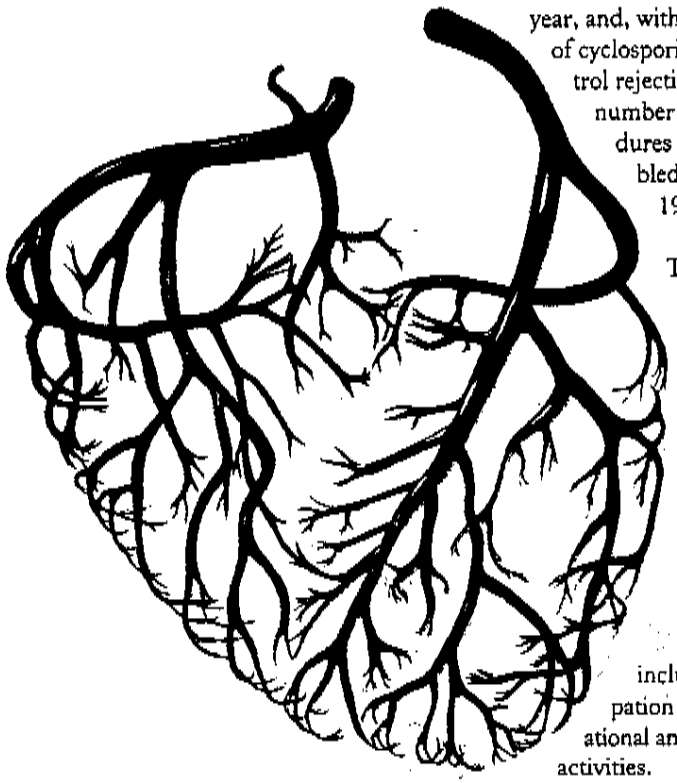
The Denervated Heart

Today patients with a heart transplant are likely to return to work and play—and to have a normal incidence of injury. Physical therapists who work with them must understand how the transplanted heart works and take precautions.

By Peggy Clough, MS, PT

Cardiac transplantations currently are performed in 148 medical centers throughout the United States (239 centers worldwide). Approximately 6,282 cardiac transplants have been performed in the United States since 1967. This number has increased every year, and, with the advent of cyclosporin A to control rejection, the number of procedures almost doubled in 1983, 1984, 1985, and 1986. The five-year survival rate for the patient with a cardiac transplant is 75.25%. Many patients return to a normal life style that includes participation in recreational and avocational activities.



Given these facts, patients probably will have the normal incidence of fractures, strains, musculoskeletal injuries, and neurological insults as they work, participate in activities, and grow older. It is, therefore, important that physical therapists working with these patients—perhaps years after the cardiac transplantation—understand how the transplanted heart works and what special treatment precautions should be taken.

The recipient's new heart is inherently different from his or her natural heart. The new heart is healthy, with a functioning myocardium and coronary artery system. The new heart also is denervated, which means it no longer has any neural connections to the brain. Normally the heart is controlled by both the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS). The cervical and thoracic sympathetic cardiac nerves contain both afferent and efferent fibers, and stimulation of the sympathetic efferent fibers by exercise or excitement causes positive chronotropic (rate-increasing) and positive inotropic (force-increasing) effects. The vagus nerves, which are part of the PNS, also contain afferent and efferent fibers. Stimulation of the vagus-efferent fibers causes a negative chronotropic effect and, to a much lesser degree, a negative inotropic effect. The heart at rest is under PNS influence or vagal inhibition.

In cardiac transplantation, the vagus nerve and the cervical and thoracic sympathetic cardiac nerves are severed when the donor heart is removed. These nerves will not regen-

erate, and they will not be re-anastomosed with the same nerves in the recipient. Because the transplanted heart is denervated, a number of changes occur in functioning both at rest and with increased activity and exercise. At the same time, some areas of cardiac physiology remain unchanged or are minimally altered.

