoes for water wear available in many local stores) can help prevent scraping the feet along the sides or bottom of the pool. Care must be taken to gently dry the feet, especially between the toes, after swimming to prevent infection. Anyone with abrasions or open sores should not enter a swimming pool environment.

A rise in ambient (surrounding) temperature such as a client might experience in an indoor, warm, and humid pool setting also causes an increase in insulin absorption from subcutaneous injection sites. The insulin disappearance rate may be as much as 50% to 60% greater with an increase of 15° in ambient temperature.¹³¹

Additionally, the ease of movement in the water allows increased activity without the same perceived intensity of exertion for the same amount of work performed outside the water. The combination of increased temperatures and increased activity can result in hypoglycemia. The therapist and client must work closely together to maintain a balance of activity, food intake, and insulin dosage.

When a client with diabetes begins aquatic physical therapy, both the time in the water and the intensity of exercise should be systematically progressed and monitored, with one of the parameters being increased with each session according to the client's tolerance. Before pool therapy, the client must not miss any meals or snacks and must measure blood glucose levels.

A snack or beverage, such as orange juice, should be readily available throughout the therapy session for anyone developing symptoms of hypoglycemia. Glucose testing should be performed after completion of the pool program. Exercise can have a positive effect in reducing blood glucose levels in persons with type 2 DM, but sudden drops in blood glucose levels after exercise should be avoided.

With careful management, the individual should be able to adjust food intake and exercise tolerance to avoid having to increase insulin dosage. Throughout the pool program, the therapist must closely monitor each individual with diabetes for any signs of hypoglycemia (see Table 11-16). The affected individuals must be cautioned to carry out self-monitoring and to respond to the earliest perceived symptoms.

Insulin Resistance Syndrome

Insulin resistance refers to the phenomenon of having high levels of both circulating insulin and glucose in the bloodstream, but the insulin molecules cannot bind properly to the insulin receptor sites on the surface of the cell to allow glucose to enter the cells and be used for energy. A syndrome of insulin resistance has been proposed to explain the frequent association of hypertension, carbohydrate intolerance, abdominal obesity, dyslipidemia, and accelerated atherosclerosis associated with type 2 DM.

Although a primary insufficiency of insulin secretion is the pathology in the development of type 2 DM, obesity is a major risk factor for the development of this type of DM, caused in part by the associated insulin resistance. In 1988 the combination of hypertension, glucose intolerance, hyperinsulinemia, and dyslipidemia was called *syndrome X* by Gerald Reaven, MD, a diabetes expert, who predicted an increased incidence of coronary heart disease.²⁰²

In the following years, syndrome X was redefined as a prediabetic state and called *metabolic syndrome*. Criteria for metabolic syndrome include abdominal obesity; elevated triglyceride levels, and low HDLs, hypertension, insulin resistance (with or without glucose intolerance), and proinflammatory markers such as increased C-reactive protein levels or coagulation factors (see Box 12-2).

Even this definition has been through numerous iterations and is still hotly debated. The National Cholesterol Education Program, the World Health Organization, and the American Heart Association all have slightly different versions of the criteria for metabolic syndrome. In contrast, the American Diabetes Association and the European Association for the Study of Diabetes published position statements concluding that there is no disorder called metabolic syndrome. They state that, "there is no solid evidence that any of the metabolic syndrome health factors contribute more together than they do individually. In other words, the whole is not greater than the sum of its parts."¹¹⁷ The issue is still under debate; see Chapter 12 for further discussion of metabolic disorder.

Obesity and insulin resistance are the underlying factors responsible for the diagnosis of metabolic syn-

drome. Several definitions of metabolic syndrome have been proposed, but all include insulin resistance or glucose intolerance, hypertension, dyslipidemia, and central obesity. For this reason, the term *insulin resistance syndrome* (IRS) was suggested by the American College of Endocrinology and the American Association of Clinical Endocrinologists to more aptly describe the prediabetic state.⁶⁴ While IRS has many of the same characteristics of metabolic syndrome, diagnosis is based on a fasting glucose level ($100 \text{ mg/dl} < \text{IRS} < 126 \text{ mg/dl}$).

Insulin resistance, a generalized metabolic disorder in which the body cannot use insulin efficiently, appears to play a key role in metabolic syndrome. Although not everyone with insulin resistance has metabolic syndrome, most people with metabolic syndrome are also resistant to the action of insulin.

Regardless of the definition or criteria, most agree that obesity is the single modifiable factor that sets off the cascade. The syndrome is associated with alterations in the abdominal fat cells. With increased fat storage, these cells become distorted in shape, and the receptor site for insulin becomes "warped" or out of proper alignment, so the insulin molecule "key" no longer fits in the receptor. Insulin resistance makes it more difficult to lose weight because the cells are not getting enough fuel and the individual perceives hunger when adequate amounts of circulating glucose exist.

The affected individual may develop elevated blood pressure and problems with reactive hypoglycemia. When the excess insulin is suddenly used, glucose rushes into the cells and the blood glucose drops suddenly. This sequence creates intense sweet cravings, and the cycle repeats itself with increasing insulin resistance.²⁵⁷

The most important implications of recent research indicate that a diagnosis with a syndrome is not necessary in order to treat the individual risk factors. At this prediabetic stage, changes in lifestyle will have the greatest impact on halting any disease progression. In fact, it may be the only time in the disease progression where changes in daily activity levels and nutritional status may have an impact.

SPECIAL IMPLICATIONS FOR THE THERAPIST 11-17

Insulin Resistance Syndrome/ Metabolic Syndrome

Physical therapists have a unique opportunity to address IRS/metabolic syndrome through reasonable dietary advice and carefully prescribed exercise counseling. After assessment, physical therapists should guide individuals toward an activity program that includes near-daily exercise that is progressive to a weekly expenditure exceeding 1200 kilocalories of aerobic activity.¹¹⁰

The therapist can provide education regarding the importance of weight loss, exercise, and dietary changes needed to help control dyslipidemia and hypertension. With appropriate lifestyle changes, people can reduce their risk of CVD, prediabetic states, and diabetes.

Studies have not yet determined the ideal exercise program for IRS/metabolic syndrome. Moderate aerobic exercise three times/week based on the ACSM guidelines increases insulin activity in nonobese, non-diabetic subjects despite the fact that there were no changes in weight, BMI, waist-to-hip ratio, lipid profile, or oxygen consumption after 2 months of exercise.⁹⁹

The mechanisms responsible for the improvement in insulin sensitivity after exercise training have been studied extensively but are not fully understood. Research focusing on insulin resistance in skeletal muscle and in particular its relation to changes in aerobic fitness in type 2 diabetes is ongoing.^{182,215}

Hyperglycemia

Two primary life-threatening metabolic conditions, DKA and hyperosmolar hyperglycemic state (HHS), can develop if uncontrolled or untreated DM progresses to a state of severe hyperglycemia (greater than 300 mg/dl).¹²⁴ Between DKA and HHS is a continuum of metabolic abnormalities.

Diabetic Ketoacidosis

Definition and Overview. DKA is most commonly seen in type 1 diabetes when complications develop from severe insulin deficiency. About one-half of the people who require hospitalization for DKA develop this hyperglycemic emergency secondary to an acute infection or failure to follow their prescribed dietary or insulin therapy.²⁵⁹

Most episodes of DKA occur in persons with previously diagnosed type 1 DM. However, the condition may occur in new cases of type 1 and in persons with type 2 DM (under stressful conditions in the latter such as during a myocardial infarction). It is characterized by the triad of hyperglycemia, acidosis, and ketosis.²³⁰

Etiologic Factors. Any condition that increases the insulin deficit in a person with diabetes can precipitate DKA. Causes of DKA commonly include taking too little insulin; omitting doses of insulin; failing to meet an increased need for insulin because of surgery, trauma, pregnancy, stress, puberty, or infection; and development of insulin resistance caused by insulin antibodies. Other precipitating causes are listed in Box 11-8.

The most common precipitating factor is infection, which occurs in up to half of all cases and may seem like a trivial condition such as mild cellulitis or upper respiratory tract infection. Omission of insulin, either because of noncompliance or because people mistakenly believe that insulin is not required on sick days when they are not eating well, is another important and preventable cause of DKA.

In young individuals with type 1 DM, psychologic problems complicated by eating disorders may be a contributing factor in 20% of recurrent ketoacidosis. Factors that may lead to insulin omission in younger people include fear of weight gain with improved metabolic control, fear of hypoglycemia, rebellion from authority, and stress of chronic disease. In approximately 15% to

30% of cases, no identifiable cause of DKA can be determined.²³⁰

Pathogenesis. The initiating metabolic defect in DKA is an insufficient or absent level of circulating insulin. Insulin may be present, but not in a sufficient amount for the increase in glucose resulting from the stressor (see Box 11-8). Inadequate insulin creates a biologic state of starvation, which triggers the excess secretion of counter-regulatory hormones, particularly glucagon, in an attempt to get more glucose to the cells and tissues. The abnormal insulin-to-glucagon ratio, with excess circulating cate-

cholamine, Cortisol, and GH levels, initiates a host of complex metabolic reactions, leading to hyperglycemia, acidosis, and ketosis.

When the body lacks insulin and cannot use carbohydrates for energy, it resorts to fats and proteins. The process of catabolizing fats for fuel gives rise to incomplete lipid metabolism, dehydration, metabolic acidosis, and electrolyte and acid-base imbalances. (See more complete discussion in the section on Pathogenesis of Diabetes Mellitus in this chapter.)

Clinical Manifestations. The signs and symptoms of DKA vary, ranging from mild nausea to frank coma (Table 11-20). Common symptoms are thirst, polyuria, nausea, and weakness that have progressed over several days. This condition also may develop quickly, with symptoms progressing to coma over the course of only a few hours. Other symptoms may include dry mouth; hot, dry skin; fruity (acetone) odor to the breath, indicating the presence of ketones; overall weakness, possible paralysis; confusion, lethargy, or coma; and deep, rapid respirations (Kussmaul's respirations). Fever is seldom present even though infection is common, primarily a result of peripheral vasodilation. Severe abdominal pain, possibly accompanied by nausea and vomiting, easily mimics an acute abdominal disorder.

MEDICAL MANAGEMENT

DIAGNOSIS, TREATMENT, AND PROGNOSIS. Prevention of DKA through client education is the key to avoiding this serious condition. Once DKA is suspected, the diagnosis must be established quickly, with immediate treatment after diagnostic confirmation (blood glucose level >250 mg/dL, pH <7.3 , bicarbonate level <18 mEq/L, and serum ketones).

Treatment includes fluid administration, insulin therapy, and correction of metabolic abnormalities

Box 11-8

PRECIPITATING CAUSES OF DIABETIC KETOACIDOSIS*

- Inadequate insulin under stressful conditions
- Infection
- Missed insulin doses
- Trauma
- Medications
 - β -blockers
 - Calcium channel blockers
 - Pentamidine (NebuPent, Pentam)
 - Steroids
 - Thiazides (diuretics)
- Alcohol abuse (inability to manage insulin because of mental change; alcoholic ketoacidosis)
- Hypokalemia
- Myocardial ischemia
- Surgery
- Pregnancy
- Pancreatitis
- Renal failure
- Stroke

*Listed in descending order.

Table 11-20 Clinical Symptoms of Life-Threatening Glycemic States

Hyperglycemia		Hypoglycemia
Diabetic Ketoacidosis (DKA)	Hyperosmolar, Hyperglycemic State (HHS)	Insulin Shock
Gradual onset*	Gradual onset	Sudden onset
Headache	Thirst	Pallor
Thirst	Polyuria leading quickly to decreased urine output	Perspiration
Hyperventilation	Volume loss from polyuria leading quickly to renal insufficiency	Piloerection
Fruity odor to breath	Severe dehydration	Increased heart rate
Lethargy/confusion/coma	Lethargy/confusion	Palpitations
Abdominal pain and distention	Seizures	Irritability/nervousness
Dehydration	Coma	Weakness
Polyuria	Blood glucose level >250 mg/dL	Hunger
Flushed face	Arterial pH >7.30	Shakiness
Elevated temperature		Headache
Blood glucose level >250 mg/dL		Double/blurred vision
Arterial pH <7.30		Slurred speech
		Fatigue
		Numbness of lips/tongue
		Confusion
		Convulsion/coma
		Blood glucose level <70 mg/dL

Modified from Goodman CC, Snyder TE: *Differential diagnosis for physical therapists*, ed 4, Philadelphia, 2007, WB Saunders.

*Less gradual than HHS.

(potassium, bicarbonate, and phosphate), in addition to correction of any underlying illnesses (e.g., infection). Before the discovery of insulin in the 1920s, DKA was almost universally fatal. This complication is still potentially lethal with an average mortality rate between 5% and 10%.

SPECIAL IMPLICATIONS FOR THE THERAPIST 11-18

Diabetic Ketoacidosis

PREFERRED PRACTICE PATTERNS

SE: Impaired Motor Function and Sensory Integrity Associated with Progressive Disorders of the Central Nervous System

SI: Impaired Arousal, Range of Motion, and Motor Control Associated with Coma, Near Coma, or Vegetative State

The therapist will be an active member of the health care team, emphasizing to anyone with type 1 DM the need for regular, daily self-monitoring of blood glucose, adherence to the diabetes management program, and early recognition of and intervention for mild ketosis. The therapist also must be able to recognize early signs and symptoms of DKA in addition to signs of infection, a major cause of DKA (see Box 8-1). The first sign of an infection in a foot or leg or an upper respiratory, urinary tract, or vaginal infection should be reported immediately to the physician.

DKA can cause major potassium shifts accompanied by muscular weakness that can progress to flaccid quadripareisis. The weakness is initially most prominent in the legs, especially the quadriceps, and then extends to the arms with involvement of the respiratory muscles. (See Chapter 5 for further discussion of hypokalemia in addition to a discussion of the other conditions associated with DKA such as dehydration, metabolic acidosis, and electrolyte and acid-base imbalances.)

Hyperosmolar Hyperglycemic State. HHS is another acute complication of diabetes, a variation of DKA. HHS is characterized by extreme hyperglycemia (800 to 2000 mg/dl), mild or undetectable ketonuria, and the absence of acidosis. It is seen most commonly in older adults with type 2 DM.^{111,124}

The precipitating factors of HHS may be similar to those for DKA such as infections, inadequate fluid intake, medications (see Box 11-8), or stress. HHS may be the first indication of undiagnosed diabetes, and it may occur in the case of someone who is receiving total parenteral nutrition (hyperalimentation) or who is on renal dialysis and receiving solutions containing large amounts of glucose.

The major difference between HHS and DKA is the lack of ketosis with HHS. Because some residual ability exists to secrete insulin in type 2 DM, the mobilization of fats for energy is avoided. When adequate insulin is lacking, blood becomes concentrated with glucose.

Because glucose molecules are too large to pass into cells, osmosis of water occurs from the interstitial spaces and cells to dilute the glucose in the blood. Osmotic diuresis occurs, and eventually the cells become dehydrated. If not treated promptly, the severe dehydration leads to vascular collapse and death.

Clinical manifestations of HHS are polyphagia, polydipsia, polyuria, glucosuria, dehydration, weakness, changes in sensorium, coma, hypotension, and shock (see Table 11-20). Lactic acidosis also can develop if tissue perfusion is compromised.

Treatment is with short-acting insulin, electrolyte replacement, and careful fluid replacement to avoid congestive heart failure and intercerebral swelling in older adults, who often have other cardiovascular or renal disorders.

SPECIAL IMPLICATIONS FOR THE THERAPIST 11-19

Hyperosmolar Hyperglycemic State

The therapist should be alert to any signs of HHS in the aging adult who may have a previous diagnosis of type 2 DM. Early recognition and treatment to restore fluid and electrolyte balance are important for a good prognosis in this condition. (See also Special Implications for the Therapist: Diabetes Mellitus in this chapter.)

METABOLIC SYSTEM

As noted earlier, the endocrine system works with the nervous system to regulate and integrate the body's metabolic activities. Metabolism is the physical and chemical (physiologic) processes that allow cells to utilize food to continually rebuild body cells and transform food into energy. Metabolism is broken down into two phases: the anabolic (tissue-building) and catabolic (energy-producing) phases. The *anabolic phase* converts simple compounds derived from nutrients into substances the body cells can use, whereas the *catabolic phase* is a consumptive phase when these organized substances are reconverted into simple compounds with the release of energy necessary for the proper functioning of body cells.⁹⁵

The body gets most of its energy by metabolizing carbohydrates, especially glucose. A complex interplay of hormonal and neural controls regulates the homeostasis of glucose metabolism. Hormone secretions of five endocrine glands dominate this regulatory function (see Table 11-10). The rate of metabolism can be increased by exercise, elevated body temperature (e.g., high fever or prolonged exertional exercise), hormonal activity (e.g., thyroxine, insulin, or epinephrine), and increased digestive action after the ingestion of food.

Fluid and Electrolyte Balance

Fluid and electrolyte balance is a key component of cellular metabolism. Homeostasis, maintaining the body's

chemical and physical balance, involves the proper functioning of body fluids to preserve osmotic pressure, acid-base balance, and anion-cation balance. The goal of metabolism and homeostasis is to maintain the complex environment of body fluid that nourishes and supports every cell.

Body fluids, classified as intracellular and extracellular, contain two kinds of dissolved substances: those that dissociate (separate) in solution (electrolytes) and those that do not. For example, when dissolved in water, glucose does not break down into smaller particles but sodium chloride dissociates into sodium cations (positively charged) and chloride anions (negatively charged).

The composition of these electrolytes in body fluids is electrically balanced, so the positively charged cations (sodium, potassium, calcium, and magnesium) equal the negatively charged anions (chloride, bicarbonate, sulfate, phosphate, and carbonic acid). Although these particles are present in relatively low concentrations, any deviation from their normal levels can have profound physiologic effects.

Because many situations in the body cause both normal and abnormal fluid shifts, it is important to have a clear understanding of fluid compartments. The recognition of pathologic conditions, such as edema, dehydration, ketoacidosis, and various types of shock, can depend on the understanding of these concepts.

In the healthy body, fluids and electrolytes are constantly lost or exchanged between compartments. This balance must be maintained for the body to function properly. The amount used in these functions depends on such factors as humidity; body and environmental temperature; physical activity; metabolic rate; and fluid loss from the GI tract, skin, respiratory tract, and renal system. Normal balance is achieved through fluid intake and dietary consumption. Alterations in fluid and electrolyte balance are discussed more completely in Chapter 5.

Acid-Base Balance

The proper balance of acids and bases in the body is essential to life. The body maintains the pH of extracellular fluid (fluid found outside cells) between 7.35 and 7.45 through a complex chemical regulation of carbonic acid by the lungs and base bicarbonate by the kidneys. The pH is essentially a measure of hydrogen ion concentration in body fluid. Nutritional deficiency or excess, disease, injury, or metabolic disturbance may interfere with normal homeostatic mechanisms and cause a lowering of pH called *acidosis* or a rise in pH called *alkalosis*.

Various bodily functions operate to keep the pH at a relatively constant level. Acid-base regulatory mechanisms include chemical buffer systems, the respiratory system, and the renal system. These systems interact to maintain a normal acid-base ratio of 20:1 bicarbonate to carbonic acid. The consequences of an acid-base metabolism disorder can result in many signs and symptoms encountered by the therapist. These conditions are discussed more completely in Chapter 5.

Aging and the Metabolic System

Aging as measured by loss of physiologic function has not yet been defined precisely, so the distinction between usual, normal, and ideal metabolic changes remains undetermined. Studies of the aging population have shown that several physiologic parameters, such as body weight, basal metabolism, renal clearance, and cardiovascular function, decline with age. Protein-calorie nutritional status has pervasive effects on metabolic regulatory systems; nutritional status often declines with age, which contributes to metabolic dysfunction.¹¹⁸

Because the respiratory and renal systems are largely responsible for maintaining acid-base balance, changes in these systems associated with aging also have an impact on metabolic function. A common measure for metabolic loss in tissues is the decline in $V_{O_{\text{max}}}$, the maximum oxygen extraction capacity of the lungs.

Loss of muscle mass associated with aging can affect stroke volume capacity and oxidative metabolism.¹⁸⁶ The low level metabolic acidosis that appears to occur in many people with advancing age may play a role in age-associated bone loss, a factor that has received little attention from those who study bone loss and aging.¹⁵⁶

Oxidative stress has been implicated in the pathogenesis of a number of diseases and has been labeled the *free radical theory of aging* (discussed in Chapters 2 and 6); studies indicate that protection from the consequences of excess metabolic activity results in a slowing of the aging process, particularly in the postreproductive period of life.^{34,77} Links between oxidative stress and aging focus on mitochondria in a theory called the *mitochondrial theory of aging*. Mitochondria, the principal site of adenosine triphosphate (ATP) synthesis (also containing DNA and RNA), is the cellular site of energy production from oxygen and the principal site of free radical damage.⁵¹

Free radical derivatives of oxygen are generated as a result of normal metabolic activity, producing destructive oxidation of membranes, proteins, and DNA. These free radicals (unstable oxygen molecules robbed of electrons) attempt to replace their missing electrons by scavenging the body and taking electrons from healthy cells, causing a chain reaction called *oxidation* (see Fig. 6-2).

The formation of free radicals can be triggered by many exogenous (outside) factors such as cigarette smoke, air pollution, anticancer drugs, ultraviolet lights, pesticides and other chemicals, uncontrolled diabetes, radiation, and emotional stress. The major defenses against these destructive byproducts of normal metabolism are the protective enzymes, which remove the free radicals and remove, repair, and replace cell constituents.

Impairment of cellular function and metabolism occurs as proteins and DNA (which turn over slowly or not at all) are damaged over time.⁶¹ The use of antioxidants found naturally in fruits and vegetables or ingested as a nutritional supplement to counteract this process is believed to increase longevity but remains under scientific investigation.^{167,168}

Signs and Symptoms of Metabolic Disease

Clinical manifestations of metabolic disorders vary, depending on the specific pathology present. Fluid and electrolyte disorders, disorders of acid-base metabolism leading to metabolic (nonrespiratory) alkalosis or acidosis, and their associated signs and symptoms are discussed in Chapter 5.

SPECIFIC METABOLIC DISORDERS

Metabolic bone disease is discussed in Chapter 24, and **disorders of purine and pyrimidine metabolism** resulting in gout and pseudogout are discussed in Chapter 27.

Metabolic Bone Disease

Metabolic disorders involving the connective tissue may result in pathologic loss of bone mineral density, such as occurs in osteomalacia or osteoporosis, or acceleration of both deposition and resorption of bone, as seen in Paget's disease. These disorders differ in pathogenesis and treatment and are discussed in Chapter 24.

Metabolic Neuronal Diseases

Metabolic neuronal diseases are rare and are not likely seen in a therapy practice. Phenylketonuria (PKU), Wilson's disease, and porphyrias are the three most often encountered and are briefly discussed in this section.

