ATRIAL NATRIURETIC PEPTIDE AND ITS POSSIBLE ROLE IN POST EXERCISE HYPOTENSION

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DEDICATION

I would like to dedicate this thesis to my grandparents Gerald and Marion MacDonald, who have instilled the old Scottish tradition and morals in me. Their encouragement, concern and love will always be appreciated more than words can say.

And, to Joan Elizabeth Heimbecker, who was tragically taken from us on March 30, 1994. You will always serve as an inspiration of dedication, individuality and courage.

ABSTRACT

The mechanisms which cause post exercise hypotension (a phenomenon of prolonged, decreased resting blood pressure following physical exertion) are unknown. Atrial natriuretic peptide (ANP) is known to exert potent natriuretic and vasodilatory properties which play an integral role in fluid regulation and blood pressure control. Elevations in plasma ANP concentration have been shown to occur during dynamic endurance exercise, and to a lesser extent during heavy resistance exercise. The purposes of this investigation were to 1) examine the effects of resistance and endurance exercise on the release of ANP, 2) examine the effects of resistance and endurance exercise on post exercise blood pressure and 3) evaluate the potential correlations of ANP release with any observed changes. Thirteen males (24.3±2.4yrs.) performed 15 min of unilateral leg press (65% 1RM) and, one week later ~15 min (based on summed cardiac cycles of the resistance trial) of cycle ergometry (65% $\dot{V}O_{2\ Peak}$). Blood pressure was measured using an intra-arterial catheter during exercise and for 1 h post exercise. Arterial blood was drawn at rest, 5, 10 and 15 min of exercise and 1½, 3, 5, 10, 15, 30, 45 and 60 min post exercise for subsequent analysis of hematocrit and αANP. No differences occurred in blood pressure responses between trials, but significant decrements in blood pressure occurred post exercise compared to pre exercise. Systolic pressure was ~20

mmHg lower from 10 min post exercise until measurements terminated at 60 min post exercise. Mean pressure was also significantly attenuated by ~7 mmHg from 30 min post exercise onwards. Only slight (non significant) elevations in αANP concentration were detected immediately following exercise with no elevation present by 5 min post exercise. It was concluded that post exercise hypotension occurs with acute bouts of either resistance or endurance exercise and that αANP does not appear to be directly related to this hypotensive effect.

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PREFACE

The following is a list of abbreviations and operational definitions used throughout this manuscript:

2D - two dimensional
ANF - atrial natriuretic factor
ANH - atrial natriuretic hormone
ANP - atrial natriuretic peptide
AV - atrial volume
BL - baseline
CO_2 - carbon dioxide
D - during
DBP - diastolic blood pressure
$\overline{DBP}$ - average diastolic blood pressure
EDV - left ventricular end diastolic volume
EF - ejection fraction
ESV - left ventricular end systolic volume
h - hours
HR - heart rate
HSD - honestly significant difference
MAP - mean arterial pressure
Mhz - megahertz
O_2 - oxygen
P - post
PEH - post exercise hypotension
PSBP - peak systolic blood pressure
$\dot{Q}c$ - cardiac output
RM - repetition maximum
RPM - revolutions per minute
RPP - rate pressure product
s - seconds
SBP - systolic blood pressure
$\overline{SBP}$ - average systolic blood pressure
SD - standard deviation
SEM - standard error of the mean
SV - stroke volume
TPR - total peripheral resistance
TSBP - trough systolic blood pressure
$\dot{V}O_{2\ Peak}$ - maximal oxygen consumption reached during cycle ergometry

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1.0 REVIEW OF LITERATURE

1.1 INTRODUCTION

The discovery of a "new hormone" - Atrial Natriuretic Peptide, with natriuretic and vasodilatory properties and the finding that physical exercise can acutely reduce post exercise arterial blood pressure are two exciting new discoveries in the field of exercise physiology. Although considerable data exist describing both atrial natriuretic peptide (ANP) and post exercise hypotension (PEH), little is known about the underlying and causative mechanisms of each. The possibility exists that the apparent hypotension after exercise may be mediated, at least in part, by ANP. The following review will address each topic independently and subsequently discuss the potential link between them.

1.2 ATRIAL NATRIURETIC PEPTIDE

1.2.1 INTRODUCTION

In 1981, deBold found a noticeable increase in renal excretion of sodium and urine in rats injected with extracts of rat atria. Since injections of ventricular extracts were found to cause no change in any of the measured variables, he coined the term Atrial Natriuretic Factor (ANF) for this extract (deBold, 1981). This compound has since been called Atrial Natriuretic Hormone (ANH) (Bates et al., 1986), Atrial

Natriuretic Peptide (ANP) (Wilkins et al., 1986; Brooks et al., 1990; MacDonald et al., 1995), Cardionatrin (Needleman et al., 1989) and Atriopeptin (Perrault et al., 1991, 1992).

In humans, resting concentrations of ANP approximate 9-75 $pg \cdot ml^{-1}$ (Goetz, 1988) and little fluctuation is observed during waking hours. There does, however, appear to be a diurnal rhythm, with the greatest concentration occurring at approximately 4 am. Dog and rodent concentrations of circulating ANP are higher than those of humans. It has been quantified in the dog that for each 1 Torr increase in atrial pressure, plasma ANP increases by ~10-15 $pmol \cdot L^{-1}$ (30-45 $pg \cdot ml^{-}$) (Goetz, 1988). No such correlation has been performed in humans.

1.2.2 BIOCHEMICAL STRUCTURE AND PROPERTIES

Within 3 years of its discovery, extraction, purification and identification were undertaken. As shown in figure 1, human atrial natriuretic factor is now known to be a C-terminus, 28 amino acid peptide with a cysteine to cysteine disulfide bridge forming a 17 amino acid ring (deBold, 1985).

Source ANP is produced primarily in the atria in a prepro form containing 151 amino acids, and is quickly converted to the 126 amino acid pro form and subsequently stored in specific membrane bound atrial granules. Limited research indicates that minute quantities may also be produced in the central nervous system

and the kidney (Goetz, 1988). Recent evidence by Baker et al. (1991) has indicated that 2 peptides at the N-terminus of the pro form (numbers 1 - 30 and 31 - 67) may

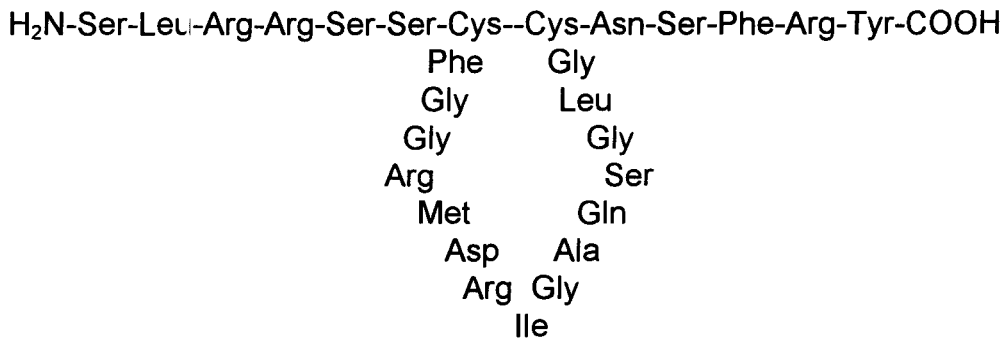


Figure 1. The structure of circulating ANP.

play a smaller but more prolonged role in vasodilation and natriuresis. Upon release from the atrial granules in response to atrial distension or pressure, the pro form is cleaved by an unknown enzyme contained in the myocardium (Yandle, 1994; Needleman et al., 1989).

Degradation The degradation of ANP is very rapid, as indicated by a half life of 2-3 min (Yandle et al., 1986). Clearance of ANP appears to occur by at least 2 separate mechanisms. At the brush border of the microvillar membranes of the kidney, and on vascular smooth muscle cells, the enzyme endopeptidase 24.11 cleaves ANP between the Cys-Phe and Ser-Phe residues to yield inactive products (Yandle, 1994; Michel & Arnal, 1990). It is interesting to note that endopeptidase 24.11 also acts on other vasoactive hormones such as angiotensin (I & II), bradykinin and endothelin (Yandle, 1994). Additionally, receptors have been identified which aid in

the metabolism of all natriuretic peptides. These 3 receptors have been identified and labelled natriuretic peptide receptors A (NPR-A), B (NPR-B) and C (NPR-C). It is known that both the NPR-A and NPR-B receptors possess an extracellular peptide binding domain for ANP attachment. Internally, there appears to be a protein kinase-like domain as well as a guanylate cyclase domain (Yandle, 1994). Although the protein kinase-like domain serves a purpose which has yet to be determined, Guyton and Hall (1996) state that when any hormone attaches to a receptor on the enzyme guanylate cyclase (located in the membrane), this results in the formation of cyclic guanosine monophosphate (cGMP) inside the cell. This cGMP, in turn, alters the degree of phosphorylation of several enzymes, thus inhibiting contraction of smooth muscle. The NPR-C receptor has been termed the "clearance" receptor (Smyth & Keenan, 1994) and functions only to degrade ANP, as opposed to exhibiting any vasodilatory properties. Yandle (1994) suggests that this receptor binds all natriuretic peptides, after which they are internalized and delivered to the lysosomes for degradation. The receptor itself is then recycled to continue the process. The actual amount of ANP cleared through this mechanism is, as yet, undetermined (Smyth & Keenan, 1994).

It has also been suggested (Muller et al., 1992) that insulin degrading enzyme has the ability to cleave ANP and thus render it inactive. Although this finding was observed in rats, it is plausible that this may also occur in humans since the cleavage occurs at the Ser-Phe bond which is present in the ANP sequence of

both species. This enzyme has similar degradation characteristics to the endopeptidase activity previously described (Muller et al., 1992).

1.2.3 MECHANISMS OF ACTION

Release Secretion of ANP from the atrial granules is thought to occur in response to several different stimuli. An elevated heart rate (or tachycardia) has been suggested as a release factor. This hypothesis arose from the observation that both ANP concentrations and heart rate increase with exercise, but evidence that heart rate *per se* is the stimulus is controversial. Bates et al. (1986) indicated that among other variables, heart rate was a single independent predictor of ANP concentration. Similarly, Fyhrquist et al. (1987) and Saito et al. (1987) found significant correlations of 0.96 and 0.73 respectively, between heart rate and circulating ANP concentrations. In the study by Saito et al. (1987), this correlation was the strongest of several measured variables. Additional evidence arises from cardiac arrhythmia patients where artificial atrial pacing has been found to increase circulating ANP (Espiner et al., 1986). In contrast, when heart rate is depressed through cardiac β-receptor blockade increases in ANP concentrations were also found to be exaggerated (Berlin et al., 1993a, 1993b; Tsai et al., 1990; Bouissou et al., 1990; Deray et al., 1990) during rest and during exercise despite a decreased heart rate in each condition.

In a study which combined bi-plane echocardiographic imaging with β-blockade, Berlin et al. (1993a) found that atrial dimensions were increased compared to the normal condition, presumably due to the increased filling time and decreased contractility. This lends support to the most widely accepted secretory stimulus for ANP - atrial distension. In order to assess the effects of atrial distension on ANP release, many techniques have been used. Non exercise measures have employed balloon catheterization of the atria (Edwards et al., 1988), water immersion (Asai et al., 1994; Vita et al., 1989; Orlandini et al., 1987), pharmacological (Anderson et al., 1986) and pathological (Wilkins et al., 1986) blood volume expansion and the supine posture (Fyhrquist et al., 1987; Ogihari et al., 1986). Each of these techniques augments venous return to the heart and thus causes increased atrial distension. The atrial distension caused by these methods significantly elevates circulating ANP concentrations approximately proportional to the increased volume load on the heart.

Other possible causes for the release of ANP remain somewhat controversial. Indirect evidence of a linkage between exaggerated sodium intake and plasma ANP concentrations can be found in studies where sodium has been depleted (Richards et al., 1987) or augmented (Cuneo et al., 1988). Pathologically, conditions of pulmonary hypertension (Haass et al., 1988; Adnot et al., 1987; Matsubara et al., 1987; Bates et al., 1986; Raine et al., 1986) and activation of chemoreceptors in the carotid sinus in response to low PO_2 levels (Milledge, 1992;

Lawrence & Shenker, 1991) have been implicated in increasing the concentration of circulating ANP. Atrial distension, however, is the only factor which appears to be widely accepted as a definitive stimulus for the secretion of ANP.

