Profiling the Hypertensive Patient in Sports

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There are approximately 35 million Americans with hypertension, many of whom are either unaware of their disease or inadequately treated. It is estimated that fewer than 29 per cent of these individuals are on adequate therapy.[36] As a result, the average physician can expect to see as many as 20 to 40 patients per week with hypertension.[20] Likewise, many subjects participating in a sport profile are healthy individuals who have had little or no contact with the medical community. Considering that hypertension represents a major risk factor for premature death and disability, it is important that blood pressure measurements be obtained on all subjects undergoing a sports profile. Early diagnosis and treatment of hypertension can have a beneficial impact on long-term morbidity and mortality. Safe application of exercise stress testing techniques requires a careful assessment of the cardiovascular system.

Although a detailed discussion of the hypertension evaluation is beyond the scope of this article, several points bear emphasizing. In individuals with known hypertension, current medication therapy and drug side effects should be noted. As will be discussed later, several antihypertensive agents are known to interfere with the normal physiologic response to exercise. If no past history of high blood pressure exists, a family history of hypertension should be sought. Although a precise genetic mechanism has not been identified, a familial tendency towards hypertensive disease can often be found. The association of hypertension and other disease states should also be evaluated. Hypertension is known to develop in diseases such as diabetes mellitus, chronic renal disease, hyper- and hypothyroidism, Cushing disease, primary aldosteronism, and renal artery stenosis, to name a few. The incidence of these secondary causes of high blood pressure is estimated to be 5 to 10 per cent of all cases of hypertension. Finally, it is particularly important to take note of any medication being taken by the subject,

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whether it is a prescription or an over-the-counter preparation. Contraceptives containing estrogen can, in some women, be associated with an elevation of blood pressure. Nasal sprays and other often used cold preparations may increase blood pressure in susceptible individuals. Finally, oral steroids, whether prescribed for a specific disease or taken illicitly as an anabolic agent for body building, are an avoidable cause of hypertension.

A precise definition of high blood pressure remains somewhat arbitrary. Actuarial data have indicated a continuum of mortality risks associated with blood pressure, even at levels below 140/90 mm Hg. Nonetheless, pressures above 160/95 mm Hg on repeat determinations indicate hypertension. Values between 140/90 and 160/95 mm Hg are defined as mild hypertension.

MEASUREMENT OF BLOOD PRESSURE

The measurement of blood pressure is largely based on the work of a Russian physician, Nicolai Korotkoff, who in 1905 noted that sounds could be generated from the brachial artery when an occluding pressure over the artery was slowly reduced.[20] The first tapping sound heard (Korotkoff phase I) identifies the systolic pressure. The disappearance of sound (Korotkoff phase V) is generally agreed to represent the diastolic pressure. An earlier muffling of sound (Korotkoff phase IV) has been correlated at rest with pressures 5 to 10 mm Hg higher than direct intra-arterial diastolic measurements.[21] If heard, both phase IV and phase V can be recorded; that is, 140/100–90. However, during exercise and other hyperkinetic states, Korotkoff phase V falls below actual intra-arterial diastolic blood pressure.[21] Under these circumstances, the phase IV correlates best with diastolic pressure and should be used for blood pressure measurements obtained during exercise testing.

Adherence to the guidelines published by the American Heart Association[21] will help to minimize introduction of errors into the measurement of blood pressure. It is recommended that the commonly used aneroid manometer be calibrated yearly against a mercury manometer. The tube of the mercury manometer should be regularly inspected for debris and obstruction to the air vent or filter. To guarantee accurate readings, the mercury meniscus must rest at zero and the column should move freely. With either manometer, the cuff needs to be of appropriate size. The cuff width should cover an area approximately two thirds of the distance from the axilla to the antecubital fossa, with the lower edge placed approximately 2.5 cm above the antecubital space.[20] Recommended cuff widths and lengths related to the arm circumference have been published.[21] Reference to these guidelines is of particular importance in the muscular athlete with large biceps and triceps in whom the use of a standard cuff might result in an erroneously high blood pressure reading.

When measuring blood pressure, the subject should be relaxed in a comfortable room, either seated or supine. Blood pressure should be checked in both arms and the higher of the two used for all future determinations. After the cuff is placed securely about the arm, the arm should be positioned and supported at heart level. As much as a 10.6 per

cent increase in the blood pressure reading can be observed when the arm is unsupported.[48] With the examiner palpating the brachial artery, the cuff is rapidly inflated to approximately 30 mm Hg above the disappearance of the pulse. The cuff is then slowly deflated at a rate of 2 to 3 mm Hg per second.[21] The first sound heard is taken as the systolic pressure and the disappearance of sound is the diastolic pressure. Finally, the blood pressure should be measured after the subject has stood for two to five minutes to check for an orthostatic change in pressure secondary to vascular disease, medication, or a pheochromocytoma. Once again, it is important to support the arm at heart level to avoid an error in this measurement. Since erect pressures are used in many stress tests, internal standardization of these techniques prior to testing is recommended. As noted earlier, the Korotkoff Phase IV should be used for the diastolic blood pressure during exercise.

CARDIOVASCULAR RESPONSE TO STRENUOUS EXERCISE

The major determinants of blood pressure (BP) are cardiac output (CO) and peripheral vascular resistance (PVR), in the following relationship: $BP = CO \times PVR$. That is to say, if, as is the case during exercise, there is a fall in PVR, CO must increase appropriately to maintain a constant blood pressure. During a strenuous bout of dynamic leg exercise, the need of working muscle for increased oxygen and substrate delivery is fullfilled by a rapid local vasodilation and an increase in blood flow to these muscles.[6] To effect an integrated rise in CO, there is a simultaneous vasoconstriction of vessels in nonworking muscles, the splanchnic bed, and the skin. The resulting increases in venous return, heart rate, and cardiac contractility permit an appropriate rise in stroke volume and CO. The net integration of these hemodynamic factors results in a rise in systolic blood pressure with little change in diastolic pressure (Fig. 1). The rise in plasma renin activity during progressive dynamic exercise may constrict peripheral vessels through the elaboration of angiotensin II.[16] Lund-Johansen, in characterizing the response to strenuous exercise, observed that heart rate, total peripheral resistance, and blood pressure are higher in the hypertensive patient at all levels of work when compared with normotensive subjects.[26] Although the heart rate response to exercise is greater, stroke volume and cardiac index rise less during exercise in the hypertensive subject.