Phenylketonuria

PKU is an autosomal recessive disease resulting from a genetic defect in the metabolism of the amino acid phenylalanine (Phe). This condition is transmitted recessively through apparently healthy parents, who show signs of the disease only on testing. The lack of an enzyme (phenylalanine hydroxylase) necessary for the conversion of the amino acid Phe into tyrosine results in an accumulation of Phe in the blood with excretion of phenylpyruvic acid in the urine. If untreated, the condition results in mental retardation and other manifestations such as tremors, poor muscular coordination, excessive perspiration, mousy odor (resulting from skin and urinary excretion of phenylpyruvic acid), and seizures.

Although PKU cannot be cured, a simple screening test for PKU can be administered to newborns and is required by law in most states in the United States and in all provinces in Canada. Currently, between 160 and 400 of the 4 million babies born in the United States each year are affected. The practice of discharging newborns in 24 hours is resulting in an increase in the number of babies at risk of PKU.

Treatment is primarily through Phe restriction of the infant's diet to control the effects of PKU and is prescribed on an individual basis with the additional administration of a dietary protein substitute. The start of newborn screening for PKU during the early 1970s has given rise to an increasing number of people who have

been identified and successfully treated for the disease in childhood. Initiation of nutritional therapy before conception for women assures a successful pregnancy outcome.¹²³ A need remains for maternal screening before pregnancy to identify undiagnosed maternal PKU and subsequent prophylactic treatment to prevent maternal PKU syndrome.⁹⁶

The prognosis for people with PKU has improved greatly with early institution of treatment after birth. However, hyperphenylalaninemia can cause white matter abnormalities, psychiatric illness, and decreased performance on neuropsychologic tests for people with PKU compared with subjects without PKU. It has been shown that the diet necessary to reduce Phe levels cannot be terminated after adolescence without elevation of plasma levels resulting in poor neuropsychologic performance.⁵²

Wilson's Disease

Wilson's disease, also known as **hepatolenticular degeneration**, is a progressive disease inherited as an autosomal recessive trait (both parents must carry the abnormal gene). This condition produces a defect in the metabolism of copper, with accumulation of copper in the liver, brain, kidney, cornea, and other tissues. Although the pathogenesis of Wilson's disease is still uncertain, it seems likely that defective biliary excretion of copper is involved.

The disease is characterized by the presence of Kayser-Fleischer rings around the iris of the eye (from copper deposits), cirrhosis of the liver (see Chapter 17), and degenerative changes in the brain, particularly the basal ganglia. Liver disease is the most likely manifestation in the pediatric population and neurologic disease is most common in young adults. Cerebellar intoxication from deposition of copper in the brain results in athetoid movements and an unsteady gait.

Other CNS symptoms may include pill-rolling tremors in the hands, facial and muscular rigidity, dysarthria, and emotional and behavioral changes. Musculoskeletal effects occur in severe disease and may include muscle atrophy and wasting, contractures, deformities, osteomalacia, and pathologic fractures.²³⁰

Treatment is pharmacologic (e.g., lifetime administration of vitamin B6 and D-penicillamine) and is aimed at reducing the amount of copper in the tissues by promoting its urinary excretion. Managing hepatic disease is also important; if left untreated, Wilson's disease progresses to fatal hepatic failure.

SPECIAL IMPLICATIONS FOR THE THERAPIST 11-20

Wilson's Disease

PREFERRED PRACTICE PATTERNS

4C: Impaired Muscle Performance

4D: Impaired Joint Mobility, Motor Function, Muscle Performance, and Range of Motion Associated with Connective Tissue Dysfunction

4G: Impaired Joint Mobility, Muscle Performance, and Range of Motion Associated with Fracture

Continued.

SE: Impaired Motor Function and Sensory Integrity Associated with Progressive Disorders of the Central Nervous System

For the person with Wilson's disease, physical or vocational rehabilitation may be required. In the advanced stage of this disease, self-care is promoted to prevent further mental and physical deterioration. An exercise schedule is essential to encourage consistent focus on rehabilitation. Sensory deprivation or over-load should be avoided and prevention of injuries that could occur as a result of neurologic deficits is important (see Box 12-14).

of enzyme deficiencies, an accumulation of excessive amounts of porphyrins and their precursors occurs. This accumulation results in generalized clinical symptoms.

Neurologic abnormalities, acute abdominal pain, skin fragility, and photosensitivity and psychiatric problems are symptoms that characterize the porphyrias. Various drugs and chemicals can cause porphyria (e.g., large amounts of alcohol, hemodialysis, or other chemical toxins) or can trigger acute, potentially life-threatening attacks in susceptible individuals. Diagnosis is suspected when clinical symptoms are combined with substantial increases in porphyrins or porphyrin-precursors in the blood and urine.³⁹

Porphyrias

Porphyrias are a group of hereditary and sometimes acquired diseases characterized by enzymatic abnormalities in biosynthesis of the heme molecule. Normally, porphyrins and their precursors are necessary for the synthesis of the heme molecule. In porphyrias, because

References

To enhance this text and add value for the reader, all references are included on the companion Evolve site that accompanies this textbook. The reader can view the reference source and access it on-line whenever possible. There are a total of 271 cited references and other general references for this chapter.

CHAPTER 12

The Cardiovascular System

CATHERINE C. GOODMAN • IRINA V. SMIRNOVA

The cardiovascular system functions in coordination with the pulmonary system to circulate oxygenated blood through the arterial system to all cells. The deoxygenated blood is then collected from the venous system and delivered to the lungs for reoxygenation (Fig. 12-1). Pathologic conditions of the cardiovascular system are varied, multiple, and complex. This chapter presents cardiovascular structure and function according to how diseases affect each individual part, including diseases of the heart muscle, cardiac nervous system, heart valves, pericardium, and blood vessels.

Other factors, such as surgery, pregnancy, and complications from other pathologic conditions (e.g., acquired immunodeficiency syndrome [AIDS], cancer treatment, metabolic diseases, collagen vascular diseases [now more commonly referred to as diffuse connective tissue diseases; see Box 12-17]) can also adversely affect the normal function of the cardiovascular system. Discussion of these additional factors is limited in this chapter (see specific chapters for each subject).

A section reporting gender differences as these relate to the cardiovascular system and diseases has been added. Whenever possible, ethnicity as it relates to cardiovascular diseases is included in each section. Ethnic differences are an area just coming under closer review, and the knowledge available is limited at this time.

SIGNS AND SYMPTOMS OF CARDIOVASCULAR DISEASE

Cardinal symptoms of cardiac disease usually include chest, neck, or arm pain or discomfort; palpitations; dyspnea; syncope (fainting); fatigue; cough; and cyanosis. Edema and leg pain (claudication) are the most common symptoms of the vascular component of cardiovascular pathologic conditions. Symptoms of cardiovascular involvement should be reviewed by system as well (Table 12-1).

Chest pain or discomfort (e.g., tightness, pressure sensation) is a common presenting symptom of cardiovascular disease and must be evaluated carefully. Chest pain of systemic origin may be cardiac or noncardiac and may radiate to the neck, jaw, upper trapezius, upper back, shoulder, or arms (most commonly the left arm). Radiating pain down the arm is in the pattern of ulnar nerve

distribution. Noncardiac chest pain can be caused by an extensive list of disorders and is not covered in this text.

Cardiac-related chest pain may arise secondary to ischemia, myocardial infarction (MI), pericarditis, endocarditis, mitral valve prolapse, or aortic dissection with or without aneurysm. Location and description (frequency, intensity, duration) vary according to the underlying pathologic condition (see each individual condition).

Chest pain is often accompanied by associated signs and symptoms, such as nausea, vomiting, diaphoresis, dyspnea, fatigue, pallor, or syncope. Cardiac chest pain or discomfort can also occur when coronary circulation is normal, as in the case of anemia causing lack of oxygenation of the myocardium (heart muscle) during physical exertion, although this situation is uncommon.

Angina (see Angina Pectoris section for more details) is a chest pain or discomfort occurring when a heart muscle does not get enough oxygen. It is a symptom of coronary artery disease (CAD). It usually starts behind the breastbone, but it may project in the arm, shoulder, neck, jaw, throat, and back. It is described as pressure, squeezing, or tightness in the chest. Some people may mistake it for indigestion. Shortness of breath, weakness, light-headedness, and sweating may occur.

Palpitations, the presence of an irregular, fast, or "extra" heartbeat, may also be referred to as arrhythmias or dysrhythmias, which may be caused by a relatively benign condition (e.g., mitral valve prolapse, caffeine, anxiety, exercise, athlete's heart [increase in left ventricular mass as a result of intensive training])²⁶¹ or a severe condition (e.g., CAD, cardiomyopathy, complete heart block, ventricular aneurysm, atrioventricular valve disease, mitral or aortic stenosis).

Palpitations may occur as a response to the bursts of adrenaline that occur with drops in estrogen levels, as a response to excess or erratic production of adrenaline-type compounds associated with panic disorder, or as a result of hyperthyroidism through other mechanisms. Up to one third of heart transplant recipients are aware of their resting heartbeat, despite the absence of cardiac innervation.³²

Palpitations have been described as a bump, pound, jump, flop, flutter, butterfly, or racing sensation of the heart. Associated symptoms may include light-headedness or syncope. Palpated pulse may feel rapid or irregular, as if the heart has skipped a beat. Some people report

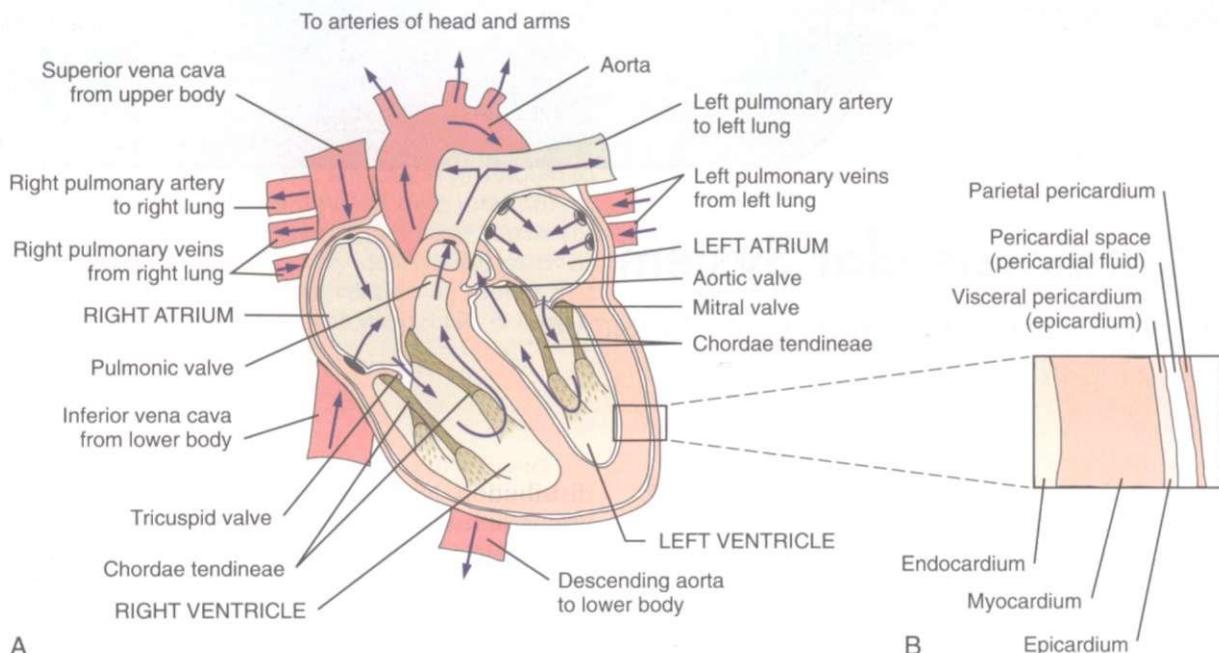


Figure 12-1

A, Structure and circulation of the heart. Blood flows from the superior and inferior venae cavae into the right atrium through the tricuspid valve to the right ventricle. The right ventricle ejects the blood through the pulmonic valve into the pulmonary artery during ventricular systole. Blood enters the pulmonary capillary system, where it exchanges the carbon dioxide for oxygen. The oxygenated blood then leaves the lungs via the pulmonary veins and returns to the left atrium. From the left atrium, blood flows through the mitral valve into the left ventricle. The left ventricle pumps blood into the systemic circulation through the aorta to supply all the tissues of the body with oxygen. From the systemic circulation, blood returns to the heart through the superior and inferior venae cavae to begin the cycle again. **B,** Sagittal view of the layers of the heart wall.

fluttering sensations in the neck rather than in the chest or thoracic area.

Dyspnea, also referred to as breathlessness or shortness of breath, can be cardiovascular in origin, but it may also occur secondary to pulmonary pathologic conditions (see also Chapter 15), trauma, fever, certain medications, or obesity. Early onset of dyspnea may be described as a sensation of having to breathe too much or as an uncomfortable feeling during breathing after exercise or exertion. Shortness of breath with mild exertion (dyspnea on exertion [DOE]) can be caused by an impaired left ventricle that is unable to contract completely. The result is an abnormal accumulation of blood in the pulmonary vasculature. Pulmonary congestion and shortness of breath then ensue. With severe compromise of the cardiovascular or pulmonary system, dyspnea may occur at rest.

Dyspnea may be a predictor of death from cardiac or other causes. In a large study of over 17,000 adults undergoing myocardial perfusion single-photon emission computed tomography (SPECT) during stress and at rest, those with no history of CAD who presented with dyspnea had four times the risk of sudden death from cardiac causes compared to asymptomatic individuals. They also had twice the risk compared to participants already diagnosed with typical angina.²

The severity of dyspnea is determined by the extent of disease; the more severe the heart disease, the more readily episodes of dyspnea occur. More extreme dyspnea includes paroxysmal nocturnal dyspnea and orthopnea. Paroxysmal nocturnal dyspnea, which is sudden, unex-

plained episodes of shortness of breath, awakens a person sleeping in a supine position, because the amount of blood returning to the heart and lungs from the lower extremities increases in this position. This type of dyspnea frequently accompanies congestive heart failure (CHF).

During the day, the effects of gravity in the upright position and the shunting of excessive fluid to the lower extremities permit more effective ventilation and perfusion of the lungs, keeping the lungs relatively fluid free, depending on the degree of CHF. *Orthopnea* is the term used to describe breathlessness that occurs during recumbency and is relieved by sitting upright, using pillows to prop the head and trunk. Orthopnea can occur anytime during the day or night.

Cardiac syncope (fainting or, in a milder form, light-headedness) can be caused by reduced oxygen to the brain when the heart's pumping ability becomes compromised. Conditions resulting in cardiac syncope include arrhythmias (particularly short bursts of ventricular tachycardia), orthostatic hypotension (sudden drop in blood pressure), aortic dissection, hypertrophic cardiomyopathy, CAD, vertebral artery insufficiency, and hypoglycemia. When the heart does not pump as much blood, blood pressure drops low enough to cause fainting.

Predictors of cardiac syncope include a history of stroke or transient ischemic attacks, use of cardiac medication, and high blood pressure. Marginally associated risk factors also include lower body mass index (BMI), increased alcohol intake, and diabetes or elevated plasma glucose level. Any client with aortic stenosis (a condition in which an aortic valve becomes narrowed or constricted)

Table 12-1 Cardiovascular Signs and Symptoms by System

System	Symptom
General	Weakness Fatigue Weight change Poor exercise tolerance
Integumentary	Pressure ulcers Loss of body hair Cyanosis (lips, nail beds)
Central nervous system	Headaches Impaired vision Light-headedness or syncope
Respiratory	Labored breathing, dyspnea Productive cough
Cardiovascular	Chest, shoulder, neck, jaw, or arm pain or discomfort (angina) Palpitations Peripheral edema Intermittent claudication
Genitourinary	Urinary frequency Nocturia Concentrated urine Decreased urinary output
Musculoskeletal	Muscular fatigue Myalgias Chest, shoulder, neck, jaw, or arm pain or discomfort Peripheral edema Intermittent claudication
Gastrointestinal	Nausea and vomiting Ascites (abdominal distention)

is more likely to experience light-headedness associated with postural hypotension as a result of a sudden change in position or increased intraabdominal pressure (Valsalva maneuver).

During the period of initiation and regulation of cardiac medications (e.g., vasodilators), side effects such as orthostatic hypotension may occur. Implantable loop recorders are available to assess falls associated with syncope of unknown cause. Implantable recorders allow for continuous electrocardiogram (ECG) monitoring for recurrent but infrequent syncope.

Noncardiac conditions, such as anxiety and emotional stress, migraine headaches, seizures, or psychiatric conditions, can cause hyperventilation and subsequent light-headedness.

Vasovagal syncope is a term that is used for persons who have a very strong parasympathetic response that leads to vasodilation throughout the body. It can occur after a prolonged period of sitting or standing. Normally, in such a situation, blood tends to pool in the legs, requiring a heart rate and vasoconstriction sufficient to push the blood back to the heart, but when vasovagal syncope occurs, it is because the heart rate slows and vessels dilate, causing hypotension and cerebral hypoperfusion with subsequent fainting and/or falling.

The individual has a vagal response to the vascular system and passes out but regains consciousness right away (after being recumbent). Some individuals may experience this type of parasympathetic reaction when having blood drawn for testing or when donating blood. This type of syncope is not as serious as cardiac syncope (except as a potential source of injury from falling).

Fatigue provoked by minimal exertion indicates a lack of energy that may be cardiac in origin (e.g., CAD, aortic valve dysfunction, cardiomyopathy, myocarditis), or it may occur secondary to neurologic, muscular, metabolic, or pulmonary pathologic conditions. Often fatigue of a cardiac nature is accompanied by associated symptoms, such as dyspnea, chest pain, palpitations, or headache.

Cough (see also Chapter 15) is usually associated with pulmonary conditions but may occur as a pulmonary complication of a cardiovascular pathologic condition. Left ventricular dysfunction, including mitral valve dysfunction as with resulting pulmonary edema, may result in a cough when aggravated by exercise, metabolic stress, supine position, or paroxysmal nocturnal dyspnea. The cough is often hacking and dry when associated with left ventricular dysfunction and failure. Cough may be productive of large amounts of frothy, blood-tinged sputum in full-blown pulmonary edema. In the case of CHF, cough develops because a large amount of fluid is trapped in the pulmonary tree, irritating the lung mucosa. A persistent, dry cough can develop as a side effect of some cardiovascular medications (e.g., angiotensin-converting enzyme [ACE] inhibitors) (see Table 12-5).

Cyanosis is a bluish discoloration of the lips and nail beds of the fingers and toes in the Caucasian population that accompanies inadequate blood oxygen levels (reduced amounts of oxygenated hemoglobin). Look for grey color tones (instead of pink/red) along the gum line (buccal mucosa) in the mouths of African Americans, Hispanics, or other dark-skinned individuals. Although cyanosis can accompany cardiac, pulmonary, hematologic, or central nervous system (CNS) disorders, visible cyanosis most often accompanies cardiac and pulmonary problems.

Peripheral edema is the hallmark of right ventricular failure; it is usually bilateral and dependent and may be accompanied by jugular venous distention (JVD; see Fig. 12-13), cyanosis (of lips, appendages), and abdominal distention from ascites (see Fig. 17-5). Right upper quadrant pain, described as constant, aching, or sharp, may occur secondary to an enlarged liver with this condition. Right-sided heart failure and subsequent edema can also occur as a result of cardiac surgery, venous valve incompetence or obstruction, or cardiac valve stenosis. Noncardiac causes of edema include pulmonary hypertension and lung dysfunction resulting in right-sided heart failure, as well as kidney dysfunction, cirrhosis, burns, infection, lymphatic obstruction, and allergic reaction.

Claudication, sometimes described as cramping or leg pain, is brought on by a consistent amount of exercise or activity. It develops as a result of peripheral vascular disease (PVD) (arterial or venous), often occurring simultaneously with CAD.⁶⁸ Claudication can be more functionally debilitating than other associated symptoms, such as angina or dyspnea, and may occur in addition to

these other symptoms. The presence of pitting edema along with leg pain is usually associated with venous disease. Pitting edema leaves a dent on the skin after the area has been pressed with a thumb for several seconds. This happens due to fluid collected in the tissue. The dent will slowly fill back.

Other noncardiac causes of leg pain (e.g., sciatica, anterior compartment syndrome, gout, peripheral neuropathy, pseudoclaudication) must be differentiated from pain associated with PVD. Low back pain associated with *pseudoclaudication* often indicates spinal stenosis. The typical person affected is approximately 60 years old and bothered less by back pain than by a discomfort occurring in the buttock, thigh, or leg that (like true claudication) is brought on by walking but (unlike true claudication) can also be elicited by prolonged standing. The discomfort associated with pseudoclaudication is frequently bilateral and improves with rest or with flexion of the lumbar spine.

SPECIAL IMPLICATIONS FOR THE THERAPIST 12-1

Signs and Symptoms of Cardiovascular Disease

Evaluation and Monitoring

As part of the evaluation, the physical therapist will assess cardiac signs and symptoms, assess the degree of risk of an adverse cardiac event, assess the type and degree of impairment (dysfunction at the level of the tissue, organ or organ system, and circulation), and assess the level of disability (difficulty performing activities of daily life) and functional limitations (restrictions in the ability to perform specific actions).⁹²

Older adults with cardiac impairment should be examined by a physician. Exercise testing to diagnose the specific level of pathology and impairment will aid the therapist in prescribing an individual exercise program with specific parameters (mode, intensity, duration, frequency) determined based on the results of examination and testing.¹⁰⁸

In some cases, monitoring individuals closely and minimizing risk of an adverse event are a priority (e.g., the person with oxygen transport impairment with or without symptoms). If the individual is symptomatic, recommendations are given to minimize life-threatening risks; interventions are directed at the underlying impairments whenever possible.

As a general guideline, the therapist monitors the unstable cardiac client (whether or not an initial ECG readout is available) during initial exercise to keep intensity lower than the threshold at which cardiac symptoms appear. In other cases, when the degree of risk is low, the need for monitoring may be reduced accordingly and treatment can be less conservative.⁹²

The evaluation and intervention strategies for clients with the cardiac symptoms described go beyond the scope of this text, and the physical therapist is referred to any of the specific cardiopulmonary texts available. Special implications included in this chapter should

be supplemented by other such materials. An excellent review of physiologic measures in a cardiopulmonary setting in relation to the Preferred Practice Patterns listed in the Guide is also available.⁹²

Signs and Symptoms

Cervical disk disease and arthritic changes can mimic atypical *chest pain* requiring screening for medical disease. Pain of cardiac origin can be experienced in the shoulder because the heart (and diaphragm) are supplied by the C5 to C6 spinal segment, which refers visceral pain to the corresponding somatic area. Chest pain attributed to trigger points and other noncardiac causes is discussed in detail elsewhere.¹²⁹

Palpitations lasting for hours or occurring in association with pain, shortness of breath, fainting, or severe light-headedness or dizziness require medical evaluation. Palpitations in any person with a personal history of cardiac disease or a family history of unexplained sudden death require medical referral. Clients describing palpitations or similar phenomena may not be experiencing symptoms of heart disease.

