Postexercise Hypotension

Key Features, Mechanisms, and Clinical Significance

Michael J. Kenney, Douglas R. Seals

Recent investigations have demonstrated that there is a sustained reduction in arterial blood pressure after a single bout of exercise, i.e., postexercise hypotension (PEH). The purpose of this discussion is to integrate the available information on this topic and to review studies using sustained stimulation of somatic afferents in experimental rats as a model to study the role of somatic afferents in PEH. PEH occurs in response to several types of large-muscle dynamic exercise (i.e., walking, running, leg cycling, and swimming) at submaximal intensities greater than 40% of peak aerobic capacity and exercise durations generally between 20 and 60 minutes. PEH is observed in both normotensive and hypertensive humans and in spontaneously hypertensive rats but is generally greater in magnitude in hypertensive subjects. The maximal exercise-induced reductions in systolic and diastolic arterial blood pressures have been on average 18 to 20 and 7 to 9 mm Hg, respectively, in hypertensive humans and 8 to 10 and 3 to 5 mm Hg, respectively, in normotensive humans. PEH has been reported to persist for 2 to 4 hours under laboratory conditions. Whether PEH is sustained for a prolonged period of time under free-living conditions remains controversial, although the results of one study indicate that PEH can persist for up to 13 hours. Possible mechanisms involved in mediating postexercise and poststimulation reductions in arterial blood pressure include decreased stroke volume and cardiac output; reductions in limb vascular resistance, total peripheral resistance, and muscle sympathetic nerve discharge; group III somatic afferent activation; altered baroreceptor reflex circulatory control; reduced vascular responsiveness to α-adrenergic receptor-mediated stimulation; and activation of endogenous opioid and serotonergic systems. It appears that the magnitude of PEH in hypertensive subjects is clinically significant; however, more investigation is required to determine if the duration is sufficient under real-life conditions to contribute to the reduction in blood pressure observed with chronic exercise conditioning. (Hypertension. 1993;22:653-664.)

KEY WORDS • exercise • hypotension • blood pressure • hemodynamics

Clinicians have studied exercise in the area of hypertension for many years. Most of this interest has focused on two issues: (1) regulation of arterial blood pressure during acute exercise, i.e., whether hypertensive patients have exaggerated arterial blood pressure responses to exercise, and (2) the use of chronic exercise as a nonpharmacologic approach to lowering arterial blood pressure at rest and during daily physical activity. In recent years, however, clinical scientists and physiologists alike have become interested in a third component of the exercise response—the sustained reduction of arterial blood pressure after a single bout of exercise, i.e., postexercise hypotension (PEH).

In contrast to the aforementioned aspects of the exercise response that have received considerable discussion, insight into the key features and possible clinical significance of PEH remains fragmentary. Therefore, the purpose of this discussion will be to integrate the available information on this topic, emphasizing its fundamental properties, speculating on the underlying mechanisms, and commenting on its possible relevance in the treatment of essential hypertension.

Definition and Documentation

For purposes of this review, PEH is defined as a reduction in systolic and/or diastolic arterial blood pressure below control levels after a single bout of exercise (Fig 1). PEH has been documented in anecdotal reports, clinical accounts, and experimental investigations. Because exercise is associated with activation of somatic afferents, electrical stimulation of the sciatic nerve and of hind limb skeletal muscles in the rat has been used to study the role of somatic afferents in mediating PEH. In this regard, poststimulation hypotension (PHS) is defined as a reduction in systolic and/or diastolic arterial blood pressure below control levels after electrical stimulation of the sciatic nerve or hind limb skeletal muscles (Fig 2).

Key Features of Postexercise and Poststimulation Hypotension

The following factors play a role in determining the occurrence, pattern, and magnitude of the arterial blood pressure responses after exercise and electrical stimulation.

Nature of the Exercise Stimulus

Mode. In humans, PEH has been observed in response to several types of large-muscle dynamic exercise, includ-
ing walking and running,* leg cycling,16-19,21,26,27,30,31 and swimming.34 Little information is available concerning the arterial blood pressure responses after resistance exercise in humans. O'Connor et al.35 observed slight elevations in systolic and diastolic arterial blood pressures immediately after 30 minutes of upper and lower body resistance exercise, with a rapid return toward preexercise control levels during the remainder of the 2-hour postexercise measurement period. In a second study, Hill and colleagues36 reported significant reductions in both systolic and diastolic arterial blood pressures immediately after 11 to 18 minutes of weight training exercise at 70% of one-repetition maximum. Thereafter, systolic and diastolic arterial blood pressures abruptly returned toward control levels but remained slightly (systolic) to moderately (diastolic) depressed throughout a 1-hour postexercise recovery period. Thus, PEH has not been conclusively established after acute resistance exercise in humans. In the rat, PEH is induced by voluntary running wheel exercise26 and forced treadmill running,25 whereas PSH is elicited by electrical stimulation of the gastrocnemius and biceps femoris skeletal muscles38,37 and of the sciatic nerve.38-42

Intensity. In both humans and rats, PEH has been observed in response to exercise at submaximal intensities between 40% and 70% of maximal oxygen consumption, peak oxygen consumption, age-predicted maximal heart rate, or resting heart rate reserve.* In addition, arterial blood pressure in humans is reduced after maximal treadmill and leg cycling exercise to exhaustion.19-28,30-31

The intensity of sciatic nerve stimulation used to elicit PSH is usually defined as a multiple of the minimal current required to evoke a muscle twitch.41 PSH occurs in response to sciatic nerve stimulation at current intensities between four and 25 times the twitch threshold.