In isometric or static exercise, the response differs from that seen with dynamic exercise, in that at any level of submaximal exercise there is a notably greater rise in systolic as well as diastolic pressure.[6] The pressor response seen with isometric exercise is associated with an increase in CO, due predominantly to an exaggerated rise in heart rate.[1, 6] Unlike dynamic exercise, a fall in total peripheral resistance was not observed during static leg exercise in the study by Bezucha et al.[1] Increased sympathetic activity, possibly related to earlier recruitment of Type II fibers, may explain the cardiovascular responses to static exercise.[16, 32, 44] As a result of these hemodynamic events, isometric exercise, such as weightlifting, produces a greater increase in blood pressure and heart rate than comparable levels of

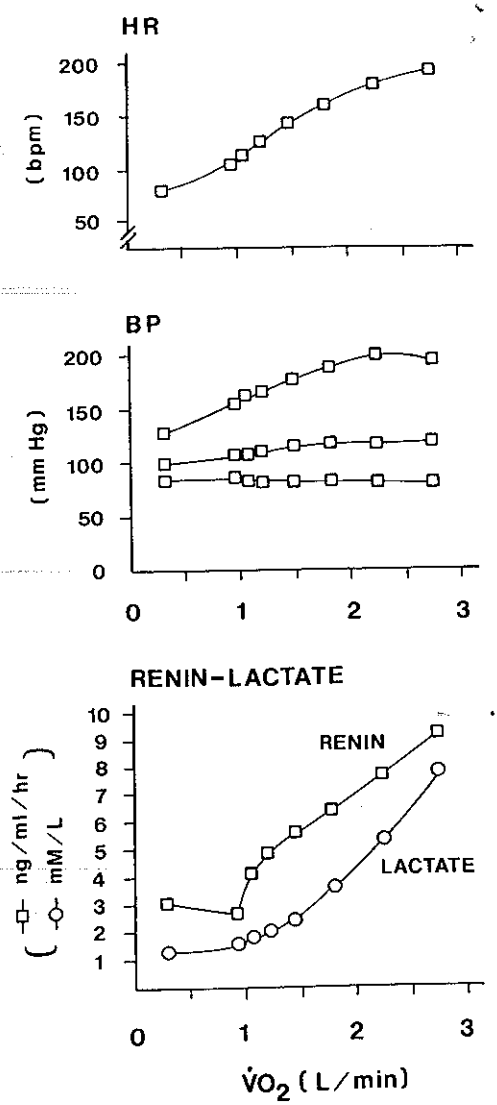

Figure 1. Heart rate (HR), blood pressure (BP), plasma renin activity, and plasma lactate levels are plotted as a function of oxygen consumption ($\dot{V}O_2$). The blood pressure panel depicts systolic, mean arterial, and diastolic pressure. Each point represents the mean of results from eight subjects during progressive cycle ergometry (*From* Gleim, G. W., Zabetakis, P. M., DePasquale, E. E., et al: Plasma osmolality, volume, and renin activity at the anaerobic threshold. J. Appl. Physiol., in press.)

dynamic leg exercise. Thus, heavy resistance forms of exercise should be avoided by the hypertensive patient.

Considerable attention has been directed toward the use of exercise stress testing in understanding the physiology of early hypertension and predicting the development of fixed hypertension in individuals at risk.[47] Wilson and Meyer studied the initial blood pressure response to exercise in 3820 individuals.[57] When compared with subjects with both a normal resting and peak exercise blood pressure, individuals with an initial elevated exercise blood pressure ($\geq$ 225/90) were found to have twice the risk of developing resting hypertension at the end of the 32 month follow-up period. Studies employing grip, mental stress, and tilt have also noted

differences between normotensive subjects and individuals who later develop hypertension.[13]

CARDIOVASCULAR RESPONSE TO EXERCISE CONDITIONING

The beneficial effects of exercise conditioning on the cardiovascular system have been suggested by numerous epidemiologic studies. Paffenbarger studied the rates and relative risks of fatal heart attacks as a function of physical activity in 6351 longshoremen between 1951 and 1972.[42] The data demonstrated a lower risk of fatal heart attack among those longshoremen involved in tasks associated with high levels of physical activity. In addition, several retrospective studies assessing levels of physical activity and blood pressure suggest that active individuals, in general, have lower blood pressures than sedentary individuals.[33]

Prospective studies in both rats and humans have supported these earlier observations. Tipton and coworkers observed that exercise-trained Wistar-Kyoto and Sprague-Dawley rats experienced a significant reduction in resting pressure when compared with nontrained rats.[51] It is particularly interesting that 12 weeks of exercise training blunted the rise in blood pressure in genetically hypertensive rats as they matured. Nontrained rats experienced an expected rise in blood pressure over the 12-week period. Studying the effect of six months of exercise training in 23 hypertensive men involved in a two day a week walk-jog program, Boyer and Kasch demonstrated a mean drop in systolic pressure of 13.5 mm Hg and in diastolic pressure of 11.8 mm Hg.[2] Normotensive exercise-trained control subjects experienced a reduction of 6 mm Hg in their diastolic pressure with no significant change in systolic pressure. Choquette and Ferguson observed a similar effect in 37 borderline hypertensive subjects.[5] After the participants performed six months of home calisthenics, the investigators noted a mean reduction in resting systolic pressure of 15 mm Hg and diastolic pressure of 8 mm Hg. During acute dynamic exercise, blood pressure rose appropriately from values at rest but remained below preconditioning values at all levels of exercise. Similarly, as illustrated in Figure 2, our group at the Institute of Sports Medicine and Athletic Trauma observed a reduction in systolic, diastolic, and mean arterial pressure following five weeks of treadmill exercise training in a group of hypertensive hemodialysis patients.[58] At week ten, mean arterial and diastolic pressure remained significantly lower than the initial values. An improvement in peak oxygen consumption and exercise tolerance was also noted in these patients.[59] However, the beneficial effect on blood pressure was maintained only during the period of continued participation in the training program (Fig. 3). Discontinuation of exercise resulted in a gradual rise in blood pressure back toward precondition levels. This required reinstitution of antihypertensive medication in two patients.