Palpitations can be considered physiologic (i.e., fewer than six occurring per minute may be considered within the normal function of the heart), or they may occur as a result of an overactive thyroid, secondary to caffeine sensitivity, as a side effect of some medications, during menopause when estrogen levels decline, and through the use of drugs, such as cocaine.

Encourage the client to report any such symptoms to the physician if this has not already been brought to the physician's attention. ECG monitoring of the heart's electrical impulses along with a diary of symptoms while wearing the monitor is most often used to identify the underlying condition. See also the section on Arrhythmias: Disturbances of Rate or Rhythm in this chapter.

Before referring the client to the physician, the therapist can help the client characterize the symptom or symptoms by asking a series of questions: Is the sensation long-lasting or transient? Palpitations that begin and end abruptly are more often true sustained arrhythmias. Episodes that gradually appear and disappear tend to be normal alterations in heart rhythm.

Does anything precipitate the symptom or symptoms? Eliminating possible triggers (e.g., caffeine) one at a time may reduce or eliminate palpitations. Is there an association between hormonal status and palpitations (e.g., onset or change in frequency associated with ovulation or start or stop of menstruation)? If exercise brings on the palpitations, ventricular tachycardia may be the underlying cause.

On the other hand, sometimes starting an exercise program reduces the frequency of palpitations. Some people find that deep breathing, coughing, or relaxation can stop the symptom when it begins. If fainting occurs with the palpitations and there is a family history of sudden death, there may be an inherited cardiomyopathy or primary arrhythmia. For the experienced clinician, auscultation may provide additional useful information. Gathering this type of information

for the physician's consideration can be very helpful in making the medical diagnosis.

Dyspnea may be a sign of poor physical conditioning, obesity, or asthma or allergies. Anyone who cannot climb a single flight of stairs without feeling moderately to severely winded or who awakens at night or experiences shortness of breath when lying down should be evaluated by a physician. Anyone with known cardiac involvement in whom progressively worse dyspnea develops must also notify the physician of these findings.

Dyspnea relieved by specific breathing patterns (e.g., pursed-lip breathing) or by specific body positions (e.g., leaning forward on arms to lock the shoulder girdle) is more likely to be pulmonary than cardiac in origin. Because breathlessness can be a terrifying experience, any activity that provokes the sensation is avoided, which quickly reduces functional activities. Pulmonary rehabilitation can favorably influence both exertional and clinically assessed dyspnea. The therapist is key in preventing this vicious circle and in delaying decline of function in the cardiopulmonary population. Specific measures for the determination of dyspnea are available.⁹⁰

Syncope without any warning period of light-headedness, dizziness, or nausea may be a sign of heart valve or arrhythmia problems but rarely occurs as a result of myocardial ischemia. Sudden death can occur; therefore medical referral is recommended for any unexplained syncope, especially in the presence of heart or circulatory problems or if the client has any risk factors for heart attack or stroke.

Physical therapy orthopedic examination of the cervical spine may include vertebral artery tests for compression of the vertebral arteries that can contribute to the development of syncope. Specific test procedures are available.^{27,206,282} Traditionally, if signs of eye nystagmus, changes in pupil size, or report of visual disturbances and symptoms of dizziness or light-headedness occurred, this was considered an indication of vertebral artery compromise requiring special care with any subsequent intervention. However, the effect of these tests (known as the vertebral basal artery test, vertebral artery compression test, Wallenberg test, or de Kleyn hanging head test) on blood flow velocity has come under question. For example, the extension-rotation test as a valid clinical screening procedure to detect decreased blood flow in the vertebral artery has been reviewed with variable results. Although one study found it to be a useful test of the adequacy of collateral circulation,²⁸³ it has been suggested that other factors, such as individual sensitivity to extreme head positions, age, and vestibular responsiveness, could affect the results of this test for vertebral artery compression.^{86,330} Larger studies are needed to determine whether subjects testing positive significantly differ from those testing negative.

Athletes may experience neurocardiogenic syncope (neurally mediated hypotension; also known as vasodepressor syncope, vasovagal attack), a benign

noncardiac cause of fainting in athletes. This disorder of autonomic cardiovascular regulation (i.e., blood pressure control system) is precipitated by prolonged standing after exertion, a warm environment, or stress, or it may occur during or after exercise, and is not life-threatening. Fainting during exertion, however, should always be evaluated by medical personnel.

Fatigue beyond expectations during or after exercise, especially in a client with a known cardiac condition, must be closely monitored. It should be remembered that P-blockers prescribed for cardiac problems can also cause unusual fatigue symptoms. For the client experiencing fatigue without a prior diagnosis of heart disease, monitoring vital signs may indicate a failure of the blood pressure to rise with increasing workloads.

Such a situation may indicate inadequate cardiac output to meet the demands of exercise. Cardiac output is the amount of blood that the heart is able to pump per minute and is directly affected by stroke volume (the amount the ventricle pumps out with each heartbeat) and the heart rate (the number of heartbeats per minute). However, poor exercise tolerance is often the result of deconditioning, especially in the older adult population. Further testing (e.g., exercise treadmill test) may be helpful in determining whether fatigue is related to cardiac problems.

Peripheral edema in the form of a 3-lb or greater weight gain or gradual, continuous gain over several days with swelling of the ankles, abdomen, and hands, and shortness of breath, fatigue, and dizziness may be a red flag symptom of CHF. When such symptoms persist despite rest, medical referral is required. Edema of a cardiac origin may require ECG monitoring during exercise or activity (the physician may not want the client stressed when extensive ECG changes are present), whereas edema of peripheral origin requires medical treatment of the underlying cause.

Claudication is always accompanied by diminished peripheral pulses in the presence of vascular disease, usually accompanied by skin discoloration and trophic changes (e.g., thin, dry, hairless skin). Core temperature, peripheral pulses, and skin temperature should be assessed. Cool skin is more indicative of vascular obstruction; warm to hot skin may indicate inflammation or infection. Abrupt onset of ischemic rest pain or sudden worsening of intermittent claudication may be due to thromboembolism and must be reported to the physician immediately.

If persons with intermittent claudication have normal-appearing skin at rest, exercising the extremity to the point of claudication usually produces marked pallor of the skin over the distal one third of the extremity. This postexercise cutaneous ischemia occurs in both upper and lower extremities and is due to selective shunting of the available blood to the exercised muscle and away from the more distal parts of the extremity.

AGING AND THE CARDIOVASCULAR SYSTEM

Cardiovascular disease, especially coronary atherosclerosis, is the most common cause of hospitalization and death in the older population in the United States. With the aging of America, by the year 2030 nearly 50% of all Americans will be 45 years old or older. By that time the number of people 65 years and older will more than double and the population 85 years and older is expected to triple.²³⁵ With this increase in the number of older persons, cardiovascular disease is likely to be even more of a major health problem in the future, as it accounts for over 80% of cardiovascular deaths in people aged 65 years and above.¹⁸⁶

Specific Effects of Aging

Aging of the heart is associated with a number of typical morphologic, histologic, and biochemical changes, although not all observed changes with age are associated with deterioration in function. The high prevalence of hypertension and ischemic heart disease makes distinction between normal aging changes and the effects of underlying cardiovascular disease processes difficult.

Disease-independent changes in the aging heart associated with a reduction in function include (1) reduction in the number of myocytes and cells within the conduction tissue, (2) the development of cardiac fibrosis, (3) a reduction in calcium transport across membranes, (4) lower capillary density, (5) decreases in the intracellular response to β -adrenergic stimulation (sometimes referred to as blunted β -adrenoceptor responsiveness), and (6) impaired autonomic reflex control of heart rate.¹⁸⁶

Other characteristic changes, such as epicardial fat deposition and "brown atrophy" caused by intracellular lipofuscin deposits, appear to be signs of the aging process but without any obvious effects on function. The hearts of older persons, even fit, healthy, and active adults, pump less blood to the skin and require the heart of the older person to work much harder under the same circumstances (e.g., exercise in warm environments) than that of a younger person.

Although the specific organ changes associated with aging are discussed here, disease and lifestyle may have a greater impact on cardiovascular function than aging. Research now shows that even children need to control their modifiable risk factors for heart disease.

Heart studies of adolescents and young adults who have died from accidental causes demonstrate that heart disease begins earlier than formerly expected. Cholesterol deposits and blood vessel changes have been demonstrated in early adolescence with substantial changes observed by age 30 years in some people.

As the arteries age, increased collagen and calcium content and progressive deterioration of the arterial media combined with atherosclerotic plaque formation result in stiff arterial walls, increased systolic blood pressure, and increased fatigue of arterial walls, all of which accelerate arterial damage, producing a self-perpetuating cycle.

Effects of Aging on Function

None of the changes described earlier has clinical relevance at rest but may have considerable consequences during cardiovascular stress, such as occurs with increased flow demand (e.g., exercise, postoperative), demand for acute autonomic reflex control (e.g., change in posture), or severe disease (e.g., uncontrolled hypertension, tachyarrhythmias, myocardial ischemia). Physiologic aging is accompanied by a progressive decline in resting organ function. Consequently, the reserve capacity to compensate for impaired organ function, heat, drug metabolism, and added physiologic demands is impaired, and functional disability will occur more quickly and take longer to resolve.²⁴⁹

According to experts at the National Institute on Aging, age is the greatest risk factor for cardiovascular disease.^{186,234} The heart also undergoes some changes associated with advancing age in individuals who do not exercise and who have risk factors for cardiac disease. Moderate thickening of the left ventricular wall (exaggerated in hypertensive clients) and increased left atrial size occur as a result of myocyte enlargement (hypertrophy) or replacement by fibrous tissue. Decreased ventricular filling compensated by increased systolic blood pressure occurs as a result of the changes in the ventricular wall. Left ventricular functioning is compromised in the presence of stress such as vigorous exercise or disease. Arrhythmia or hypertension may occur as a result.

The vasculature changes with aging as the arterial walls stiffen with age and the aorta becomes dilated and elongated. The incidence and severity of atherosclerosis do increase with aging, and this contributes to changes in vasculature function.

Calcium deposition and changes in the amount of and loss of elasticity in elastin and collagen most often affect the larger and medium-sized vessels. The unpredictable interaction between age-related and disease-associated changes in all organ functions (including the heart) and the altered neurohormonal response to various forms of stress in the aging older adult may result in atypical clinical presentations of disease that delay diagnosis and medical intervention.^{198,249}

Resting cardiac function (e.g., cardiac output, heart rate) shows minimal age-related changes. Changes in functional capacity are more apparent during exercise than at rest. The maximal heart rate or the highest heart rate during exercise does decline with age, possibly because of a decreased cardiovascular response to catecholamines. This decline in maximal heart rate is reflected in the target zone heart rates for exercising senior citizens. See Appendix B for calculation of target heart rates for sedentary and physically fit older adults. The effect of the Frank-Starling mechanism is unaltered with age and is used effectively during exercise to maintain cardiac output through a higher stroke volume.

The Frank-Starling law states that the greater the myocardial fiber length (or stretch), the greater will be its force of contraction. The more the left ventricle fills with blood, the greater will be the quantity of blood ejected into the aorta. This is like a rubber band: the more it is stretched, the more strongly it recoils or snaps back. Thus

a direct relationship exists between the volume of blood in the heart at the end of diastole (the length of the muscle fibers) and the force of contraction during the next systole.

Effects of Exercise on Aging

It is commonly accepted that a decline in maximal oxygen uptake, heart rate, and reduced maximal cardiac output with aging occurs during exercise, even in older athletes. These cardiovascular alterations parallel changes that occur with deconditioning or disuse, including the decrease in maximal oxygen intake and maximal cardiac output. These functions normalize with increased activity, and exercise can reverse some of the age-associated changes in the heart at least partially,¹⁸⁶ supporting the hypothesis that age-related cardiovascular changes are simply the result of inactivity.

In older people, aerobic exercise training lowers heart rate at rest, reduces heart rate and levels of plasma catecholamine at the same absolute submaximal workload, improves heat tolerance,³³¹ and, at least in men, improves left ventricular performance during peak exercise.²⁹⁸ It may be that the effect of training is relatively greater in older subjects.

Finally, although the benefits of physical activity and exercise among older persons are becoming increasingly clear, the role of exercise stress testing and safety monitoring for older people who want to start an exercise program is unclear. Current guidelines regarding exercise stress testing may not be applicable to the majority of adults aged 75 years or older who are interested in restoring or enhancing their physical function through a program of physical activity and exercise.

Recommendations and precautions to minimize the risk of adverse cardiac events among previously sedentary older adults who do not have symptomatic cardiovascular disease and are interested in starting an exercise program are available.¹²⁴ The therapist is very instrumental in conducting an examination and performing exercise testing to identify the specific level of pathology, impairment, or functional limitations.³⁴ An individual exercise prescription is made (mode, intensity, duration, frequency) based on the results of the examination and testing.^{108,192}

GENDER DIFFERENCES AND THE CARDIOVASCULAR SYSTEM

Interest in gender differences in all of medicine but especially the cardiovascular system has come to the forefront in the new millennium. Only a small, representative portion of the new information now available can be presented here; the reader is referred to other more complete sources.^{194,195}

Female hearts not only are smaller than male hearts but also are constructed differently and respond to age and hypertrophic stimuli differently. Structural differences in the mitral valve may explain why women are more prone to mitral valve prolapse than men. At puberty, a young woman's QT interval lengthens, and the woman

with a long QT interval is at greater risk for a serious form of ventricular arrhythmia (known as *torsades de pointes*) and sudden cardiac death, especially when taking drugs that prolong the QT interval.³⁶

The QT interval is a measure of the duration of ventricular depolarization and repolarization. A prolonged period of time for depolarization prolongs the suprathreshold period of an action potential and upsets the critical influx and efflux of electrolytes during action potential activity that may predispose a person to ventricular tachycardia.

Left ventricular mass increases with age in healthy women but remains constant in men. Under increased cardiac loading conditions (e.g., hypertension, aortic stenosis) this disparity between genders is even more obvious, especially in adults older than 50 years.¹⁴⁵ The risk for drugs other than cardiac and psychotropic ones to cause prolongation of the QT interval has recently been recognized. Women also have a three times greater risk of potentially fatal arrhythmias from some cardiac and psychotropic medications. It is anticipated that the list of drugs known to produce such effects will grow.²⁹⁶ Complications from antiarrhythmic drug use are most common during the first 3 days or after a dosage increase.

Women also tend to have a higher incidence of bleeding episodes from thrombolytic agents (see Table 12-5). Women also have different outcomes with surgery and percutaneous transluminal coronary angioplasty (PTCA), with more repeat procedures of PTCA, possibly due to smaller arteries, more advanced disease compared to men, or different tolerance to medications.¹⁹⁰ Women, in contrast to men, with premature coronary disease are at higher risk of developing vascular and ischemic complications after percutaneous coronary intervention.¹⁸⁹

Coronary Artery Disease in Women

It was long believed that CAD was a more benign process in females, but this has been soundly disproved. A woman presenting with angina postmenopausally has the exact same mortality as a man presenting with angina in his sixties. CAD is the single leading cause of death and a significant cause of morbidity among women in the United States.

Certain characteristics and clinical conditions may place women at higher risk of CAD development or progression, such as depression, being black, menopausal status, age, type 2 diabetes mellitus, and thyroid function. In addition, female gender may adversely influence the relative benefits of some risk modification interventions in older adults (e.g., cholesterol lowering, sedentary behavior, smoking cessation).^{164,349}

Underrecognition and underdiagnosis of CAD in women contribute to the high mortality rate,²²² and underuse of guideline-based preventive and therapeutic strategies for women probably contributes to their less favorable CAD outcomes.³⁵⁵ Researchers are actively studying specific risk factors for women.

A new predictive model for women that combines newer risk markers with traditional risk factors and family history is being investigated. A family history of heart

Table 12-2 Ischemic Heart Disease

	Coronary Artery Disease	Coronary Microvascular Disease
Clinical presentation	Chest pain often described as "crushing" radiating to the left arm, jaw, upper back; can present differently in women (see Figs. 12-7 and 12-11)	Diffuse discomfort
Pathology	Cold sweat, nausea Plaque buildup extending in toward the blood vessel lumen	Extreme fatigue Depression Dyspnea Older adult: confusion or increased confusion
Diagnosis	Stress test, coronary angiography	Microvascular constriction (narrowing of smaller coronary arteries); plaque deposited uniformly around inside of the artery walls
Treatment	Surgery (angioplasty, CABG), medication (statins)	Stress test, functional vascular imaging (e.g., multidirectional CT scan of the heart, stress echocardiography,* SPECT) Medication (antihypertensives, antiinflammatories, statins)

Data from Harvard Women's Health Watch: New view of heart disease in women, *Harv Womens Health Watch* 14(6):1-3, 2007.

CT, Computed tomography (serves as a noninvasive angiogram; moves around the heart generating a three-dimensional image of the heart and coronary arteries); SPECT, single-photon emission computed tomography (injects a radioactive tracer into bloodstream to chart the flow of blood in the heart and coronary vessels); CABG, coronary artery bypass graft.

*Stress echocardiography uses ultrasound to produce images of the heart after an exercise stress test.

attack prior to age 60 has been added to the list of risk factors of which women should be aware. The Reynolds Risk Score could help target women who could benefit from more aggressive preventive treatment, including diet, exercise, and a statin or other cholesterol-lowering medication.²⁸¹ You can calculate your own score if you are a woman, or help your female clients do so, at www.reynoldsriskscore.org.

Coronary Microvascular Dysfunction

A "stealth" form of heart disease called *coronary microvascular dysfunction or disease* (previously called syndrome X) has been identified in women. This type does not show up on angiograms. Classic signs of reduced blood flow to the heart (ischemia) are not present. Instead there are false-positive stress test results (significantly abnormal results on the stress test but clear arteries on an angiogram). It may be that the tiny blood vessels to the heart become constricted, reducing blood flow.

Scientists suspect ischemia may have different effects on women compared to CAD (Table 12-2). It was previously believed that women with chest pain but clear arteries had an aggravating case of coronary microvascular syndrome but it was not considered harmful.

Research in the Women's Ischemia Syndrome Evaluation (WISE) study, a federally funded investigation into ischemic heart disease in women, is ongoing to explain this phenomenon.^{31,271,305,306} Autopsy comparisons of women and men have shown that women who die of heart attacks are more likely to have plaque buildup uniformly around the inside of the blood vessel, possibly as a result of chronic inflammation. Inflammation may not be the only cause of coronary microvascular dysfunction. Risk factors such as anemia and polycystic ovarian syndrome have been identified as well.¹⁴¹ Women with this type of heart disease are at increased risk for heart attack, stroke, and reduced quality of life.

Gender Differences

Many studies have suggested that women with acute MI receive less aggressive therapy than men and have a poorer

outcome when treatment is received. Until recently, women in all age groups have been less likely to undergo diagnostic catheterization than men, and this difference was especially pronounced among older women (more than 85 years). Women have been less likely than men to receive preventive care (drug treatment for lipid management; risk factor management through exercise, nutrition, and weight reduction), invasive treatments (revascularization procedures), and thrombolytic therapy within 60 minutes of heart attack (or stroke).^{118,355}

Women delay longer than men before seeking help for symptoms of acute MI, referred to as *decision delay*, further compromising effective treatment and improved outcomes.²⁸⁸ This is especially true given the evidence that first heart attacks in women may be more severe and that women are more likely to die in the first weeks and months after a heart attack. The WISE study has provided detailed evaluation of gender-related risk factors for ischemic heart disease.³⁰⁶

For many years, women and minorities were underrepresented in studies conducted on heart disease and stroke, but this has changed over the last decade along with concomitant expansion of prevention and educational outreach programs for heart attack, stroke, and other cardiovascular diseases in women. The use of noninvasive testing in women was controversial because of a perception of diminished accuracy, limited female representation, and technical limitations.

Large observational studies now report marked improvements in the accuracy of results for women undergoing exercise treadmill, echocardiography, and nuclear testing as a result of expanding risk parameters in the test interpretations and improved diagnostic accuracy of such tests.²²² Because of technologic advances, improved surgical techniques, greater awareness of gender differences in heart disease, and increased funding for gender-based research, these trends are improving, and women now seem to do as well as men after surgical (revascularization) procedures to restore blood flow to the heart.

Although the American Heart Association reports a decline in death rates in women for CAD and stroke,

women are still twice as likely as men to die within 1 year of having a heart attack, and women are at greater risk for second heart attacks and for disability because of heart failure. The death rate among black women is 33.7% higher for stroke and 69% higher for heart disease than among white women.^{12,17}

Many women die of CAD without any warning signs, and by age 65 years one in four women has heart disease (the same proportion as in men). CAD claims the lives of nearly 250,000 women annually in the United States,²²² compared with 40,200 for breast cancer and 63,000 for lung cancer. Despite these statistics, misperceptions still exist that cardiovascular disease is not a real problem for women and that, despite the fact that some risk factors for CAD can be prevented, CAD is not curable. For these reasons, education and prevention²²⁸ are vitally important to reduce risk of heart disease.

Coronary Artery Surgery and Women

The number of women undergoing coronary artery bypass graft (CABG, pronounced "cabbage") has continued to increase (from 146,000 in 1995 to 427,000 in 2004).^{13,15} Women may experience more chest wall discomfort as a common side effect of CABG than men; it is most often reported in those women who had an internal mammary artery (IMA) graft.

Women undergoing bypass surgery have a death rate about twice as high as that of men.³⁹ This has been attributed to the fact that women generally have smaller bodies, meaning smaller coronary arteries on which it may be technically more difficult to operate. Data from the WISE study also suggest that women may have both CAD and unrecognized microvessel disease, in which case, opening the arteries is not sufficient.

Hormonal Status

Influence of Hormones on Coronary Artery Disease

Estrogen has been considered to have a cardioprotective benefit for women via a variety of mechanisms. It stimulates the formation of high-density lipoprotein (HDL), the good cholesterol, which carries plaque away from the artery wall and back to the liver to be broken down and excreted, while also stimulating low-density lipoprotein (LDL) receptors in the liver and possibly the blood vessel walls. These receptors bind the LDL, the bad cholesterol, and remove it from the circulation, preventing its damaging effects in plaque formation.

Estradiol acts as a calcium channel blocker to relax artery walls, which helps dilate the arteries, improves blood flow throughout the brain and body, and helps to reduce blood pressure. Estrogen maintains the normal balance of prostacyclin and thromboxane, two chemicals that regulate clot formation. Estrogen increases arterial wall production of prostacyclin, which improves blood flow and reduces platelet aggregation. Estrogen receptors locate different regulatory molecules that attract and bind to estrogen in the cells of the smooth muscle layer of blood vessels. Atherosclerosis may develop because blood vessel cells cannot extract needed estrogen from the blood without the necessary receptors.

Another possible mechanism by which estrogen protects against heart disease before menopause is the release of endothelium-derived relaxing factor (EDRF, thought to be nitric oxide), a chemical stimulated by estrogen and responsible for dilating blood vessels to maintain normal pressure and flow. As women lose the biologically active estradiol, gender differences become gender similarities and the incidence of cardiovascular disease increases dramatically, matching the incidence among men within 10 years of menopause without hormone replacement therapy.