*References 12, 13, 15-18, 20, 21-23, 25, 27, 32, 33.

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old.28-41 Electrical stimulation of the gastrocnemius and biceps femoris muscles at current intensities between 3 and 25 mA also elicits PSH.34,37

Duration. Reductions in arterial blood pressure have been observed after a wide range of exercise durations. PEH has been reported with exercise durations as short as 3 to 10 minutes15,24 and as long as 170 minutes,28 but most studies have used exercise durations between 20 and 60 minutes.12,13,15-23,25-27,29-33 PSH has been observed with stimulation lasting 3039,41 and 6034,37,38 minutes.

Importance of the Subject Population

PEH has been observed in young and middle-aged normotensive humans,15,16,19,21-23,28,31,32 patients with borderline essential hypertension,20,26,30 and patients with established (sustained mild to moderate) essential hypertension* as well as in older subjects with essential hypertension.12 In contrast, several studies have reported no significant change in arterial blood pressure after a single bout of exercise in normotensive humans.17,18,27 Moreover, Hara and Floras22 reported that diastolic and mean but not systolic arterial blood pressures were reduced after exercise in normotensive humans, whereas Floras et al20 reported postexercise reductions in systolic but not diastolic arterial blood pressure in borderline hypertensive subjects. PEH occurs in both men† and women,12,18,19,26,31 indicating a lack of gender specificity. PEH is also observed in spontaneously hypertensive rats (SHR)25,29 PSH occurs in conscious34,37,38,41 and anesthetized40 SHR, conscious Wistar-Kyoto normotensive rats,41 and anesthetized prehypertensive Dahl salt-sensitive rats.39 In contrast, PSH is not observed in renal hypertensive38 and Dahl salt-resistant39 rats. Because Dahl salt-sensitive rats and SHR exhibit a genetic predisposition for development of hypertension whereas Dahl salt-resistant and renal hypertensive rats do not, these results suggest that the magnitude of PSH may be related to the genetic predisposition of the animal to hypertension.39

Nature of the Arterial Pressure Responses

Peak changes in arterial pressure. In studies to date, peak exercise-induced reductions in systolic and diastolic arterial blood pressures have been on average 18 to 20 and 7 to 9 mm Hg, respectively, in hypertensive humans‡ and 8 to 10 and 3 to 5 mm Hg, respectively, in normotensive humans.15,19,21-23,27,28,31,32 Studies in borderline hypertensive humans have reported peak postexercise reductions in systolic and mean arterial blood pressures of approximately 1020,30 and 16 mm Hg,26 respectively. In one study, SHR exhibited a peak exercise-induced reduction in mean arterial blood pressure of 16 mm Hg.25

In response to muscle and/or sciatic nerve stimulation, the peak reduction in mean arterial blood pressure is on average 18 to 20 mm Hg in SHR34,37,38,40,41 and 7 to 9 mm Hg in Wistar-Kyoto rats.41 After sciatic nerve stimulation in prehypertensive Dahl salt-sensitive rats, the peak reduction in mean arterial blood pressure is 20 mm Hg.39

Collectively, these observations indicate that (1) in normotensive humans and rats the peak postexercise reduction in arterial blood pressure is generally less than that observed in their hypertensive counterparts and (2) the magnitude of the peak exercise-induced decrease in arterial blood pressure in hypertensive rats is approximately equal to that observed in hypertensive humans.

Average changes in arterial pressure. Several studies have reported average decreases in arterial blood pressure during the postexercise measurement period. Between 30 and 90 minutes after moderate cycling exercise in humans with mild to moderate essential hypertension, Cléroux et al18 reported that the hypotensive response averaged −11 mm Hg for systolic and −4 mm Hg for diastolic arterial blood pressures. Moreover, the reduction in pressure was maintained during the period between 2 and 3 hours after exercise, with systolic arterial blood pressure 9 mm Hg and diastolic arterial blood pressure 4 mm Hg below control values. In older humans with essential hypertension, systolic arterial blood pressure was reduced an average of 13 mm Hg from control values for 3 hours after exercise at 70% maximal oxygen consumption (Fig 1). Mean arterial blood pressure has been reported to be reduced an average of 8 mm Hg for at least 4 hours after submaximal cycling exercise in borderline hypertensive humans,26 whereas Pescatello et al27 reported that systolic arterial blood pressure was reduced an average of 6 mm Hg over 8.7 hours and diastolic arterial blood pressure was reduced an average of 9 mm Hg over 12.7 hours after submaximal exercise in mildly hypertensive men (Fig 3). Mean arterial blood pressure is reduced on average 14 mm Hg for 50 minutes and 4 mm Hg for 38 minutes after spontaneous wheel running in SHR and Wistar-Kyoto rats, respectively.29