Measuring intra-arterial blood pressures, Ressl et al. observed that the rises in pressure and heart rate during acute dynamic exercise were blunted following a one-month bicycle training program.[45] Of particular note in this study was the reduction in tension time index (TTI) and rate pressure

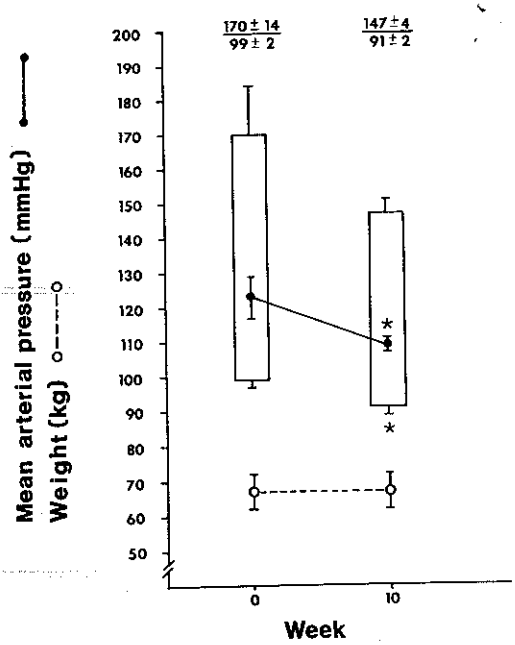

Figure 2. The blood pressure response to a 10-week exercise conditioning program in five hemodialysis patients is shown. Measurements of systolic, diastolic, and mean arterial pressure (closed circles) were obtained at rest in the sitting position before an exercise fitness evaluation at weeks zero and 10. Weight measurements (open circles) represent the mean ± SEM of three predialysis values for each patient during the week of observation. $P < 0.05$.

product (RPP) after training. Kitamura has demonstrated that a linear relationship exists for coronary blood flow and myocardial oxygen consumption with each of the independent variables—heart rate, RPP, and TTI.[22] With increasing levels of exercise, the rise in heart rate and blood pressure is associated with a linear rise in myocardial oxygen demand and coronary blood flow. Thus, at any given level of external work, a patient with untreated hypertension will have a higher RPP than a normotensive subject, resulting in increased myocardial oxygen demand and myocardial work. As demonstrated by Ressl et al., myocardial stress or left ventricular work can be reduced through exercise training by lowering the RPP and TTI.[45] Similarly, our group noted a significant reduction in RPP at a comparable level of submaximal exercise following a ten-week exercise conditioning program in hypertensive hemodialysis patients (Fig. 4).

Thus, the evidence indicates that exercise conditioning is associated with a reduction in blood pressure and myocardial work. As to the mechanisms responsible for these changes, there is no unifying thesis. Fixed essential hypertension is characterized by an elevated resting total peripheral resistance and a normal cardiac output. Considering the measurable hemodynamic changes that occur with exercise conditioning, it appears that alterations in overall autonomic balance as well as non-neurogenic factors may be responsible for the reduction in blood pressure.[8, 46] A decrease in baroreceptor sensitivity,[50] a fall in resting cardiac output,[9] a reduction in sympathetic activity,[43, 46] increased beta-2 or decreased alpha-receptor sensitivity,[24, 25, 26] and an alteration in non-neurogenically mediated vascular compliance[8, 50] have all been implicated as mecha-

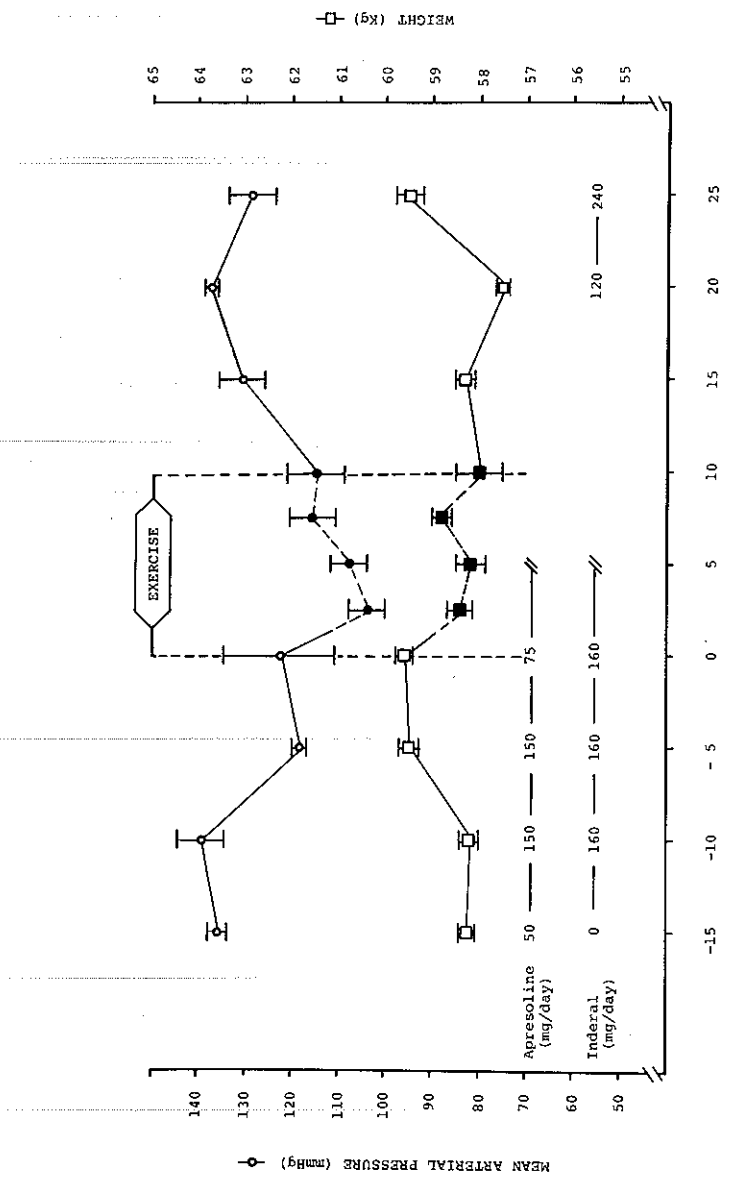

Figure 3. The blood pressure response to a 10-week exercise conditioning program in a hypertensive hemodialysis patient is shown. Mean arterial pressures and weights represent the mean ± SEM of three predialysis measurements during the week of observation. Closed circles and closed squares represent measurements during the exercise conditioning program. There was no correlation between the changes in blood pressure and weight.