Myocardial ischemia may be more easily induced when estrogen concentrations are low, a finding that may be important for timing the assessment and evaluating treatment in women with CAD. The early follicular phase, when estradiol and progesterone concentrations are low, may be associated with poor exercise performance as measured by onset to myocardial ischemia. These findings are preliminary and have not been reproduced or confirmed.

Hormone Replacement for Postmenopausal Women

The use of hormones for cardioprotection has been under investigation for many years. Because heart attacks tend to occur 10 years later in women than in men, it was assumed that the protective effect of estrogen was responsible. Exogenous (externally administered) estrogen has been reported to improve plasma lipid profiles, carbohydrate metabolism, and vascular reactivity, but surprisingly, hormonal therapy does not alter the progression of CAD or protect against MI or coronary death. The Heart and Estrogen/Progestin Replacement Study (HERS) failed to demonstrate cardioprotection and even showed an early adverse outcome in women with documented CAD who received daily hormone replacement therapy (HRT). Several large randomized clinical trials for primary and secondary prevention showed mixed results.³⁴⁷

Fifty percent of all women who have had a hysterectomy (without removal of the ovaries) and all women who have an oophorectomy (ovary removal) become endocrinologically menopausal by 3 years after surgery, regardless of age. Their heart disease risk increases when they become menopausal regardless of their age or the means by which menopause occurs.

Oral Contraceptives

Studies show that women smokers over 35 years who use oral contraceptives are much more likely to have a heart attack or stroke than nonsmokers who use birth control pills. In the last 20 years, cardiovascular complications in all women taking oral contraceptives have become less common because current contraceptives contain the lowest dose of estrogen possible without breakthrough bleeding.¹⁷

At this dose, the risk of thromboembolic disease is reduced to about 40 events per 100,000 women per year, approximately the same risk as in the general population.⁵⁵ However, much debate continues about the use of so-called third-generation (newest) oral contraceptives containing low doses of estrogen and a type of progestin known as *desogestrel*. Women taking this contraceptive are twice as likely to develop superficial venous blood clots

compared to women taking second-generation oral contraceptives containing progestins, such as levonorgestrel and norethindrone. It is estimated that 425 ischemic strokes can be attributed to oral contraceptive use each year in the United States, even with the newer low-estrogen preparations.¹²⁵

Hypertension in Women

More women than men eventually develop hypertension in the United States because of their higher numbers and greater longevity. White coat hypertension (rise in blood pressure when being evaluated by a physician or other health care worker) is more prevalent among women, and black women are more likely to have hypertension than black men.

Alcohol, obesity, and oral contraceptives are important causes of rise in blood pressure among women. Alcohol is known to have specific toxic effects on heart muscle fibers, and excessive alcohol consumption is increasing in women; yet women are less likely than men to be identified as alcohol abusers at early stages of the illness and are less often referred for alcohol treatment until later stages of abuse, when cardiac and other severe complications have occurred.³⁴¹

Women with left ventricular hypertrophy are at greater risk of death than men. ACE inhibitors and angiotensin receptor blockers are contraindicated in pregnancy and should be avoided in women with childbearing potential.²⁷² A recent study found that infants who were exposed to the ACE inhibitors during the first trimester were at increased risk of major congenital malformations that affected the cardiovascular and nervous systems.⁸⁵

In the WISE study, early onset of high systolic blood pressure or pulse pressure (the difference between systolic and diastolic blood pressures) has been linked with a higher risk of having significant CAD.

Cholesterol Concerns for Women

Total cholesterol is broken into HDL, or good cholesterol, which carries cholesterol away from the cells, and LDL, or bad cholesterol, which carries cholesterol to the cells. A helpful way to remember the function of these is to think of HDL as "Healthy" or beneficial cholesterol and LDL as "Lousy" or detrimental cholesterol. Lipoproteins are complexes that help dissolve, transport, and utilize the cholesterol molecule.

The National Heart, Lung, and Blood Institute estimates that more than half of all women over age 55 years need to lower their blood cholesterol. Reference guides for cholesterol testing and recommendations based on lipid levels have not been standardized for women with the exception of the HDL. The recommended level for initiating treatment in women is less than 50 mg/dl and for men is less than 40 mg/dl. Whether the current established guidelines on other lipids (based on data derived from studies of men) are most appropriate for women remains unknown.

After menopause, women have higher concentrations of total cholesterol than men do, but the significance of this finding remains unknown. Research results at this

time suggest that women need higher levels of the good cholesterol (HDL) for protection against heart disease and that other blood markers, such as serum triglycerides and C-reactive protein (CRP), may play more meaningful roles in defining women's heart disease risk. Low levels of HDL cholesterol are predictive of CAD in women and appear to be a stronger risk factor for women older than 65 years than for men of the same age.²²⁹

DISEASES AFFECTING THE HEART MUSCLE

Ischemic Heart Disease

Coronary arteries carry oxygenated blood to the myocardium. When these arteries become narrowed or blocked, the areas of the heart muscle supplied by that artery do not receive sufficient amount of oxygen and become ischemic and injured, and infarction may result. Major disorders of the myocardium owing to insufficient blood supply are collectively known as ischemic heart disease, coronary heart disease (CHD), or coronary artery disease (CAD).

Despite improved clinical care, heightened public awareness, and widespread use of health innovations, atherosclerotic diseases (resulting in narrowing of arteries) and their thrombotic complications remain the number one cause of mortality and morbidity in the United States (see Table 2-1).

An estimated 12 million persons in the United States have CAD. Of the 1.1 million CAD events that occurred during 2001, approximately 650,000 were first events and 450,000 were recurrences. Each year approximately 220,000 fatal CAD events occur suddenly among unhospitalized people. Eleven million Americans who are alive today have a history of angina pectoris, MI, or both, and an estimated 2 million middle-aged and older adults (more than 75 years) have silent myocardial ischemia.²²⁶

Although CAD death rates in the United States have decreased since reaching a peak during the late 1960s (146.2 cases per 100,000 in 1948 with a peak of 220.3 in 1963 to 87 cases per 100,000 in 1996), a decline in the incidence of coronary disease has not been achieved. In 1940, the rate of cardiovascular disease was 26.4 per 100,000 people compared to 173.5 in 2000.¹⁶

The declining mortality rate does not apply to those adults with diabetes and has been attributed to improvements in lifestyle (e.g., reduced smoking in men, improved treatment for lipid lowering, improved coronary care), whereas the increased incidence may be related to the increasing number of people who are surviving past age 65 years.

Nonatherosclerotic causes of coronary artery obstruction and subsequent ischemic heart disease are uncommon (Box 12-1). For example, mediastinal radiotherapy for left-sided breast cancer, Hodgkin's disease, or non-Hodgkin's disease may be an independent risk factor in the development of ischemic heart disease.

Radiotherapy causes cardiac perfusion defects 6 months after treatment in most people, but it remains unknown if these changes are transient or permanent. Improvements in radiation technique have reduced com-

Box 12-1**NONATHEROSCLEROTIC CAUSES OF CORONARY ARTERY OBSTRUCTION**

- Kawasaki disease
- Coronary embolism
 - Infective endocarditis
 - Prosthetic valves
 - Cardiac myxomas
 - Cardiopulmonary bypass
 - Coronary arteriography
- Metabolic syndrome
- Insulin resistance syndrome (hyperinsulinemia)
- Trauma to coronary arteries
 - Penetrating
 - Nonpenetrating
- Arteritis
 - Syphilis
 - Polyarteritis nodosa
 - Lupus erythematosus
 - Rheumatoid arthritis
- Connective tissue diseases
- Radiotherapy

plications, especially late cardiac deaths. At the present time, the benefit of treatment for operable breast cancer for individuals who may be cured of the disease appears to outweigh the risks of long-term cardiac sequelae.³⁶⁷ Researchers continue to investigate the need to optimize adjuvant radiotherapy for early breast cancer by considering the dose both to the cancer and to the heart.

Arteriosclerosis

Arteriosclerosis represents a group of diseases characterized by thickening and loss of elasticity of the arterial walls, often referred to as hardening of the arteries. Arteriosclerosis can be divided into three types: (1) atherosclerosis, in which plaques of fatty deposits form in the inner layer or intima of the arteries; (2) Monckeberg's arteriosclerosis, involving the middle layer of the arteries with destruction of muscle and elastic fibers and formation of calcium deposits; and (3) arteriolosclerosis or arteriolar sclerosis, characterized by thickening of the walls of small arteries (arterioles). All three forms of arteriosclerosis may be present in the same person but in different blood vessels. Frequently the terms *arteriosclerosis* and *atherosclerosis* are used interchangeably, although technically atherosclerosis is the most common form of arteriosclerosis.

Atherosclerosis

Atherosclerosis, defined as thickening of the arterial wall through the accumulation of lipids, macrophages, T lymphocytes, smooth muscle cells, extracellular matrix, calcium, and necrotic debris, can affect any of the arteries in a condition known as cardiovascular disease.

When the arteries of the heart are affected it is referred to as coronary artery disease (CAD) or coronary heart disease (CHD); when the arteries to the brain are affected, cerebrovascular disease develops. Atherosclerosis of blood vessels to other parts of the body can result in PVD, aneurysm, and intestinal infarction. Atherosclerosis as it

affects the heart vessels is discussed in this section. The effect of atherosclerosis on other blood vessels is discussed individually elsewhere.

Etiologic and Risk Factors. In 1948, the U.S. government decided to investigate the etiologic factors, incidence, and pathologic findings of CAD by studying residents of a typical small town in the United States: Framingham, Massachusetts. In 1971 a second generation of adult children and their spouses of the original participants were added. Results from this ongoing research have identified important modifiable and non-modifiable risk factors associated with death caused by CAD.

Modifiable risk factors that can be controlled are referred to now as "risk factors for which intervention has been shown to *reduce* incidence of CAD"; other risk factors that can be managed are now referred to as "risk factors for which intervention is *likely to reduce* incidence of CAD" or "risk factors for which intervention *might reduce* incidence of CAD." Some risk factors cannot be altered (nonmodifiable), such as age, gender, family history of heart disease, ethnicity, and exposure to infectious agents (Table 12-3).

As the Framingham study continues to gather and analyze new data, results are reported that help modify existing health risk appraisal models relating risk factors to the probability of developing CAD. With these new models, blood lipid levels, diabetes, and, in women, systolic blood pressure and cigarette smoking are emphasized once again as independent predictors of risk.

The Framingham study is engaged in quantifying the independent contributions of plasma homocysteine (an amino acid by-product of protein metabolism); lipoprotein (a) (Lp[a]), a cholesterol-rich plasma lipoprotein that encourages overgrowth of cells in the artery walls; insulin resistance; small, dense LDL; CRP, a producer of inflammation; fibrinogen; and genetic determinants of cardiovascular disease.¹⁷⁴

In a national sample of older women and men (65 to 84 years), black and Mexican American women and black men were at the greatest risk for cardiovascular disease. These findings parallel a previously documented increased risk of cardiovascular disease among younger ethnic minority populations. Differences in socioeconomic status (as measured by educational level and family income) do not explain the higher prevalence of cardiovascular disease risk factors in these ethnic minority

³²⁰

groups.

Higher prevalence of certain risk factors in black women, particularly diabetes and obesity, may explain their increased risk of CAD, but ethnic differences in CAD for Hispanics remain unknown. The Newcastle Thousand Families Study confirms that adult lifestyles are more important than socioeconomic variables,¹⁸⁷ but further research to identify ethnic differences in cardiovascular disease risk factors is needed.

Modification of Risk Factors That Reduce Incidence of Coronary Artery Disease. Cigarette smoking remains the leading preventable cause of CAD. Tobacco products increase heart rate and blood pressure; decrease the oxygen-carrying capacity of blood; increase poisonous gases and elements of the blood such as carbon monox-

Table 12-3 Coronary Artery Disease Risk Factors

MODIFIABLE RISK FACTORS		NONMODIFIABLE RISK FACTORS	NEW PREDICTORS OF RISK FACTORS
Risk Factors for Which Intervention Has Been Shown to Reduce Incidence of CAD	Risk Factors for Which Intervention Is Likely to Reduce Incidence of CAD	Risk Factors for Which Intervention Might Reduce Incidence of CAD	Risk Factors Under Investigation
Cigarette smoking	Obesity (see Table 12-4)	Psychologic factors and emotional response to stress	Elevated homocysteine ($>15 \mu\text{mol/L}$)
Elevated total serum cholesterol level	Physical inactivity	Discriminatory medicine*	C-reactive protein
Elevated LDL cholesterol level	Diabetes or impaired glucose tolerance; insulin resistance	Oxidative stress	Fibrinogen
Hypertension	Low HDL ($<40 \text{ mg/dl}$ [men]; $<50 \text{ mg/dl}$ [women])	Excessive alcohol consumption or complete abstinence	Lipoprotein (a), or Lp(a) ($>30 \text{ mg/dl}$)†
	Hormonal status; oral contraceptives; hysterectomy or oophorectomy; menopause without hormone replacement (especially before age 40 yr)	Elevated triglycerides	Troponin T
	Thrombogenic factors	Sleep-disordered breathing	Plasminogen activator inhibitor (PAI); marker for recurrence of MI
		Poor nutrition	D-dimer (fibrin)
			Dermatologic indicators
			Greying of the hair
			Thoracic hairiness
			Earlobe creases
			Male impotence
			Ankle/brachial blood pressure index (ABI) (see Box 12-15)

CAD, Coronary artery disease; LDL, low-density lipoprotein; HDL, high-density lipoprotein; MI, myocardial infarction.

*Discriminatory medicine is not technically a risk factor for CAD but rather results in a different natural history for some individuals.

†Applies to whites and Asians but not to blacks.

ide, cyanide, formaldehyde, and carbon dioxide; cause narrowing of blood vessels; and increase the work of the heart.

Nicotine enhances the process of atherosclerosis by a direct effect on the blood vessel wall, increasing the circulating levels of fibrinogen and tendency for plaque formation in the coronary arteries. Nicotine also increases the expression of LDL receptors on smooth muscle cells lining the plaque, priming the cells for the entry of LDL cholesterol. By-products of tobacco products in the blood act as potent oxidizing agents. This oxidation damages the intimal lining of the arterial walls, exposes collagen, and results in platelet aggregation. People who quit smoking will reduce their risk of CAD by one half after 1 year and equalize their risk of CAD to that of a non-smoker in 15 years (see Table 3-4).

Elevated total serum cholesterol levels (more than 200 mg/dl) place a person at greater risk for heart disease; this risk doubles when cholesterol levels exceed 240 mg/dl and the ratio of total cholesterol to HDL cholesterol is more than 4.5 (Table 12-4). It is now well known that therapy to lower LDL levels can stabilize, reduce, or even reverse the progression of atherosclerotic plaques and coronary stenosis and reduce recurrent cardiac episodes. Cholesterol levels are influenced by heredity, diet, exercise, alcohol consumption,^{91,183} obesity, medications, menopausal status, thyroid function, and smoking. Impaired thyroid function is a cause of elevated cholesterol and arterial stiffness, especially in women older than 50 years who smoke.^{248,343}

Hypertension, or high blood pressure, causes the heart to work harder and may injure the arterial walls, making them prone to atherosclerosis. Epidemiologic studies document a strong association between high levels of both systolic and diastolic blood pressure and risk of CAD (and stroke) in both men and women.

Hypertension is aggravated by obesity and is associated with diabetes and regular alcohol use. It can be initiated or aggravated by the use of oral contraceptives, especially in women who smoke. Women who have undetected or uncontrolled hypertension are five times more likely to experience angina, heart attack, or sudden death than women with normal blood pressure. Weight reduction, dietary interventions, and pharmacologic intervention have important roles in the prevention and treatment of hypertension.

Modification of Risk Factors That Are Likely to Reduce Incidence of Coronary Artery Disease. Physical inactivity, sedentary lifestyle, and obesity are parallel, interrelated epidemics in the United States that contribute to increased risk of CAD.

Obesity (see discussion in Chapter 2) alone can lead to CAD, because the excess weight makes the heart work harder to pump blood throughout the body. Obesity is commonly associated with diabetes mellitus, high blood pressure, and high fat (triglycerides and cholesterol) levels. The prevalence of obesity has increased among both men and women in the United States in the past decade. More than one half of adult Americans are overweight or obese, and more than one half of this

Table 12-4 Heart Disease Prevention Target Measurements*

Risk Factors	Targets
Body Measurements	
• Body mass index (BMI): multiply your weight in pounds by 700, then divide that number by the square of your height in inches	18.5-24.0 (see also Table 2-3)
• Waist/hip ratio (WHR): divide your waist measurement in inches by your hip measurement in inches	≤0.8
Lipids, Lipoproteins	
• Total cholesterol	<200 mg/dl
• High-density lipoprotein (HDL) cholesterol	≥40 mg/dl (men)† ≥50 mg/dl (women)†
• Low-density lipoprotein (LDL) cholesterol	≤129 mg/dl (optimal: 100 mg/dl; <70 mg/dl for women at high risk for heart attack or stroke)
• Triglycerides	≤200 mg/dl (<150 mg/dl, preferred target)
• Total cholesterol/HDL ratio	<4.5
Blood Pressure	See Table 12-8

*These target measures are for healthy adults without evidence of heart disease.

†The current standard for all adults is set at ≥35 mg/dl. Proposed targets of ≥40 mg/dl for men and ≥50 mg/dl for women are the new guidelines from the American Heart Association³⁰⁰ and are developed for adults and children over age 2 (no upper age limit). Some experts recommend 55 mg/dl or higher for women, but this remains unproven and is under investigation.

population is overweight with associated medical conditions.²³⁸

The U.S. Department of Health and Human Services reports that one out of every five children is obese, and the obesity rates have increased 147% from 1971 to 1994 among children ages 6 to 11 years.²⁹ Target body measurements (adults) for the prevention of heart disease are listed in Table 12-4. Increasing research and knowledge related to nutrition have led to identification of several dietary factors that influence CAD risk. The epidemiologic evidence confirms that diets low in saturated fat and high in fruits, vegetables, whole grains, and fiber are associated with a reduced risk of CAD.

Physical inactivity is a major risk factor equal to cholesterol, cigarette smoking, and high blood pressure. Because a higher proportion of U.S. adults lead a sedentary lifestyle (60%) than have hypertension (10%), have hypercholesterolemia (excessive cholesterol in the blood) (10%), or smoke one pack or more of cigarettes per day (18%), increasing the general population's physical activity level may have a greater effect on reducing the incidence of CAD than the modification of the other three risk factors.

Regular aerobic exercise lowers resting pulse rate and blood pressure, improves the ratio of good to bad cholesterol, and helps prevent and control diabetes and osteoporosis. The risk of heart attack and death from heart disease declines steadily as the frequency of vigorous exercise increases. Occasional exercise (one or two times per week) reduces the risk of heart attack by 36%, moderate exercise (three or four times per week) reduces it by 38%, and regular, vigorous exercise (five or more times per week) reduces it by 46%. The benefit of habitual exercise toward reducing heart attack was greatest among those who worked out for 11 to 24 minutes and did not change or increase further after 24 minutes of exercise.⁵

Impaired glucose metabolism (e.g., insulin resistance, hyperinsulinemia, glucose intolerance) is reported to be atherogenic. Diabetes mellitus, impaired glucose tolerance, and high-normal levels of glycated hemoglobin are powerful contributors to atherosclerotic cardiovascular events in the Framingham study.³⁶³

The association is complex, and the pathways by which elevated insulin adversely affects both CAD risk factors and the risk of developing CAD remain unknown. The risk for CAD in participants younger than 65 years was double in men and triple in women with diabetes compared with their nondiabetic counterparts. Individuals with type 2 diabetes mellitus have a risk of MI equivalent to that of someone without diabetes who has had a previous MI.

Diabetes confers the same risk of cardiovascular disease as aging 15 years.⁴² Kidney disease accompanied by hypertension is a serious complication affecting the cardiovascular system among people with diabetes. More than 80% of persons who have diabetes die of some form of cardiovascular disease. Bypass surgery provides significantly better survival than angioplasty for individuals with diabetes in some subgroups. This may be attributed to the more extensive CAD among people with diabetes and the greater tendency for their arteries to restenose after angioplasty.

Low levels of HDL cholesterol (and high levels of triglycerides) produce twice as many cases of CAD as any other lipid abnormality; this effect is exaggerated in women (see Table 12-4). *Hormonal status* in the menopausal or postmenopausal woman is now known to be a likely contributing risk factor in the development of CAD. The mechanism through which a protective effect is mediated by estrogen has not been explained completely (see previous discussion in this chapter).

Modification of Risk Factors That Might Reduce Incidence of Coronary Artery Disease. Psychologic factors and

emotional stress (e.g., depression, anxiety, personality factors and character traits, social isolation, chronic life stress) contribute significantly to the pathogenesis and expression of CAD. People who are negative, insecure, and distressed (type D personality) are three times more likely to experience a second heart attack than non-D types.⁹⁶

Other personality traits likely to affect the heart are free-floating hostility associated with anger and a sense of time urgency (two major components of the type A personality). The long-held belief that anger can increase the risk of acute MI and can be an immediate trigger of heart attacks has been verified.³⁶¹

The relationship between these entities and CAD can be divided into behavioral mechanisms, whereby psychosocial conditions contribute to a higher frequency of adverse health behaviors such as poor diet and smoking, and direct stress-induced pathophysiologic mechanisms, which contribute to neuroendocrine activation, hemodynamic and catecholamine responses, and platelet activation.³¹⁶ Personality traits are more difficult to change than other psychologic risk factors, such as depression or anxiety.⁹⁶

Improved technologies and research demonstrate that acute mental or emotional stress triggers myocardial ischemia, promotes arrhythmogenesis, stimulates platelet function, and increases blood viscosity through hemoconcentration. Moderate to severe depression is associated with altered cardiac autonomic modulation, including elevated heart rate, elevated norepinephrine, and reduced heart rate variability, known risk factors for cardiac morbidity and mortality.

In the presence of atherosclerosis in people with CAD, acute stress also causes coronary vasoconstriction. Hypersensitivity of the sympathetic nervous system to perceived adversity (manifested by exaggerated heart rate and blood pressure responses to psychologic stimuli) is an intrinsic characteristic among these individuals; in addition, the calming response of the parasympathetic nervous system is diminished in persons who are hostile and the parasympathetic counterbalance does not stop the effects of adrenaline on the heart.

These emotions trigger the stress response, increasing blood pressure and heart rate and altering platelet function. Increasing evidence suggests that cognitive behavioral therapy and anger management may benefit cardiac clients by improving medical outcome. (See also Special Implications for the Therapist: Stress, Coping, and Self-Efficacy in Chapter 2.)

Discriminatory medicine, the idea that women (and minorities) are treated less aggressively than men for heart problems, has been strongly debated. On the one hand, it has been suggested that a woman's symptoms are more likely to be misinterpreted, overlooked, or dismissed as psychosomatic and that women are less likely to undergo diagnostic procedures. On the other hand, lower rates of cardiac catheterization among women may be related to women's lower rate of positive exercise test results and older age at the time of symptomatic presentation rather than bias based on gender. As mentioned earlier in this chapter, there is evidence to suggest that this trend is changing toward improved gender equity.