Time course of the response. Little information is available concerning the time at which the lowest recorded levels of arterial blood pressure occur after a single bout of exercise. The results of several studies indicate that the nadir of the postexercise systolic and diastolic arterial blood pressure responses generally occurs within the first 60 to 70 minutes of recovery.12,21,23,26,31 In these studies the lowest recorded levels of arterial blood pressure were generally followed by increases toward control levels before measurements were stopped. In other studies it is difficult to determine when the nadir of the PEH response occurred because the first data point recorded was 30 to 60 minutes after the cessation of exercise17,18,20 or the last recorded data point was either the lowest or very nearly the lowest recorded value of arterial blood pressure.15,16,27,30

In general, the nadir for mean arterial blood pressure after muscle and sciatic nerve stimulation in hypertensive rats ranges between 30 and 180 minutes.34,38,40,41 In normotensive rats, the peak reduction in mean arterial blood pressure has been reported to occur within 2 hours after sciatic nerve stimulation.41

Little information is available on the time course for reattainment of arterial blood pressure to control levels, because few studies have continued measurements to this standardized end point. In mildly to moderately hypertensive humans, diastolic and mean arterial blood pressures were reduced from control levels when the measurements were stopped 12.7 hours after the cessa-
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Fig 3. Line graph shows systolic (SBP), mean (MAP), and diastolic (DBP) arterial blood pressures recorded in mildly hypertensive men before, during, and for approximately 13 hours after a single bout of cycling exercise (EX). Note the sustained postexercise reductions in arterial blood pressures compared with values recorded before exercise (REST). Reprinted with permission from Pescatello et al.27

In this section, we review potential mechanisms by which exercise and somatic afferent stimulation may induce sustained reductions in arterial blood pressure.

Efferent Mechanisms

Systemic and regional hemodynamics. Because arterial blood pressure is a function of the product of cardiac output and total peripheral resistance, reductions in arterial blood pressure observed after exercise and electrical stimulation of somatic and muscle afferents must result from decreases in cardiac output, total peripheral resistance, or both. To date, however, the experimental findings concerning the regional and systemic hemodynamic adjustments responsible for PEH have been inconsistent.
Forearm vascular resistance and total peripheral resistance have been reported to be significantly increased compared with control values after intermittent submaximal treadmill exercise in hypertensive humans. In older subjects with essential hypertension, the increase in total peripheral resistance was associated with a significant reduction in cardiac output. Because heart rate generally remained either above or unchanged from control values after exercise, the reduction in cardiac output was primarily mediated by a decrease in stroke volume. Neither reductions in cardiac preload nor increases in cardiac afterload could account for the reduced stroke volume, suggesting that alterations in myocardial contractility may have contributed to this hypotensive response. In this regard, decreased left ventricular systolic function after prolonged exercise has been documented in healthy humans. After treadmill exercise in SHR, vascular resistance in the iliac, superior mesenteric, and renal beds was not markedly changed from control levels, whereas heart rate was significantly reduced. It is not known if this bradycardic response is associated with a reduction in cardiac output.

In contrast to these observations, Coats and coworkers reported significant increases in heart rate and cardiac output and decreases in arterial blood pressure and total peripheral resistance after maximal leg cycle ergometry in normotensive humans. The increase in cardiac output was mediated by the sustained tachycardia, as stroke volume remained unchanged from control levels after exercise. The reduction in total peripheral resistance involved vasodilation in the nonactive limbs, as forearm vascular resistance was significantly reduced after exercise. Consistent with these observations, Cleroux et al. reported decreases in arterial blood pressure, total peripheral resistance, and forearm vascular resistance (Fig 4) and increases in cardiac output, heart rate, and stroke volume after bicycle exercise at 50% of peak oxygen uptake in humans with mild to moderate hypertension. Reductions in mean arterial blood pressure and total peripheral resistance also have been observed for at least 4 hours after submaximal exercise in borderline hypertensive humans. Moreover, Hara and Floras recently reported reductions in diastolic and mean arterial blood pressures, calf vascular resistance, and total peripheral resistance and tachycardia-mediated increases in cardiac output after submaximal treadmill exercise in normotensive humans.

It is not clear what accounts for the inconsistent hemodynamic changes observed after a single bout of exercise. It does not appear to be solely an influence of exercise intensity, as variable changes in both cardiac output and systemic vascular resistance have been reported after moderate intensities of dynamic exercise. Moreover, there appear to be no consistent relations among the observed hemodynamic changes and the exercise mode and duration. The subject population involved could play a role, as older subjects with essential hypertension demonstrate postexercise reductions in cardiac output and increases in total peripheral resistance. Body position also may contribute to the differences observed in postexercise systemic hemodynamics; the study that reported decreased cardiac output and increased total peripheral resistance after exercise evaluated subjects during seated rest rather than supine as in several other studies that observed the opposite relation.