Effects As shown in figure 2, the most prominent effects of ANP are potent vasodilation (Atlas & Laragh, 1986), decreased renin-angiotensin activity (Asai et al., 1994; DePaoli et al., 1991), decreased aldosterone activity (Lawrence & Shenker, 1991), vasopressin release inhibition (Cantin & Genest, 1987) and a fluid shift to increase extravascular fluid (independent of urine output). These factors, in turn, lead to a decrease in blood pressure (Asai et al., 1994) heart rate, cardiac

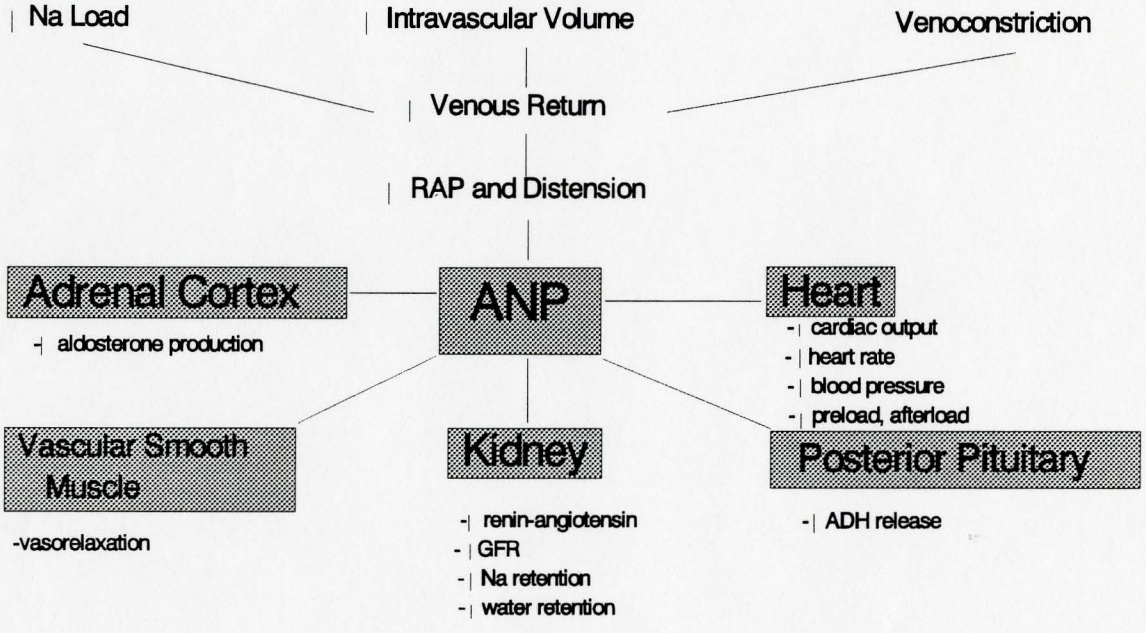


Figure 2. The effects of ANP on physiologic measures (Adapted from Birney & Penney, 1990).

output, preload and afterload (Saito et al., 1987). Pharmacological doses of ANP have been shown to stimulate the glomerular filtration rate to cause natriuresis and diuresis (Espiner et al., 1986; deBold, 1981). Controversy exists as to whether physiological levels elicit the same renal effects since 3 to 5 fold increases in circulating ANP have been shown to produce a delayed and only modest natriuretic response, and at times, none at all (Chan et al., 1994; DePaoli et al., 1991).

It has been reported that a prolonged hypotensive response to ANP secretion persists long after the 2-3 min half life (Davis, 1989) of the hormone. To date, this phenomenon is attributed to an unidentified effect of ANP on the central nervous system.

1.2.4 EXERCISE AND ANP

It is generally accepted that endurance exercise elicits increases in ANP secretion which are somewhat proportional to the relative exercise intensity and duration. Limited, and contradictory research, also indicates that trained subjects may display attenuated secretion levels at equivalent relative intensities (despite elevated resting concentrations) when compared to non-trained controls (Rogers et al., 1991; Vollmer-Larson et al., 1989). Conversely, Freund and colleagues (1988, 1987) have found no differences between the trained and the untrained population.

Intensity It appears as though the intensity of the exercise dictates the magnitude of the ANP secretion, with greater intensities eliciting greater ANP concentrations (Freund et al., 1991; Tanaka et al., 1986). Although little systematic work has been

done comparing the response to different exercise intensities, there is some evidence to suggest that a plateau may develop at some point prior to maximal exercise (Tanaka et al., 1986). Plasma elevations have been observed with intensities ranging from 25% of peak exercise (Freund et al., 1991) to maximal exercise (i.e. Goodman et al., 1993; Mannix et al., 1990; Richards et al., 1987). Freund et al. (1991) indicated a trend of increasing ANP levels from rest, to 1.6 fold at 25% of $\dot{V}O_{2\ Peak}$, and to a 7 fold expansion at 80% of $\dot{V}O_{2\ Peak}$.

Duration Few studies have examined the effects of exercise duration on ANP secretion, and combined results are difficult to interpret. Perrault et al. (1991) indicated that, during 90 min of cycle ergometry at 67% of $\dot{V}O_{2\ Peak}$, ANP concentrations rose during the initial 30 min of exercise, after which a plateau occurred. However, Goodman et al. (1993) found that over a bout of 150 min of exercise at 70-74% of maximal heart rate, subjects encountered substantial elevations of ANP at 50 min (+104%) with a decrement at 100 min (+89%) before increasing again to 150% at the cessation of exercise. It is also interesting to note that the greatest elevations (+207%) were found 3 min post exercise. It is possible that more frequent sampling may have detected this heightened response during exercise.

Mode There is a great lack of information dealing with exercise other than endurance exercise. Short term, high intensity exercise (10 x 6 s sprints with 30 s recovery) has been shown to increase concentrations of ANP at the cessation of the

exercise session (Brooks et al., 1990), but these increases were minimal compared to those normally found with endurance exercise.

In an attempt to find a link between arterial blood pressure and ANP release, MacDonald et al. (1995) used resistance exercise as the stimulus. Subjects performed 5 sets of 10 repetitions at 80% 1 repetition maximum (RM) on a leg press apparatus. Blood was drawn at rest, 2.5 minutes after sets 1 and 3 and 1, 3, 5, 10, 15, 30, 45 and 60 min after set 5, from the antecubetal vein. Blood pressure was approximately 169/93 mmHg immediately following exercise and remained elevated until approximately 10.5 min post exercise. Plasma concentrations of ANP increased significantly ($p=0.007$) from a pre-exercise value of 11.5, to 18.6 $pg \cdot ml^{-1}$ at 5 min post exercise. This 5 min value was also significantly elevated above concentrations observed after set 1 and 1, 10 and 45 min post exercise. These findings suggest that since little cardiac volume overload occurs during such exercise (Lentini et al., 1993) the large elevations in arterial blood pressure which occur (MacDougall et al., 1985) may also be a stimulus for ANP release. Further work in this area is warranted in order to adequately examine the causes of ANP secretion during different forms of exercise.

1.3 POST EXERCISE HYPOTENSION

1.3.1 INTRODUCTION

The term post exercise hypotension (PEH) has been used to describe the transient decrease in blood pressure observed by many investigators during recovery from acute exercise. Although there have been a number of descriptive studies of this phenomenon, little is known about possible underlying mechanisms.

Anecdotally, the first well documented observation of post-exercise hypotension was made by Fitzgerald (1981) in which 4-year records were presented. These indicated the pronounced effect of exercise on the lowering of his own labile hypertension. Fitzgerald (1981) also suggested that many hypertensive airline pilots avoid suspension by performing aerobic exercise shortly before their medical examination in order to decrease their blood pressure. Since that time, well controlled studies of PEH have been very limited and often present contradictory findings. This review will attempt to summarize the current state of knowledge regarding post-exercise hypotension.

1.3.2 SUBJECT POPULATION

Normotensive vs. Hypertensive Subjects A number of studies have established that PEH occurs in individuals with borderline (Boone et al., 1993; Somers et al., 1991, 1985; Floras et al., 1989;) and established hypertension (Floras & Wesche 1992; Pescatello et al., 1991; Hagberg et al., 1987; Wilcox et al., 1987, 1982; Bennett et al., 1984; Webster et al., 1980). The phenomenon appears less pronounced in normotensive subjects. Floras, in 1991 with Senn, and again in 1992 with Wesche, found no evidence of PEH in normotensive humans after 45 min of treadmill exercise at 70% of resting heart rate reserve. Pescatello et al. (1991) suggested that normotensives actually exhibit an elevated systolic blood pressure for 12.7 h after exercise. No change in the diastolic or mean blood pressure was found over this time period. Conversely, Hara and Floras (1992), using the same protocol as Floras and colleagues (1992, 1991) found significant reductions in blood pressure in their normotensive population. Also, Brown et al. (1994), Boone et al. (1992), Landry et al. (1992) and Convertino and Adams (1991), using cycle ergometry at various power outputs between 60 and 100% $\dot{V}O_{2\,Peak}$, found a significant decrement in post-exercise blood pressure. Bennett et al. (1984), using intermittent exercise, also detected PEH in normotensive males. However, 5 sessions of 10 min of treadmill exercise (with 3 min rest between each) were needed to elicit it, whereas hypertensive subjects required only a single session.

Gender Post-exercise hypotension has been found to occur in both males (Cable et al., 1994; Hara and Floras, 1992; Boone et al., 1992; Cléroux et al., 1992; Pescatello et al, 1991; Somers et al., 1991; Coats et al., 1989; Floras et al., 1989; Seals et al., 1988; Hagberg et al., 1987; Kaufman et al., 1987; Wilcox et al., 1987; Bennett et al., 1984; Wilcox et al., 1982; Fitzgerald, 1981; Hannum et al., 1981) and females (Mooney & Unnithan, personal communication; Cléroux et al., 1992a, 1992b; Coats et al., 1989; Hagberg et al., 1987, Somers et al., 1985; Paulev et al., 1984). It has recently been observed by Mooney and Unnithan (personal communication), that highly trained, normotensive females displayed PEH whereas their normotensive sedentary controls did not. This further supports a lack of gender specificity.

Species There has also been substantial evidence to suggest that post-exercise hypotension is not confined to humans since various researchers have encountered hypotension following treadmill exercise and/or electrical stimulation in normotensive (Yao et al., 1982a) and spontaneously hypertensive rats (Boone et al., 1995; Collins & DeCarlo, 1993; Tipton et al., 1991; Hoffman et al., 1990, 1988; Overton et al., 1988; Shyu et al., 1986, 1984; Yao et al., 1982a, 1982b).

1.3.3 EXERCISE STIMULUS

Endurance Exercise The majority of studies of PEH have utilized submaximal cycle ergometry exercise protocols, at intensities varying between 40 and 100% of $\dot{V}O_{2\ Peak}$ (Piepoli et al., 1994, 1993; Franklin et al., 1993; Boone et al., 1992; Pescatello et al., 1991; Somers, et al., 1991; Coats et al., 1989; Urata et al., 1987). A number of researchers have also used treadmill running as the exercise stimulus, using protocols eliciting 70% of resting heart rate reserve (Floras & Wesche, 1992; Floras & Senn, 1991; Floras et al., 1989), 75% $\dot{V}O_{2\ Max}$ (Cable et al., 1995). Both modes of exercise require dynamic contractions and a large active muscle mass.

Resistance Exercise As reviewed by MacDougall (1994), during endurance exercise, systolic blood pressure increases almost linearly with the exercise intensity. It has, therefore, been suggested that it is the increase in blood pressure during exercise which alters baroreceptor activity both during and post exercise (Convertino et al., 1991). If this hypothesis is correct, resistance exercise, which evokes the greatest pressor responses, should also provoke PEH since the upward setting of the pressure receptors during exercise may endure for some time post exercise. Data supporting this are still somewhat inconclusive. Brown et al. (1994) indicated that PEH occurred after 3 sets of arm curls, hamstring curls, squats, lateral pull-downs and bench press at both 40 and 70% of 1RM values (20-25 reps @ 40%; 8-10 reps @ 70%). Nevertheless,

they also noted that the PEH response to the resistance exercise did not differ from that produced by the endurance exercise, suggesting that the magnitude of the pressor response was not responsible for the PEH. O'Connor et al. (1993) observed minimal elevations in both systolic and diastolic blood pressure immediately following 30 min of whole body resistance exercise, with a return towards resting levels during the 2 h recovery period. This further supports the idea that the magnitude of the pressor response plays little or no role in mediating PEH. Additional work using resistance exercise by Hill and colleagues (1989) indicated that both systolic and diastolic blood pressure were significantly reduced immediately following a bout of resistance exercise, and approached resting levels throughout the remainder of the 60 min post exercise measurement period. This sudden decrement in pressure immediately after heavy resistance exercise concurs with the observations of MacDougall et al. (1985), and can be attributed to the sudden perfusion of the previously occluded muscle mass and a transient pressure undershoot. Because of its brevity (8-12 s), this pressure undershoot is most likely the result of baroreceptor and cardiopulmonary reflex action in response to the extreme pressures achieved during the resistance exercise (MacDougall et al., 1985) and is not the same phenomenon as true PEH.

Electrical Stimulation Electrical stimulation of skeletal muscle has also been used in the rat to investigate its effect on PEH. Sciatic nerve stimulation, varying

in intensity from 4 to 25 times the minimum current intensity required for eliciting a twitch, has been shown to result in PEH (Hoffman & Thoren, 1986; Shyu et al., 1984; Yao et al., 1982a, 1982b, 1981). Similarly, Hoffman et al. (1990) and Hoffman and Thoren (1988) have used electrically-induced contractions of the biceps femoris and the gastrocnemius muscles to induce PEH in rats.

It is, therefore, apparent that different exercise types and intensities can elicit the PEH phenomenon.