Research to understand ethnic differences remains limited.

Oxidative stress, or the oxidation of LDL particles as part of the atherosclerotic formation, is under active investigation. Oxidative stress is considered a significant risk factor for cardiovascular disease. However, antioxidant nutrients failed to provide benefits for cardiovascular disease in several human trials.

This apparent paradox between the role of antioxidants in reducing oxidative stress and the failure of many antioxidant supplementations warrants further research. Meanwhile, according to the current American Heart Association scientific statement, antioxidant vitamin supplements to prevent cardiovascular disease are not recommended.¹⁹⁹ See further discussion of the oxidation process in Chapter 6.

Moderate alcohol consumption decreases the risk of heart disease in some people. This is attributed to alcohol's beneficial effects on hemostasis, including platelet aggregation, coagulation factors, and fibrinolytic system.²⁸⁹ Alcohol intake increases activity of an enzyme called *tissue-type plasminogen activator* (*t-PA*) that helps to keep blood flowing smoothly by initiating dissolving of clots (fibrinolysis). The highest levels of endogenous *t-PA* protein have been found among daily consumers of red wine, and the lowest levels have been found among subjects who never (or rarely) consume alcohol.³

Although a small amount of alcohol taken daily with meals may elevate levels of HDL cholesterol and the bioflavonoids in red wine reduce atherosclerosis, most researchers oppose recommending drinking as a public health measure to fight heart disease and stress that no one, particularly people with a personal or family history of alcohol abuse, should drink alcohol to improve cholesterol. It should always be remembered that heavy alcohol consumption and binge drinking increase risk of blood clot formation, cardiac arrhythmia, elevated blood pressure, and cardiovascular disease. Dietary supplements containing flavonoids and antioxidants are now available without the sugar in grape juice or the alcohol in wine.

The cardioprotective benefits appear to be effective only in men over age 45 years and women over age 55 years when limited to one or two drinks per day.¹⁵¹ Greater concentrations of alcohol cause direct coronary artery constriction, which may explain the relationship between ethanol and sudden coronary ischemia that is seen clinically. In addition, the depressive effect of excessive alcohol on the function of myocardial cells decreases myocardial contractility and can be very disabling. Chronic abuse of alcohol is also related to a higher incidence of hypertension, which places greater stress on a heart already compromised by CAD. Chemical dependency is also associated with increased stress on the diseased heart.

In addition, several epidemiologic studies have suggested that *sleep-disordered breathing* is a risk factor for cardiovascular disease, particularly hypertension, stroke, and heart failure.

Nonmodifiable Risk Factors. The risk of cardiovascular disease or CAD increases with *increasing age*, and the person older than 40 years is more likely to become

symptomatic. *Gender* as a nonmodifiable risk factor is reflected in the fact that heart disease is more prevalent among men; women generally experience heart attacks 10 years later than men, possibly because of the biologic protection factor provided premenopausally by estrogen.

By age 45 years, heart disease affects one woman in nine. By age 65 years, this ratio becomes one in three, more closely approximating rates among men. These statistics represent the outcome when no hormone replacement therapy is initiated, but as previously mentioned, the effectiveness of hormone replacement therapy in reducing morbidity and mortality associated with CAD is still under investigation.

A *family history* of cardiovascular disease (i.e., one or more members of the immediate family with the disease) is associated with increased incidence of heart disease. It is proposed that a mix of environmental and genetic factors leads to atherosclerosis of the coronary arteries in a complex, unpredictable, and unknown series of interactions. For selected individuals, genetic predisposition, especially abnormalities in lipoprotein metabolism, can play a very important role in their risk of developing atherosclerosis.

Current research is exploring the possibility of "candidate genes" that may be associated with an increased risk of CAD. Current technology and information from the Genome Project now allow linkage in family studies to be supplemented with accurate localization of a disease-causing or susceptibility (candidate) gene.

For example, apolipoprotein E-4 (*apo E-4*), one of three forms of a gene involved in clearing cholesterol from the body, is associated with an increase in LDL and total cholesterol. Another candidate gene (*DSCAM*) present in individuals with Down syndrome and CAD has been identified, and a mutation in the ABC-1 (adenosine triphosphate [ATP]-binding cassette transporter 1) protein involved in lipoprotein metabolism can disrupt normal transport and processing of cholesterol. In the future, inherited markers in combination with traditional risk factor assessment will be used first to prevent and then to manage vascular disease through better utilization of diagnostic testing and individualized pharmacologic intervention.

Ethnicity is a risk factor, and certain ethnic groups have a higher rate of heart disease. The risk of heart disease is highest among blacks, who are three times more likely to have extremely high blood pressure, a major risk factor for CAD, and who have a higher prevalence of other risk factors, such as diabetes mellitus, obesity, and cigarette smoking.

Native Americans have an unusually high rate of diabetes and obesity, although lower total and LDL cholesterol levels appear to offset the difference. Conflicting comparisons of CAD mortality between Mexican Americans and non-Hispanic whites have been reported. Despite their adverse cardiovascular risk profiles, especially a greater prevalence of diabetes, Mexican Americans are reported to have lower mortality rates from CAD. However, when death certificates are more carefully examined and coded, Mexican Americans have rates equal to or higher than those of non-Hispanic whites.²⁵³

Hispanics are less likely than whites to receive catheterization and angioplasty procedures.¹⁰⁹

Infections (bacterial and viral) as a cause of atherosclerosis and thereby CAD in some people have been supported by experimental and clinical data. This discovery came about as researchers identified the presence of a common virus (cytomegalovirus) in arterial plaque as a contributing factor to angioplasty failure. Atherosclerosis, now recognized as an inflammatory process, and injury to the inner layer of the artery may be triggered by acute or chronic infection, particularly in more susceptible disease states such as diabetes.

Epidemiologic studies have suggested a link between chronic *Helicobacter pylori* infection²⁶⁰ or prior infection with *Chlamydia pneumoniae* and ischemic heart disease, but this idea is speculative, and research results have been correspondingly conflicting. Although *C. pneumoniae* infection has been associated with the initiation and progression of atherosclerosis, results of clinical trials investigating antichlamydial antibiotics as adjuncts to standard therapy in patients with CAD have been inconsistent,²³ and evidence available to date does not demonstrate an overall benefit of antibiotic therapy in reducing mortality or cardiovascular events in adults with CAD.

New Predictors. Investigators may have identified markers for heart disease present in apparently healthy people, that is, components of blood or other factors that can help identify risk of CAD before symptoms develop (see Table 12-3). Serum cholesterol has been used for a long time, but many more potential predictors of risk are being examined. *Homocysteine* (Hcy), an amino acid that is generated as the body metabolizes another amino acid, methionine (found in animal-derived foods), occurs naturally in blood and tissues and is more common in people with CAD. Elevated levels of homocysteine may be as much of a risk factor as high cholesterol or smoking.

High-sensitivity C-reactive protein (hsCRP), an acute-phase reactant that reflects low-grade systemic inflammation, is produced by the liver in response to trauma, tissue inflammation, and infection, and seems to predict hypertension, diabetes, heart attacks, and strokes before they occur.²⁸⁰ People with even slightly elevated blood levels of CRP appear to be at increased risk for CAD and its complications regardless of age, gender, general health, or the presence of other CAD risk factors.

Cigarette smokers have elevated levels of CRP, and individuals experiencing a heart attack who have high levels of CRP have a slower than normal response to antithrombotic medication. Preliminary data suggest that the relative effectiveness of secondary preventive therapies, such as cholesterol-lowering drugs and aspirin, may depend on an individual's baseline CRP level.⁶

Fibrinogen, a blood protein essential for proper clotting, may predict first heart attacks (and strokes) in people with unstable CAD and is a risk factor for future cardiovascular problems in those who have not yet developed CAD.

Lipoprotein (a), (Lp[a]), an LDL cholesterol particle with an additional protein attached, slows the breakdown of blood clots. People with high levels of Lp(a) are at greater risk for MI than those with lower levels of Lp(a).

Pulse pressure (less than 60 mm Hg), a measure of arterial stiffness (*systolic blood pressure less diastolic blood pressure*), has been investigated as an independent predictor of CHD risk. Pulse pressure has been shown to predict risk for cardiovascular events in men; this association has not been well established in women. Results of postmenopausal women with CAD evaluated in the Heart and Estrogen/Progestin Replacement Study showed that pulse pressure has a predictive value for heart failure and stroke, but is not associated with mortality associated with CAD.²³³

Dermatologic indicators of coronary risk, such as greying of the hair, hair loss (baldness), thoracic hairiness, and diagonal ear lobe crease are additional but weak risk indicators of CAD in men under age 60 years, independent of age and other established coronary risk factors. Short stature may also be an early indicator of heart disease risk. Available data on the mentioned skin conditions as markers for elevated coronary disease risk have come under question.^{30,138}

Erectile dysfunction (impotence) is a hemodynamic event that can warn of ischemic heart disease in some men. Researchers may eventually call impotence a "penile stress test" that can be as predictive as a treadmill exercise stress test.²⁴⁶

Metabolic syndrome has received increased attention within the last few years (see also discussion in Chapter 11). Several terms have been proposed previously for it: the "deadly quartet," syndrome X, insulin resistance syndrome, and hypertriglyceremic waist.¹³⁵ The term *metabolic syndrome* is most commonly used in the cardiovascular field.

Metabolic syndrome can be viewed as an aggregation of multiple cardiovascular risk factors of endogenous origin in one individual. Until recently, the metabolic syndrome has been considered a complex disorder (not a discrete entity with a single cause but truly a syndrome, i.e., a grouping of the risk factors) with no single factor as a cause.¹³⁵

However, latest research using confirmatory factor analysis, while supporting the current clinical definition of the metabolic syndrome, suggests the existence of a single latent factor that underlies all of the core components of the metabolic syndrome.²⁶⁷ The existence and the nature of this single factor remain to be proved.

Metabolic syndrome is a group of interrelated factors of metabolic origin—*metabolic risk factors*—that appear to directly promote the development of the atherosclerotic cardiovascular disease. Another group of factors, the *underlying risk factors*, can precipitate the metabolic syndrome.

Metabolic risk factors include dyslipidemia (elevated serum triglycerides, apolipoprotein B, and LDL; low level of HDL cholesterol), elevated blood pressure, and elevated plasma glucose, a prothrombotic state, and a proinflammatory state.¹³⁵ The most important *underlying risk factors* are abdominal obesity and insulin resistance; other associated conditions include physical inactivity, aging, hormonal imbalance, and genetic or ethnic predisposition.¹³⁵ Excess visceral fat is considered more strongly associated with the metabolic syndrome than any other adipose tissue compartment.^{66,157}

Box 12-2

CRITERIA FOR CLINICAL DIAGNOSIS OF METABOLIC SYNDROME

The presence of any three of these five components constitutes a diagnosis of metabolic syndrome:

- Waist size of more than 40 inches in men and 35 inches in women
- Low levels of high-density lipoprotein cholesterol (healthy or good cholesterol): less than 40 mg/dl in men and 50 mg/dl in women
- Blood pressure of 130/85 mm Hg or greater
- A fasting blood glucose measure of 100 mg/dl or more
- Triglyceride levels of 150 mg/dl or more

People with the metabolic syndrome have a twofold increase in relative risk for cardiovascular events, and in individuals without established type 2 diabetes mellitus, a fivefold increase in risk for developing diabetes as compared with people without the syndrome.

In 2001 the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATPIII)²³⁶ proposed a set of diagnostic criteria based on common clinical measures, including waist circumference, triglycerides, HDL, blood pressure, and fasting glucose level (Box 12-2). Abnormalities in any three of these five measures constitute a diagnosis of the metabolic syndrome. Presently, the American Heart Association and the National Heart, Lung, and Blood Institute adhere to the NCEP ATPIII criteria.¹³⁵

Most of the time, metabolic syndrome is manifested in the presence of some degree of obesity and physical inactivity. In addition to the lifestyle changes (exercise, smoking cessation) drug therapy for risk factors may be required.

The primary goal of clinical management of the metabolic syndrome is to reduce the risk for atherosclerotic cardiovascular disease. When encountering clients presenting with abdominal obesity, physical therapists should appreciate that waist circumference maybe associated with lipid abnormalities.¹⁵⁷

A possible link has been recently demonstrated between psychosocial stressors from everyday life and the metabolic syndrome. Employees with chronic work stress have more than double the odds of the syndrome compared with those without the stress.⁷³

Pathogenesis. The exact mechanism by which the development of cardiovascular disease/CAD can be explained has yet to be determined. The recent implication of infectious agents in initiating the inflammatory cascade may help explain the pathogenesis in some (but not all) cases.²⁹³ Clinical and laboratory studies have shown that inflammation plays a major role in the initiation, progression, and destabilization of atheromas. CRP has been found in a variety of cardiovascular diseases. However, whether CRP is a contributing cause or an after-effect remains undetermined.

Mutations in the PCSK9 gene (chromosome 1) have been linked with naturally high levels of LDL in some people. Other PCSK9 variations have been discovered

that cause naturally *low* levels of LDL by increasing the number of LDL receptors in the liver, making the liver better able to attract excess LDL.⁷⁸

Many new studies emphasize the fact that cholesterol deposits are only one of many mechanisms through which acute CAD develops. New information points to the endothelium as a modulating factor in the pathogenesis of CAD through the production of nitric oxide and angiotensin II, which maintain the homeostatic environment influencing the progression of CAD. This imbalance tends to promote CAD in individuals who have multiple risk factors.

Endothelium-derived nitric oxide is an important mediator of exercise-induced changes in skeletal muscle blood flow. This molecule, composed of one nitrogen atom and one oxygen atom, is responsible for the natural dilation of blood vessels.

Nitric oxide is an antilipid that provides a nonstick coating to the lining of blood vessels, much like Teflon. These two effects have helped explain how nitric oxide might prevent heart attacks and strokes and why nitroglycerin works—nitroglycerin is converted to nitric oxide inside vascular tissue, where it relaxes smooth muscle in arteries and causes blood vessels to dilate.

In the normal artery, the endothelial lining is tightly packed with cells that allow the smooth passage of blood and act as a protective covering against harmful substances circulating in the bloodstream. The normal endothelium presents a nonreactive surface to blood, but injury triggers the thrombotic process.

In the earliest stage of atherosclerosis, damage to arteries arises from a combination of factors. In some cases, the initial damage comes from LDL cholesterol that has been modified by free radicals (see Fig. 6-2). Free radicals are abundant in people who smoke and who have high blood pressure or diabetes. In other cases, high levels of homocysteine or bacteria may contribute to early damage of arterial linings.

In general, most current theories include the following major events in the development of an atherosclerotic plaque (Fig. 12-2): Arterial wall damage occurs either from injury caused by harmful substances in the blood or by physical wear and tear as a result of high blood pressure. This injury to the blood vessel wall permits the infiltration of macromolecules (especially cholesterol) from blood through the damaged endothelium to the underlying smooth muscle cells. Naked collagen acts like flypaper for platelets, causing them to aggregate at the site of injury and plug up the wound.

The core of a coronary thrombus (clot) is composed of platelets, forming a so-called white thrombus. Early-stage plaque formations known as fatty streaks consist of foam cells (white blood cells coated with LDL particles, smooth muscle cells that move in from deeper layers of the artery wall, and platelets).

Cholesterol-filled plaques can take decades to form, sitting snugly in an artery wall for years. What makes a plaque break open and leak its contents into the bloodstream, causing a clot that can block an artery supplying the heart or brain, remains unknown. Experts speculate it could be a spike of high blood pressure or a surge of chemical messages that accompany anger, stress, or other

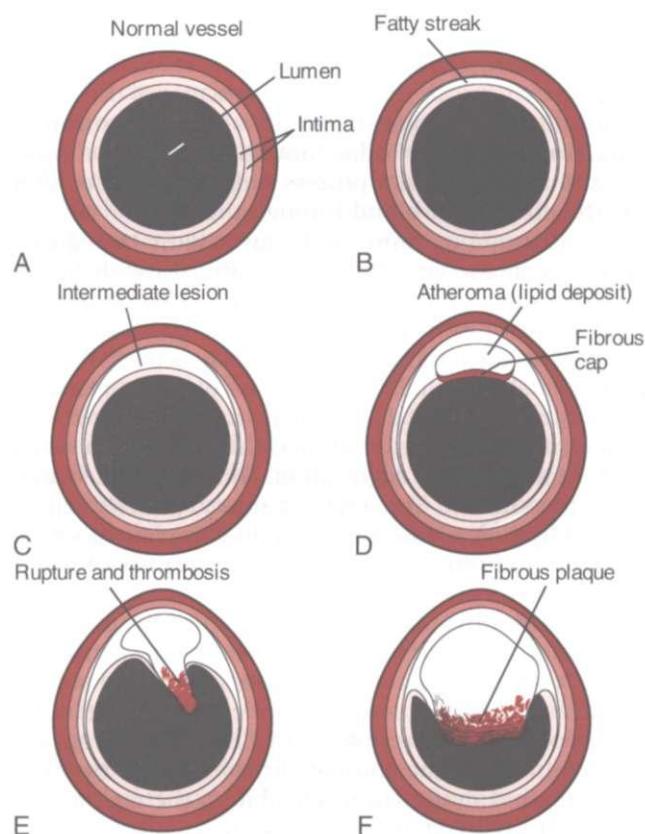


Figure 12-2

Updated model of atherosclerosis. Atherosclerosis begins with an injury to the endothelial lining of the artery (intimal layer) that makes the vessel permeable to circulating lipoproteins. New technology using intravascular ultrasound shows the entire atherosclerotic plaque and has changed the way we view things. The traditional model held that an atherosclerotic plaque in the blood vessel, particularly a coronary blood vessel, kept growing inward and obstructing flow until it closed off and caused a heart attack. This is not entirely correct. **A**, It is more accurate to say that in the normal vessel **B**, penetration of lipoproteins into the smooth muscle cells of the intima produces fatty streaks and the start of a coronary lesion forms. **C** and **D**, The coronary lesion grows outward first in a compensatory manner to maintain the open lumen. This is called *positive remodeling*. The blood vessel tries to maintain an open lumen until it can do so no longer. A little roof or “fibrous cap” separates the plaque from the inside of the lumen. A blood clot called an *intraplaque thrombosis* can form inside the plaque; the clot may never leave the plaque. **E**, The plaque (atheroma) begins to build up, gradually pressing inward into the lumen with obstruction of blood flow and possible rupture and thrombus potentially leading to myocardial infarction or stroke. Capped plaques are not as likely to rupture as the softer type packed with viscous cholesterol and white blood cells but only capped with a thin layer of collagen. **F**, Vascular disease today is considered a disease of the wall. Some researchers like to say the disease is in the donut, not the hole of a donut, and that is a new concept. (From Goodman CC, Snyder TE: *Differential diagnosis for physical therapists: screening for referral*, ed 4, Philadelphia, 2007, Saunders. Data from Horn HR: Insulin resistance, diabetes, and vascular disease: the rationale for prevention. Available on-line at http://www.medscape.com/viewarticle/466799_2. April 2007.)

intense emotion. It could be the result of cholesterol crystallization inducing cap rupture and/or erosion.¹²⁰³

Although platelet activation is a normal response to injury, in atherosclerosis, once the platelets adhere, they also release chemicals that alter the structure of the blood vessel wall, so that what starts out as a small erosion in the wall can end up a swollen mound of platelets, muscle cells, and fibrous clots, a process called *proliferation* that obstructs the flow of blood through the vessel.

After a thrombus forms and causes static or reduced blood flow in the vessel, the clot stabilizes with fibrin. This is commonly referred to as a *red thrombus* because of the presence of entrapped red blood cells. Within the thrombus is thrombin, which remains active and can activate platelets. Platelets also release plasminogen activator inhibitor 1 (PAI-1), a potent natural inhibitor of fibrinolysis, and vasoactive amines that can lead to vessel spasm, further platelet aggregation, and thrombus formation or reocclusion. This cycle of injury, platelet activation, and lipid deposition can lead to complete blockage of a vessel and result in ischemia and necrosis of tissue supplied by the obstructed blood vessel.

Clinical Manifestations. Atherosclerosis by itself does not necessarily produce symptoms. For manifestations to develop, there must be a critical deficit in blood supply to the heart or other structures supplied by affected blood vessels. For example, symptoms of CAD may not appear until the lumen of the coronary artery narrows by 75%. Then, pain and dysfunction referable to the region supplied by an occluded artery may occur.

When atherosclerosis develops slowly, collateral circulation develops to meet the heart's needs. Complications from atherosclerosis occur because it is a progressive disorder that results in more severe cardiac disease if it is not prevented or untreated. Common sequelae of atherosclerosis affecting coronary arteries include angina pectoris, MI or heart attack, and sudden death.

Men experience angina as the first symptom of CAD in one third of all cases and heart attack or sudden death in the majority of cases, whereas one half of all women experience angina and remain asymptomatic or present with atypical symptoms in the remaining cases.

Atypical symptoms of angina in women include breathlessness, pain in the left chest, upper abdominal pain, and back or arm pain (more rarely, isolated pain in the right biceps muscle) in the absence of substernal chest pain. The pain may be more diffuse and is described as sharp or fleeting, unrelated to exercise, unrelieved by rest or nitroglycerin but relieved by antacids, and characterized by palpitations without chest pain. The pain may be repeated and prolonged. Chest pain in women with chronic stable angina is more likely to occur during rest, sleep, or periods of mental stress.

MEDICAL MANAGEMENT

PREVENTION. Overwhelming evidence indicates that cardiovascular disease and CAD are largely preventable; therefore whenever possible, prevention of cardiovascular disease and CAD is the goal for everyone. And atherosclerosis is not a disease of middle to old age; it begins in adolescence and young adulthood and develops slowly but progressively throughout the body.

Preventing heart disease means controlling LDL before atherosclerosis gets a chance to do much damage. Reduction in the plasma level of LDL (at or below 100 mg/dl) throughout the lifespan through the use of diet, exercise, and statins or other cholesterol-lowering drugs is the proposed ways to do this.⁷⁸

Healthy People 2010 has identified the following goals for heart disease and stroke: improvement of cardiovascular health and quality of life through the prevention, detection, and treatment of risk factors; early identification and treatment of heart attacks and strokes; and prevention of recurrent cardiovascular events. An excellent guide to evidence-based primary prevention of cardiovascular disease and similar recommendations for prevention of cerebrovascular disease (i.e., stroke) are available.^{131,136,148,258,259}

Health perceptions, health care-seeking behavior, and willingness to participate in long-term preventive therapies are significantly influenced by age, cultural, and socioeconomic factors. Many physicians underestimate the life expectancy in older adults. For example, the average 65-year-old can expect to live an additional 15 to 20 years and function independently for more than 70% of this time.