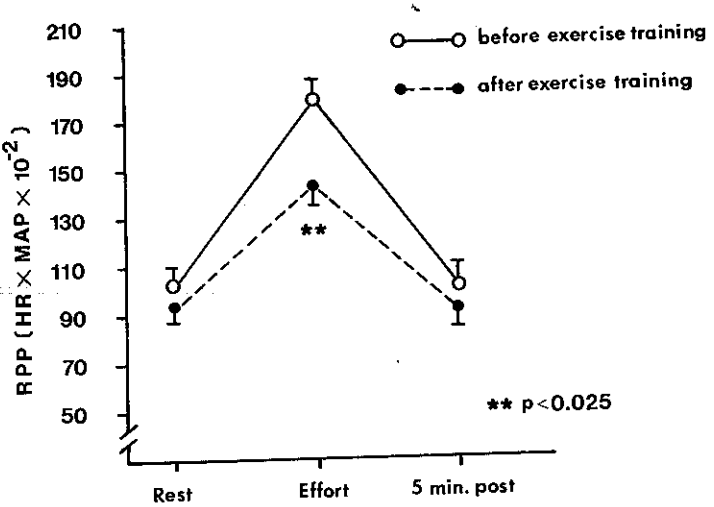

Figure 4. Rate pressure product (RPP) is shown at rest, at a similar level of oxygen consumption (18.0 ± 1.0 ml/kg/minute) during a treadmill test (effort), and five minutes after effort in five hemodialysis patients. $P < 0.025$.

nisms responsible for the reduction in blood pressure following exercise conditioning.

HEMODYNAMIC EFFECTS OF ANTIHYPERTENSIVE AGENTS DURING EXERCISE

Although antihypertensive medication has been shown to reduce morbidity and mortality associated with moderate to severe hypertension,[53, 54] there remains some controversy regarding the beneficial effects of pharmacologic treatment of mild hypertension when compared with the risks of long-term medication. The observed reduction in mortality reported in the Hypertension Detection and Follow-up Program (HDFP) study[18] was not confirmed by the Multiple Risk Factor Intervention Trial (MRFIT) study.[38] Differences in experimental design as well as other factors may explain the lack of agreement. It is expected by many that subsequent reports from other centers will support the conclusion that even mild hypertension should be evaluated and, in many patients, treated. Nonetheless, the side effects of pharmacologic treatment, including hypokalemia, hypertriglyceridemia, hypercalcemia, and hyperuricemia, cannot be ignored.

As noted earlier, aerobic exercise training is associated with a reduction in resting blood pressure and myocardial work during submaximal exercise. These beneficial hemodynamic effects make conditioning an attractive alternative or adjunct to the treatment of hypertension in selected patients. The safe application of exercise testing and conditioning of subjects taking antihypertensive medication requires an appreciation of the effects of these agents on the hemodynamic changes during strenuous exercise. Figure 5