Normal Cardiac Function in the Denervated Heart

The basic rhythm of the myocardium and the intrinsic control systems remain intact. The sinoatrial (SA) node undergoes spontaneous depolarization and spreads this wave of electrical activity in the normal pattern to the atrioventricular (AV) node and then to the ventricles of the heart via the Purkinje fibers. The vascular resistance of the coronary arteries remains responsive to changes in perfusion, pressure, hypoxia, and ischemia.

The Starling effect is retained. With an increased venous return (pre-load), the contractile force of the myocardium will increase, causing an increase in the stroke volume and a corresponding increase in the cardiac output.

The Anrep effect is retained. With a rise in aortic pressure (afterload), the contractile force of the myocardium will increase, causing an increase in stroke volume and a corresponding increase in the cardiac output.

The Bowditch effect is retained. An increased heart rate will augment the contractile force of the myocardium, again increasing the cardiac output. At rest, stroke volume and cardiac output remain within normal limits.

Altered Cardiac Function in the Denervated Heart

The patient with a denervated heart does not experience angina or heart pain because the cervical sympathetic cardiac afferent fibers are no longer intact. The patient can experience a myocardial infarction, but there will be no pain to warn the patient that the myocardium is becoming ischemic.

With the loss of SNS influence via the cervical and thoracic sympathetic cardiac nerves, the patient loses the ability 1) to increase the conduction velocity through the atria and AV node, 2) to increase the heart rate, and 3) to increase the force of contraction via neural control. The patient is, therefore, unable to reach normal peak heart rate values with exercise.

With the loss of PNS influence via the vagus nerves, the patient loses the ability 1) to decrease the conduction velocity, 2) to decrease the heart rate, and 3) to decrease the force of contraction via neural control. Because the heart normally is more influenced by the PNS, the transplant recipient has a higher heart rate at rest compared with the normal heart. The heart rate may be 90 beats per minute (bpm) rather than 70 bpm.

The denervated heart develops an increased sensitivity to the catecholamines (epinephrine and norepinephrine) in the circulating blood. The supersensitivity occurs because the denervated heart is slower than the innervated heart to remove these hormones from the blood via re-uptake by the nerve endings (adrenergic receptors). This hormonal system serves as the back-up system used by the patient to raise the heart rate when he or she wishes to exercise. The catecholamines are released from the suprarenal adrenal medullae and the adrenergic nerve endings. Epinephrine increases the heart rate and the force of myocardial contraction. Norepinephrine increases the total peripheral vascular resistance, which causes afterloading and triggers the Anrep effect.

The denervated heart exhibits increased electrical stability and is much less susceptible to ventricular arrhythmias (including ventricular fibrillation) even with coronary occlusion. When ventricular fibrillation does occur in the denervated heart, it often is a sign of significant rejection.

The electrocardiogram (ECG) shows two P waves. The P wave from the SA node of the patient's natural heart is slower because it is still under neural control and, therefore, is under parasympathetic influence. The P wave from the denervated heart's SA node is faster and independent of neural control. It is this P wave that results in the QRS complex and the ventricular contraction.

The Valsalva maneuver and carotid sinus massage, both of which normally decrease heart rate, have no effect on the heart rate of the denervated heart. Moving from a supine to a standing position or anticipating increased activity, which normally increases heart rate, has no effect on the heart rate of the denervated heart.

Cardiac Function with Exercise

With exercise, the heart rate rises much more slowly because this change is dependent on increased catecholamines in the blood rather than on the nervous system. The hormonal system is much slower than the neural system. This means that a 5- to 10-minute warm-up period is essential for the patient with a cardiac transplant. Without a gradual warm-up, the patient's cardiac output might not be able to deliver sufficient oxygen to the exercising muscles, resulting in anaerobic exercise, lactic acid build-up, exercise intolerance and, ultimately, collapse of the patient. Also, because only the secondary system for raising heart rate is intact, the patient with a denervated heart never reaches normal peak heart rate values with exercise.

With exercise, the cardiac output rises more slowly. This is due to the slow rise in heart rate, which slows the Bowditch effect. This leaves only the Starling effect of pre-load (more blood returning from the exercising muscles per minute) to increase the cardiac output by increasing the stroke volume. Stroke volume in the denervated heart at any level of exercise is decreased in comparison with stroke volume of a normal heart at the same level of exercise because of the lack of sympathetic influence.