Cleroux et al believe that the experimental design of several studies may have influenced postexercise hemodynamic alterations. In the studies by Bennett et al and Hagberg and coworkers, baseline measurements were established over a brief period of time immediately before exercise. Cleroux et al suggest that the preexercise cardiac output and forearm blood flow values reported in these studies are relatively high because of the anticipation of the impending bout of exercise or the stress of being in an unfamiliar laboratory setting; thus, the "artificially" higher preexercise values could mask postexercise increases in these variables. In their own study, they compared hemodynamics after exercise to those of a nonexercise control period completed on a separate day. However, differences in experimental design may not account for all the observed variances among studies, as Coats et al reported no significant differences in arterial blood pressure, cardiac index, forearm vascular resistance, or systemic vascular resistance during a control period immediately before exercise compared with a control session completed on a
been reported to be slightly increased, 33 unchanged, 26 with essential hypertension, plasma volume remained unchanged, and 60 minutes after treadmill exercise in borderline hypertensive subjects. The level of arterial blood pressure during control and after exercise is listed below the EKG tracing. Note that SNA and arterial blood pressure were lower 60 minutes after exercise compared with control levels. Reprinted with permission from Floras et al. 20

separate day. It is clear that additional data are needed to define more completely the nature of the systemic and regional hemodynamic alterations mediating PEH, as well as the role of differing methodology in determining the nature of these responses.

The results of several studies suggest that reductions in plasma volume are not necessary to observe PEH. Cléroux et al 17,18 reported that, in hypertensive humans after cycling exercise at 50% of maximal oxygen uptake, arterial blood pressure was reduced, whereas plasma volume remained unchanged from control values. In subjects 60 minutes after treadmill exercise at approximately 70% of maximal heart rate, Kaufman et al 23 and Hara and Floras 22 reported reductions in sympathetic and diastolic arterial blood pressures, respectively, without significant changes in plasma volume. In older humans with essential hypertension, plasma volume remained slightly increased from control for 1 hour after exercise at 50% of maximal aerobic capacity and was reduced on average 4% for 3 hours after exercise at 70% of maximal aerobic capacity. 12 However, systolic arterial blood pressure was reduced from control levels after both intensities of exercise. Moreover, plasma volume was reduced a similar magnitude in control subjects after 4 hours of sitting, whereas systolic and diastolic arterial blood pressures remained unchanged from control levels. Taken together, these results suggest that reductions in plasma volume appear not to play a key role in PEH.

**Sympathetic nerve activity.** The results of several studies indicate that inhibition of basal sympathetic nerve discharge may contribute to PEH and PSH in hypertensive populations. Floras et al 20 reported significant reductions (10 mm Hg) in systolic arterial blood pressure and muscle sympathetic nerve activity in borderline hypertensive subjects 60 minutes after treadmill exercise (Fig 5). Moreover, simultaneous reductions in arterial blood pressure and sympathetic nerve discharge (renal and splanchnic) have been observed after prolonged sciatic nerve stimulation in SHR 40,41 and prehypertensive Dahl salt-sensitive rats. 39 The results of studies using plasma levels of norepinephrine as an indirect measure of sympathetic nerve activity have been inconsistent, as postexercise plasma levels have been reported to be slightly increased, 20 unchanged, 33 and reduced 18 from control values in borderline hypertensive, hypertensive, and mildly hypertensive humans, respectively.

In normotensive humans, Hara and Floras 22 reported that diastolic and mean arterial blood pressures were reduced, whereas muscle sympathetic nerve activity and plasma norepinephrine levels remained unchanged from control levels after submaximal exercise, suggesting that PEH can occur in normotensive humans in the absence of reductions in sympathetic nerve activity.

**Humoral and local factors.** Circulating hormones, local metabolic factors, or both may play a role in mediating PEH. Unfortunately, the studies to date have not provided information that clarifies the influence of these mechanisms on PEH.

Plasma concentrations of epinephrine have been reported to be unchanged 33 and increased 18 after exercise that elicits PEH. PEH is observed after β-receptor antagonism with enalapril and atenolol, 33 suggesting that β-adrenergic receptor-mediated vasodilation does not play a key role in this response. Mean plasma vasopressin levels have been reported to be unchanged 20 and increased 33 after exercise that elicits PEH. Although vasopressin produces vasoconstriction of isolated arterial segments in vitro, 44 the increase in arterial blood pressure after vasopressin administration in intact animals is less than expected. 46 In this regard, vasopressin has been reported to sensitize the arterial baroreceptor reflex, increase forearm blood flow, and decrease forearm vascular resistance. 57-49 Whether vasopressin plays a role in PEH has not been determined.

Other humoral factors may also play a role in PEH. For example, acute exercise increases plasma levels of immunoreactive atrial natriuretic peptide, 50,51 which has potent local vasodilator effects and can induce decreases in arterial blood pressure. 53 However, Hara and Floras 22 reported reductions in diastolic and mean arterial blood pressures after submaximal exercise in normotensive subjects despite the fact that plasma levels of atrial natriuretic peptide were reduced compared with control levels.