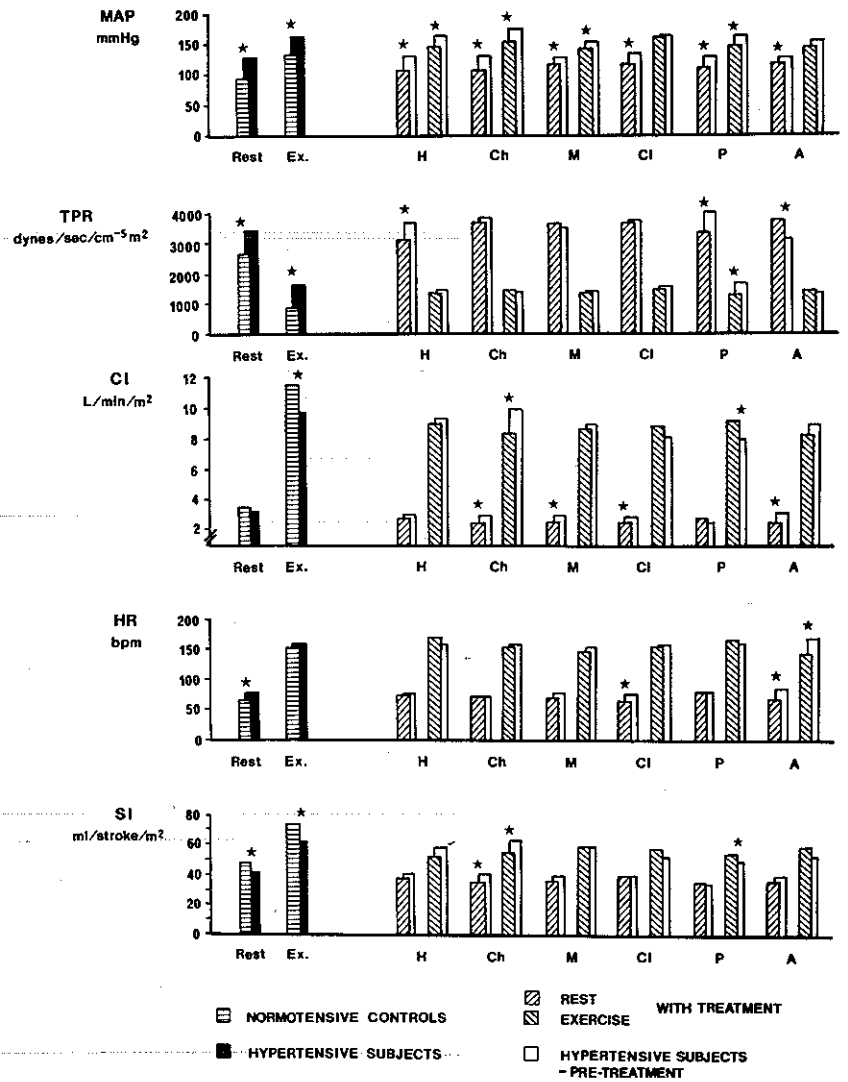

Figure 5. Hemodynamic responses are shown at rest (sitting) and during peak exercise (900 kpm/minute) following long-term antihypertensive therapy in subjects with essential hypertension. The cardiovascular measurements at rest and during peak exercise (Ex.) in normotensive control subjects are compared with measurements of untreated hypertensive subjects (age 40 to 49 years) in the first set of bar graphs in each panel. The antihypertensive medications include hydrochlorothiazide (H), chlorthalidone (Ch), methyldopa (M), clonidine (Cl), prazosin (P), and alprenolol (A). MAP = mean arterial pressure; TPR = total peripheral resistance; CI = cardiac index; HR = heart rate; SI = stroke index. Asterisks denote significant differences between groups of data as indicated by the author. Based on data from Lund-Johansen.[26-31]

illustrates the cardiovascular effects of several antihypertensive agents at rest and at peak exercise in subjects with essential hypertension, as reported by Lund-Johansen.[26] For comparison with normal physiology, the hemodynamic responses to exercise in untreated hypertensive subjects and normotensive controls is also displayed. At rest, the untreated hypertensive subjects are characterized by a higher mean arterial pressure (MAP) and heart rate (HR) than that seen in the normotensive state, the elevated pressure being due to an elevation in total peripheral resistance (TPR). During exercise, MAP rises to levels greater than those seen in the normotensive controls. Although TPR falls, it remains significantly elevated over levels measured in the control subjects. In addition, the rise in cardiac index (CI) and stroke index (SI) are less than those seen in the normotensive controls.

Diuretics

Diuretics act acutely to reduce plasma volume by inducing a naturesis and diuresis. The reduction in plasma volume and subsequent reduction in cardiac output reduces blood pressure. Within one to six months, plasma volume and cardiac output return to near baseline levels, but blood pressure remains controlled through an overall reduction in total peripheral resistance.[52, 55] Hydrochlorothiazide and polythiazide both reduced blood pressure via a reduction in TPR with a minor lowering of cardiac index and stroke index.[27] Heart rate was unaffected. The response to exercise in subjects taking thiazide diuretics was not unlike that observed in normotensive individuals (see Fig. 5). However, unlike hydrochlorothiazide, chlorthalidone mediates blood pressure reduction predominantly through a lowering of cardiac output, both at rest and during exercise.[27]

The importance of a normal potassium concentration in maintaining muscle blood flow during exercise has been demonstrated by Knochel et al.[23] Potassium-depleted animals suffered muscle ischemia and necrosis following stressful exercise. Although most hypertensive patients taking diuretics do not demonstrate significant reductions in serum potassium levels, low normal levels are often found. A sudden and unexpected reduction in potassium has been implicated in the arrhythmia and sudden death seen in this patient population.[17] Therefore, it is advisable that patients on diuretics who participate in athletic activities, especially in a warm environment, have close monitoring of their serum potassium levels. Supplementation should be initiated to maintain a normal level of this important anion. Evaluating the resting serum potassium in this patient population prior to stress testing is also strongly advocated.

Sympathetic Inhibitors

The hypotensive properties of methyldopa were noted in 1960 by Oates et al.[40] It was initially believed to act through decarboxylase inhibition in peripheral sympathetic nerves; however, it is now generally accepted that methyldopa acts in the central nervous system.[15] After metabolism in the central adrenergic neurons to alpha-methylnorepinephrine, this agent stimulates central alpha-adrenergic receptors, thus inhibiting sympathetic outflow and producing a fall in blood pressure. Peripherally, alpha-methyl-

norepinephrine may play a minor role as a weaker vasoconstrictor than norepinephrine, causing a reduction in TPR.[15]

The response during exercise of patients treated with alpha-methlydopa (see Fig. 5) is similar to that of normotensive subjects with a rise in CO and fall in TPR.[28] An appropriate rise in blood pressure and pulse is seen during exercise, with levels remaining below those seen before treatment. It is of some interest that in these studies by Lund-Johansen, the major hemodynamic effect of alpha-methyldopa at rest was a reduction in CO, with the fall in mean arterial pressure being correlated with changes in cardiac index. Total peripheral resistance actually rose over pretreatment levels in a number of patients. This observation in patients treated for 11 to 12 months is at odds with acute studies that have demonstrated a fall in blood pressure via a reduction in TPR with preservation of CO.[34] Regardless of these differences, alpha-methlydopa appears to be a relatively safe agent for use in the exercising subject.

Clonidine, a newer alpha-adrenergic agonist, similarly acts centrally to produce a reduction in blood pressure. By stimulating central alpha-adrenergic receptors, peripheral sympathetic activity is inhibited, lowering pressure predominantly through a reduction in CO.[41] In the erect position, there is an additional fall in TPR. During exercise (see Fig. 5), a physiologic rise in cardiac index, heart rate, and blood pressure is observed in patients on chronic clonidine therapy.[29] As is the case with methyldopa, clonidine does not produce severe orthostatic hypotension after exercise, indicating that reflex venoconstriction of capacitance vessels is intact.[15, 37] Owing to these features, clonidine can be safely used in patients undergoing exercise stress testing or conditioning.

Reserpine, a rauwolfia alkaloid, acts to reduce blood pressure by depleting stores of catecholamines in many organs, such as the brain, adrenal medulla, and myocardium.[15] Chronic use of this drug is associated with a reduction in CO.[7] Although the use of reserpine had fallen out of favor for a number of years, it is now being prescribed with more regularity. There are few data available on the influence of reserpine on the physiologic responses to exercise. However, the partial inhibition of cardiovascular reflexes and postural hypotension observed with reserpine[15] make it important to evaluate the response in the individual patient closely before prescribing a long-term conditioning program. Another rauwolfia alkaloid, syrosingopine, has been studied during acute exercise.[4] The response to nine minutes of exercise at 1500 ft. lb. per minute was essentially identical to that seen during the control period.