1.3.4 MAGNITUDE OF RESPONSE

Normotensive vs. Hypertensive Subjects Evidence suggests that the magnitude of the PEH response is dependent upon the individual's baseline blood pressure status. In studies of borderline hypertensive subjects (Boone et al., 1993; Somers et al., 1991, 1985; Floras et al., 1989), an average decrease in systolic pressure of 12 mmHg was observed, with a peak decline of 18 mmHg (Somers et al., 1991). Decrements in diastolic pressure varied from a maximal value of 14 mmHg (Somers et al., 1991) to negligible results (Boone et al., 1993; Floras et al., 1989). Individuals with essential hypertension displayed an average drop in post exercise pressure of 21 mmHg and 11.7 mmHg for SBP and DBP, respectively (Floras & Wesche, 1992; Pescatello et al., 1991; Hagberg et al., 1987; Bennett et al., 1984; Wilcox et al., 1982), with peak reductions being 40 mmHg for SBP (Bennett et al., 1984; Wilcox et al., 1982) and 15 mmHg for DBP (Bennett et al., 1984). Unfortunately, a standardized measurement protocol

has not been used across studies, and resting posture has not always been controlled. In hypertensive subjects, Bennett et al. (1984) noted a PEH difference of 15/6 mmHg (in systolic/diastolic pressure) between the sitting and standing postures with the seated position eliciting the greater decrement in pressure. The response of normotensives who exhibited PEH was somewhat attenuated and averaged 8.6 mmHg and 7.9 mmHg for SBP and DBP, respectively (Boone et al., 1992; Hara & Floras, 1992; Coats et al., 1989; Kaufman et al., 1987; Bennett et al., 1984; Wilcox et al., 1982; Hannum & Kasch, 1981).

Studies in rats suggest that spontaneously hypertensive rats (SHR) exhibit a greater magnitude of PEH than their normotensive counterparts. Following exercise or electrical stimulation, the average decrement in mean arterial pressure (MAP) in the SHR was approximately 21 mmHg (Boone et al., 1995; Collins & DeCarlo, 1993; Overton et al., 1988; Hoffman et al., 1988; Shyu et al., 1986, 1984; Yao et al., 1982a, 1982b;) whereas the normotensive rats showed a decrease of only 8 mmHg (Yao et al., 1982).

1.3.5 TIME COURSE FOR PEH

There are conflicting reports regarding the time point following exercise where blood pressure drops below normal and the length of time that this lower pressure persists. It also appears that this may vary with the subject population.

Onset It is generally accepted that in both hypertensive and normotensive individuals, PEH does not manifest itself immediately following exercise. Although some investigators have reported lower than baseline blood pressures as early as 2-5 min (Piepoli et al. 1994; Piepoli et al., 1993) or 6 min (Boone et al., 1993) following exercise, most studies indicate that PEH is not evident until some time point between 30 min and 1 h post exertion (Franklin et al., 1993; Floras & Wesche, 1993; Somers et al., 1991; Pescatello et al., 1991; Overton et al., 1988; Fitzgerald, 1981). The time course for PEH in rodents may be different from that in humans in that the hypotensive effect may occur much closer to the cessation of exercise. Both Collins and DeCarlo (1993) and Hoffman and Thoren (1988) indicated that a drop in blood pressure is apparent immediately following active treadmill running (Collins & DeCarlo, 1993) and evoked stimulation (Hoffman & Thoren, 1988) in rats.

Duration Very little information is available as to the duration of PEH since the majority of studies have terminated measurements at a pre-defined time point. In the longest reported post-exercise period to date, Pescatello et al. (1991) have shown that diastolic and mean pressures were still depressed in hypertensive patients when measurements were terminated 12.7 h after 30 min

of cycling at 40 or 70 percent of $\dot{V}O_{2\,Peak}$. Similarly, Piepoli et al. (1994, 1993), Boone et al. (1993), Franklin et al. (1993), Cléroux et al. (1992), Coats et al. (1989) and Somers et al. (1985) found sustained reductions in blood pressure at the termination of measurement 30 - 180 min post exercise. In one study (Hagberg et al., 1987) systolic blood pressure returned to resting values after 2 h of a 3 h protocol, and diastolic pressure was back to normal after ~75 min. According to Somers et al. (1991), post exercise hypotension is not sustained in either normal or hypertensive individuals since a significant decrement in pressure was only found between 30 and 60 min post exercise during a 12 h measurement protocol. Unfortunately, this study was confounded by the fact that, at the cessation of the first hour of measurement, subjects were sent home to monitor their own blood pressure, with a different measuring apparatus from that used during the initial hour. Additionally, Floras and Wesche (1992) and Mooney and Unnithan (personal communication), reported only one time point indicating PEH. The limitation of these studies was the failure to monitor pressure for an extended period, since actual PEH, or a trend, was still evident at the cessation of measurement.

From these results, it may be concluded that PEH may persist anywhere from approximately 1 to 13 h, with hypertensives generally exhibiting a longer response than normotensives.

1.3.6 MEASUREMENT TECHNIQUES

The inconsistencies in the literature on PEH may, to a large extent, be attributable to the methods used for measuring blood pressure. Virtually all studies which have examined PEH have used auscultation in conjunction with either manual or automated sphygmomanometry methods (i.e. Piepoli et al., 1994, 1993; Floras & Senn, 1991; Somers et al., 1991; Floras & Senn, 1991; Floras et al., 1989; Kaufman et al., 1987). Auscultation may result in an underestimation of up to 13% for systolic blood pressure in both the resting and exercising conditions (Wiecek et al., 1990; Robinson et al., 1988; Holland & Hummerfelt, 1964). It is also known that blood pressure recordings vary with the respiration cycle, increasing during inspiration and decreasing during expiration. The magnitude of these variations will depend upon the inspired volume. Additionally, discrepancies between direct and indirect pressure monitoring are apt to be greater after exercise, since heart rate may be elevated (i.e. Piepoli et al., 1994; Hagberg et al., 1987), thus allowing for less time between beats to obtain a measurement. Minimal, but nevertheless significant reductions in post exercise blood pressure might go undetected.

1.3.7 POSSIBLE MECHANISMS FOR PEH

Cardiac Output vs. Total Peripheral Resistance Mean arterial pressure (MAP) is a direct function of cardiac output ($\dot{Q}c$) and total peripheral resistance

(TPR) and can be described in the equation: MAP = $\dot{Q}c$ x TPR. Therefore, a change in blood pressure must be mediated by a change in one or both of these variables. As with many aspects of PEH, the results of investigations of possible causative mechanisms are inconsistent and contradictory. Using non-invasive techniques to assess changes in cardiac output, (i.e. aortic Doppler), a number of researchers have attempted to evaluate the relationship between $\dot{Q}c$ and TPR. Hagberg et al., in 1987, found that during PEH, cardiac output was lower than normal due to a decrease in stroke volume (SV) (heart rate (HR) was also lower than normal or unchanged). Since a decrease in plasma volume could not entirely account for this alteration in SV, changes in venous return or contractility were hypothesized to be responsible. Floras and Wesche (1992) concurred with these findings and found similar results in young hypertensive adults. In contrast, Piepoli et al. (1994, 1993) and Cléroux et al. (1992), demonstrated that PEH occurred in spite of increases in cardiac output resulting from persistent tachycardia after exercise, so a decrease in TPR was most likely responsible for the effect.

The decrease in TPR has been supported by others using regional assessment of blood flow and/or vascular resistance. The work of Cléroux et al. (1992b) and Coats et al. (1989) are in agreement with those findings illustrating decreased total peripheral resistance. Both of these studies indicated a decrease in forearm vascular resistance post exercise. These changes were

apparently not related to a thermoregulatory effect, since the post exercise measurements in forearm vascular resistance differed from baseline, but not from the other post exercise measurements until the cessation of recording (60 and 90 min respectively). At these time points, it was assumed that body temperature had returned to basal levels. It should be noted that in both of these investigations, the exercising muscle mass was in the lower body, whereas the vascular resistance measurements were made in the upper body, thus indicating that the vasodilatory effects may occur throughout the body.

Work by Overton et al. (1988), using the rodent model, contradicts the hypothesis of TPR mediated PEH and supports the hypothesis that a decrement in $\dot{Q}c$ is responsible for PEH, since no change was found in regional vascular resistance of the mesenteric, renal or iliac arteries. Additionally, a significantly lower heart rate was observed in the rats following exercise.

Opioids Although inconclusive, it has been postulated that endogenous opioids may have an effect on the cardiovascular system and that their increase during and following exercise might inhibit sympathetic activity. Naloxone, an opioid receptor antagonist, has recently been used as an inhibitor of β-endorphins and other opioids. Boone et al. (1995), has indicated a reversal of the PEH effect in rats via inhibition by naloxone. However, Hara and Floras (1992), using the human model, failed to find such a reversal of PEH through naloxone inhibition.

Hormones There is also little evidence that PEH may be hormonally mediated. A review of the current literature dealing with ANP release and exercise reveals that although its concentration has returned to resting levels before the appearance of PEH, the long lasting effect of ANP on the CNS may still mediate PEH. PEH has been observed independent of plasma catacholamine concentrations. Epinephrine concentrations have been reported to be increased (Cléroux et al., 1992) or unchanged (Wilcox et al., 1987), and norepinephrine levels have been shown to be increased (Paulev et al., 1984), decreased (Cléroux et al., 1992) or unchanged (Wilcox et al., 1987) during PEH.

Potassium Since potassium also exerts a dilatory effect on vascular smooth muscle, elevations following exercise could theoretically be linked to decreased peripheral resistance. Potassium is released by tissue in response to low oxygen concentration. After release, it is then believed to diffuse back to the precapillary sphincters, the metarterioles and arterioles to have vasodilatory effects (Guyton & Hall, 1996). During exercise, plasma potassium concentration has been shown to increase significantly. This increase is proportional to the exercise intensity (Medbo & Sejersted, 1990), but is short lived and is often found to undershoot basal levels within minutes of recovery (Hallen et al., 1994; Medbo & Sejersted, 1990). Unfortunately, the majority of studies failed to measure potassium concentrations after a trend towards baseline was observed. Only 2 studies to date have examined potassium concentrations when the PEH phenomenon was exhibited. Again, contradictory results arose since levels were

either increased (Wilcox et al., 1987) or unchanged (Paulev et al., 1984). The effects of potassium require further extensive examination.

It is evident that a distinctive mechanism has yet to be found to account for PEH. In those studies that do exist, a lack of standardized methods and measurements have probably contributed to the uncertainty that exists. It is also apparent that much more work is warranted to deduce the mechanisms of PEH.

Post exercise hypotension may have important clinical implications. The heightened response by hypertensive individuals may allow for exercise to be used as a non-pharmacological intervention to treat their condition.

Since PEH occurs following a variety of exercise types, intensities and durations, a brisk walk could seemingly evoke PEH. This, coupled with the fact that PEH may persist for up to 13 h and beyond, could lead to the recommendation that those individuals suffering from hypertension should partake in light to moderate exercise for short periods of time (15 to 30 min) at evenly spaced intervals during the day. Despite these initial findings, much work is warranted in order to better understand the occurrence of PEH and to elucidate the mechanisms involved.

1.4 SUMMARY

ANP The previous review has indicated that ANP is a hormone released from atrial myocytes in response to atrial distension. Limited evidence also indicates that ANP may be released in response to increased heart rate, increased blood pressure, elevated Na^+ intake, pulmonary hypertension and a decreased PO_2. ANP affects various body centres in the following manner:

a) aldosterone production is suppressed in the adrenal cortex

b) there is a vasorelaxation of smooth muscle

c) kidney function is regulated by:

decreasing renin - angiotensin activity

increasing GFR

decreasing Na^+ retention

decreasing H_2O retention

d) suppressed vasopressin release of the posterior pituitary

These factors lead to changes in cardiac performance by decreasing cardiac output, heart rate, blood pressure and cardiac preload and afterload.

ANP is degraded very rapidly (2-3 min) by two separate mechanisms. Endopeptidase 24.11 cleaves ANP, rendering it inactive. Also, specific natriuretic peptide receptors (NPRs) degrade ANP through lysosomal activity.

PEH. It has been shown to occur in both normotensive and hypertensive humans and rats. Although contradictory reports exist, PEH may be more predominant in the hypertensive population.

It has been documented that PEH occurs after both resistance and endurance exercise at relative intensities between 40 and 100 percent of maximum. In humans, the onset of PEH occurs between 30 min and 1 h post exertion and may persist for up to 13 hours or more.

Contradictory reports have failed to elucidate an accepted cause of PEH. Suggested mechanisms include decreased catacholamine concentration, increased endogenous opioids and potassium concentrations, all of which may influence either cardiac output or total peripheral resistance.

1.5 Purpose

The purpose of this study was three fold.

Purpose A Initially, this investigation attempted to evaluate the stimulus for the secretion of ANP during exercise. A number of studies have shown an increase in circulating ANP with endurance exercise (Perrault et al., 1994, 1991; Goodman et al., 1993; Freund et al., 1988) suggesting that this response is most likely due to increased atrial distension associated with the enhanced venous return. In theory, supine body position will cause greater venous return to the heart, resulting in greater atrial distension and thus, elevated concentrations of ANP. Although this is a legitimate hypothesis, Bussieres-Chaffe et al. (1994) and Ray et al. (1990), found significantly elevated (75% and 66% respectively) concentrations of ANP at peak exercise in the supine position compared to upright. Perrault et al. (1991), also observed this trend. According to both

Steingart et al. (1984), and Poliner et al. (1980), using radionuclide ventriculography, resting stroke volume is significantly increased in the supine position. This increase is, however, negligible during supine cycle ergometry at power outputs above 25 watts (including peak exercise). This suggests that atrial distension is not the primary mechanism for ANP secretion in this instance. Data from Lentini et al. (1993), indicates that during heavy resistance exercise, end diastolic volumes remain quite constant despite marked increases in blood pressure. Also using this model, MacDonald et al. (1995), have observed significant elevations in ANP, suggesting that blood pressure *per se*, independent of atrial distension may elicit increased ANP secretion.