Adults older than 80 years can expect to live 7 to 10 more years and function independently for one half of that time. Older individuals are less likely to be referred to cardiac rehabilitation and exercise-training programs and less likely to attend than younger adults. Therefore, preventive cardiology, including primary and secondary preventive efforts directed at the older adult, is important.¹⁹³

Primary and secondary prevention programs are needed that are modified for the language, cultural, and medical needs of people of all age groups and ethnic backgrounds but especially for older ethnic minorities who are at increased risk for cardiovascular disease.³²⁰ Ethnic comparisons of health behaviors and prevalence of risk factors among teenagers support the need for health promotion intervention among urban ethnic teenagers.¹⁰⁵

Women are less likely than men to receive health care advice on risk reduction while they are still healthy (i.e., before a significant cardiac event), even though they are more likely to die with the first heart attack. For this reason, new guidelines for prevention of heart disease in women were published in 2007.²²⁹

The bottom line is that even for people with a strong genetic component, modifying risk factors can slow the growth and spread of atherosclerotic plaque and reduce the risk of heart attack or stroke. The goal is to prevent cholesterol-filled plaque from rupturing, a key event that leads to the formation of blood clots that can block a coronary or carotid artery. Many people with significant nonmodifiable risk factors for heart disease but who follow a heart-healthy lifestyle live longer and in better health with better quality of life compared with those individuals who do not follow a heart-healthy plan.

DIAGNOSIS. Current national guidelines advise everyone over age 20 to have his or her cholesterol checked to establish a baseline with follow-up (retesting) once every

5 years (more often for those with risk factors for heart disease).

Advances in technology are rapidly changing the diagnostic tools available to physicians for diagnosing and evaluating CAD. Coronary angiography (angiogram or arteriogram; x-ray examination of the arteries with dye injection) has been the most widely used anatomic test to assess the degree of obstructive coronary disease and left ventricular contractility.

Angiograms are limited by their inability to detect which plaques represent vulnerable sites for rupture, and all forms of chest pain in women are associated with a lower prevalence of positive findings on angiography, making the diagnosis challenging. Tests using ultrasound or nuclear agents are less reliable in women because signals are blocked by breast tissue. Angiography is much more accurate than echocardiography; echocardiography improves the diagnostic accuracy of stress tests.

Echocardiography is a group of interrelated applications of ultrasound imaging (including Doppler, contrast, stress, and real-time three-dimensional [RT-3D] echocardiography). Advances in echocardiography have expanded its use in assessment of regional myocardial function, analysis of diastolic function, and quantification of regional myocardial function in different pathologic conditions, including ischemic heart disease.

Echocardiography has the potential to image myocardial perfusion along with wall motion and wall thickening. Stress echocardiography showing responses of the heart can be performed during or after a number of different physical stressors. This is important, because responses of the heart to stressors are probably even more important than how the heart functions at rest.

Until this technology is available everywhere, exercise treadmill testing to record symptoms and the electrical activity of the heart under stress continues to offer a means of assessing risk of future cardiac events in most groups (obese, sedentary, middle-aged or older men and women; studies among ethnic groups are under way).¹³⁰

Heart rate recovery after submaximal exercise has been confirmed as a predictor of mortality. This measurement is routinely obtained during exercise testing; it is determined by subtracting the heart rate 2 minutes after exercise from the heart rate at the end of exercise. Abnormal heart rate recovery is defined as a reduction of 12 beats/min or less from the heart rate at peak exercise as compared to the heart rate measured 2 minutes after exercise cessation.

People with an abnormal heart rate recovery are four times as likely to die as those with a normal heart rate recovery. This screening tool can be used with healthy adults as well as with those who have known heart disease.^{79,80} A delay in decline of systolic blood pressure after graded exercise is another independent correlate of CAD.

Other diagnostic test procedures available include ultrafast computed tomography (fast CT; "heart scan"), which allows for a computer image accommodating for the heart's pumping cycle. Multidirectional or multidetector CT (also referred to as the "new angiogram") generates up to 64 slicelike images of the heart. A computer then reconstructs these slices to create a detailed 3D

image of the heart and coronary arteries. Although less expensive, this new technology is not yet considered a replacement for angiography as it exposes people to increased doses of radiation compared to a traditional coronary angiogram.

Magnetic resonance angiography (MRA) uses a powerful cylinder-shaped magnet able to vibrate in distinctive ways to create a signal that is translated into a picture. This technique is also synchronized to the heart cycle, able to detect plaques. High-speed rotational angiography may be the next technologic diagnostic technique. High-speed rotational angiography is a newly available angiographic modality that gives a dynamic multiple-angle perspective of the coronary tree during a single contrast injection.²⁰⁵

With a standard angiogram, the camera is placed at different angles and takes a series of pictures of the heart. Dye is injected with each angle photographed. High-speed rotational angiography allows the camera to sweep across the heart in an arc taking all the (digital) pictures with one injection. The digital component allows the cardiovascular surgeon to stop and look at each frame.

In the future advanced technology may be able to determine which plaques are most likely to rupture. Thermography using probes to check the temperature of arteries may also reveal vulnerable plaques that are at risk for rupture, since these will be inflamed with elevated temperatures. The routine measurement of newer predictors, such as Lp(a) and CRP, is not recommended at this time for prognostic use and will be delayed until the clinical benefits of altering these concentrations are made available.

MODIFICATION OF RISK FACTORS. Modifying risk factors whenever possible can decrease the risk of cardiovascular disease/CAD, especially prevention or cessation of cigarette smoking, management of diabetes and hypertension, and modification of diet. For example, folate deficiency was believed to be a major determinant of the increased risk of cardiovascular disease related to elevated total homocysteine (tHcy) because these nutritional components benefit both the vascular wall structure and the blood coagulation system.¹⁰¹

Folate, riboflavin, vitamin B6, and vitamin B12 are essential in homocysteine metabolism. But recent studies using folic acid supplements, though successful in reducing homocysteine levels, did not lower the risk of recurrent cardiovascular disease after acute MI. A harmful effect from combined B vitamin treatment was observed. The American Heart Association no longer recommends folic acid supplements for individuals with elevated levels of homocysteine.

Changing dietary habits by reducing fat intake can result in regression and disappearance of fatty streaks consisting of lipid-laden macrophages, T lymphocytes, and smooth muscle cells before these components progress to form a fibrous plaque.

Dietary changes are recommended for everyone, including children and adults, since it is now recognized that blood vessel changes associated with heart disease begin as early as 15 years of age and the progression of the lesions is strongly influenced by the same risk factors

that predict risk of clinically manifest coronary disease in middle-aged adults.^{317,368} In addition, at least 25% of all Americans under age 19 years are overweight or obese.

There is a need for early and aggressive control of all risk factors in young persons for long-range prevention of CAD and related diseases. The Unified Dietary Guidelines have been published as nutritional guidelines by experts from the American Heart Association, American Cancer Society, American Dietetic Association, American Academy of Pediatrics, and National Institutes of Health.⁹³

In addition, an excellent guide to risk reduction outlining goals, screening, and recommendations for lifestyle factors and pharmacologic interventions is available.²²⁹ The National Heart, Lung, and Blood Institute also has a validated health risk appraisal instrument (ATPIII scale) that is easy to use.²³⁹

EXERCISE AND PHYSICAL ACTIVITY. Exercise and physical activity according to recommendations from the Centers for Disease Control and Prevention (CDC) (i.e., moderate-intensity exercise for at least 30 minutes on most days of the week) have been shown to reduce the risk for coronary events, ischemic stroke,¹⁵⁴ metabolic syndrome and insulin resistance, and diabetes mellitus for men and women.^{209,344}

The American College of Sports Medicine's position on the quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness and flexibility in healthy adults recommends aerobic endurance training at least 2 days/wk at 50% or higher $\dot{V}O_2$ and for at least 10 minutes. $\dot{V}O_2$ is a measure of oxygen uptake sometimes described as aerobic capacity, ventilatory uptake, or physical working capacity. Maximal oxygen consumption is referred to as $\dot{V}O_{2\text{max}}$. This measurement reflects the integration of three components of the delivery system that transports O_2 from the outside air to the working muscles: pulmonary ventilation, blood circulation, and muscle tissue.

In recent years the view that physical activity has to be vigorous to achieve a reduction in risk of CAD has been under question. Substantial evidence supports the benefit of continued regular physical activity that does not need to be strenuous or prolonged and includes daily leisure activities, such as walking or gardening. Taking up regular light or moderate physical activity in middle or older age confers significant benefit for cardiovascular disease.³⁴³

The National Runners' Health Study reports that substantial health benefits occur (in men) at exercise levels that exceed the CDC guidelines, suggesting that intense exercise offers one set of benefits whereas lengthy exercise provides another.³⁶² Other studies report the benefits of shorter periods of physical activity in decreasing the risk of CAD as being equal to one longer, continuous session of exercise, as long as the total caloric expenditure is equivalent.¹³²

The effect of exercise on cholesterol has been documented, but it remains unclear which component of exercise is the underlying beneficial mechanism. Exercise frequency may be more important than intensity in improving HDL cholesterol and cholesterol ratios,¹⁷⁹ and resistive exercise training has been reported to raise HDL

cholesterol levels, but studies in these areas have been limited.^{128,263} Even so, many health benefits from physical activity can be achieved in shorter bouts at less intensity.¹⁰

More studies are required to identify the ideal prescriptive exercise. Interestingly, endothelial damage has been reported after intense aerobic exercise, raising additional questions about exercise for athletes with cardiovascular risk factors.³⁷ It is likely that in the future, different exercise regimens for specific heart disease risk factors will be individually prescribed.

Exercise alone independent of weight loss or diet changes can have significant beneficial effects on cardiovascular risk factors in overweight people with elevated cholesterol levels.⁵³ Exercise is the one single intervention with the ability to influence the greatest number of risk factors (e.g., aids in smoking cessation, alters cholesterol levels, reduces blood pressure, helps control blood glucose levels, reverses the effects of a sedentary lifestyle, contributes to weight loss, helps in managing stress-induced increases in heart rate and blood pressure).

In fact, researchers at the University of Texas using RT-3D echocardiography to compare the effects of medications with the effects of exercise on coronary artery perfusion declare exercise to be "the most powerful drug available in preventing cardiac events."⁷⁴ Exercise can lessen depression, anger, and stress, which frequently interfere with recovery, and heart attack survivors who follow the CDC exercise guidelines reduce their risk of a fatal second episode by up to 25%.¹⁶⁵

PHARMACOTHERAPY AND CHEMOPREVENTION. Chemoprevention is an established method in the primary and secondary prevention of cardiovascular (and cerebrovascular) disease. Clinical trials have proven conclusively that both fatal and nonfatal coronary events and strokes can be prevented.³³⁶ Pharmacologic management is used to reduce the risk of clotting, to treat hypertension, and to decrease serum cholesterol level when it exceeds 200 mg/dl.

Medications are now available (3-hydroxy-3-methyl-glutaryl coenzyme A [HMG-CoA] reductase inhibitors, better known as "statins") that have been proven effective not only in lowering LDL levels and raising HDL levels but also in reducing cardiac events (primary and secondary prevention of MI).

However, caution has to be executed when a combination of drugs is used. Recent findings showed increased rate of death in patients receiving atorvastatin (Lipitor) in combination with torcetrapib, an HDL booster, compared with those receiving the Lipitor alone. The drug company subsequently halted clinical drug trials of experimental cholesterol treatment with torcetrapib. Target measurements to reduce risk factors developed by the American College of Cardiology and the American Heart Association are listed in Table 12-4.

Low-dose aspirin, 75 to 81 mg/day, was found to be just as effective in prevention of cardiovascular disease as high doses that result in increased incidence of bleeding events, primarily related to gastrointestinal (GI) tract toxicity.⁶¹ The American Heart Association now recommends low-dose aspirin therapy of 81 mg/day or 100 mg every

other day for all women age 65 or older. Studies show that aspirin will not prevent heart attacks in low-risk women under age 65, but it may be considered for all women at risk for stroke who are not at increased risk of bleeding.

TREATMENT. Medical management is directed toward the specific blood vessel occlusion and depends on complications, for example, occlusive disease of the peripheral vasculature, arterial disease in diabetic clients, occlusive cerebrovascular disease, or visceral artery insufficiency (intestinal ischemia) (see discussion of each individual complication).

Surgery. Surgical management of atherosclerosis of the coronary arteries may include PTCA (Fig. 12-3), CABG (Fig. 12-4), and coronary stents (Fig. 12-5). The current generation of drug-coated stents are bare metal covered with a polymer (plastic) coating that holds and releases a drug to inhibit the growth of endothelial cells. Several companies are working on polymers that are more compatible with the body and less likely to trigger clots. Others are testing polymers that dissolve and disappear after some time.

Angioplasty is performed 10 times more often than bypass surgery; angioplasty combined with a stent reduces the incidence of restenosis, especially for people with diabetes who have a high restenosis rate when treated by standard balloon angioplasty.³³⁷ The use of a combined antiplatelet treatment with aspirin and glycoprotein lib/

IIIa receptor blockers (Table 12-5) is a standard pharmacologic regimen after coronary artery stenting for the prevention of thrombosis (*thrombosis* is the formation of a clot; *thrombus* is the clot).

For the person with significant coronary and carotid artery disease, the importance of treating symptomatic

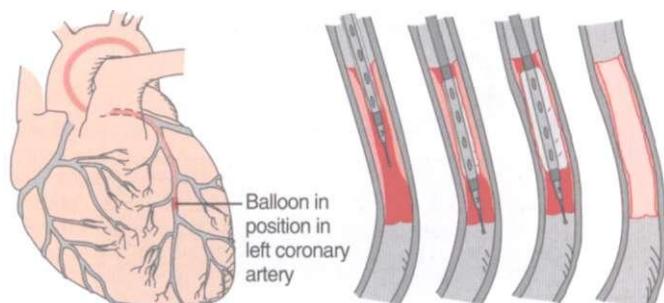


Figure 12-3

Percutaneous transluminal coronary angioplasty (PTCA) can open an occluded coronary artery without opening the chest, an important advantage over bypass surgery. **A**, Once coronary angiography has been performed to determine the presence and location of an arterial occlusion, a guide catheter is threaded through the femoral artery into the left coronary artery. **B**, When the angiography shows the guide catheter positioned at the site of occlusion, the uninflated balloon is centered in the obstruction. **C**, A smaller double-lumen balloon catheter is inserted through the guide catheter. **D**, The balloon is inflated, compressing the plaque against the arterial wall and deflated until the angiogram confirms a reduced pressure gradient in the vessel. **E**, The balloon is removed, and the artery is left unoccluded.

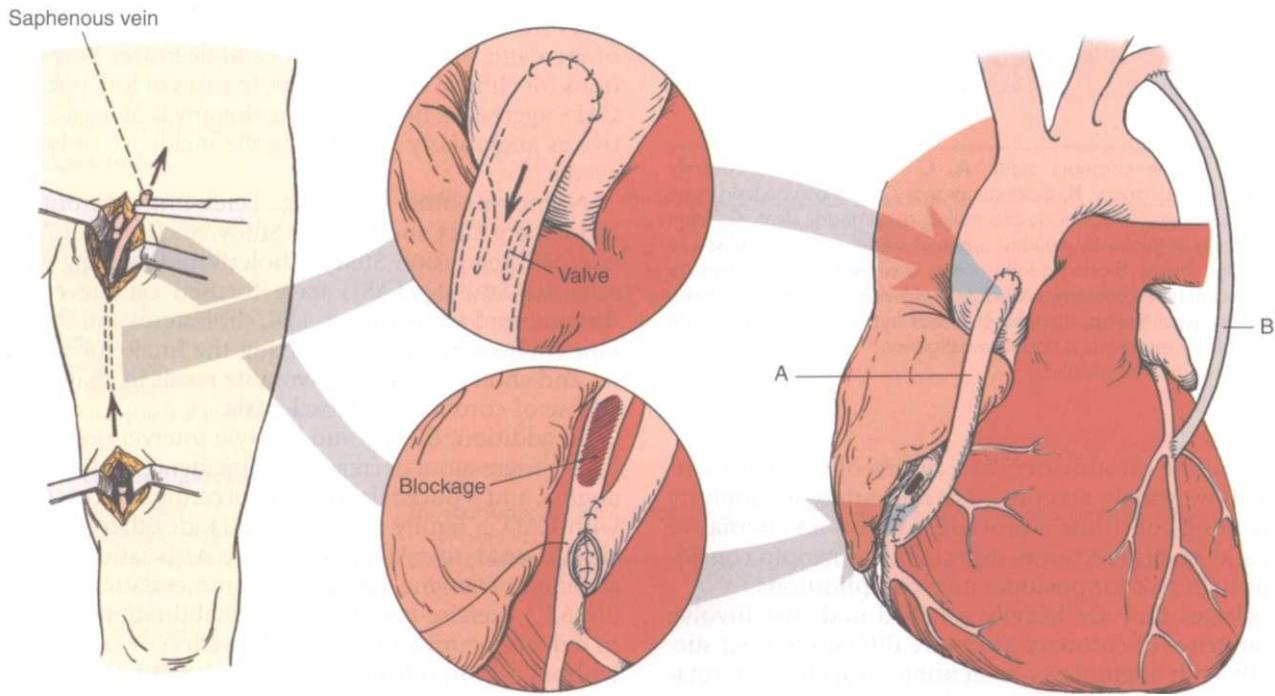


Figure 12-4

Coronary artery bypass graft (CABG). This procedure involves taking a portion of a vein or artery from the chest or leg and grafting it onto the coronary artery. In this illustration, (A) a section of the saphenous vein is used as a graft to route blood around areas of blockage. Bypassing the clogged vessel provides an alternative route (B) for blood to reach the heart muscle. The internal mammary artery can be used as an alternate vein site for grafting. CABG has been a major surgery requiring a sternotomy but is being refined to possibly become an off-pump bypass grafting through a partial sternotomy. It is considered most effective in individuals who have several severely blocked coronary arteries and a previously damaged heart muscle or when repeated revascularization has failed. (From Black JM, Hawks JH, Keene AM: *Medical-surgical nursing: clinical management for positive outcomes*, ed 6, Philadelphia, 2001, Saunders.)

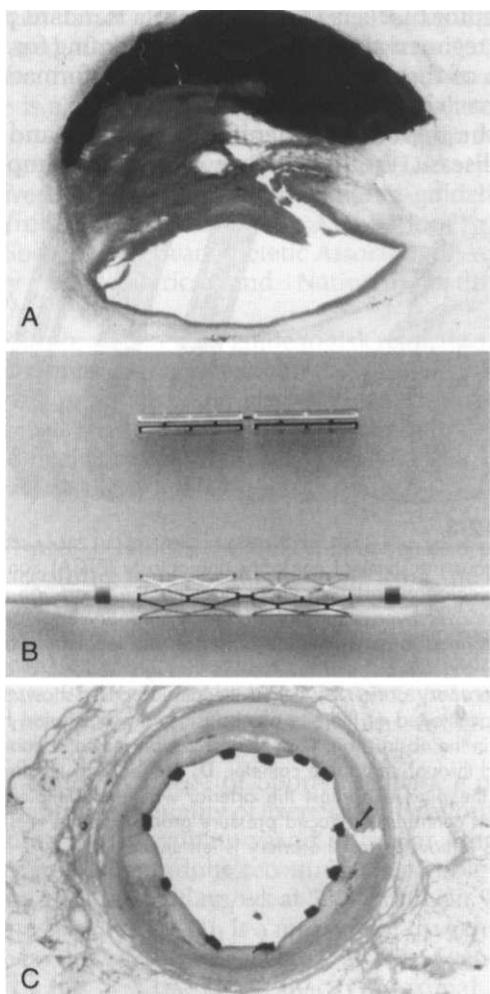


Figure 12-5

Application of the coronary stent. **A**, Cross-section of a severely occluded coronary artery. **B**, Blocked coronary artery can be held open using a balloon-expandable device called a coronary stent. **C**, Stent shown here is in place to maintain opened vessel, allowing blood to pass through freely. Biodegradable stents are under development to reduce or eliminate problems associated with metal stents.³⁴² Delivery of drugs or gene therapy to inhibit intimal hyperplasia and prevent postangioplasty restenosis is under investigation.^{83,107} (Courtesy Thomas Jefferson University, Philadelphia.)

stenosis of the carotid artery as a means of stroke prevention is now widely accepted. Carotid artery angioplasty and stenting constitute a procedure that is an alternative to carotid endarterectomy, especially for people considered at high risk for postoperative complications.

Blockages that are heavily calcified and that involve long stretches of coronary artery are difficult to treat successfully with angioplasty or stenting. In such cases, rotational atherectomy can be accomplished using a device called a *rotoblator* (catheter tipped with a tiny rotary blade). This procedure makes sharp cuts in plaque, shaving away the blockage and producing a relatively smooth luminal surface.

Other surgical techniques such as mechanical thrombectomy using a device (Angiojet System) that removes blood clots in the coronary (or carotid) arteries before

angioplasty are viable options in some cases but carry a higher rate of major complications, especially for women.

Intravascular ultrasound, a technology that combines echo with catheterization, may eventually allow diagnosis and therapy to be combined as the cardiologist uses a camera on the tip of a catheter to precisely target atherosclerotic blockage. In keeping with the new data on the time of day that cardiac events occur (i.e., thrombus formation is more likely to occur in the morning hours), researchers are now investigating the possibility that post-operative complications are related to the time the procedure takes place.³²⁷

Although surgical intervention has been a mainstay for the treatment of CAD, researchers are questioning the necessity of heart surgery and studying the benefits of pharmacologic intervention combined with exercise and lifestyle changes. The role of exercise in the prevention of atherosclerosis has been discussed, but the role of exercise as a treatment modality is equally important.

Cardiac Rehabilitation. Cardiac rehabilitation exercise training consistently improves objective measures of exercise tolerance, without significant cardiovascular complications or other adverse outcomes. Appropriately prescribed and conducted exercise training is recommended as an integral component of the treatment of atherosclerosis and CAD.⁴ See further discussion in Special Implications for the Therapist, this section.

Results from the Stanford Coronary Risk Intervention Project (SCRIP) conducted over 4 years have demonstrated that intensive multifactor risk reduction favorably alters the rate of luminal narrowing in coronary arteries of men and women with CAD and decreases hospitalizations for clinical cardiac events. In cases of low-risk, stable CAD, aggressive lipid-lowering therapy is at least as effective as angioplasty in reducing the incidence of ischemic events.⁵⁴

Numerous other trials (e.g., Leiden Intervention Trial, Heidelberg Diet and Exercise Study, St. Thomas's Atherosclerosis Regression Study, Cholesterol Lowering Atherosclerosis Study [CLAS]) have focused on the effect of diet-induced reductions in LDL cholesterol and the resultant changes in CAD. Restricting the intake of saturated fat and cholesterol has a favorable result in changing the course of coronary atherosclerosis.

In addition, dietary and lifestyle interventions slowed CAD progression, decreased the incidence and severity of angina, and reduced the number of cardiac events. Anyone with CAD, a family history of CAD, or other risk factors should read the American Heart Association scientific statement Diet and Lifestyle Recommendations Revision 2006.¹⁹⁹ Exercise-based cardiac rehabilitation is effective in reducing cardiac deaths, but the effect of exercise alone without a comprehensive cardiac rehabilitation intervention has not been evaluated.¹⁶⁷

Because pharmaceutical agents, surgery, and lifestyle changes including diet and exercise have been unable to maintain blood flow without restenosis in some people, new technologic approaches to intervention are being investigated. Emerging treatments for reclosure (restenosis) include antiproliferative (drug)-coated stents and photoangioplasty.