Vasodilators

By direct relaxation of vascular smooth muscle, hydralazine produces a reduction in blood pressure, the diastolic being affected to a greater extent than the systolic pressure.[15] Although TPR falls, heart rate, stroke volume, and CO all increase. Postural hypotension is generally avoided because of the preferential reduction in arteriolar resistance. Maintainence of venous tone permits adequate venous return and an increase in CO. Unless hypotension is pronounced, blood flow to the cerebral, coronary, splanchnic, and renal systems increases.

Prazosin is an alpha-adrenergic blocking agent that acts on vascular smooth muscle to produce arterial dilation and, unlike hydralazine, venodilation.[15] It is currently held that prazosin is relatively selective as a blocking agent of postsynaptic alpha-1 adrenergic receptors, with little or no action at presynaptic alpha-2 receptors. By inhibiting norepinephrine-induced vasoconstriction at the alpha-1 receptor but not the negative feedback control of norepinephrine release at the alpha-2 receptor, prazosin minimizes reflex tachycardia secondary to the reduction in TPR. In addition, the increase in plasma renin activity seen with hydralazine is not observed during prazosin therapy.[15]

Chronic prazosin therapy results in a reduction of blood pressure associated with a fall in TPR and a modest rise in cardiac index.[31] Heart rate is unaffected at rest and the normal hemodynamic response to acute exercise is maintained (see Fig. 5). When compared with pretreatment studies, lower levels of blood pressure and TPR were observed at all workloads.[31] In addition, cardiac index and stroke index were both significantly higher during exercises, with a 14 per cent increase in cardiac index and an 11 per cent increase in stroke index at 900 kpm per minute after treatment with prazosin. In the experience of Lund-Johansen, prazosin therapy was most effective in reducing TPR when compared with hydrochlorothiazide, methyldopa, clonidine, and alprenolol.[31] The use of prazosin in the active hypertensive patient appears warranted in view of its lack of adverse effects on the physiologic response to exercise. It should be cautioned that volume-depleted patients can experience a syncopal episode after the first dose of this drug. Otherwise, prazosin is generally well tolerated.

Beta-Adrenergic Blocking Agents

The attention given the beta blocking agents over the past two decades is largely due to the impact that these agents have had on a wide spectrum of disease, including hypertension, arrhythmias, and angina pectoris. Propranolol, the first widely used beta-adrenergic antagonist, belongs to a group of relatively nonselective beta-adrenergic agents that includes alprenolol, nadolol, oxyprenolol, penbutolol, pindolol, sotalol, and timolol.[15] Propranolol (Inderal) and naldolol (Corgard) are currently available in the United States. These nonselective agents block cardiac beta-1 receptors as well as peripheral beta-2 receptors, such as those located in skeletal muscle and bronchial smooth muscle. These peripheral effects can produce a transient rise in blood pressure due to unopposed alpha-1 vasoconstriction, can interfere with bronchodilation by sympathomimetic amines, and can inhibit hypoglycemic-induced glycogenolysis.[15] In contrast, the selective beta-1 adrenergic blocking agents, metoprolol (Lopressor), atenolol (Tenormin), and acebutolol (Sectral), are cardioselective in usual therapeutic doses.

The beta-adrenergic agents have been shown to reduce blood pressure, heart rate, and CO with prolongation of mechanical systole.[15] Sympathetic reflex compensation for this reduction in CO and heart rate results in an increase in peripheral resistance and an attendant reduction in tissue blood flow.[30, 39] Except for the notable benefits derived by patients with angina,

maximal exercise tolerance is reduced in otherwise healthy subjects taking these agents.[10, 14, 19] Studies by Ekblom et al. demonstrated a 12 per cent reduction in CO at maximal exercise in propranolol-treated subjects undergoing bicycle ergometry.[10] These subjects were able to reach their pre-propranolol maximal oxygen uptake but did so at a reduced maximal heart rate and lower blood pressure and with a shorter performance time; that is, they were unable to work for as long a period of time at the highest workload. Similar results have been observed with acebutolol, pindolol, and atenolol.[14, 19]

Alprenolol, studied by Lund-Johansen,[30] similarly adversely affects the physiologic response to exercise (see Fig. 5). Mean arterial pressure at rest is decreased via a reduction in heart rate and cardiac index. Typical of the beta-blockers, this reduction in blood pressure is associated with a significant increase in TPR. During acute exercise, the expected fall in TPR and rise in both cardiac index and heart rate were blunted in subjects on alprenolol. Studies comparing selective (metoprolol) and nonselective (propranolol) beta-blockers have demonstrated no significant difference in the effects of these agents on the hemodynamic response during dynamic and isometric exercise.[35] Therefore, these alterations in exercise hemodynamics need to be considered when performing a sports profile on subjects taking beta-adrenergic blocking agents.

Renin-Angiotensin System Inhibitors

Captopril is one of a class of drugs developed to inhibit the renin-angiotensin system at specific locations. As a converting enzyme inhibitor, captopril competitively blocks the conversion of the decapeptide angiotensin I to the octapeptide angiotensin II, a potent vasoconstrictor. An increase in kallikrein-kinins, substances with vasodilating properties, has also been observed as a result of captopril inhibition of kininase II, an enzyme similar to converting enzyme.[49] Thus, in the presence of captopril, angiotensin II and aldosterone levels are suppressed, while plasma renin activity and kinins are increased.

In hypertensive patients judged to be renin-dependent, captopril therapy has been demonstrated to be quite effective in lowering blood pressure.[3] The acute hemodynamic effect of captopril is a reduction in systolic and diastolic pressure through a decrease in systemic vascular resistance.[11, 12] Resting CO, stroke volume, and heart rate are not significantly affected. During graded exercise in these studies by Fagard et al., blood pressure rose appropriately but remained below pretreatment levels.[11, 12] The fall in TPR and rise in both CO and heart rate during exercise did not differ from the response seen before captopril administration. Furthermore, maximal oxygen consumption and exercise time were unaffected by captopril.[11] Thus, captopril therapy appears to be a suitable antihypertensive agent for the active patient by providing control of blood pressure at rest and during exercise without adversely affecting the hemodynamic responses to exercise.