It was hypothesized that by examining the ANP response to cycle ergometry and heavy resistance exercise, it would be possible to uncouple the effects of a blood pressure, versus volume, load on the heart as a stimulus for ANP release.

Purpose B The second purpose of this study was to evaluate the separate effects of the 2 exercise modalities (endurance and resistance) on PEH. For PEH to have some clinical benefit, it should occur after short duration exercise at an intensity which will not increase the likelihood of cardiovascular complications in hypertensive individuals, yet assist in blood pressure regulation. Most previous studies have focused on moderate volume endurance exercise (Floras & Wesche, 1992; Floras & Senn, 1991; Floras et al., 1989) between 75%

$\dot{V}O_{2\,Max}$ (Cable et al., 1995) and maximal exercise (Fleg & Lakatta, 1986). These intensities may be difficult and even dangerous for those hypertensives who are obese, cardiac patients or elderly. Since it has been shown previously that the hypotensive response to exercise is attenuated in the normotensive population (Brown et al., 1994; Boone et al., 1992, Landry et al., 1992; Convertino and Adams 1991; Pescatello et al., 1991; Hagberg et al., 1987; Bennett et al., 1984; Wilcox et al., 1982), it was felt that if the PEH phenomenon could be exhibited in moderately active, normotensive individuals, the results could be extrapolated to the hypertensive population and thus provide probable clinical significance.

Purpose C The third purpose of this study was to evaluate any link between PEH and ANP levels post exertion. If ANP concentrations remained elevated at the onset of PEH, it seemed plausible that this hormone may be responsible, at least in part, for any observed PEH.

2.0 METHODS

2.1 SUBJECTS

Thirteen recreationally active males aged 24.3±2.4 (mean±SD) years, with a mean height of 175.9±5.0 cm and a mean weight of 74.2±7.9 kg volunteered as subjects for the study. In accordance with the McMaster University Humar Ethics Committee, subjects were advised of the risks associated with the study and provided written informed consent (Appendix B).

2.2 PRELIMINARY TESTING

2.2.1 MAXIMAL OXYGEN UPTAKE ($\dot{V}O_{2\ Peak}$) ASSESSMENT

The maximal oxygen uptake of each subject was determined by an incremental cycle ergometry test to exhaustion. Using an electrically braked cycle ergometer (Erich Jaeger, Hoechberg, Germany), subjects pedalled at a cadence greater than 60 revolutions per minute (RPM). At the completion of each 2 min interval, the power output was increased by 20-60 Watts. Volitional exhaustion was deemed to be the point at which subjects could no longer maintain a pedal cadence of 60 RPM.

Expired gases were collected using one-way air flow valves (Hans Rudolph #2700, Hans Rudolph Inc., Kansas City, Mo.) and analyzed on line via an IBM PS1 computer (International Business Machines, Armonk, NY) using a TurboFit software

package (Vacumetrics, Ventura, Ca.) coupled with an AMETEK S3A/1 oxygen analyzer (Applied Electrochemistry, Pittsburg, Pa.) and a Hewlett Packard 78356A carbon dioxide analyzer (Hewlett Packard, Mississauga, Ont.). Both analyzers were calibrated prior to and following each test using gases of known O_2 (12.10%) and CO_2 (5.10%) content. The highest 1 min, averaged score was deemed to be the maximal oxygen uptake ($\dot{V}O_{2\ Peak}$) and 65% of this was taken as the 65%$\dot{V}O_{2\ Peak}$ value which was the target oxygen consumption during the endurance trial.

2.2.2 DETERMINATION OF THE MAXIMAL UNILATERAL LEG PRESS (1RM)

The maximal unilateral leg press was deemed to be the greatest weight that a subject could lift once with the dominant leg, through the entire range of movement. Determination of this value was accomplished through a progressive incremental protocol on a commercial leg press apparatus (Global Gym, model 3221-168, Global Gym Fitness Equipment Inc., Weston, Ontario) with at least 3 min between attempts. Sixty five percent of this value was termed the 65% 1RM to be used in the resistance exercise trial.

2.3 ECHOCARDIOGRAPHIC MEASUREMENTS

Two subjects underwent echocardiographic assessment during rest and while performing unilateral leg press at 65% of 1RM, and cycle ergometry at 65% of $\dot{V}O_{2\ Peak}$. Echocardiographic measurements were taken using a Pass II

Ultrasound Imaging System (General Electric, model 46-253036G1, Rancho Cordova, California) with a hand-held 2.5 megahertz (MHz) transducer. Two dimensional (2D) echocardiographic images of the apical 4 chamber view from the left apical position in the 8th or 9th intercostal space were recorded on ½ inch videocassette tape, using a Sony VHS 1000 videotape recorder (Sony Corporation, Tokyo, Japan) for subsequent playback and analysis. Selected images were chosen from rest and at times approximating 10 min into exercise. Images were analyzed using a Cineview image analysis system (Freeland, Prism Imaging Inc., Louisville, Colorado). Tracings were made of the right atrium and the left ventricle for determination of atrial volume (AV), end diastolic volume (EDV) and end systolic volume (ESV). Stroke volume (SV) was calculated as the difference between the ESV and the EDV. Ejection fraction (EF) was defined as SV/EDV x 100, expressed as a percentage.

2.4 CONTROL OF DIET

Subjects provided typical 4 day diet records. From these, average daily caloric intake was calculated and pre-packaged diets were designed in order to control for caffeine and sodium intake. Since high protein ingestion has been shown to increase ANP secretion (Tam et al., 1990), subjects were asked to refrain from ingesting animal protein for 3 days prior to consumption of the pre-packaged diet. During the day immediately preceding the test day, and the test

day, subjects consumed the provided diet. The provided diet contained approximately 75% carbohydrate, 20% fat and 5% protein and was low in dietary sodium.

2.5 TEST PROTOCOL

After having fasted for at least 7 h, subjects reported to the laboratory and underwent auscultatory resting blood pressure measurement. Percutaneous injection of ~1.0 ml of localized anaesthetic (Xylocaine®, Astra Pharmaceuticals, Mississauga, Ontario) was administered followed by catheterization of the brachial or radial artery (n=10 brachial, n=3 radial) with a 1½ inch, 20 gauge Angiocath® (Becton Dickenson, Sandy, Utah). This catheter was then attached to a saline-Heparin®(Wyeth-Ayerst, Toronto, Ontario) drip equipped with a Novotrans® pressure transducer (MX 800, Medex Inc., Hilliard, Ohio) for the direct measurement of blood pressure. This transducer was placed at mid-sternal level and coupled to an amplification system (Acudata, model 143, Honeywell Inc., Denver, Colorado) and an on-line data acquisition package (Windaq/200, DataQ Instruments Inc., Akron, Ohio) sampling at a frequency of 300 hertz (Hz). Additionally, an esophageal probe was introduced via the nasal passage and advanced to a level approximating the mid-sternum. This probe was equipped with a Mikro-tip® pressure sensor (Model MPC-500, Millar Instruments Inc., Houston, Texas) for the measurement of intra-esophageal

pressure (which approximates intra-thoracic pressure). The probe was also coupled to the amplification and recording system of the intra-arterial pressure measurements.

Calibration of both pressure monitoring systems was completed using a mercury manometer prior to each trial. The intra-arterial catheter was calibrated to show a linear response between 0 and 300 mmHg. The intra-esophageal probe was linearly calibrated between 0 and 180 mmHg.

Reference electrodes placed in the V5 positions, were affixed to a digital heart rate recorder. This recorder was coupled to a signal triggered counting device (Lafayette Instrument Company, Model 54430, Lafayette, Indiana) for the determination of summed cardiac cycles.

The initial testing session required subjects to complete 15 min of unilateral leg press using commercially available exercise equipment (Global Gym, model 3221-168, Global Gym Fitness Equipment Inc., Weston, Ontario) at 65% of their predetermined 1RM. Timing of the lifting, lowering and lockout phases of the exercise was established using a hand held metronome (Seiko, Tokyo, Japan). The metronome emitted an audible stimulus at a frequency of 1 Hz. Subjects were asked to maintain a cadence of 2 during the lifting phase, 1 during the lockout and 3 during the lowering phase in time with the metronome. During the session, subjects were free to alternate to the contralateral limb as

fatigue occurred. At the cessation of exercise, subjects were asked to remain seated quietly for one hour, for continued monitoring.

Intra-arterial blood and esophageal pressures were monitored continuously throughout the session with 30 s windows saved to disk at rest, 5, 10, and 15 min into exercise and 1½, 3, 5, 10, 15, 30, 45 and 60 min post exercise for later analysis. Arterial blood was sampled approximately 15 s before and after each pressure-monitoring time point. The equi-volume blood samples taken pre and post each pressure-monitoring period were mixed to approximate a single sample taken at each of the time points listed above. The blood was obtained from the arterial catheter site and collected in chilled collection vials which contained EDTA (Vacutainer®, Becton Dickenson, Rutherford, New Jersey). Upon completion of the trial, the blood was centrifuged at 4°C for 30 min. Plasma was then extracted and stored at -50°C for later analysis.

The second testing session occurred one week later with catheterization, pressure, heart cycle monitoring and blood collection procedures being identical to the previous session. This trial required subjects to perform a bout of cycle ergometry at a power output which elicited 65%$\dot{V}O_{2\ Peak}$. Ergometry was performed using an electrically braked cycle ergometer (Erich Jaeger, Hoechberg, West Germany), while maintaining a pedalling cadence greater than 60 RPM. Expired gases were collected using the system described above to

ensure that the target of 65% $\dot{V}O_{2\,Peak}$ was maintained. Collection times for pressures and blood samples in this trial were dependent upon the number of cardiac cycles recorded in the resistance exercise trial (e.g. if during the resistance exercise, blood pressure was taken at 5 min, at which point 800 cardiac cycles had occurred, the aerobic session would collect pressure measurements at a time point corresponding to 800 cardiac cycles). This was employed since ANP release has been shown to be stimulated by atrial distension. This distension is related to the filling of the atria during late diastole. If the hypothesis of a decreased right atrial volume during resistance exercise and increased right atrial volume during endurance exercise (based on observations of the left ventricle by Lentini et al., 1992) is correct, an uncoupling of a pressure load and a volume load on the heart could be achieved by using these 2 different exercise modalities. Since one would expect the total amount of ANP released to be a function of both the magnitude of the load and the duration over which it is imposed, summed cardiac cycles were held constant between the two trials in order to hold the number of diastolic filling times constant. At the cessation of exercise, subjects remained quietly seated as in the initial trial.

To maintain consistency, samples were labelled corresponding to the resistance exercise trial with the following coding: BL, D5, D10, D15, 1:30P, 3P,

5P, 10P, 15P, 30P, 45P, 60P, where BL = baseline, D = during exercise and P = post exercise.

2.6 BLOOD PRESSURE ANALYSIS

Blood pressure waveforms were analyzed using a Windaq data analysis program (DataQ Instruments Inc., Akron, Ohio) and its adjunct programs (Peak/Valley Capture, Integrate and Calculation). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were calculated as the highest point in the waveform and the lowest point in the waveform, respectively. Mean arterial pressure (MAP) was determined as the quotient of the integrated pressure and the duration of the time interval. The rate-pressure product (RPP) was calculated as the product of SBP and heart rate (HR) and divided by 1000. Peak systolic blood pressure (PSBP), trough (or lowest) systolic blood pressure (TSBP), average systolic blood pressure ($\overline{SBP}$), peak diastolic blood pressure (PDBP), trough diastolic blood pressure (TDBP) and mean diastolic blood pressure ($\overline{DBP}$) were calculated from the Peak/Valley Capture program over each time interval (see Appendix E, pg. 128 for graphic representation of peak and trough values).

2.7 BLOOD ANALYSIS

From the whole blood, capillary tubes were filled and subsequently centrifuged (Autocrit®, Becton Dickenson, Franklin, N.J.) for hematocrit

determination in order to calculate possible shifts in plasma volume. The plasma was analyzed for α-human ANP using a commercially available human αANP [^{125}I] radioimmunoassay system (Amersham Chemicals, Oakville, Ont.), which employed a double incubation period. Gamma scintillation was performed using a LKB Gamma Counter (LKB Wallac Oy, Turku, Finland). Concentrations of α-human ANP were determined from plotted standard curves

2.8 SUBSEQUENT TESTING

In order to assess the effects of 75 min of sitting on its own (e.g. without being preceded by exercise) on blood pressure, following the 2 sessions described above, 2 subjects returned to the laboratory for additional testing. Following arterial catheterization, subjects remained seated in an identical manner to the previous 2 trials. Blood pressure and hematocrit were monitored as above for 75 min in order to determine the extent to which possible reductions in plasma volume due to a static seated position could have contributed to the response.

2.9 STATISTICAL ANALYSIS

All statistical analyses described below were completed using the Statistica (Statsoft® Inc.) data analysis program. The Tukey Honestly Significant Difference (HSD) method was used to assess the location of any significant

differences. A probability level of $p \leq 0.05$ was considered statistically significant. All values are expressed as mean $\pm$ standard deviation unless otherwise stated.

2.9.1 PRELIMINARY ECHOCARDIOGRAPHIC DATA

A single 2 factor, repeated measures ANOVA with trial (leg press and cycle ergometry) and time (rest and 10 min of exercise) as the repeated measures was performed on each of the following variables: AV, EDV, ESV, SV and EF.