Endothelium-derived relaxing factor is an endogenous vasodilator released by the vascular endothelium. 53-56 It is a powerful vasodilator agent that plays a role in the vascular relaxation produced by acetylcholine and other endothelium-dependent vasodilators such as bradykinin, histamine, and substance P. 53,56 The
chemical mediator of endothelium-derived relaxing factor is nitric oxide. Moncada et al have proposed that there is a nitric oxide–dependent tone in the cardiovascular system that plays a role in the regulation of arterial blood pressure. Mechanical factors associated with increased arterial blood flow are thought to be one possible mechanism by which these substances are released from the endothelium. It is possible that the hyperemia associated with physical exercise stimulates their release, and this may contribute to the vasodilation of skeletal muscle during and possibly after exercise.

Reduced vascular responsiveness to adrenergic receptor activation may also play a role in PEH. Howard and Di Carlo measured changes in rabbit iliac blood flow velocity induced by bolus injections of the α-adrenergic receptor agonist phenylephrine during control conditions and after a single bout of treadmill exercise. The reduction in iliac blood flow velocity at the same dose of phenylephrine was attenuated after exercise compared with nonexercise control days, suggesting that the ability of the hind limb vasculature to constrict in response to activation of α-adrenergic receptors is reduced after acute exercise in conscious rabbits. Phenylephrine-induced alterations in iliac blood flow velocity were obtained without changes in mean arterial pressure or heart rate as the hind limb was functionally isolated. This allowed for evaluation of the direct effects of acute exercise on vascular function without eliciting baroreceptor reflex–mediated changes in arterial pressure. Recent data from the same laboratory indicate that acute exercise also attenuates phenylephrine-induced contraction of rabbit isolated aortic rings. The fact that after acute exercise hind limb vascular responsiveness to α-adrenergic receptor activation is attenuated and muscle sympathetic nerve activity has been reported to be reduced suggests that both local and neural alterations in skeletal muscle may contribute to PEH.

Two metabolic factors proposed to be involved in the local control of skeletal muscle blood flow during exercise are the potassium ion and adenosine, both of which produce vasodilation. Whether the potassium ion plays a role in PEH is not clear. Mean plasma levels of potassium have been reported to be unchanged and increased after submaximal exercise that elicits PEH. Moreover, plasma potassium was unchanged compared with prestimulation control levels at 15 and 180 minutes after cessation of electric muscle stimulation in the hind limb of the SHR that produced PSH. A possible influence of adenosine in mediating PEH has not been determined.

It is clear that additional studies are needed to define more completely a role for various humoral and local factors in mediating PEH.

Peripheral Afferent Mechanisms

Somatic afferent stimulation. Somatic afferents are involved in mediating PSH because this response is elicited by electrical stimulation of the cut, central end of the sciatic nerve in anesthetized rats, whereas PSH is not observed after sham sciatic nerve stimulation. Stimulation parameters that activate predominantly A-delta (or group III) afferent fibers appear to mediate this effect. The hypotension observed in response to direct electrical stimulation of hind limb skeletal muscle is also of neurogenic origin, as this response is eliminated if the sciatic nerve has been anesthetized before the onset of stimulation.

Sustained stimulation of muscle afferents during exercise is well established. Contracting skeletal muscle stimulates both mechanoreceptor and metaboreceptor (chemosensitive) sensory afferents. Studies in anesthetized cats have established that static and rhythmic contractions of cat hind limb muscles reflexly increase arterial blood pressure, heart rate, and renal sympathetic nerve activity. Substantial evidence indicates that these responses are mediated by stimulation of group III and IV muscle afferents. Whether stimulation of muscle afferents contributes to PEH has not been established. However, dynamic exercise and electrical stimulation of somatic afferents are known to produce a number of similar responses, including (1) sustained increases in arterial pressure and heart rate, and (2) postcontraction/stimulation reductions in arterial pressure, and (3) an increase in pain threshold. Collectively, these observations suggest that exercise-induced stimulation of muscle afferents may play a role in PEH. If so, it is not clear whether this effect is mediated by a sustained activation of these afferents during the postexercise period or, alternatively, by a decrease in afferent activity on cessation of exercise.

Baroreceptor afferent stimulation. The rise in arterial blood pressure above resting levels during short-term exercise is thought to be mediated by an upward resetting of the baroreceptor reflex operating (set) point. One current hypothesis is that central command causes this via a direct effect on the medullary areas involved in baroreceptor reflex control. It is unclear whether the converse of this, ie, a downward resetting of the baroreceptor reflex at the cessation of exercise, could be involved in mediating PEH. The removal of central command and/or other central inputs at the offset of exercise should cause the operating point for arterial pressure to return to resting levels. However, the mechanism by which these resting levels could be perceived as inappropriately high, thus resulting in further lowering of pressure (PEH), is not as obvious. Nevertheless, a downward resetting of the set point for baroreceptor reflex control of blood pressure remains a possible factor in PEH.

Cléroux et al reported that the stimulus-response relation between central venous pressure (stimulus for cardiopulmonary baroreceptors) and forearm vascular resistance was shifted downward to lower forearm vascular resistance at a given level of central venous pressure after exercise compared with control conditions. This apparent alteration in baroreceptor reflex regulation of forearm vascular resistance was observed in hypertensive but not normotensive subjects and was primarily due to changes in the control of skeletal muscle blood flow. These results raise the possibility that exercise-induced modulation of the baroreceptor reflex control of muscle sympathetic nerve activity may affect skeletal muscle vascular resistance after exercise in hypertensive subjects.