SUMMARY

Performing a sports profile in the hypertensive patient requires a careful assessment of the cardiovascular system. Special attention must be

directed to the etiology of the disease as well as to the treatment regimen. Many individuals seeking a sports profile may, in fact, be either unaware of their hypertension or inadequately treated. Insufficient pretesting evaluation of these individuals might well place them at a higher risk for complications of testing. Modification of standard testing procedures would, therefore, be warranted, and in view of the augmented rise in both systolic and diastolic pressure with isometric exercise, avoidance of this form of exercise is advised in the untreated hypertensive patient. Finally, recognizing that antihypertensive medication can adversely affect the hemodynamic response to exercise should permit appropriate application and interpretation of the sports profile.

REFERENCES

1. Bezucha, G. R., Lenser, M. C., Hanson, P. G., et al.: Comparison of hemodynamic responses to static and dynamic exercise. J. Appl. Physiol., *53*:1589, 1982.
2. Boyer, J. L., Kasch, F. W.: Exercise therapy in hypertensive men. J.A.M.A., *211*:1668, 1970.
3. Case, D. B.: Clinical use of angiotensin blocking agents. N.Y. State J. Med., *77*:2100, 1977.
4. Chidsey, C. A., Frye, R. L., Kahler, R. L., et al.: Influence of syrosingopine on the cardiovascular response to acute hypoxemia and exercise. Circ. Res., *9*:989, 1961.
5. Choquette, G., and Ferguson, R. J.: Blood pressure reduction in "borderline" hypertensives following physical training. Can. Med. Assoc. J., *108*:699, 1973.
6. Clausen, J. P.: Circulatory adjustments to dynamic exercise and effect of physical training in normal subjects and in patients with coronary artery disease. *In* Sonnenblick, E. H., and Lesch, M. (eds.): Exercise and Heart Disease. New York, Grune and Stratton, 1977, pp. 39–75.
7. Cohen, S. I., Young, M. W., Law, S. H., et al.: Effects of reserpine therapy on cardiac output and atrioventricular conduction during rest and controlled heart rates in patients with essential hypertension. Circulation, *37*:738, 1968.
8. Edwards, M. T., Diana, J. N.: Effect of exercise on pre- and postcapillary resistance in the spontaneously hypertensive rat. Am. J. Physiol., *234*:H439, 1978.
9. Ekblom, B., Astrand, P. O., Saltin, B., et al.: Effect of training on circulatory response to exercise. J. Appl. Physiol., *24*:518, 1968.
10. Ekblom, B., Goldberg, A. N., Kilbom, A., et al.: Effects of atropine and propranolol on the oxygen transport system during exercise in man. Scand. J. Clin. Lab. Invest., *30*:35, 1972.
11. Fagard, R., Lijner, P., and Amery, A.: Hemodynamic response to captopril at rest and during exercise in hypertensive patients. Am. J. Cardiol., *49*:1569, 1982.
12. Fagard, R., Lijnen, P., Vanhees, L., et al.: Hemodynamic response to converting enzyme inhibition at rest and exercise in humans. J. Appl. Physiol., *53*:576, 1982.
13. Falkner, B., Kushner, H., Onesti, G., et al.: Cardiovascular characteristics in adolescents who develop essential hypertension. Hypertension, *3*:521, 1981.
14. Franz, I. W., Lohmann, F. W., and Koch, G.: Effects of chronic antihypertensive treatment with acebutolol and pindolol on blood pressures, plasma catecholamines, and oxygen uptake at rest and during submaximal and maximal exercise. J. Cardiovasc. Pharmacol., *4*:180, 1982.
15. Gilman, A. G., Goodman, L. S., and Gilman, A.: The Pharmacological Basis of Therapeutics, 6th ed. New York, MacMillan Publishing Co., Inc., 1980.
16. Gleim, G. W., Zabetakis, P. M., DePasquale, E. E., et al.: Plasma osmolality, volume, and renin activity at the anaerobic threshold. J. Appl. Physiol., in press.
17. Holland, O. B., Nixon, J. V., and Kuhnert, L.: Diuretic-induced vertricular ectopic activity. Am. J. Med., *70*:762, 1981.