2.9.2 BLOOD AND PRESSURE DATA

All blood and pressure data were analyzed using single 2 factor repeated measures ANOVAs. Trial (leg press and cycle ergometry) and time (rest, D5, D10, D15, 1:30P, 3P, 5P, 10P, 15P, 30P, 45P and 60P) served as the repeated measures. The variables analyzed were: concentration of αANP, MAP, RPP, HR, PSBP, TSBP, $\overline{SBP}$, PDBP, TDBP and $\overline{DBP}$.

2.9.3 SUBSEQUENT TESTING DATA

The follow-up pressure data completed on 2 subjects were analyzed with a single factor, repeated measures ANOVA with time (as above) as the repeated measure. The variables analyzed were identical to those indicated above.

3.0 RESULTS

3.1 EXERCISE TIME ANALYSIS

Matching the duration of the 2 exercise modes to total cardiac cycles resulted in a finding that exercise time was significantly different ($p=0.0007$) for cycling (13 min, 47 s$\pm$1:10) compared to the resistance exercise (a constant at 15 min, 15 s).

3.2 PLASMA αANP CONCENTRATION ANALYSIS

Because of faulty preservative reagents, ANP analysis was confounded in 7 subjects. In the remaining 6 subjects, no statistically significant differences in plasma αANP concentrations were found between the resistance and endurance trials ($p=0.34$). Additionally, plasma concentrations of αANP failed to indicate a significant increase with exercise ($p=0.42$). It should be noted however, that one subject (who exercised at the highest power output and was a highly trained cyclist) did exhibit a more than 5 fold rise in αANP concentration during endurance exercise (Figure 3). The coefficient of variation for this assay was ~4.9%.

3.3 BLOOD PRESSURE ANALYSIS

3.3.1 SYSTOLIC AND DIASTOLIC BLOOD PRESSURE

Analysis of $\overline{SBP}$ produced a significant main effect ($p<0.00001$) for time, indicating an increase in pressure at all time points during exercise as well as a reduction from baseline at the 10P, 15P, 30P, 45P and 60P time points. Collapsed across modality, maximal $\overline{SBP}$ was ~225 ± 31 mmHg and occurred during the initial 5 min of exercise. Conversely, the greatest decrement in $\overline{SBP}$ was evident at the 30P time point and was ~20 mmHg below resting values. Additionally, the $\overline{SBP}$, recorded 5 min into the endurance exercise was significantly ($p<0.00001$) elevated from the corresponding time point during the resistance trial (Figure 4).

Average diastolic blood pressure analysis indicated a significant main effect for time ($p<0.00001$) for $\overline{DBP}$, but unlike systolic pressure it did not decrease below baseline during recovery. Across exercises, increases in $\overline{DBP}$ were found only during the exercise period with maximal values reaching 93 ± 15 mmHg at the D5 reading. The difference between exercise modalities failed to reach significance. Post hoc analysis of the significant ($p<0.00001$) interaction did indicate that the average diastolic pressures incurred via resistance exercise were elevated above both resting values and those reached during cycle ergometry. Endurance exercise failed to increase diastolic pressure (Figure 4).

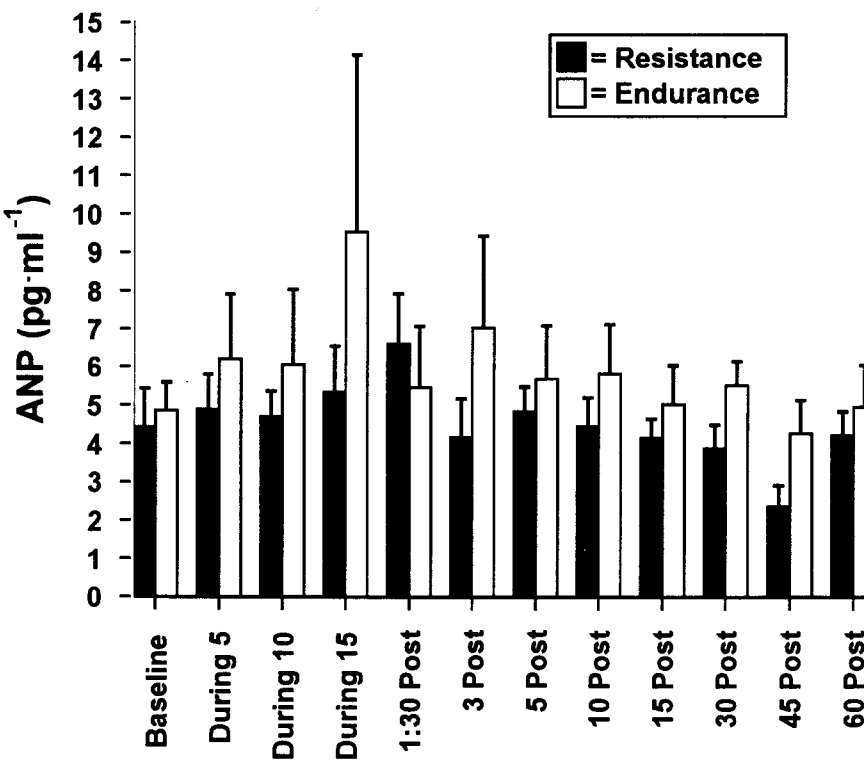


Figure 3. The response of atrial natriuretic peptide (mean±SEM) to resistance and endurance exercise. (Note: n=6).

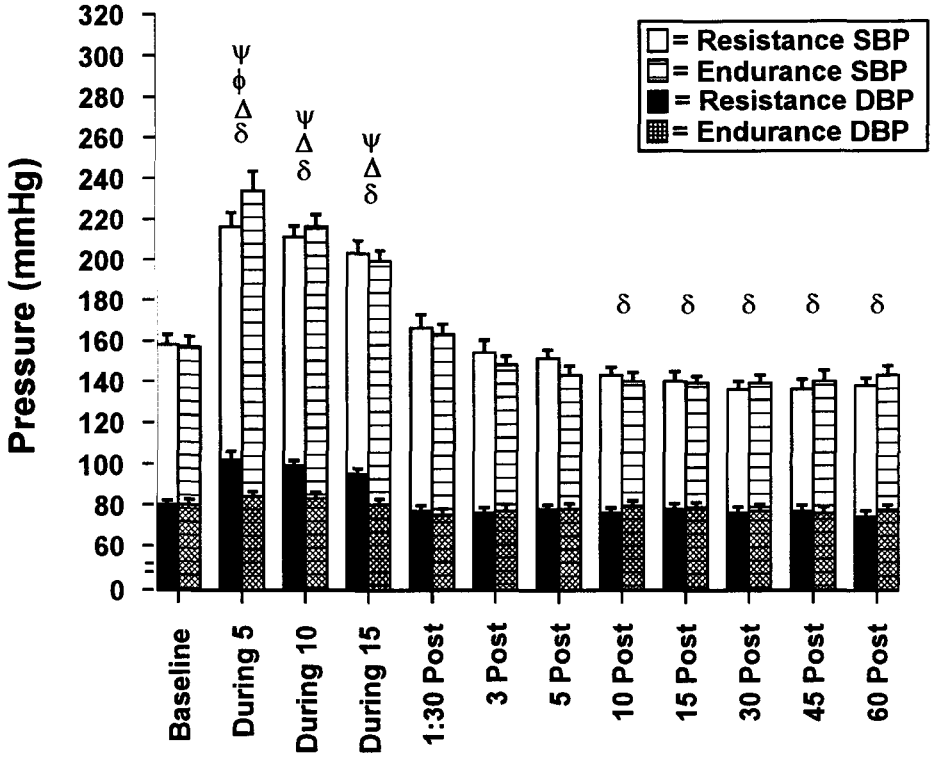


Figure 4. The response of blood pressure (mean±SEM) to resistance and endurance exercise (δ denotes pooled systolic data is significantly different from baseline; ϕ denotes systolic pressure of resistance trial is significantly different from that of the endurance trial; Δ denotes pooled diastolic data is significantly different from baseline; Ψdenotes diastolic pressure of resistance trial is significantly different from that of the endurance trial).

Additionally, a main effect for time ($p<0.00001$) was found for PSBP, indicating that, collapsed across modality, peak systolic pressure was significantly increased at all time points during exercise and significantly decreased from resting levels at 15, 30, 45 and 60 min post exercise. Average maximal pressure during exercise reached 258 $\pm$ 39 mmHg at the D5 time point. Post hoc analysis of the significant interaction ($p<0.00001$) revealed that during exercise, each recording of PSBP attained during resistance exercise was elevated above that achieved during the endurance exercise .

Significant differences in PDBP were also found between both trial ($p=0.003$) and time ($p<0.00001$) with the resistance trial eliciting greater PSBPs. The main effect for time is indicative of higher pressures during exercise, with most of the contribution from the resistance trial. Post hoc analysis of the significant interaction ($p<0.00001$) indicated that the differences occurred throughout the exercise period, with the resistance exercise yielding a maximal increase in PDBP of approximately 51 mmHg above the endurance exercise. No increases from resting values were measured during the endurance exercise session. Additionally, diastolic pressures did not decline below baseline values during the post exercise monitoring period.

Changes in TSBP did not differ between exercise modalities as indicated by the lack of a significant trial effect. A significant main effect ($p<0.00001$) for time was found indicating that, collapsed across exercise type, the TSBP was

elevated during exercise whereas it was substantially decreased from 10 to 45 min inclusive, post exercise. Analysis of the significant interaction ($p<0.00001$) indicated that during exercise, the TSBP was elevated during the resistance exercise above the endurance exercise, at all time points.

The minimal value for diastolic pressure (TDBP) indicated a significant ($p=0.002$) decrement across modalities, between baseline values and those obtained during the final point measured during exercise (D15). No effects were observed for exercise modality or interactions.

3.3.2 PULSE PRESSURE

Pulse pressure indicated a significant change ($p<0.00001$) over time. Collapsed across trial, after an average initial increase of approximately 54 mmHg from baseline at the D5 time point, pulse pressure began to decline, returning to resting levels immediately post exercise, and declining below initial values by as much as 17 mmHg during the period of 15 to 45 min post exercise, inclusive. The significant interaction ($p<0.00001$) occurred at the time points D5 and D10 at which point pulse pressure was significantly greater during the endurance exercise condition. In the resistance trial there were decreases in pulse pressure between 15P and 60P. The endurance trial was

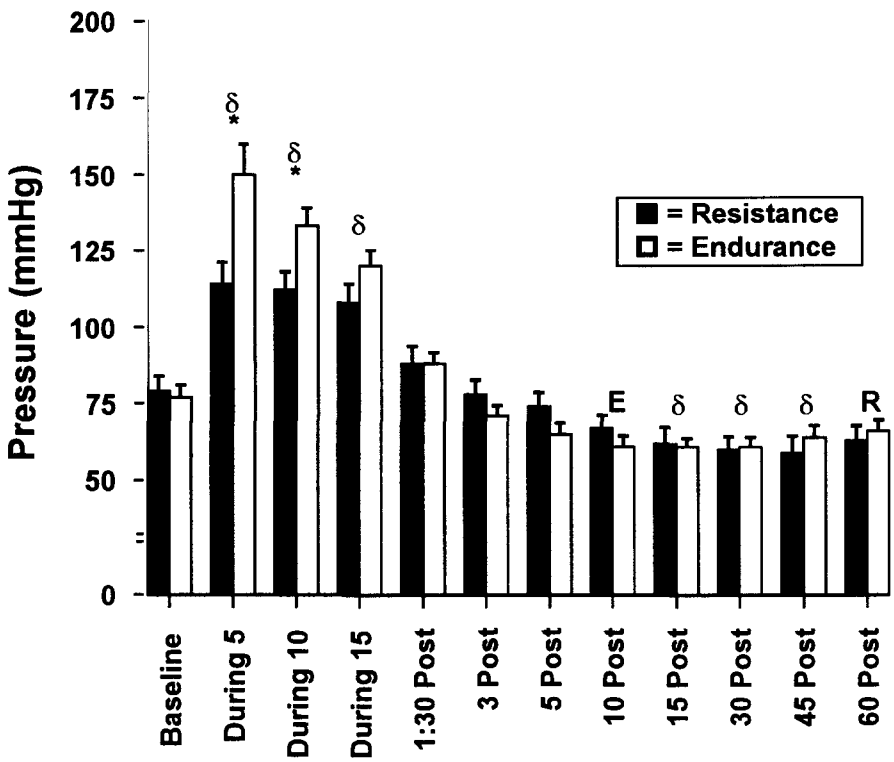


Figure 5. The response of pulse pressure (mean±SEM) to resistance and endurance exercise (★ denotes resistance is significantly different from endurance, δ denotes pooled data is significantly different from baseline, **R** denotes resistance trial is significantly different from baseline, **E** denotes endurance trial is significantly different from baseline).

similar, but decrements were indicated between 10 and 30 min post exercise (Figure 5).

3.3.3 MEAN ARTERIAL PRESSURE

MAP increased ($p<0.00001$) from 103 ± 8 mmHg to a peak value of 127 ± 13 mmHg during exercise (D5). The increases at the D10 and D15 time points were also significant. MAP was reduced at 30, 45 and 60 min post resistance exercise, with a maximal decrement of approximately 7 mmHg (@ 45P) below baseline. Significant interactions ($p<0.00001$) confirmed that resistance exercise elicited greater MAP responses than cycling exercise (Figure 6).