Table 12-5 Common Cardiovascular Medications

Medications: Trade Names (Generic Names)	Indications and Side Effects*
α-Adrenergic Blockers (-zoxin) Cardura (doxazosin) Hytrin (terazosin HCl) Minipress (prazosin HCl)	Indication: to lower blood pressure by dilating peripheral blood vessels, reducing peripheral resistance Side effects: headache, palpitations, fatigue, nausea, weakness, drowsiness, palpitations, † dizziness, ‡ fainting†
Angiotensin-Converting Enzyme (ACE) Inhibitors (-pril) Capoten (captopril) Lotensin (benazepril) Vasotec (enalapril maleate) Prinivil, Zestral (lisinopril) Altace (ramipril) Accupril (quinapril)	Indications: to treat high blood pressure and heart failure; prevent constriction of blood vessels and retention of sodium and fluid; improve sympathetic heart rate response during exercise in the early phase of MI to prevent heart failure Side effects: persistent, dry cough, skin rash, loss of taste, weakness, headaches, palpitations, † swelling of feet or abdomen, † dizziness or fainting† (because of low blood pressure), numbness or tingling of the hands, feet, or lips, renal failure; may cause congenital cardiovascular defects if taken during the first trimester of pregnancy ⁸⁵
Angiotensin II (AT-II) Receptor Antagonists (-sartan) Atacand (candesartan) Avapro (irbesartan) Cozaar (losartan) Diovan (valsartan) Micardis (telmisartan) Teveten (eprosartan) Verdia (tasosartan)	Indications: to vasoconstrict arterioles by blocking the effects of AT-II; enhance renal clearance of sodium and water Side effects: dizziness, ‡ insomnia, † anxiety, † confusion, † stroke, ‡ hypotension, ‡ visual changes, ‡ GI/GU effects, † cough, † upper respiratory infection, † myalgia; many other various but less common side effects
Antiarrhythmics Cardioquin (quinidine) Procan (procainamide HCl) Rythmol (propafenone HCl)	Indication: to alter conduction patterns in the heart Side effects: nausea, palpitations, vomiting, rash, † insomnia, † dizziness, ‡ symptoms of CHF (shortness of breath, swollen ankles, coughing up blood)‡
Anticoagulants (Antithrombotics) Coumadin (warfarin sodium) Unfractionated heparin (Lovenox [enoxaparin]) Low-molecular-weight heparin (Fragmin [dalteparin], Orgaran [danaparoid], Normiflo [ardeparin]) Hirudin (Refludan [lepirudin])	Indication: to prevent blood clot formation Side effects: easy bruising, joint or abdominal pain, ‡ difficulty in breathing or swallowing, ‡ paralysis, ‡ unexplained swelling, unusual or uncontrolled bleeding, ‡ rib and vertebral fractures (long-term use of anticoagulants) ⁶³
β-Blockers (-olol) Inderal (propranolol HCl) Lopressor (metoprolol tartrate) Tenormin (atenolol) Kerlone (betaxolol) Cartrol (carteolol) Corgard (nadolol) Coreg (carvedilol) Levatol (penbutolol) Blocadren (timolol) Not registered (clinical trial status): bucindolol	Indications: to relax the blood vessels of the heart muscle by blocking sympathetic conduction at β-receptors on the SA node and myocardial cells, producing a decline in the force of contraction and a reduction in heart rate; decrease blood pressure, dysrhythmias, and angina; decrease myocardial oxygen demand Side effects: insomnia, nausea, fatigue, slow pulse, weakness, increased cholesterol and blood glucose levels, nightmares, † depression, † sexual dysfunction, † asthmatic attacks, ‡ dizziness‡
Calcium Channel Blockers (-pine) Procardia (nifedipine) Cardizem (diltiazem HCl) Calan, Verelan (verapamil) Norvasc (amlodipine) Plendil (felodipine) Cardene (nicardipine)	Indications: to dilate coronary arteries to lower blood pressure and suppress some arrhythmias Side effects: fluid retention, palpitations, headache from vasodilation, flushes, rash, † dizziness‡
Central Antiadrenergic Agents Aldomet (methyldopa) Catapres (clonidine) Wytensin (guanabenz acetate) Tenex (guanfacine)	Indication: to lower high blood pressure by dilating the blood vessels Side effects: drowsiness, depression, sexual dysfunction, fatigue, dry mouth, stuffy nose, fever, upset stomach, change in bowel habits, weight gain, fluid retention, dizziness‡
Digitalis Compounds (Cardiac Glycosides) Lanoxin (digoxin) Crystodigin (digitoxin)	Indications: to strengthen the heart's pumping force to increase cardiac output and decrease electrical conduction through the AV node; slows heart rate to allow heart to fill completely; too fast a heart rate does not give the heart enough time to fill completely, then the heart does not pump enough blood out of the heart to supply the body

Continued.

Table 12-5 Common Cardiovascular Medications—cont'd

Medications: Trade Names (Generic Names)	Indications and Side Effects*
Diuretics	Side effects: fatigue, lethargy, weakness, headache, † visual disturbances (blurred vision, yellow-green halos, blind spots in visual field or scotomata, double vision), † cardiac disturbances (bradycardia, irregular heart rhythms), ‡ hypotension, † anorexia, nausea, vomiting, † diarrhea, † CNS disturbance† (depression, irritability, confusion, restlessness, drowsiness, seizures‡), electrolyte disturbances (hypokalemia)†
Thiazide diuretics (e.g., HydroDIURIL [hydrochlorothiazide]) Potassium-sparing diuretics (e.g., Aldactone [spironolactone]) Loop diuretics (e.g., Lasix [furosemide], Bumex [bumetanide], Demadex [torsemide])	Indications: to increase the excretion of sodium and water and control high pressure and fluid retention Side effects: drowsiness, dehydration, electrolyte imbalances, gout, nausea, pain, hearing loss, blood glucose abnormalities, elevated cholesterol and lipoprotein levels, muscle cramps, † dizziness, ‡ light-headedness‡
Lipid-Lowering Drugs	Indication: to interfere with the metabolism of blood fats in various ways by lowering cholesterol, low-density lipoprotein, and/or triglyceride levels in the blood or by blocking the absorption of cholesterol that comes from food; non-lipid lowering effects include improving endothelial function, antiproliferative actions on smooth muscle, and reducing platelet aggregation Side effects: nausea, vomiting, † diarrhea, † constipation, † flatulence, abdominal discomfort, myalgia, increased liver enzymes; more rarely, statins can cause myositis or rhabdomyolysis (a debilitating muscle-wasting condition resulting in acute renal failure), peripheral neuropathy, sleep disturbances (insomnia, bad or vivid dreams), or rash; statins may stimulate bone growth and reduce osteoporosis (under investigation)
Nitrostat, Nitro-Bid (nitroglycerin) Iso-Bid, Isordil (isosorbide dinitrate)	Indication: for dilation of coronary arteries Side effects: headache, dizziness, † orthostatic hypotension, † tachycardia†
Platelet Inhibitors (Antiplatelet Agents)	Indication: to prevent platelet aggregation and subsequent clot formation Side effects: gastric irritation (aspirin), † bleeding or hemorrhage, ‡ leg or pelvic pain, † rash, atrial fibrillation, ‡ tachycardia, ‡ dizziness, † confusion†
Aspirin Ticlid (ticlopidine) Plavix (clopidogrel) Glycoprotein IIb/IIIa receptor blockers ("super aspirin") ReoPro (Abciximab) Integrilin (Eptifibatide) Aggrastat (Tirofiban)	Indication: used to break down and dissolve already formed blood clots Side effects: bleeding (GI, GU, intracranial, surface), ‡ headache, † fever, † nausea, † low back pain†
Thrombolytics	Indication: to dilate the peripheral blood vessels (used in combination with diuretics) Side effects: headache, drowsiness, nausea, vomiting, diarrhea, hair growth (minoxidil only), increased heart rate, † swollen ankles, ‡ dizziness, ‡ difficulty in breathing‡
Nitroglycerin Isordil, Iso-Bid (isosorbide dinitrate) Minoxidil (oral)	Indication: combination of effects including rapid dilation of arteries and veins; promotes diuresis; used in decompensated CHF and arrhythmias Side effects: dose-related hypotension†
Human B-Type Natriuretic Peptide (BNP; Vasodilator/Diuretic; Genetically Engineered Form of Naturally Occurring Cardiac Hormone)	
Natrecor (nesiritide)	

MI, Myocardial infarction; HCl, hydrochloride; GI, gastrointestinal; GU, genitourinary; CHF, congestive heart failure; SA, sinoatrial; AV, atrioventricular; CNS, central nervous system.

*The therapist is more likely to see potential side effects not otherwise present since these develop when the person is physically challenged. Any unusual signs or symptoms and potential side effects should be documented and reported to the prescribing physician.

†Document and call physician when possible.

‡Call physician immediately; document findings.

Drug-coated stents resist colonization of the stent (smooth muscle cells cover the surface) and prevent restenosis but can lead to the formation of blood clots. The drugs that prevent the accumulation of scar tissue around the stent also delay healing over the stent site. When tissue does not heal quickly, blood collects and thickens around the stent site, causing a stent-related thrombosis that can cause a heart attack. People with drug-coated stents often take antiplatelet medication (e.g., clopidogrel [Plavix] in combination with aspirin) to prevent this from happening.

Photoangioplasty uses a photosensitive drug that selectively accumulates in atherosomatous plaque and remains inactive until exposed to an endovascularly delivered far-red light that reduces or destroys the deposits without damage to the normal vessel wall.¹⁴³

Gene Therapy. Gene therapy (i.e., gene transfer-based antirestenosis therapy) is one strategy with the potential to prevent some of the sequelae after arterial injury, induce growth of new vessels, or remodel preexisting vessels.¹⁰⁷ Several groups have injected a gene that makes a protein called *vascular endothelial growth factor (VEGF)*. When injected directly into the heart, this gene prompts the heart to sprout tiny new blood vessels to bypass the blocked vessels, a process referred to as *therapeutic angiogenesis* or *biologic revascularization*.^{243,368}

Alternatively, endothelial stem cells derived from bone marrow and injected into the region bordering an infarction have been shown to regenerate new myocardium or new blood vessels in animal studies. The increase in oxygen and nutrients accompanying this new tissue formation has the potential of preventing death of myocardial cells, reducing myocardial remodeling and scarring, and improving heart function by levels of 30% to 40%.^{116,247}

Genetic approaches will continue to identify genes and pathways involved in the predisposition to and pathophysiology of atherosclerosis. Targets for therapeutic intervention based on gene profiling continue to be the focus of research at this time.²²³

Complementary and Integrative Medicine. Finally, a review of alternative or complementary integrative medicine, sometimes referred to as mind-body therapies, and their effects on heart disease, blood pressure, lipid levels, morbidity, and mortality is available.²⁰²

These techniques remain under investigation and include prayer or meditation and/or religious attendance at church or services; yoga, Tai Chi, and other forms of martial arts; acupuncture; social support and/or support groups; cognitive-behavioral therapy; imagery; hypnosis; physiologic quieting; relaxation techniques; music therapy; and others (Table 12-6).

PROGNOSIS. The American Heart Association reports compelling scientific evidence that comprehensive risk factor interventions in people with cardiovascular heart disease extend overall survival, improve quality of life, decrease the need for interventional procedures, and reduce the incidence of subsequent MI. Even so, despite the well-documented benefit of preventive measures and cardiac rehabilitation, compliance with recommendations for reducing risk factors and utilization rates of

rehabilitation programs remain low, especially among women.²²⁹

Prognosis depends on the site and extent of myocardial necrosis, but nearly 500,000 deaths each year in the United States are attributable to CAD/CHD. Fatality rates for CAD remain low before age 35 years, but these figures increase exponentially until age 75 years, with men generally experiencing mortality at approximately twice the rate of women until age 65 years. Total CAD mortality in women after age 65 years now exceeds that of men. Of the nearly 20,000 persons eligible for heart transplants, only 10% receive a new heart each year. Advanced atherosclerosis is usually fatal if vessels to the brain or heart are affected, but new technology and new surgical intervention may reduce mortality in the decade ahead.

Surgical procedures are considered safe, and although complications can occur, the rates of complications (e.g., reintervention or repeat procedures, reexploration for bleeding) following CABG surgery have declined substantially in the last 15 years despite higher client risks. In the case of angioplasty, the risks of failure, reoperative procedures, and operative mortality are higher with advanced age, female gender, diabetes mellitus, elevated serum cardiac enzymes following the procedure, and impaired left ventricular dysfunction.³¹⁴

PTCAs are associated with greater rates of restenosis, especially among women, who are at greater risk for complications and have a higher mortality rate. Most studies attribute the higher mortality rate to the fact that women more often undergo the surgery during an emergency, they are usually older at the time of diagnosis than men, they are more likely to have other complicating conditions (e.g., hypertension, diabetes), and they may have smaller, more delicate coronary arteries, making surgery more difficult.

The higher rates of morbidity and mortality associated with angioplasty have resulted in the use of the balloon-expandable stent, which is associated with a low restenosis rate and a favorable clinical outcome with event-free survival rate at 1 year. The need for repeat revascularization has also been significantly reduced.

SPECIAL IMPLICATIONS FOR THE THERAPIST

12-2

Atherosclerosis (Cardiovascular Disease, Coronary Artery Disease)

PREFERRED PRACTICE PATTERN

6A: Primary Prevention/Risk Reduction for Cardiovascular/Pulmonary Disorders

Other practice patterns may be necessary depending on the clinical manifestations and disease outcomes (see discussion of each specific disease). The therapist can be very instrumental in guiding individuals through a preoperative wellness program, including client education, risk factor reduction, and exercise program. See also the section on Stroke in Chapter 32.

Continued.

Table 12-6 Medical Management of Cardiovascular Conditions*

Coronary Artery Disease (CAD)/Myocardial Infarction (MI)	Angina Pectoris	Hypertension	Congestive Heart Failure	Arrhythmias
Lifestyle changes (see text)	Lifestyle changes	Lifestyle changes	Lifestyle changes	Cardioversion (electrical or pharmacologic)
Prescriptive exercise	Prescriptive exercise	Prescriptive exercise	Prescriptive exercise	
Medications:	Medications:	Medications (frequent combination therapy):	Medications:	Medications:
Thrombolytics	Vasodilators	Diuretics	Cardiac glycosides	Class I: sodium channel blockers
β-Adrenergic blockers	β-Adrenergic blockers	β-Adrenergic blockers	Diuretics	Class II: β-adrenergic blockers
Angiotensin-converting enzyme (ACE) inhibitors	Calcium channel blockers	Renin-angiotensin system inhibitors	Renin-angiotensin system inhibitors	Class III: agents prolonging depolarization
Platelet aggregation inhibitors	Platelet inhibitors	ACE inhibitors	ACE inhibitors	Class IV: calcium channel blockers
Anticoagulants	Anticoagulants (unstable angina)	Angiotensin II receptor blockers (ARBs)	Vasodilators	
Lipid-lowering agents (especially statins)	Lipid-lowering agents (unstable angina)	Oral renin inhibitors	Human B-type natriuretic peptide (BNP)	
		Centrally acting agents	β-Adrenergic blockers	
		Vasodilators		
		Calcium channel blockers		
		α ₁ -Blockers		
Surgery:	Surgery:	Surgery:	Surgery:	Surgery:
Percutaneous transluminal coronary angioplasty (PTCA)	Revascularization procedures for unstable angina; see CAD/MI, this table	Transplantation	Revascularization procedures (see CAD/MI, this table)	Maze procedure (surgical or catheter)
Coronary artery bypass graft (CABG)	TMR		IABP	Pacemaker
Coronary stent implantation			Left ventricular assistive device (see Chapter 21)	ICD
Atherectomy			Cardiac resynchronization therapy (CRT)	Ventricular resynchronization therapy
Mechanical thrombectomy			Implantable cardioverter-defibrillator (ICD)	
Transmyocardial revascularization (TMR)			Transplantation	
Photoangioplasty			EECP	
Intraaortic balloon pump (IABP)				
Transplantation				
Gene therapy	External counterpulsation (EECP)			
Stem cell therapy				

Adapted from Susan Queen, PT, PhD, University of New Mexico, Albuquerque, NM, 2007, with permission.

The term blocker is synonymous with antagonist.

Platelet aggregation inhibitors, anticoagulants, and thrombolytics are used to treat overactive clotting but have distinct uses and mechanisms of action.

Platelet aggregation inhibitors block platelet aggregation and platelet-induced clotting, anticoagulants inhibit the synthesis of clotting factors, and thrombolytics facilitate clot breakdown after the formation of a clot.

*The use of complementary-integrative therapies in the adjunctive treatment of each of these conditions is under investigation at this time [see text discussion in Atherosclerosis: Treatment]. Research centered on pharmacologic and surgical approaches to these conditions is changing rapidly. This information represents a broad overview and may not include every option available.

Postoperative Considerations

Cardiac rehabilitation (phases I to IV) is an important component of intervention for anyone treated medically for CHF, arrhythmias, unstable angina, CAD, MI, valvular disease, or heart transplantation. This multidisciplinary program of education and exercise is designed to promote the development of and maintenance of a desirable level of physical, social, and psychologic function in those individuals with an acute cardiovascular illness.

Specific goals of cardiac rehabilitation include stratifying risk, improving emotional well-being and psychologic factors, reducing CAD risk factors, and decreasing symptoms. In addition, older adults often have reduced functional capacity and quality of life scores compared with younger CAD clients, making this an important goal for those individuals.^{191,193}

Implementation of phase I by physical therapists begins day 1 to 3 following CABG (or other) surgery or an MI. Primary emphasis is on postsurgical mobilization; client education is essential given the presence of comorbidities and the need for individualized prescriptive exercise.

During this phase the therapist uses and teaches the client sternal precautions (Box 12-3¹⁶¹; see also the section on The Cardiac Client and Surgery in this chapter) and adjusts the intensity of mobilization to optimize recovery from surgery and tissue injury, thereby minimizing length of stay without compromising the client.¹⁶⁰

In the past, chest physical therapy was recommended routinely for persons who had abdominal or cardiothoracic surgery, but the efficacy of chest physical therapy for reducing complications after coronary artery surgery has been repeatedly studied and never been proven. With advances in surgical techniques, smaller incisions, reduced postoperative pulmonary dysfunction, and earlier mobilization, techniques such as postural drainage and manual techniques now are limited to clients who are very acutely ill and cannot participate in early mobilization.⁷⁷

Postoperative brachial plexus injury can occur following cardiac surgery that requires a sternotomy when prolonged sternal separation or asymmetric traction of the sternal halves causes nerve compression or overstretching. Uncomplicated cases are usually transient and do not require intervention by a therapist. In rare cases, peripheral neuropathy will persist, resulting in impaired function and disability. As cardiac operative techniques continue to improve and move toward noninvasive methods, this type of injury will become obsolete.

Home monitoring of symptoms for the first weeks after surgery is essential following the guidelines in Box 12-4. The physician should be notified if the client experiences one or more of the signs and symptoms outlined. Transfusion is no longer a standard part of open heart surgery, so hematocrit levels are usually low (25% to 29%) following this procedure, requiring modification of exercise guidelines (see Table 40-8)

Continued.

Box 12-3

STERNAL PRECAUTIONS

- It is important to know whether the chest has been closed; the skin may be sutured, but the underlying chest structures may not be closed.
- To evaluate chest wall stability at rest, the therapist places his or her hands on the client's chest and asks the client to cough. Observe chest movement; any type of asynchronous movement between the two chest sides is a sign of an unstable chest requiring sternal precautions. These precautions vary from center to center and sometimes from surgeon to surgeon based on the surgical procedure performed but usually include the following:
 - No pulling up in bed during acute care is allowed; client must roll into side-lying position and use the top arm to assist in pushing up while allowing the feet to drop off the side of the bed as a pendulum type of assist.
 - Hand-held assistance during mobilization may be required initially in place of assistive devices, such as walkers or canes.
 - No pushing, pulling, or lifting more than 10 lb (some precautions list 5 lb) for 6 weeks postoperatively is allowed; this includes vacuuming, lifting pets (or walking pets on a leash), lifting or pushing furniture, lifting bowling balls, pushing or pulling doors, lifting children, and lifting anything that weighs more than 1 gallon of milk.
 - No driving motorized vehicles (e.g., automobile, golf cart, or other similar large conveyance) for 4 weeks postoperatively (at some centers, for 6 to 8 weeks) is permitted; during this time, person should not sit in the front seat of any vehicle and especially in vehicles equipped with airbags.
 - Full neck, shoulder, and torso range of motion may be permitted as long as the sternum is stable but not if a sternectomy with skin or muscle flap is present; presence of a flap limits range of motion to 90 degrees (flexion or abduction) or until the point of movement at the chest wall or rib cage.
 - Avoid shoulder horizontal abduction with extreme external rotation.
 - Progression is based on client tolerance and signs of wound healing; once the incision is fully healed, scar mobilization is permissible. The usual precautions for scar mobilization apply, including mobilizing the tissue in the direction of the scar before using any cross-transverse techniques and mobilizing toward the scar rather than away from the scar to avoid overstretching the healing tissue.
 - Use of the more conservative precautions is advised with anyone who has diabetes mellitus, severe osteoporosis, or other equally compromising comorbidities.
 - Women with larger breasts are at higher risk for dehiscence poststernotomy; however, more research is needed on using supportive undergarments to reduce sternal skin stress.¹⁶¹
 - Sternal support or harness may be useful to treat pain associated with sternotomy wounds, especially while coughing.²¹⁸

Box 12-4**INDICATIONS FOR DISCONTINUING OR MODIFYING EXERCISE*****Symptoms**

- New-onset or easily provoked anginal chest pain
- Increasing episodes, intensity, or duration of angina (unstable angina)
- Discomfort in the upper body, including chest, arm, neck, or jaw; chest pain unrelated to chest incision
- Fainting, light-headedness, dizziness
- Sudden, severe dyspnea
- Severe fatigue or muscle pain
- Nausea or vomiting
- Back pain during exercise
- Bone or joint pain or discomfort during or after exercise
- Severe leg claudication

Clinical Signs

- Pallor; peripheral cyanosis; cold, moist skin
- Staggering gait, ataxia
- Confusion or blank stare in response to inquiries
- Resting heart rate >130 beats/min or <40 beats/min
- More than six arrhythmias (irregular heartbeats; palpitations) per minute
- Frequent premature ventricular contractions (PVCs)
- Uncontrolled diabetes mellitus (blood glucose >250 mg/dl)
- Oxygen saturation <90% (98% is normal); some variability (individual and geographic)
- Acute infection or fever >100°F (37.8°C)
- Persistent drainage or change in drainage from any incision
- Increased swelling, tenderness, and redness around any incision site
- Inability to converse during activity
- Blood pressure (BP) abnormalities
 - Fall in systolic BP with increase in workload; specifically, a decrease of 10 mm Hg or more below any previously recorded BP accompanied by other signs or symptoms
 - Rise in systolic BP above 250 mm Hg or diastolic BP above 115 mm Hg
- Signs of central nervous system involvement (e.g., confusion or delirium, cognitive decline, encephalopathy, seizure, stroke)

Other

- Person indicates need or desire to stop
- Recent myocardial infarction (within 48 hours)

Adapted from Gibbons RJ: ACC/AHA 2002 guideline update for exercise testing. American College of Cardiology Foundation. Available on-line at www.acc.org. Accessed June 6, 2007.