Oxygen uptake and oxygen pulse are decreased throughout exercise in the patient with a heart transplant compared with the person who does not have a heart transplant. There is less oxygen to deliver to the exercising musculature, which results in a lower anaerobic threshold and a decreased exercise tolerance in the patient.

Maximum level of exercise tolerance decreases by about 30%. Because the patient reaches his or her anaerobic threshold sooner, he or she consistently shows more of a build-up of anaerobic metabolic waste products (lactic acid) than does the person with an innervated heart.

Ventilation and the ventilatory equivalent are significantly higher throughout exercise in the patient with a cardiac transplant compared with the person who does not have a cardiac transplant. The patient with a cardiac transplant breathes harder and moves more air but gets less oxygen into the bloodstream because of the decreased cardiac output and decreased oxygen uptake.

Sufficient data are not yet available on ST-segment changes during exercise in patients with denervated hearts. It is known that the denervated heart is more electrically stable. The denervated heart may be less prone to ST-segment depression during exercise, even if the myocardium becomes hypoxic.

Regular aerobic exercise over time can decrease the rise in systolic blood pressure for a given work load. This normal conditioning effect also is present in the patient with a heart transplant but can be more important to such a patient because immunosuppressive drugs, which are taken by the patient with a cardiac transplant to reduce infection, increase systolic and diastolic blood pressure.

Dynamic exercise usually increases systolic blood pressure proportionally with increasing work loads (approximately 7 to 10 mm Hg per 1 metabolic equivalent increase in work load) with little or no change in diastolic blood pressure. This change is due to the increased cardiac output and is required to meet the oxygen demands of the exercising muscles. The patient with a cardiac transplant also increases his or her systolic blood pressure when performing dynamic exercise. This increase is not as marked as it is in the person who does not have a heart transplant, and less oxygen is available to the exercising muscles, peak work loads are limited, and the anaerobic threshold is lowered.

Isometric exercise usually increases systolic and diastolic blood pressure because of the increase in peripheral vascular resistance. This remains true for the patient with a cardiac transplant. Catecholamines are not released with isometric exercise as they are with dynamic exercise. Because the patient is relying on the hormonal system to increase the heart rate and, thereby, to increase the cardiac output (which increases the oxygen supply to the exercising muscles), isometric exercise is not well tolerated by the patient with a cardiac transplant. Isometric exercise should be used very cautiously and only after a dynamic exercise warm-up period.

Isometric exercise also can decrease myocardial blood flow. The use of isometric exercises involving any significant muscle mass will increase diastolic blood pressure. This increased diastolic blood pressure can compromise myocardial blood flow. With exercise, the myocardium has increased oxygen needs, and blood flow through the coronary arteries may increase 500% to 600% above normal. Most of the coronary blood flow occurs during diastole; if diastolic pressure is increased, it will inhibit coronary blood flow and contribute to myocardial ischemia. This could be particularly dangerous in the patient with a cardiac transplant because the warning signs of angina and ST depression with myocardial ischemia do not appear.

With regular aerobic exercise, the patient with a heart transplant will reap many of the same benefits that a person without a transplant derives from regular exercise, but not always to the same level or degree. Most notably, the patient with a cardiac transplant can increase aerobic capacity, coronary circulation, muscle strength, tone, and feeling of well being and at the same time decrease blood pressure, serum triglyceride level, and obesity.

After the patient with a cardiac transplant has exercised regularly over time and has become more conditioned, release of catecholamines from the suprarenal adrenal medullae is diminished. This is a second reason to ensure an adequate warm-up period before exercise.

Recovery time after exercise is longer for the patient with a cardiac transplant than it is for the person who does not have a cardiac transplant. The heart rate decreases slowly because the re-uptake of the catecholamines is a gradual process. A planned 5- to 10-minute cool-down period is important.

Physiological Alterations Caused by Drug Therapy

The most commonly used immunosuppressive drugs are cyclosporin A and prednisone (a steroid). The actions and side effects of these drugs are important to understand because they can affect the patient's activity level and exercise program.