3.4 ADDITIONAL STATISTICAL ANALYSES

3.4.1 OXYGEN CONSUMPTION

Analysis of exercise oxygen consumption during exercise revealed both a main effect for trial ($p<0.00001$) and time ($p<0.00001$). The trial effect was indicative of greater oxygen consumption during the endurance cycling (which was ~65% of $\dot{V}O_{2\ Peak}$). Post hoc analysis of time (irrespective of trial) revealed

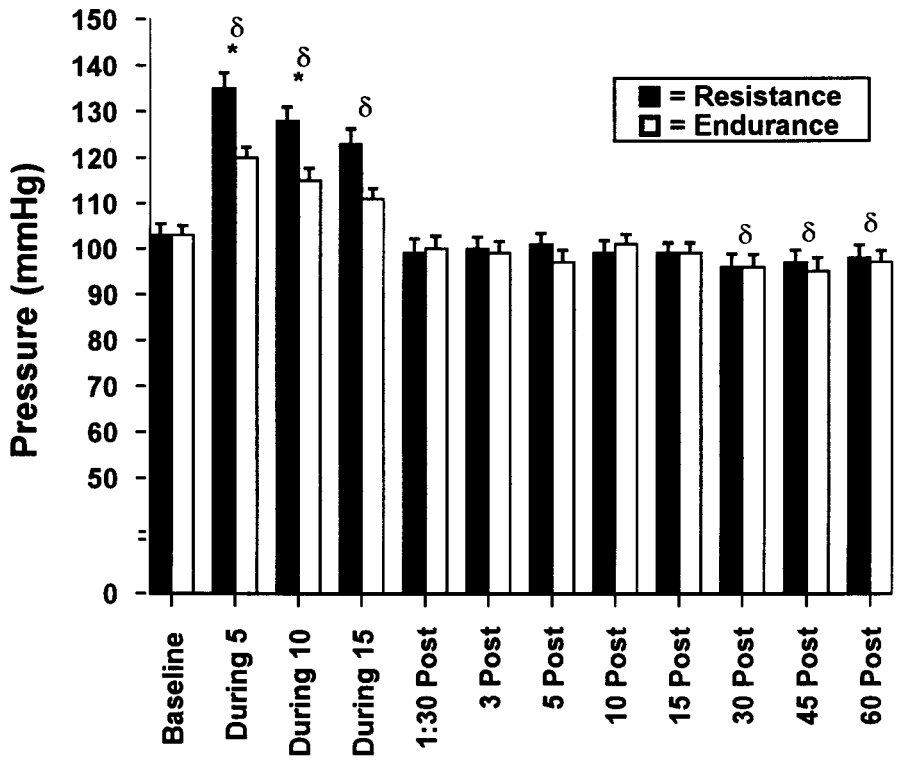


Figure 6. The response of mean arterial pressure (mean±SEM) to resistance and endurance exercise (★ denotes resistance is significantly different from endurance, δ denotes pooled data is significantly different from baseline).

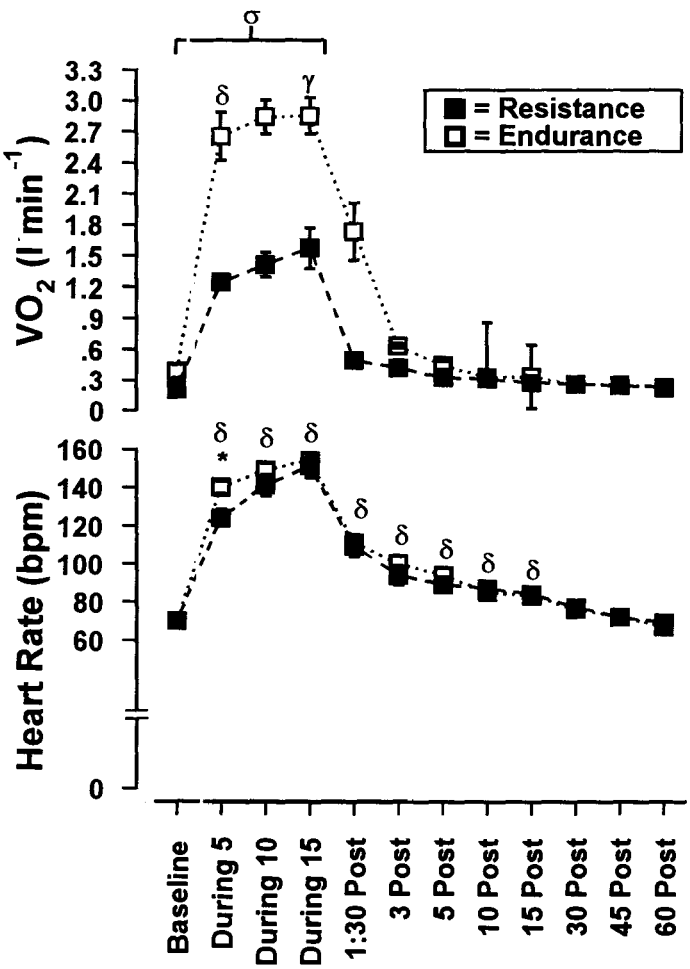


Figure 7. The response of $\dot{V}O_2$ and heart rate (mean±SEM) to resistance and endurance exercise (σ denotes a main effect for trial, δ denotes pooled data is significantly different from baseline, γ denotes pooled data is significantly different from D5). Note: post exercise $\dot{V}O_2$ is for reference only.

a significant increase from baseline to D5. This increase was further heightened at the D15 time point.

3.4.2 HEART RATE

Changes in heart rate were consistent between conditions, both during and post exercise, with the exception of the D5 point where it was significantly ($p<0.00001$) higher during the endurance trial. Resting heart rate was 69 ± 12 beats per minute (BPM). This value increased significantly ($p<0.00001$) with exercise at the D5 time point (131 ± 15 BPM) and increased further to 152 ± 16 BPM immediately prior to the cessation of exercise. In recovery, this value immediately dropped below exercise values, yet remained significantly elevated above baseline values for ~15 min (Figure 7).

3.4.3 RATE PRESSURE PRODUCT

The RPP (an index of myocardial oxygen demand) analysis indicated that there was no main effect for trial. The RPP was significantly elevated from baseline at all points during exercise ($p<0.00001$) and regained resting values by approximately 3 min post exercise (collapsing across trial). Results of the significant interaction ($p<0.00001$) indicated that the RPP of the initial 2 time

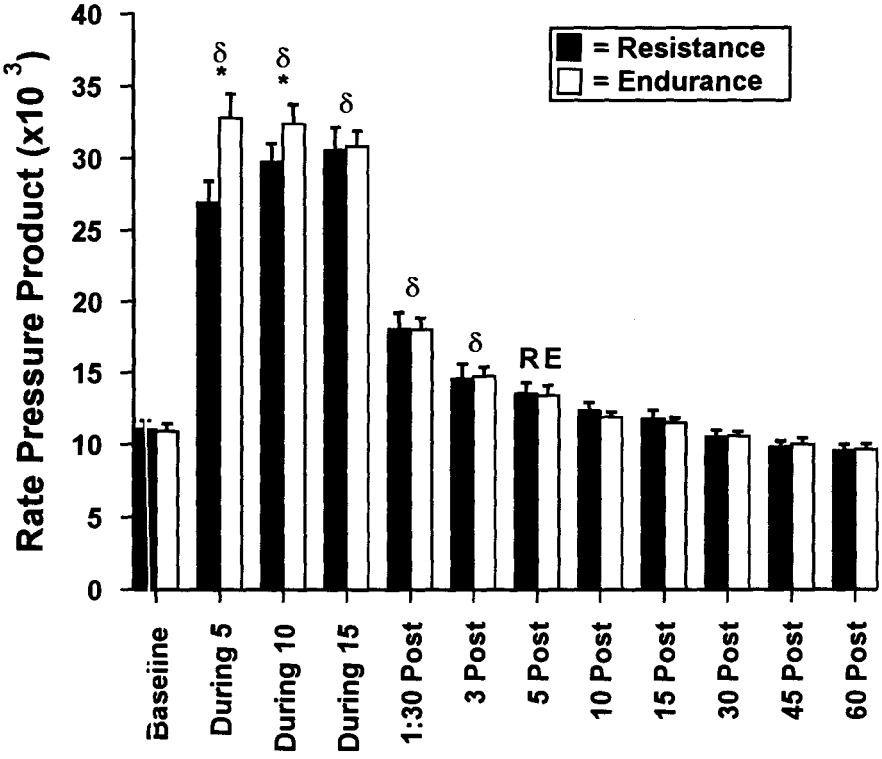


Figure 8. The response of the rate pressure product (mean±SEM) to resistance and endurance exercise (★ denotes resistance is significantly different from endurance, δ denotes pooled data is significantly different from baseline, **R** denotes resistance trial is significantly different from baseline, **E** denotes endurance trial is significantly different from baseline).

points during exercise (e.g. D5 and D10) were significantly greater during the resistance exercise session (Figure 8).

3.4.4 HEMATOCRIT

A main effect for trial indicated a significantly increased ($p=0.0004$) hematocrit during the resistance exercise. There was an additional main effect for time ($p<0.00001$), indicating that Hct was significantly elevated from the onset of exercise until the 5P time point. There was a continued decrement after 5P, but it failed to reach significance. The significant interaction ($p=0.0100$) is indicative of Hct being higher in the resistance trial than the endurance trial at D10, D15, 1:30P, 3P and 5P (Figure 9).

3.5 ECHOCARDIOGRAPHIC RESULTS

3.5.1 CARDIAC VOLUMES

Echocardiographic analysis of two subjects revealed a significant difference ($p=0.005$) between exercise modalities. Endurance cycling produced an elevated atrial volume from a baseline value of 41.2 ± 2.27 ml to 52.1 ± 2.38 ml. The leg press elicited a decrement in atrial volume to a value of 32.1 ± 0.53 ml (Figure 10).

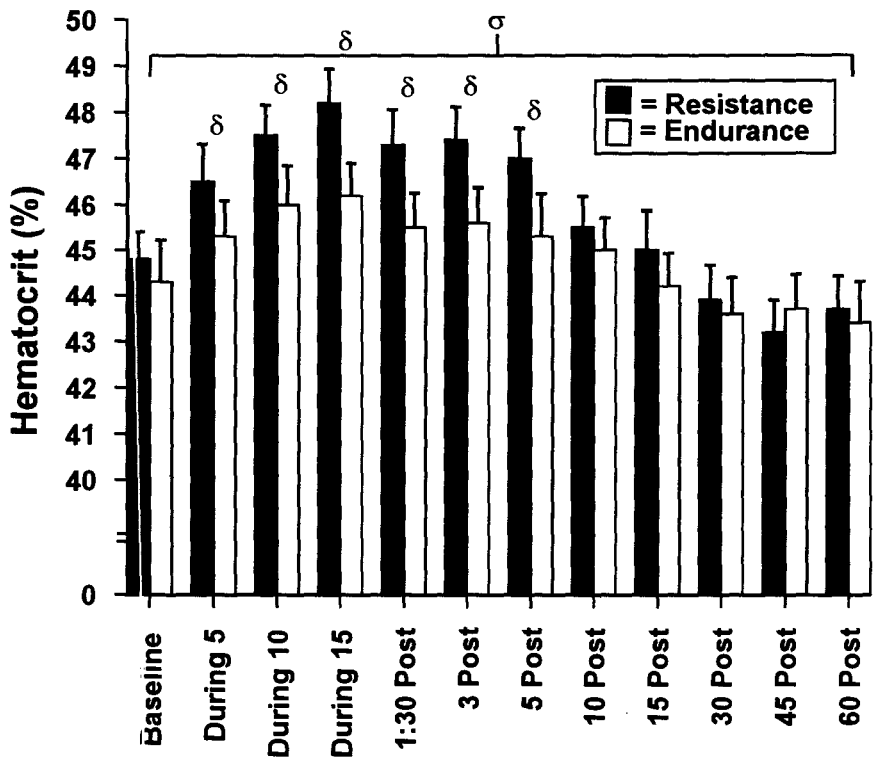


Figure 9. The response of hematocrit (mean±SEM) to resistance and endurance exercise (★ denotes resistance is significantly different from endurance, σ denotes a main effect for trial, δ denotes pooled data is significantly different from baseline).

Left-ventricular end-diastolic volume was significantly increased ($p=0.027$) by ~18 ml from baseline during the endurance cycling. The leg press exercise failed to provoke any change from resting values (Figure 10).

The left-ventricular end-systolic volume was not statistically different between rest and either of the exercise conditions. There was, however, a strong trend ($p=0.073$) towards a decreased ESV during the endurance trial and even more so during the resistance trial (Figure 10).

3.5.2 EJECTION FRACTION

Although there was no statistically significant difference between trials ($p=0.052$), there was an increase of ~18% during each of the two exercise modalities.

3.5.3 STROKE VOLUME

Differences in stroke volume also failed to meet statistical significance ($p=0.059$), most likely due to the small sample size. Stroke volume increased by ~21% during the resistance trial and by ~34% during the endurance trial (Figure 10).

3.6 DATA FROM SUBSEQUENT NON-EXERCISE TRIALS

3.6.1 AVERAGE SYSTOLIC AND DIASTOLIC BLOOD PRESSURE

Average systolic pressure of 2 individuals during the non-exercise condition indicated that hypotension was not evident, since no significant differences ($p=0.769$) were found at any time point.

Similarly, average diastolic pressure did not differ ($p=0.550$) throughout the 75 min non-exercise condition (Table 1).