*Not all signs and symptoms require immediate cessation of exercise or intervention. The therapist is advised to document any clinical signs or symptoms observed or reported along with any modifications made in the intervention and notify the physician accordingly.

unless directed otherwise by the physician. Carotid artery disease is a risk factor for CNS complications after CABG surgery, requiring close monitoring for signs and symptoms of CNS involvement.

Discharge instructions for the cardiovascular surgical population may vary according to physician and institution, but some general guidelines apply (Box 12-5). The therapist can be helpful in teaching about unexpected symptoms and ways to manage them. For example, women experiencing postoperative chest dis-

Box 12-5**DISCHARGE INSTRUCTIONS AFTER CARDIOVASCULAR SURGERY**

- **Showers:** Permitted 2 days after surgery or hospitalization. Avoid tub baths or soaking in water until incisions are healed; avoid extremely hot water.
 - **Incisions:** The incision should be kept dry but can be gently washed with mild soap and warm water (directly over the tapes); lotions, creams, oils, or powders are not permitted until the wound is completely healed unless prescribed by the physician.
 - **Care of surgical leg** (for bypass graft involving the leg): Avoid crossing the legs, which impairs circulation; avoid sitting in one position or standing for prolonged periods. Elevate the involved leg when sitting or lying down. Swelling in the grafted leg is common until collateral circulation develops. Swelling should decrease after leg elevation but may recur when standing. Progressive edema must be reported to the physician.
 - **Elastic stockings:** Worn for at least 2 weeks after discharge during the daytime and removed at bedtime.
 - **Rest:** A balance of rest and exercise is an essential part of the recovery process. Resting between activities and short naps are encouraged. Resting may include sitting quietly or reading for 20 to 30 minutes; loss of appetite is common for the first 2 weeks and may contribute to fatigue.
 - **Walking:** Walking increases circulation throughout the body and to the heart muscle and is encouraged. Activity must be increased gradually, but frequent walks of short duration are recommended initially. Pacing of activities throughout the day, combined with energy conservation, is important.
 - **Stairs:** Climbing stairs is permitted unless the physician indicates otherwise.
 - **Sexual relations:** Sexual relations can be resumed when the client feels physically comfortable (usually 2 to 4 weeks after discharge; see also text discussion).
 - **Sternal precautions:** See Box 12-3.
- Stop any activity immediately if dyspnea, palpitations, chest pain or discomfort, or dizziness or fainting develops. Notify the physician if symptoms do not subside with rest in 20 minutes.**

comfort can be reassured that this is not uncommon, will subside over time, and may be minimized by wearing a snug all-cotton undershirt under loose clothing to decrease friction.

Reassurance and education are extremely important for clients who are emotionally distressed. Although these people are successful in improving their functional status and physical capacity, they are more likely to experience angina during activities of daily living and during exercise and to be less successful in returning to work.

Prescriptive Exercise

The known benefits of regular physical activity and exercise in both primary and secondary prevention of cardiovascular disease have been thoroughly documented (and discussed in this section; see Prevention). Exercise training increases cardiovascular functional capacity and decreases myocardial oxygen demand at

any level of physical activity in apparently healthy people as well as in most people with cardiovascular disease.

Regular dynamic exercise is considered adjunctive therapy for lipid management along with dietary management and reduction of excess weight but must be maintained in order to sustain the training effects. Both short- and long-term endurance exercise can contribute to an improvement in blood lipid abnormalities.⁸

Although exercise and physical training have been shown to improve exercise capacity and recovery of the autonomic nervous activity,³²⁵ there is an increased risk that exercise may precipitate cardiovascular complications and silent symptoms of ischemia, arrhythmias, or abnormal blood pressure. Heart responses to exercise and fatigue necessitate special considerations for the formulation and execution of physical conditioning programs. Determining how heart rate and blood pressure respond to exercise (e.g., at what point symptoms of oxygen deprivation occur) forms the basis for an exercise prescription.

Frequent premature ventricular contractions (PVCs) are considered a contraindication to exercise unless approved by the physician (e.g., as in the case of automatic implantable cardioverter-defibrillators). Indications for stopping an exercise test can be used as precautions during therapy or exercise (see Box 12-4; see also Box 12-8). Therapists in all settings are encouraged to read the complete American Heart Association Exercise Standards.⁹ Risks associated with resistance exercise in older adults and recommended guidelines for resistance exercise prescription in this population of cardiac rehabilitation clients are also available.⁴⁵

Postoperative Exercise

People recovering from cardiac surgery, despite an excellent hemodynamic result, may be disabled by persistent left ventricular hypertrophy and years of pre-surgical restricted activity and deconditioning. Exercise rehabilitation is an important part of the recovery process. Easy fatigability related to muscular weakness lessens with increased physical activity. Exercise-induced symptoms of angina and light-headedness or syncope disappear immediately after surgery with a successful result.

The exercise capacity of clients soon after MI and bypass surgery is determined by the same parameters as in healthy individuals or for other cardiac problems, including time since MI, age, physical training status, and amount of myocardial dysfunction that occurs with exercise. CNS dysfunction is a common consequence of otherwise uncomplicated CABG surgery that may affect exercise capacity. The exact cause of this neurologic phenomenon remains unknown, but it may be the result of preoperative intracranial or extracranial carotid artery disease contributing to compromised hemodynamics and cerebral hypoperfusion.

Heart rate variability (HRV) may be altered (decreased) after PTCA. HRV (analysis of beat-to-beat heart rate variability) is a simple, reproducible, and noninvasive method for quantitatively assessing

cardiac autonomic regulation. The alteration in HRV can be transient or may remain for 6 months or more. A high variability in heart rate is a good sign of adaptability, implying that the autonomic nervous system control mechanisms are functioning well. Beneficial effects of exercise training in restoring HRV after coronary angioplasty have been documented.³³⁵

A program to increase the strength and flexibility of the pectoral and leg muscles is usually recommended. During this time, elastic stockings are usually worn to prevent fluid accumulation at the site of the leg incisions. Special exercises are prescribed to improve chest wall function, facilitate breathing, and prevent adhesive capsulitis, a common finding 6 to 12 weeks after a CABG or other open chest procedure.

Data to support the need for early range of motion (ROM) to prevent loss associated with surgery are limited. One small study of the effect of shoulder ROM exercises after CABG surgery reported that ROM exercises do not ameliorate the early loss of ROM associated with surgery, since the loss is a function of the surgical procedure and not lack of ROM challenge.³⁰⁴ The delay in presentation of adhesive capsulitis suggests other variables may be present during the time when clients are enrolled in phase I (inpatient) and phase II (outpatient) cardiac rehabilitation programs to account for this development.

Monitoring during Exercise

More than one half of all ischemic episodes are not accompanied by angina. Ask any client with identified CAD risk factors or diagnosed CAD to report all unusual sensations, not just episodes of chest pain or discomfort. Exercise testing should be performed before beginning an exercise program, but if this has not been accomplished and baseline measurements are unavailable for use in planning exercise, use pulse oximetry; monitor the heart rate and rhythm, respiratory rate, and blood pressure; and note any accompanying symptoms before, during, and after exercise (see Appendix B). This type of monitoring can be modified for each individual and is recommended throughout therapy intervention. Documentation of vital signs can be an excellent way to demonstrate evidence-based outcomes of intervention.

Side effects of cardiovascular medications may not appear until the cardiovascular system is challenged, such as occurs during therapy intervention. Monitoring for drug-related problems is essential, and a basic understanding of how these medications work is helpful (see Table 12-5). Striking a balance between the benefits of cardiovascular medications and acceptable or tolerable side effects can be a challenge, and the therapist must keep in mind when documenting and reporting drug-related effects that these medications often produce physiologic responses that increase the effectiveness of physical therapy. A more comprehensive discussion of this topic is available.⁷⁶

Several drugs used in the treatment of CAD are known to alter the heart rate. For example, (3-adrenergic blocking agents used in the treatment of angina

Continued.

and hypertension cause a reduction in resting and exercise heart rate. Anyone taking these medications may not be able to achieve a target heart rate above 90 beats/min; therefore, using symptoms (e.g., angina, diaphoresis, shortness of breath, dizziness, pallor, isolated [arm or leg] or overall fatigue) and rating perceived exertion may be a more appropriate means of monitoring. Avoid increases of more than 20 beats/min over the resting rate for individuals taking these medications.

Conservative limits postoperatively include a maximal heart rate of 130 beats/min, 120 beats/min for medically managed cases, or an increase of 30 beats/min for surgical cases and 20 beats/min for medical cases. A safe rate of exercise will allow the heart rate to return to the resting level within 5 minutes after stopping exercise.

Almost all antihypertensive agents, including diuretics that may have a dual action of peripheral dilation and volume depletion, can have a profound effect on postexercise blood pressure. In some healthy people, when exercise is terminated abruptly, precipitous drops in systolic blood pressure can occur owing to venous pooling. Some people with CAD have higher levels of systolic blood pressure that exceed peak exercise values; a proper cool-down after vigorous exercise is important to prevent such an occurrence.

More detailed information on the effects of various drugs on the exercise response during training in clients with CAD can be found in *Guidelines for Exercise Testing and Prescription* by the American College of Sports Medicine.⁹

Side Effects of Medication

As shown in Table 12-5, there is a wide range of commonly prescribed cardiovascular medications with an equally wide variety of potential side effects. The therapist must make note of medications used by each client and observe for any of the common adverse effects.

Of particular note is the potential for muscle pain from statins. Less than 5% of the adult population who take statins develop this problem. A more serious form of this side effect associated with statins (cholesterol-lowering medications) is called *rhabdomyolysis*, the rapid breakdown of skeletal muscle.

Myalgia as a result of taking a statin medication usually occurs within a few weeks of starting the drug. Any unexplained muscle pain, cramps, stiffness, spasm, or weakness in an adult taking a statin should be reported to the physician. This is especially true if there are any predictive risk factors.

Risk factors for this particular effect include age over 80, small body frame or frail health, presence of kidney disease, and polypharmacy. Individuals taking some forms of this medication (e.g., cerivastatin [Crestor]) are especially warned to avoid drinking grapefruit juice while taking statins as this seems to have an adverse effect.

Box 12-6

TYPES OF ANGINA PECTORIS

- Chronic (stable) angina; classic exertional angina
- New-onset (unstable) angina
- Nocturnal angina
- Postinfarction angina
- Preinfarction angina (unstable); progressive, crescendo angina
- Prinzmetal's (variant) angina; vasospastic
- Resting angina (decubitus)
- Metabolic syndrome, microvascular angina

Angina Pectoris

Definition and Incidence

As blood vessels become obstructed by the formation of atherosclerotic plaque, the blood supply to tissues supplied by these vessels becomes restricted. When the cardiac workload exceeds the oxygen supply to myocardial tissue, ischemia occurs, causing temporary chest pain or discomfort, called *angina pectoris*. The exact incidence of angina is unknown, although it is considered common, especially in people age 65 years and older; it occurs more often in men.

Overview

There are several types of anginal pain (Box 12-6). *Chronic stable angina*, classified as classic, exertional angina, occurs at predictable levels of physical or emotional stress and responds promptly to rest or to nitroglycerin. No pain occurs at rest; and the location, duration, intensity, and frequency of chest pain are consistent over time (60 days). *New-onset angina* describes angina that has developed for the first time within the last 2 weeks and is also considered unstable. *Nocturnal angina* may awaken a person from sleep with the same sensation experienced during exertion and is usually caused by increased heart rate associated with dreams or in response to underlying CHF.

Postinfarction angina occurs after MI when residual ischemia triggers an episode of angina. *Preinfarction angina* or *unstable angina*, also known as progressive angina or crescendo angina, is unpredictable and is characterized by an abrupt change (increase) in the intensity and frequency of symptoms or decreased threshold of stimulus. This angina lasts longer than 15 minutes and is a symptom of worsening cardiac ischemia.

Prinzmetal's, vasospastic, or variant angina produces symptoms similar to those of typical angina, but it is caused by coronary artery spasm. These spasms periodically squeeze arteries shut and keep the blood from reaching the heart. In this type of angina, coronary arteries are usually clear of plaque or free of physiologic changes that cause obstruction of the vessels. The pattern of Prinzmetal's angina is characterized by early morning occurrence, frequently at the same time each day, and it occurs at rest (i.e., it is unrelated to exertion).

Prinzmetal's angina is more common in women younger than 50 years; it is often associated with various

Table 12-7 Causes of Myocardial Ischemia

Decreased Oxygen Supply	Increased Oxygen Demand
Vessels	
Atherosclerotic narrowing	Hyperthyroidism
Inadequate collateral circulation	Arteriovenous fistula
Spasm caused by smoking, emotion, or cold	Exercise or exertion
Coronary arteritis	Emotion or excitement
Hypertension	Digestion of large meal
Hypertrophic cardiomyopathy	
Circulatory Factors	
Arrhythmias (\downarrow blood pressure)	
Aortic stenosis	
Hypotension	
Bleeding	
Blood Factors	
Anemia	
Hypoxemia	
Polycythemia	

From Goodman CC, Snyder TE: *Differential diagnosis in physical therapy*, ed 3, Philadelphia, 2000, Saunders.

types of arrhythmias or conduction defects. It is not a benign condition but is less likely to lead to a heart attack than angina caused by atherosclerosis because most heart attacks are caused by the rupture of an atherosclerotic plaque.

Decubitus or *resting angina* is considered atypical; it occurs most often when at rest and frequently occurs at the same time every day. This type of anginal chest pain is atypical in that it is paroxysmal in nature, not brought on by exercise, and not relieved by rest, but it is reduced when the person sits or stands up.

It is more prevalent among women, particularly those who have undergone hysterectomy. Microvascular angina associated with insulin resistance syndrome affects the microcirculatory system, a network of tiny blood vessels that branch from the large coronary vessels and that provide oxygen to each of the millions of myocardial cells. Why these vessels spasm and cause decreased blood flow remains undetermined; the cause may be a decrease in estrogen during menopause or a specific trigger from within the heart. Long-term survival rates are not reduced in women with this syndrome.

Etiologic and Risk Factors

Any condition that alters the blood (oxygen) supply or demand of the myocardium can cause ischemia (Table 12-7). Increased oxygen needs of the heart, increased cardiac output, or reduced blood flow to the heart can cause angina. CAD accounts for 90% of all cases of angina, although other conditions affecting normal vessels can also cause angina. Disorders of circulation, such as relative hypotension secondary to spinal anesthesia, antihypertensive drugs, or blood loss, can also result in decreased blood return to the heart and subsequent ischemic pain.

Onset of angina may be triggered by physical exertion or exercise, especially involving thoracic or upper extremity muscles or walking rapidly uphill; increase in pulse rate or blood pressure (e.g., psychologic or emotional stress); or vasoconstriction. The threshold for angina is often lower in the morning or after strong emotion; the latter can provoke attacks in the absence of exertion. Angina may also occur less commonly during sexual activity, at rest, or at night during sleep.

Pathogenesis

Angina is a symptom of ischemia usually brought on by an imbalance between cardiac workload and oxygen supply to myocardial tissue usually secondary to CAD (see previous discussion on pathogenesis of atherosclerosis). Disruption of a formed plaque with sudden total or near-total arterial occlusion may bring on unstable angina. Rupture leads to the activation, adhesion, and aggregation of platelets and the activation of the clotting cascade, resulting in the formation of an occlusive thrombus. If this process leads to complete occlusion of the artery, then MI occurs. If the process leads to severe stenosis but the artery remains open, then unstable angina occurs.

Metabolites within the ischemic segment of the myocardium (e.g., histamines, bradykinin, prostaglandins) and buildup of lactic acid or abnormal stretching of the myocardium irritate myocardial fibers, resulting in myocardial pain. Afferent sympathetic fibers of the autonomic nervous system enter the spinal cord from levels C3 to T4 (Fig. 12-6), accounting for the varied locations and radiation patterns of anginal pain. The effects of temporary ischemia are reversible; if blood flow is restored, no permanent damage to or necrosis of the heart muscle occurs.

Clinical Manifestations

Angina is characterized by temporary pain or, more often, discomfort that starts suddenly in the chest (substernal or retrosternal) and sometimes radiates to other parts of the body, most commonly to the left shoulder and down the ulnar border of the arm to the fingers. Pain or discomfort may also be referred to any dermatome from C3 to T4, presenting at the back of the neck, lower jaw, teeth, left upper back, interscapular area, abdomen occasionally, and possibly down the right arm (Fig. 12-7).

The sensation described is often referred to as squeezing, burning, pressing, heartburn, indigestion, or choking. It is usually mild to moderate (rarely reported as severe); it usually lasts 1 to 3 minutes, sometimes 3 to 5 minutes, but can persist up to 15 to 20 minutes. Symptoms are usually relieved by rest or nitroglycerin; in women, symptoms may be relieved by taking an antacid.

Recognizing symptoms of myocardial ischemia in women is more difficult, since the symptoms are less reliable and do not follow the classic pattern described. Many women describe the pain in ways consistent with unstable angina, suggesting that they first become aware of their chest discomfort or have it diagnosed only after it reaches more advanced stages. Some experience a sensation similar to that of inhaling cold air, rather than the more typical shortness of breath. Other women note only

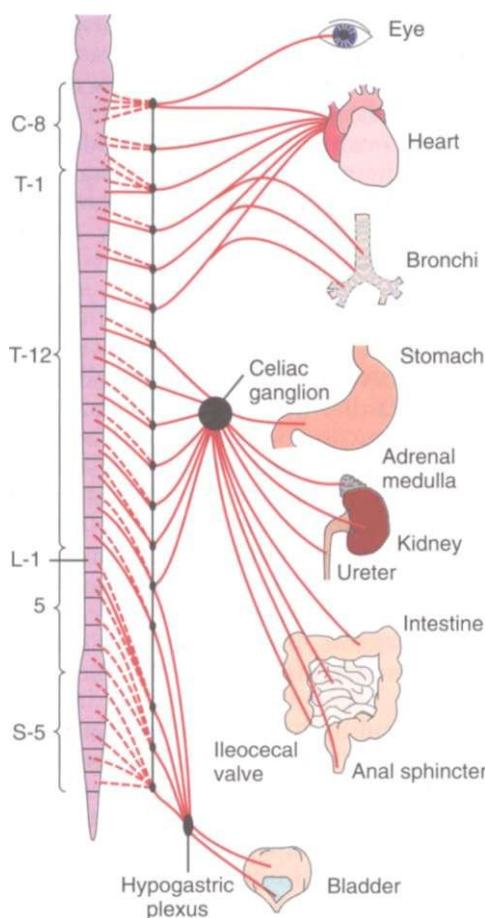


Figure 12-6

Diagram of the autonomic nervous system. The visceral afferent fibers mediating cardiac pain travel with the sympathetic nerves and enter the spinal cord at multiple levels (C3 to T4). This multisegmental innervation results in a variety of pain patterns associated with myocardial ischemia and infarction.

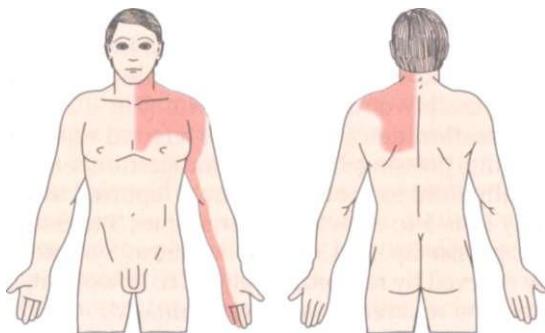


Figure 12-7

Pain patterns associated with angina. Left, Area of substernal discomfort projected to the left shoulder and arm over the distribution of the ulnar nerve. Referred pain may be present only in the left shoulder or in the shoulder and along the arm only to the elbow. Right, Occasionally, anginal pain may be referred to the back in the area of the left scapula or the interscapular region. See Fig. 12-11 for pain pattern associated with myocardial ischemia or infarction experienced by some women (see text for complete description).

weakness and lethargy, and some have observed isolated pain in the midthoracic spine or throbbing and aching in the right biceps muscle.

MEDICAL MANAGEMENT

DIAGNOSIS. The diagnosis of angina pectoris is strongly suspected by history and is supported if sublingual nitroglycerin shortens an attack and if prophylactic nitrates permit greater exertion or prevent angina entirely. Medical evaluation includes examination for signs of diseases that may produce angina or contribute to or accompany atherosclerotic disease (see the previous section on Clinical Manifestations).

Early and accurate triage to assess risk (low, intermediate, high) can help identify those people for whom medical therapy will probably fail and lead to better outcomes through a more appropriate management strategy. ECG is normal in about 25% to 30% of people with angina, so the exercise tolerance test is a more useful noninvasive procedure for evaluating the ischemic response to exercise in the client with angina. Diagnostic testing continues as for CAD (see the previous section on Atherosclerosis: Diagnosis and the section on Myocardial Infarction: Diagnosis later in the chapter).

PREVENTION AND TREATMENT. Prevention of attacks is the first step after the acute attack subsides. Treatment of underlying disorders such as hypertension is essential. The client is also encouraged to avoid situations and stressors that precipitate angina. This usually requires modifying all possible risk factors through changes in lifestyle and modifications of lifelong habits.

Short-acting sublingual nitroglycerin is the drug of choice for the acute attack, usually relieving symptoms within 1 to 2 minutes. Nitroglycerin oral spray is also available in a metered delivery system, which is especially useful for anyone having difficulty handling or swallowing pills. The spray is also easy to use in the dark and is more rapidly acting. Long-acting nitrates (e.g., oral sustained-release nitroglycerin, transdermal nitroglycerin patches, nitroglycerin ointment) are especially useful for people for whom sudden drop in blood pressure associated with taking nitroglycerin is not desirable (i.e., people with hypotension).

Pharmacologic therapy may include other vasodilators, such as (β -blockers (i.e., β -adrenergic receptor blockers) and calcium channel blockers (see Table 12-5). Intravascular thrombosis is a key element in the pathophysiology of unstable angina and its progression to MI. Anticoagulation therapy using aspirin and/or heparin is an important part of treatment for unstable angina.

Anticoagulants, such as aspirin and heparin, prevent clot formation, whereas antithrombotic agents (thrombolytics), such as urokinase and streptokinase, break down clots already formed. Aspirin blocks platelet cyclooxygenase, preventing the formation of thromboxane A₂, thereby inhibiting platelet aggregation. Heparin binds to an enzyme inhibitor, antithrombin III, enabling it to inactivate clotting factors such as thrombin or factor X.

Second-line alternatives to aspirin (sometimes referred to as "clot busters" or "super aspirins"; e.g., ticlopidine, clopidogrel) are more effective than aspirin in preventing