Several other observations are consistent with the fact that PEH is associated with altered baroreceptor

*References 12, 15, 17, 18, 20, 23, 29, 31, 32, 39, 41.
reflex control of the circulation. For example, baroreceptor reflex control of heart rate has been reported to be enhanced after a short-term bout of maximal exercise in normotensive^79 and borderline hypertensive^80 humans. With regard to regulation of regional blood flow, Bennett et al^13 reported potentiated forearm vascular resistance responses to lower body negative pressure (cardiopulmonary baroreceptor unloading) in hypertensive subjects after compared with before a single bout of exercise. It is unclear, however, exactly how these changes in baroreceptor reflex control of the circulation may contribute to PEH.

Thermoreflexes. Exercise increases metabolic heat production and internal body temperature. In humans, eccrine sweating and active vasodilatation of cutaneous blood vessels are the two primary effector mechanisms for dissipating heat under conditions of thermal stress.^80 Because activation of these mechanisms increases cutaneous vascular conductance, decreases systemic vascular resistance, and thus can reduce arterial blood pressure, thermally induced physiological adjustments may contribute to PEH.

As stated previously, several studies have reported parallel decreases in arterial blood pressure and forearm vascular resistance after exercise,^18,19 suggesting that hemodynamic changes in forearm muscle or skin or both may contribute to PEH. Sustained increases in blood flow to forearm skin would provide evidence indicating that thermoregulatory vasodilatation plays a role in PEH. In this regard, hand (primarily skin tissue) vascular resistance is significantly reduced after submaximal exercise in hypertensive and normotensive humans (Fig 4).^10 However, because forearm skin blood flow is under different regulatory control than hand blood flow, changes in the latter may not provide useful information concerning regulation of blood flow to forearm skin. Moreover, as emphasized by Cléroux et al,^18 if alterations in hand blood flow were reflected in forearm hemodynamic changes, it would be expected that forearm vascular resistance should be lower immediately after exercise compared with time points further removed from the cessation of exercise (ie, when body temperature has returned to control levels). However, this was not the case in their hypertensive subjects, as reductions in forearm vascular resistance were not significantly different at 30, 60, and 90 minutes after exercise (Fig 4). In addition, PEH occurs in response to moderate exercise with durations as short as 3 to 10 minutes. Taken together, these findings suggest that PEH is not necessarily associated with thermoregulatory vasodilatation.

Central Mechanisms
Endogenous opioid pathways. Endogenous opioids are thought to play an important role in cardiovascular regulation. The opioids are generally classified into three groups: endorphins, enkephalins, and dynorphins. Moreover, there are three widely accepted opioid receptor types referred to as μ-, δ-, and κ-receptors. The precise relation among these opioids and receptors is not well understood; however, there is some degree of specificity. For example, β-endorphin has been shown to bind selectively to μ- and δ-receptors, whereas dynorphin A and [leu]enkephalin have affinity for κ- and δ-receptors, respectively.

Poststimulation reductions in arterial blood pressure in SHR are reversed toward control levels after administration of high doses of naloxone, an opioid receptor antagonist with a high affinity for μ-receptors (Fig 6). whereas pretreatment with naloxone prevents the development of PSH. These findings suggest that endogenous opioid systems are involved in mediating PSH. However, because high doses of naloxone can antagonize δ- and κ-receptors as well as μ-receptors, these results do not indicate which opioid receptors play a role in mediating PSH. In this regard, Hoffmann et al^37 reported that selective antagonism of opioid κ-receptors completely reversed PSH in SHR, whereas the depressor response was partially reversed by antagonism of opioid δ-receptors. In contrast, PSH was not affected by the selective antagonism of opioid μ-receptors. These findings indicate that opioid κ- and to some extent δ-receptors are involved in mediating PSH in SHR.

It has been postulated that sustained somatic afferent stimulation induces activation of central endogenous opioid systems, which in turn produce sympathoinhibition. This inhibitory influence may be masked during exercise by the sympathoexcitatory influences of central command and peripheral chemoreceptor stimulation. However, once exercise is completed, the physiological effects of sustained activation of endogenous opioid systems may predominate and produce hypotensive and sympathoinhibitory responses. In this regard, plasma levels of β-endorphin have been reported to be increased after exercise in humans,^6,60 and increased levels of β-endorphin in the brain^60 and cerebrospinal fluid^60 have been reported after exercise in rats. Moreover, alterations in opioid receptor occupancy have been demonstrated in specific areas of the brain after exercise in experimental rats. PEH is attenuated in SHR by the administration of naloxone. However, the involvement of endogenous opioids in mediating reductions in arterial pressure after submaximal exercise in normotensive humans is equivocal. Boone et al reported that naloxone administration transiently reversed reductions in systolic and mean arterial blood pressures, whereas Hara and Floras reported that the administration of naloxone did not prevent postexercise.
reductions in diastolic and mean arterial blood pressures.