3.6.2 MEAN ARTERIAL PRESSURE

As with the non-exercising $\overline{SBP}$ and $\overline{DBP}$, MAP also did not significantly change ($p=0.779$) while subjects remained seated during the measurements, indicating no evidence of hypotension.

3.6.3 HEMATOCRIT

The sitting only condition failed to cause any vascular fluid shifts as indicated by a lack of significance ($p=0.099$) between hematocrit measures (Table 1).

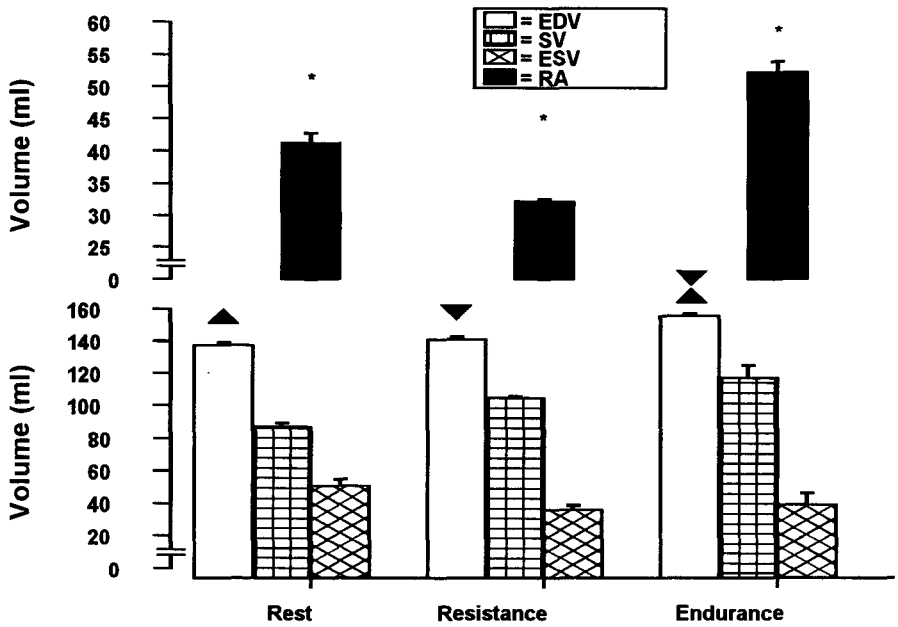


Figure 10. Echocardiographic data indicating heart volume (mean±SEM) responses to exercise. Note: like symbols denote significant differences.

	Systolic Blood Pressure (mmHg)											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	157.00	166.00	161.00	160.00	161.00	163.00	158.00	160.00	163.00	158.00	156.00	149.00
4	128.00	134.00	132.00	126.00	127.00	124.00	126.00	126.00	124.00	129.00	135.00	131.00
MEAN	142.50	150.00	146.50	143.00	144.00	143.50	142.00	143.00	143.50	143.50	145.50	140.00
STDEV	20.51	22.63	20.51	24.04	24.04	27.58	22.63	24.04	27.58	20.51	14.85	12.73

	Diastolic Blood Pressure (mmHg)											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	68.00	70.00	70.00	70.00	73.00	73.00	72.00	72.00	70.00	67.00	67.00	68.00
4	69.00	76.00	72.00	73.00	76.00	71.00	73.00	73.00	66.00	73.00	77.00	74.00
MEAN	68.50	73.00	71.00	71.50	74.50	72.00	72.50	72.50	68.00	70.00	72.00	71.00
STDEV	0.71	4.24	1.41	2.12	2.12	1.41	0.71	0.71	2.83	4.24	7.07	4.24

	Hematocrit (%)											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	47	48	44	46	45	46	46	46	46	48	44	46
4	41	42	41	41	41	42	41	42	41	42	41	42
MEAN	44	45	43	44	43	44	44	44	44	45	43	44
STDEV	4.24	4.24	2.12	3.54	2.83	2.83	3.54	2.83	3.54	4.24	2.12	2.83

Table 1. Data from subsequent non exercise trials. Note: time points are labelled to correspond to the exercise trials although no exercise occurred.

4.0 DISCUSSION

4.1 INTRODUCTION

The data indicate that when healthy young normotensive subjects perform ~15 min of moderate intensity (65% $\dot{V}O_{2\ Peak}$) cycle ergometry or continuous weightlifting (65% 1RM) exercise, minimal but non-significant increases occur in circulating ANP concentration, with baseline values being re-established within 5 min following exercise. Ten min following exercise, systolic blood pressure decreased significantly below baseline and 30 min following exercise, mean arterial pressure was also significantly lower than baseline. This post-exercise "hypotensive effect" was similar for both exercise modes until measurements were terminated at 60 min. Follow-up studies using the identical methodology in a sub-sample of subjects who simply remained in the same seated position (without performing exercise), revealed no change in resting blood pressure, thus indicating that the observed hypotensive response was due to the exercise intervention.

4.2 ECHOCARDIOGRAPHIC DATA

Echocardiography was used to determine whether Lentini's (1993) observations that traditional resistance exercise results in little or no increase in end-diastolic cardiac volume also applied to the resistance protocol used in the

present study. The finding that cardiac volumes did not increase during the resistance exercise but increased substantially during the cycle ergometry exercise indicates that an uncoupling of distension and pressure was achieved using the different exercise modalities. The differences between the two exercise modalities were striking in that atrial volumes were decreased by 22% from rest during the resistance exercise, and increased 27% during the endurance exercise. Echocardiographic results during weightlifting in the study by Lentini et al. (1993), indicated an increased PSBP/ESV ratio (an indication of enhanced myocardial contractility independent of changes in preload or afterload) and an increased EF. Similar to the work of Lentini et al. (1992), the present study found an increased ejection fraction. This increase failed to reach significance, most likely due to the small sample size. Contrary to Lentini et al.'s (1992) data, this study found no significant change in EDV in the resistance exercise, whereas, as expected, there was a significant increase during the cycling condition.

4.3 PLASMA αANP CONCENTRATION

αANP measurements in 7 subjects were found to be invalid due to contamination of the blood samples by a tainted protease inhibitor. Considerable intra and intersubject variability was evident in the responses of the remaining 6 subjects (Appendix C). The 89% increase in αANP

concentration at the 15 min point of the cycle ergometry exercise was largely due to the exaggerated response of one subject and was not statistically significant. Similarly, the 49% elevation in αANP concentration at 1 min 30 s following the resistance exercise was not statistically significant with this small number of subjects. The failure to detect an increase in αANP release with either form of exercise was unexpected, in light of the increase in right atrial volume which was observed with echocardiography during the endurance trial and the heightened blood pressures associated with the resistance exercise.

Cycle Ergometry Based on the echocardiographic data, one can expect that the subjects in the present study would have experienced significant increases in atrial volumes during the cycling exercise. Distension of the atria is considered to be the major stimulus for ANP release (Asai et al., 1994; Vita et al., 1989; Edwards et al., 1988; Fyhrquist et al., 1987). With a similar cycle ergometry protocol, Perrault et al. (1991) reported a 2 fold increase in ANP after 15 min at 67% of $\dot{V}O_{2\ Peak}$. It is possible that slight differences in sampling time may have contributed to some of the difference between Perrault's results and those of the present study. The final blood sample was taken at approximately 13 min and 47 s into exercise, whereas the 15 min time point in the investigation of Perrault et al. (1991) was the initial measurement time. It is possible that significant ANP secretion does not begin until some point between these 2 times. Furthermore, in the present study, subjects began pedalling at a power

output required to elicit 65% $\dot{V}O_{2\ Peak}$. Since $\dot{V}O_2$ measurements indicated that a steady state was not reached until approximately 2 min into exercise, the actual cycling time at 65% $\dot{V}O_{2\ Peak}$ would have been only approximately 11½ min, and possibly insufficient to provoke significant ANP secretion. A more likely explanation would be that the moderately trained subjects attained a level of $\dot{Q}c$ during exercise which was insufficient to place a significant volume load on the heart. In contrast, the trained cyclist in the present study did display the trend observed for ANP release, increasing plasma concentrations during the endurance trial by ~532%. This individual required a greater absolute power output (approximately 30%) than the average of the subject population to elicit 65% $\dot{V}O_{2\ Peak}$. The higher $\dot{Q}c$ necessary to accomplish this power output would also have been accompanied by a greater venous return to the heart and a greater stroke volume. This increased venous return would, presumably, lead to greater atrial distension and thus ANP release. This suggests that the chosen exercise intensity of 65% $\dot{V}O_{2\ Peak}$ was insufficient, and the duration of exertion was inadequate to promote ANP secretion in the majority of the subjects.

Resistance Exercise MacDonald et al. (1995) previously showed significant increases in circulating levels of ANP, using lower body resistance exercise (5 sets of 10 repetitions @ 80% 1RM double leg press) where blood pressure was presumably greatly elevated (see Lentini, 1993) but there would have been no increase in atrial dimensions. It is possible that, in the present study, the

modified protocol of 15 min of unilateral leg press exercise at 65% of 1RM did not adequately increase blood pressure to elicit ANP secretion. It is known from the work of MacDougall et al. (1985), that dynamic, bilateral leg press exercise performed at 95% 1RM (similar to the procedure employed by MacDonald et al. (1995)) can elicit pressures in excess of 320/250 mmHg. In contrast, maximal pressures in the present study were 258/148 mmHg.

Heart Rate This study refutes the suggestions by Fyhrquist et al. (1987), Saito et al. (1986) and Bates et al. (1986) that tachycardia is a major contributor to ANP secretion. The maximal averaged heart rate in the present study reached approximately 152 beats per minute. This value is greater than 75% of the age predicted maximal heart rate for this subject population (Guyton & Hall, 1996). Heart rate was not significantly different between exercise modalities.

4.4 BLOOD PRESSURE

4.4.1 BLOOD PRESSURE DURING EXERCISE

In the present study the blood pressure measurements taken during exercise are in agreement with those in the literature (e.g. MacDougall et al., 1994, Lentini et al., 1993, 1992). During dynamic cycle ergometry exercise, the systolic pressure increases substantially while diastolic pressure shows little or no change in normal subjects. This increase is mediated largely by the increased $\dot{Q}c$. Although the peripheral resistance is decreased due to

vasodilation of the exercising muscle vasculature (MacDougall, 1994), this decrease is insufficient to offset the large increases in $\dot{Q}c$. The protocol which was used for resistance exercise in the present study makes comparison with previous work difficult since 15 min of continuous unilateral leg press exercise is quite atypical. However, if the initial 5 min data are compared with previously reported values, similar results are obtained. Average pressure in the current investigation for 65% unilateral 1RM averaged 216/101 mmHg, whereas those in a study of Lentini et al. (1992) which employed 70% unilateral 1RM were found to be 202/111 mmHg. The slightly higher systolic pressures observed in the present study may be attributable to the longer duration of the exercise since blood pressure and heart rate tend to increase over time with resistance exercise. This value was recorded 5 min into exercise, whereas measurements of blood pressure by Lentini et al. (1992) were completed between 33 and 36 s into exercise.

The dramatic increase in blood pressure which is observed during resistive exercise can be attributed to several factors. Initially, there is an occlusion of the blood vessels in the contracting muscle due to mechanical compression. This is accompanied by enhanced central command from higher centres of the brain, and feedback from muscle ergoreceptors and mechanoreceptors, resulting in rapid increases in heart rate, arterial pressure and $\dot{Q}c$ - the classic pressor response (Mitchell et al., 1983). Towards the end

of exercise, subjects found it necessary to perform the Valsalva maneuver (a forced expiration against a closed glottis) in order to stabilize the trunk. This maneuver further augments the blood pressure response due to increased intrathoracic pressure which is transmitted to the arterial tree (MacDougall, 1994). Suprisingly, this heightened pressure from the evident Valsalva maneuvers was undetectable since, after the initial 5 min, both systolic and diastolic pressures were shown to significantly decline throughout exercise. This may have been caused by the increased frequency of alternating legs as the exercise was continued. The marked decrease in the number of leg presses in each "set" as subjects began to fatigue increased the frequency of the use of the "rested" limb.

4.4.2 HEMATOCRIT

The significant increase in hematocrit which was detected during the resistance exercise and which persisted until 5 min following exercise has been well documented (Ploutz-Snyder et al., 1995; Collins et al., 1989). Loss of plasma to extravascular space in muscle is thought to be caused by the increased hydrostatic capillary pressures which accompany the dramatic increases in blood pressure which occur with each lift (Ploutz-Snyder et al., 1995; MacDougall et al., 1985). Hemoconcentration is also known to occur with endurance exercise but the magnitude is considerably less (Novosadova, 1977).

The finding that fluid shifts were only transient and that normal hematocrit was regained after 5 min of recovery indicates that a decrease in total plasma volume could not have been the cause for the PEH which occurred.

4.4.3 OXYGEN CONSUMPTION

Since $\dot{V}O_2$ and $\dot{Q}c$ are tightly coupled during sub-maximal exercise, the higher $\dot{V}O_2$ during the cycle ergometry can be interpreted as evidence for a higher $\dot{Q}c$ than during the resistance exercise. Because heart rate did not differ between the 2 trials, one can conclude that SV should also have been greater during the cycling, thus providing further support for a greater volume load on the heart with this form of exercise.