Immunosuppressive drugs increase blood pressure. Regular dynamic exercise that can decrease blood pressure should be encouraged, and isometric exercise that increases blood pressure should be avoided. Because these drugs increase blood pressure, these patients also take antihypertensive drugs. Adjusting the antihypertensive drugs with the immunosuppressive drugs to achieve optimal therapeutic benefit may require several dosage modifications. Because exercise also affects blood pressure, monitoring blood pressure before, during, and after exercise sessions should be routine.

Immunosuppressive drugs accelerate atherosclerosis. Regular exercise that can decrease the serum triglyceride level should be encouraged, as should adherence to a prescribed nutritional plan.

Immunosuppressive drugs decrease the body's natural defense mechanisms against infection. Patients should be warned to avoid sources of infection (e.g., large crowds, use of others' eating utensils). They should be instructed in good hand-washing techniques and told to use face masks if they will be in contact with anyone who has a cold or an upper respiratory infection. Health care professionals should use proper protective isolation techniques.

Immunosuppressive drugs increase the

skin's sensitivity to the sun. If the patient is planning to exercise outside following discharge from the hospital, the use of a sunscreen with a high sun protection factor rating (SPF 15 or more) should be recommended.

Prednisone also is commonly used to help control transplant rejection. Over time, prednisone can cause osteoporosis, muscle mass loss, muscle weakness, and steroid myopathy. These side effects must be noted when evaluating and exercising these patients.

Three Key Reminders

The patient with a cardiac transplant can and should exercise. Such a patient should not be kept out of community exercise classes or activities. Physical therapists who treat a patient soon after cardiac transplantation or years later should remember three important things when exercising a person with a denervated heart: 1) heart rate is not a good monitor of work load during warm-up, cool-down, or the first five minutes of peak aerobic activity; 2) warm-up is *essential*, not only to decrease musculoskeletal injuries, but because time is needed for the catecholamines to increase heart rate (the cool-down period also is very important); and 3) isometric exercise is not well tolerated by the patient who has a denervated heart, and should be avoided. **CM**

Peggy Clough, MS, PT, is supervisor of the Chest and Rehabilitation Teams, Physical Therapy Division, University of Michigan Medical Center, Ann Arbor, MI.

REFERENCES

Arthur, E.K. 1986. Rehabilitation of potential and cardiac transplant recipients. *Cardiopulmonary Record* 1:11-13.

Borg, G.A.V. 1982. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 14:377-381.

Fink, A.W. 1986. Exercise responses in the tranplant population. *Cardiopulmonary Record* 1:7-10.

Haskell, W.L., W.M. Savin, J.S. Schroeder, et al. 1981. Cardiovascular responses to handgrip isometric exercise in patients following cardiac transplantation. *Circ Res* 48(Supp)1:156-161.

Kent, K.M., T. Cooper. 1974. The denervated heart. *N Engl J Med* 291:1017-1021.

Noble, B.J. 1982. Clinical applications of perceived exertion. *Med Sci Sports Exerc* 14:406-411.

Pope, S.E., E.B. Stinson, G.T. Daughters II, et al. 1980. Exercise response of the denervated heart in long-term cardiac transplant recipients. *Am J Cardiol* 46:213-218.

Savin, W.M., E.L. Alderman, W.L. Haskell, et al. 1980. Left ventricular response to isometric exercise in patients with denervated and innervated hearts. *Circulation* 61:897-901.

Savin, W.M., W.L. Haskell, J.S. Schroeder, et al. 1980. Cardiorespiratory responses of cardiac transplant patients to graded, symptom-limited exercise. *Circulation* 62:55-60.

Squires, R.W., P.R. Arthur, G.T. Gau, et al. 1983. Exercise after cardiac transplantation: A report of two cases. *J Cardiac Rehabil* 3:570-574.

Yusuf, S., A. Mitchell, M.H. Yacoub. 1985. Interrelation between donor and recipient heart rates during exercise after heterotopic cardiac transplantation. *Br Heart J* 54:173-178.