These observations suggest that activation of endogenous opioid pathways can contribute to PEH in normotensive humans and hypertensive rats. Because the magnitude of the PEH response is greater in hypertensive than normotensive humans, it is tempting to speculate that opioid receptor blockade may produce a greater effect on PEH in hypertensive humans.

Central serotonin. Central serotonergic mechanisms have been implicated in mediating PSH. Pretreatment with para-chlorophenylalanine methyl ester--HCl, a tryptophan hydroxylase inhibitor, abolishes PSH in SHR. Furthermore, administration of the serotonin precursor 5-hydroxy-DL-tryptophan before sciatic nerve stimulation augments the poststimulatory reduction in arterial blood pressure. The mechanism by which serotonin might contribute to PSH is unknown.

Clinical Significance

An important issue is whether PEH is simply an interesting short-term physiological phenomenon or might be an important factor in the blood pressure–lowering effect of chronic exercise. To contribute to the sustained lowering of arterial blood pressure observed with regular exercise, PEH must be sustained at a sufficient level for a sufficient duration throughout the day. If this were the case, an acute bout of exercise, repeated regularly, might be an important nonpharmacologic tool in the control of hypertension. To determine whether PEH has potential clinical implications, at least three important questions must be answered. First, is the PEH response of sufficient magnitude to be considered clinically significant? Second, is the duration of the hypotensive response sufficient to lower daily mean arterial blood pressure? Third, is the hypotension evoked and sustained under conditions of normal daily living (ie, outside of the laboratory)?

The peak exercise-induced reductions in systolic and diastolic arterial blood pressures calculated in this article, 18 to 20 and 7 to 9 mm Hg, respectively, would likely be considered clinically significant for hypertensive humans. Reductions in arterial blood pressure of approximately the same magnitude are associated with a reduced risk for stroke and certain other forms of cardiovascular disease. Thus, one of the criteria for therapeutic efficacy appears to be satisfied.

On the other hand, although PEH has been consistently documented for 2 to 3 hours, the average duration of the hypotensive response remains to be determined. Many studies have not reported data on the time course for reattainment of control values. One report indicates that PEH may be sustained for at least 13 hours, with diastolic and mean arterial blood pressures still remaining depressed at the end of this period. However, this duration of PEH was not confirmed in a recent investigation (see below). For a single session of exercise, repeated daily, to contribute to a sustained antihypertensive effect, arterial blood pressure would have to remain depressed for most of the subsequent 24 hours after exercise.

Finally, it is well established that the absolute levels and behavior of arterial blood pressure are influenced significantly by the environment in which the measurements are made. In this context, it is important to emphasize that most human investigations have documented PEH only under quiet resting conditions in the laboratory. This is obviously not the case in real life. The question of whether postexercise reductions in arterial blood pressure are sustained for a prolonged period of time under free-living conditions has been addressed in two recent studies.

Somers and colleagues determined the effects of incremental leg cycling exercise to exhaustion on PEH in 12 normotensive and 12 borderline or mildly hypertensive men and women. PEH was documented under resting conditions in the laboratory in both groups. The subjects then were sent home and recorded their own blood pressures for a period of 8 to 12 hours. The same procedure was repeated on a nonexercise control day. The levels of arterial blood pressure recorded at home were not different on the exercise and control days in either the hypertensive or the normotensive subjects, indicating no sustained effect of the acute exercise under normal living conditions.

In marked contrast to these results, Pescatello and colleagues documented a prolonged hypotension after a single bout of submaximal exercise in hypertensive subjects. Six normotensive men and six mildly hypertensive men cycled for 30 minutes at 40% and 70% of peak oxygen uptake. Arterial blood pressure was lower at rest in the laboratory after compared with before exercise in hypertensive but not normotensive men. Blood pressure recorded outside the laboratory with an automated ambulatory monitor for 13 hours remained significantly below preexercise baseline levels in the hypertensive subjects (Fig 3). Moreover, the average levels of arterial blood pressure were significantly lower over this 13-hour period after exercise compared with the same period on a nonexercise control day.

The two most obvious differences between the studies are the methods of outside-the-laboratory blood pressure measurements and the nature of the exercise stimulus. Concerning the latter, it has been reported that chronically performed low- to moderate-intensity exercise has a blood pressure–lowering effect, whereas higher intensity exercise has a lesser effect, no influence, or actually produces a "hypertensive" effect. If true, it is possible that the apparent discrepancies between the results of the above two studies could be explained by this factor.

Thus, the available experimental evidence is equivocal as to whether PEH is sustained for a prolonged period of time under normal living conditions. Additional investigations in which ambulatory arterial blood pressure recordings are performed outside the laboratory for 24 to 48 hours after acute exercise will be needed to answer this question. In these studies, the nature of the exercise stimulus should be carefully controlled; low- to moderate- versus high-intensity exercise should be examined as well as several modes of exercise commonly performed in daily life (eg, leg cycling versus walking or jogging). If arterial blood pressure can be shown to remain depressed for this period of time, one might reasonably conclude that the sustained blood pressure–lowering effects of physical training could, at least in part, be mediated by the hypotensive effects of single bouts of exercise repeated on a regular basis.
Possible Mechanisms Mediating Postexercise Hypotension in Human Subjects for Which There Is Some Experimental Support