18. Hypertension Detection and Follow-up Program Cooperative Group: Five-year findings of the hypertension detection and follow-up program. J.A.M.A., *242*:2562, 1979.
19. Kaiser, P.: Running performance as a function of the dose-response relationship to beta-adrenoceptor blockade. Int. J. Sports Med., *3*:29, 1982.
20. Kaplan, N. M. (ed.): Clinical Hypertension, 3rd ed. Baltimore, Williams and Wilkins, 1982.
21. Kirkendall, W. M., Feinleib, M., Freis, E. D., et al.: Recommendations for human blood pressure determination by sphygmomanometers. Circulation, *62*:1146A, 1980.
22. Kitamura, K., Jorgensen, C. R., Gobel, F. L., et al.: Hemodynamic correlates of myocardial oxygen consumption during upright exercise. J. Appl. Physiol., *32*:516, 1972.
23. Knochel, J. P., and Schlein, E. M.: On the mechanism of rhabdomyolysis in potassium depletion. J. Clin. Invest., *51*:1750, 1972.
24. LeBlanc, J., Boulay, M., Dulac, S., et al.: Metabolic and cardiovascular responses to norepinephrine in trained and nontrained human subjects. J. Appl. Physiol., *42*:166, 1977.
25. Lehmann, M., Keul, J., Huber, G., et al.: Plasma catecholamines in trained and untrained volunteers during graduated exercise. Int. J. Sports Med., *2*:143, 1981.
26. Lund-Johansen, P.: Hemodynamics in early essential hypertension. Acta Med. Scand. Suppl., 482, 1967.
27. Lund-Johansen, P.: Hemodynamic changes in long-term diuretic therapy of essential hypertension. Acta Med. Scand., *187*:509, 1970.
28. Lund-Johansen, P.: Hemodynamic changes in long-term alphamethyldopa therapy of essential hypertension. Acta Med. Scand., *192*:221, 1972.
29. Lund-Johansen, P.: Hemodynamic changes at rest and during exercise in long-term clonidine therapy of essential hypertension. Acta Med. Scand., *195*:111, 1974.
30. Lund-Johansen, P.: Hemodynamic changes at rest and during exercise in long-term beta-blocker therapy of essential hypertension. Acta Med. Scand., *195*:117, 1974.
31. Lund-Johansen, P.: Hemodynamic changes at rest and during exercise in long-term prazosin therapy for essential hypertension. Postgrad. Med. Spec. No. 45–52, Nov. 1975.
32. Mitchell, J. S., Reardon, W. C., and McClosky, I.: Reflex effects on circulation and respiration from contracting skeletal muscle. Am. J. Physiol., *233*:H374, 1977.
33. Montoye, H. J., Metzner, H. L., Keller, J. B., et al.: Habitual physical activity and blood pressure. Med. Sci. Sports, *4*:175, 1972.
34. Morin, Y., Turmel, L., Fortier, J.: Methyldopa: Clinical studies in arterial hypertension. Am. J. Med. Sci., *248*:633, 1964.
35. Morrison, S. C., Kumana, D. R., Rudnick, K. V., et al.: Selective and nonselective beta-adrenoceptor blockade in hypertension: Responses to changes in posture, cold and exercise. Circulation, *65*:1171, 1982.
36. Moser, M.: Long-term management of hypertension. N.Y. State J. Med., *77*:76, 1977.
37. Muir, A. L., Burton, J. L., Lawrie, D. M.: Circulatory effects at rest and exercise of clonidine, an imidazoline derivative with hypotensive properties. Lancet, *2*:181, 1969.
38. Multiple Risk Factor Intervention Trial Research Group: Multiple risk factor intervention trial. J.A.M.A., *248*:1465, 1982.
39. Nies, A. S., Evans, G. H., Shand, D. G.: Regional hemodynamic effects of beta-adrenergic blockade with propranolol in the unanesthetized primate. Am. Heart J., *85*:97, 1973.
40. Oates, J. A., Gillespie, L., Udenfriend, S., et al.: Decarboxylase inhibition and blood pressure reduction by alpha-methyl-3,4-dihydroxy-DL-phenylalanine. Science, *131*:1890, 1960.
41. Onesti, G., Schwartz, A. B., Kim, K. E., et al.: Antihypertensive effect of clonidine. Circ. Res., *28* (Suppl. 11):28, 1971.
42. Paffenbarger, R. S., and Hale, W. E.: Work activity and coronary heart mortality. N. Engl. J. Med., *292*:545, 1975.
43. Paynter, D. E., Tipton, C. M., and Tcheng, T. K.: Response of immunosympathectomized rats to training. J. Appl. Physiol., *42*:935, 1977.
44. Petrofsky, J. S., Phillips, C. A., and Lind, A. R.: The influence of fiber composition, recruitment order and muscle temperature on the pressor response to isometric contractions in skeletal muscle of the cat. Circ. Res., *48* (Suppl. I):132, 1981.

45. Ressl, J., Chrastek, J., and Jandova, R.: Haemodynamic effects of physical training in essential hypertension. Acta Cardiol., 32:121, 1977.
46. Scheuer, J., and Tipton, C. M.: Cardiovascular adaptation to physical training. Ann. Rev. Physiol., 39:221, 1977.
47. Schieken, R. M., Clarke, W. R., and Lauer, R. M.: The cardiovascular responses to exercise in children across the blood pressure distribution. Hypertension, 5:71, 1983.
48. Silverberg, D. S., Shemesh, E., and Iaina, A.: The unsupported arm: A cause of falsely raised blood pressure readings. Br. Med. J., 2:1331, 1977.
49. Smith, M. C., and Dunn, M. J.: Renal kallikrein, kinins, and prostaglandins in hypertension. *In* Brenner, B. M., and Stein, J. H. (eds.): Contemporary Issues In Nephrology. New York, Churchill Livingstone, 1981, pp. 168–202.
50. Tipton, C. M., Matthes, R. D., Bedford, T. G.: Influence of training on the blood pressure changes during lower body negative pressure in rats. Med. Sci. Sports Exerc., *14*:81, 1982.
51. Tipton, C. M., Matthes, R. D., Callahan, A., et al.: The role of chronic exercise on resting blood pressures of normotensive and hypertensive rats. Med. Sci. Sports, 9:168, 1977.
52. Tobian, L.: Why do thiazide diuretics lower blood pressure in essential hypertension? Ann. Rev. Pharmacol., 7:399, 1967.
53. Veterans Administration Cooperative Study Group on Anti-Hypertensive Agents: Effects of treatment on morbidity in hypertension. Results in patients with diastolic blood pressure averaging 115 through 127 mm Hg. J.A.M.A., *202*:116, 1967.
54. Veterans Administration Cooperative Study Group on Anti-Hypertensive Agents: Effects of treatment on morbidity in hypertension. Results in patients with diastolic blood pressure averaging 90 through 114 mm Hg. J.A.M.A., *213*:1143, 1970.
55. Villarreal, H., Exaire, J. E., Revollo, A., et al.: Effects of chlorothiazide on systemic hemodynamics in essential hypertension. Circulation, 26:405, 1962.
56. Wiegman, D. L., Harris, P. D., Joshua, I. G., et al.: Decreased vascular sensitivity to norepinephrine following exercise training. J. Appl. Physiol., *51*:282, 1981.
57. Wilson, N. V., and Meyer, B. M.: Early prediction of hypertension using exercise blood pressure. Prev. Med., *10*:62, 1981.
58. Zabetakis, P. M., Gleim, G. W., Pasternack, F. L., et al.: Exercise induced reduction in blood pressure in hemodialysis patients. Kidney Int., *16*:910, 1979.
59. Zabetakis, P. M., Gleim, G. W., Pasternack, F. L., et al.: Long-duration submaximal exercise conditioning in hemodialysis patients. Clin. Nephrol., *18*:17, 1982.

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