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased stroke volume and cardiac output</td>
<td>12</td>
</tr>
<tr>
<td>Decreased limb (skin and/or skeletal muscle) vascular resistance</td>
<td>18,19,22</td>
</tr>
<tr>
<td>Decreased total peripheral resistance</td>
<td>18,19,22,26</td>
</tr>
<tr>
<td>Reduced sympathetic nerve discharge</td>
<td>20,39-41</td>
</tr>
<tr>
<td>Reduced vascular responsiveness to $\alpha$-adrenergic receptor-mediated stimulation</td>
<td>57,58</td>
</tr>
<tr>
<td>Group III muscle afferents</td>
<td>34,38-41</td>
</tr>
<tr>
<td>Modulation of baroreceptor reflex control of vascular resistance</td>
<td>17</td>
</tr>
<tr>
<td>Endogenous opioid and serotonergic systems</td>
<td>16,29,37,40-42</td>
</tr>
</tbody>
</table>

Summary and Conclusions

The experimental findings reviewed here indicate that PEH is observed in normotensive humans, patients with borderline essential hypertension, and patients with established essential hypertension as well as in SHR. PEH occurs in response to several types of large-muscle dynamic exercise (eg, walking, running, cycling, and swimming) at intensities between 40% and 70% of maximal oxygen consumption as well as after exercise to exhaustion. Moreover, PEH is observed after a wide range of exercise durations from as short as 3 to 10 minutes to as long as 60 minutes. Because exercise is associated with activation of somatic afferents, electrical stimulation of the sciatic nerve and of hind limb skeletal muscles in the rat has been used to study the role of somatic afferents in mediating PEH. PSH has been observed in SHR, Wistar-Kyoto normotensive rats, and prehypertensive Dahl salt-sensitive rats.

Postexercise reductions in arterial blood pressure are generally greater in hypertensive compared with normotensive humans and animals. In studies to date, maximal exercise-induced reductions in systolic and diastolic arterial blood pressures have been on average 18 to 20 and 7 to 9 mm Hg, respectively, in hypertensive humans and 8 to 10 and 3 to 5 mm Hg, respectively, in normotensive humans. Similarly, the maximal stimulation- and exercise-induced reductions in arterial blood pressure are generally greater in hypertensive compared with normotensive rats.

Little information is available on the time course for reattainment of postexercise reductions in arterial blood pressure to control levels. The results to date indicate that PEH persists anywhere from 2 to at least 13 hours. The length of the PEH response is generally longer in hypertensive than normotensive humans. To date, the two studies that have addressed the question of whether PEH is sustained for a prolonged period of time under free-living conditions have come to opposite conclusions. No experimentally controlled investigation has determined whether arterial blood pressure remains reduced from control levels for at least 24 hours after exercise.

We have also reviewed potential mechanisms by which exercise and somatic afferent stimulation may induce sustained reductions in arterial blood pressure. Cardiac output has been reported to be decreased from control levels after exercise in older subjects with essential hypertension. The reduction in cardiac output was primarily mediated by a decrease in stroke volume. Neither reductions in cardiac preload nor increases in cardiac afterload could account for the reduced stroke volume, suggesting that alterations in myocardial contractility may contribute to PEH. Sustained decreases in limb (forearm and calf) vascular and total peripheral resistances have been reported more consistently after exercise in normotensive and hypertensive subjects. These observations suggest that a sustained vasodilation in skeletal muscle and other arterial beds may contribute to PEH. Relatedly, reductions in muscle sympathetic nerve discharge have been observed after exercise in hypertensive humans, whereas sympathetic nerve discharge is reduced from control levels after somatic afferent stimulation in SHR and prehypertensive Dahl salt-sensitive rats. The factors involved in mediating the exercise-induced changes in forearm vascular resistance and sympathetic nerve discharge have not been established; however, baroreceptor reflex control of forearm vascular resistance is altered after a single bout of exercise. Moreover, vascular responsiveness to $\alpha$-adrenergic receptor-mediated activation is reduced after exercise.

Somatic afferents are involved in mediating PSH because this response is elicited by electrical stimulation of the cut, central end of the sciatic nerve. Whether muscle afferents contribute to PEH has not been established. However, dynamic exercise and electrical stimulation of somatic afferents are known to produce a number of similar responses, including sustained increases in arterial pressure, heart rate, and sympathetic nerve activity and postcontraction/stimulation reductions in arterial pressure. Several observations support a role for endogenous opioids in mediating PSH. It is thought that sustained somatic afferent stimulation induces activation of central endogenous opioid systems, which in turn produce sympathoinhibition and hypotension. The results of one study have shown that naloxone administration can transiently reverse PEH in normotensive humans. In general, an important role for various humoral, local metabolic, and thermal factors in PEH has not been well established. The Table provides a list of possible mechanisms involved in mediating PEH for which there is current experimental support.

In conclusion, it appears that the magnitude of the PEH response observed in hypertensive subjects is significant and would likely be considered clinically important. However, more investigation is required to determine if the duration of the response is sufficient in real-life conditions...
to contribute to the reduction in arterial blood pressure observed after chronic exercise.

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