4.4.4 BLOOD PRESSURE FOLLOWING EXERCISE

PEH has been documented to a much greater extent in hypertensive subjects than in normotensive subjects. In addition, many investigations of PEH in normotensive subjects have yielded contradictory results. For example, Floras, in 1991 with Senn, and again in 1992 with Wesche found no incidence of PEH after 45 min of treadmill exercise at 70% of resting heart rate reserve. Moreover Pescatello et al. (1991) actually suggested that normotensives exhibit an increase in systolic blood pressure for 12.7 h after exercise. Conversely, Hara and Floras (1992), using the same protocol as Floras and colleagues

(1992, 1991) reported significant reductions in blood pressure in the normal population. Also, Brown et al. (1994), Boone et al. (1992), Landry et al. (1992) and Convertino and Adams (1991), using cycle ergometry at various workloads between 60 and 100% $\dot{V}O_{2\,Peak}$, found a significant decrease in post-exercise blood pressure. Many of these discrepancies may be attributable to the indirect methods often used to measure blood pressure following exercise. Additionally, no standardized body posture has been accepted for the post-exercise measurement period. The present study has shown PEH to be a significant phenomenon in the normal population.

Systolic Blood Pressure The decrements in average systolic pressure which were observed following exercise, exceed those normally reported for a normotensive population. This may be partially due to the fact that intra-arterial pressure was directly monitored in the present study. This method of sampling is more apt to detect small differences in pressure and is less affected by motion and limb position than the auscultatory methods employed in the majority of previous examinations (Boone et al., 1992; Landry et al., 1991; Kiyonaga et al., 1985).

Diastolic Blood Pressure In contrast to a number of previous studies, following exercise, the average diastolic pressures did not parallel the changes in systolic pressure (Boone et al., 1992; Hara & Floras, 1992; Coats et al., 1989; Kaufman et al., 1987; Bennett et al., 1984; Wilcox et al., 1982). A possible explanation for

this may be that the majority of studies indicating decreased diastolic pressure following exercise involved subjects in the supine position, whereas the present study maintained subjects in the sitting position. Bennett et al. (1984) has suggested that the decreases in diastolic pressure which are detected post exercise may differ by approximately 6 mmHg between the sitting and standing position, with the sitting position achieving the greatest reductions. It is possible that similar decrements could be extrapolated between the sitting and supine position. When the average decrement of diastolic pressure due to PEH in normotensive subjects of 7.9 mmHg is taken into account, it can be seen that the changes in diastolic pressure may fail to reach significance, as in the present study.

Exercise Intensity and Duration The majority of studies which have examined PEH following endurance exercise have focused on intensities which range from 40% to 70% of $\dot{V}O_{2\ Peak}$ (Kenney & Seals, 1993). PEH was observed following exercise at 65% $\dot{V}O_{2\ Peak}$ in the current investigation and therefore concurs with the previous literature (e.g. Brown et al., 1994; Boone et al., 1992; Landry et al., 1992; Convertino & Adams, 1991).

With the exception of maximal exercise tests (which generally last ~8-12 min), the majority of endurance exercise protocols which have been shown to elicit PEH have ranged from 20 to 60 min in duration (e.g. Boone et al., 1992;

Hara & Floras, 1992; Floras et al., 1989; Bennett et al., 1984; Fitzgerald, 1981). The exercise intensities used in these studies were ~75% of maximal heart rate. When it is assumed that subjects in the present study exercised at 65% $\dot{V}O_{2\ Peak}$, for approximately 11½ min, this study has documented the occurrence of PEH after a bout of exercise at moderate intensity and of shorter duration than previously reported. This may have significant clinical implications, since this is a readily obtainable target intensity and duration, even for the hypertensive and elderly population.

Duration of PEH The time course for PEH has yet to be accurately established. Preliminary data from Taylor-Tolbert et al. (in press) and Boer et al. (1995), using tightly controlled studies, have suggested that ambulatory pressure measurements are significantly reduced after exertion, for 17 h. If these data are correct, and the same duration could be achieved with the protocol used in the present study, promising interventions could be employed. It seems plausible that an exercise prescription may on its own, or in addition to pharmacological intervention, aid in the control of hypertension. If the exercise protocol in the present study could be extrapolated to the durational results of Taylor-Tolbert et al. (in press) and Boer et al. (1995), an exercise program of moderate intensity and short duration (12-15 min) performed twice daily, could be useful in alleviating symptoms of hypertension.

The present study has also documented the occurrence of PEH after a bout of resistance exercise. Previous work in this area is sparse and contradictory. Hill et al. (1989) indicated decreases in blood pressure after a bout of resistance exercise whereas O'Connor et al. (1993) found elevations in pressure following resistance exercise. More recently Boer et al. (1995) observed significantly diminished blood pressures for 17 h post resistance exercise of 8-12 repetitions of 11 exercises at 70% 1RM. The present study confirms that PEH occurs in response to resistance exercise. Moreover, significantly decreased systolic and mean pressure values recorded at the termination of measurement in the rest phase concur with reports of prolonged hypotension (e.g. Taylor-Tolbert et al., in press; Boer et al., 1995; Pescatello et al., 1991).

Mechanisms for PEH Although it was not the purpose of the present study to examine many of the possible causal mechanisms for PEH, based on the data some possibilities may be dismissed. Primarily, ANP appears not to be a significant modulator of PEH since both the resistance and endurance exercise modalities had a minimal effect on circulating levels of αANP. Moreover, any changes in ANP had disappeared by 5 min of recovery and significant declines in mean pressure did not occur until 30 min following cessation of exercise. This is in agreement with previous research (Brussieres-Chafe et al., 1994; Perrault et al., 1991, 1989) which have found a return to baseline ANP concentrations by

30 min following upright exercise. However, the possibility of a delayed effect of ANP on the cardiovascular control centres modulated by the earlier ANP release cannot be discounted. It can also be concluded that baroreceptor modulation was not the direct cause of PEH. If this were so, the increases in pressure ($\overline{SBP}$, $\overline{DBP}$ and MAP) which occurred during resistance exercise above those observed during the endurance exercise would, theoretically, cause a greater stimulation of the baroreceptors. Presumably, this would be expected to result in an exaggerated hypotensive response following the activity which elicits the highest pressor response (e.g. resistance exercise). This study, in agreement with Brown et al. (1994), found no difference between exercise modality on PEH, thus rejecting the hypothesis of baroreceptor activity modulating the PEH response. Additionally, Piepoli et al. (1993) found that a decreased baroreceptor sensitivity occurred only in the 10 min immediately post (maximal) exercise. This would negate the baroreceptor activity modulation of PEH since the PEH was not evident within this period.

It also seems plausible that a thermoregulatory effect from cutaneous vasodilation would not play a significant role in the PEH which occurred in the present study. Although rectal and skin temperatures were not monitored, the relatively moderate duration and intensity of the exercise would argue against a significant increase in core temperature and subsequent sustained cutaneous vasodilation. Additionally, it is likely that whole body heat dissipation had

returned to normal by the end of the post exercise measurement period (60 min), where PEH was still prevalent. In a study by Franklin et al. (1993), which examined the effects of climatic conditions on PEH, it was found that PEH was only present after exercise in a warm environment, where skin temperature was still elevated (and thus, presumably skin blood flow) at 60 min post exercise. Exercise in a thermo-neutral environment (as in the present study) elicited a skin temperature which was actually decreased (although not significantly) shortly after exercise. These findings suggest that cutaneous vasodilation was not responsible for PEH in the current investigation.

Finally, the fact that hematocrit did not change during the 75 min non-exercise period, nor during the recovery portion of the exercise trials in which PEH occurred, argues against a vascular pooling mechanism. One might postulate that maintaining a relatively static body position for 60 min might have caused a shift of plasma from the vascular space and thus a decreased total blood volume, and subsequent drop in blood pressure. It is apparent that this possibility can also be dismissed as a mechanism.

Further extrapolation of the mechanisms responsible for the observed PEH in the present study are not possible due to the failure to monitor catacholamines, $\dot{Q}c$, peripheral/vascular resistance and hormonal fluctuations. Further work is needed to determine the cause of PEH.

4.5 SUMMARY AND FUTURE DIRECTIONS

4.5.1 SUMMARY

The present study has documented that neither 15 min of unilateral leg press at 65% 1RM nor ~13 min 47 s of cycle ergometry at 65% $\dot{V}O_{2\ Peak}$ were sufficient to stimulate ANP secretion. These results were apparent in spite of increased atrial dimensions in the endurance trial and increased systolic and diastolic blood pressure in the resistance trial. Each of these protocols was, however, adequate to elicit PEH, which occurred between 15 and 60 min post exercise in normotensive healthy males. It is therefore apparent that in the present study, no link appeared to exist between the secretion of ANP and PEH. Although more work is warranted in this area, exercise may be of significant clinical benefit in the treatment of hypertension.

4.5.2 FUTURE DIRECTIONS

Biochemical The greatest impact in ANP research would likely stem from biochemical studies of receptor blockade, and degradation enzyme inhibitors. Physiologists must also accurately determine the stimulus for maximal secretion, and further work is needed to determine the metabolic interactions between this

and other vasoactive hormones (e.g. vasopressin, renin, angiotensin, aldosterone).

Characterization of PEH A comprehensive plan to study the potential clinical benefits of PEH is as follows. Initially, a series of well controlled studies are needed to characterize the PEH response, since controversial results have been found under various conditions using differing techniques. This could be accomplished through a series of experiments examining the effects of exercise type, duration, intensity and frequency (including activities of daily living), in a variety of subject populations (normotensive vs. borderline hypertensive vs. hypertensive).

Potential Clinical Significance of PEH It is important to establish whether or not PEH persists in an ambulatory setting. If exercise is to have some clinical benefit, PEH should be evident in individuals who spend the post-exercise period in situations of normal activity. A device which not only allows for post exercise measurements *in situ*, but will also permit practical exercise regimes of daily living and give accurate intra-arterial measurements of pressure would be ideal.

Causes of PEH

Cardiac Output vs. TPR There is a need for the determination of whether post exercise hypotension is caused by a decrease in $\dot{Q}c$ or a decrease in total peripheral resistance (or both). This should be accomplished by a precise measurement of $\dot{Q}c$ by the most direct and accurate method.

Autonomic Nervous System Modulation If the results indicate that a decrement in $\dot{Q}c$ is responsible for PEH, examination of the activity of the autonomic nervous system should be undertaken using power spectral analysis of heart rate variability.

Hormonal Mechanisms If, however, a lowering of peripheral resistance appears to be the underlying mechanism, an in-depth analysis of the hormones responsible for vasodilation would be warranted. Additional variables which would require investigation include angiotensin converting enzyme (ACE) and endothelium derived nitric oxide (generally via inhibition by L-NMMA).

4.6 CONCLUSIONS

The present investigation has documented that neither a ~13½ min bout of cycle ergometry at ~65% $\dot{V}O_{2\ Peak}$ nor 15 min of unilateral leg press at 65% 1RM is sufficient stimulus to cause elevated release of ANP. Thus, the uncoupling of a pressure and a volume load on the heart still remains to be accomplished at intensities needed to elicit significant ANP secretion.

Additionally, since ANP levels failed to increase significantly, the effect of this hormone on post-exercise blood pressure in the present study was negligible.

More interestingly, this investigation has documented that brief periods of either endurance, or resistance exercise result in PEH, which may have potential clinical application in the management of hypertension.

REFERENCES

1. Baker, B. J., W. C. Wu, C. J. Winters, H. Dinh, R. Wyeth, A. L. Sallman, and D. L. Vesely. Exercise increases the circulating concentration of the N-terminus of the atrial natriuretic factor prohormone in normal individuals. *American Heart Journal* 122: 1395-1402, 1991.

2. Bates, E. R., Y Shenker, and R. J. Grekin. The relationship between plasma levels of immunoreactive atrial natriuretic hormone and hemodynamic function in man. *Circulation* 73: 1155-1161, 1986.

3. Bennett, T., R. G. Wilcox, and I. A. Macdonald. Post-exercise reduction of blood pressure in hypertensive men is not due to acute impairment of baroreflex function. *Clinical Science* 67: 97-103, 1984.

4. Berlin, I., G. Deray, P. Lechat, G. Maistre, C. Landault, V. Chermat, C. Ressayre, and A. J. Puech. Tertatolol potentiates exercise-induced atrial natriuretic peptide release by increasing atrial diameter in healthy subjects. *Cardiology* 83 Suppl 1: 16-24, 1993.

5. Berlin, I., P. Lechat, G. Deray, C. Landault, G. Maistre, V. Chermat, C. Ressayre, and A. J. Puech. Beta-adrenoceptor blockade potentiates acute exercise-induced release of atrial natriuretic peptide by increasing atrial diameter in normotensive healthy subjects. *European Journal of Clinical Pharmacology* 44: 127-133, 1993.

6. Boer, N. F., M. D. Brown, R. J. Zimet, and J. M. Hagberg. The effect of a single bout of weight training on ambulatory blood pressure. *18th Annual Meeting: Mid-Atlantic Regional Chapter of the American College of Sports Medicine* 1995.(Abstract)

7. Boone, J. B., Jr., M. M. Probst, M. W. Rogers, and R. Berger. Postexercise hypotension reduces cardiovascular responses to stress. *Journal of Hypertension* 11: 449-453, 1993.

8. Bouissou, P., F. X. Galen, J. P. Richalet, M. Lartigue, F. Devaux, and C. Dubray. Effects of propranolol and pindolol on plasma ANP levels in humans at rest and during exercise. *American Journal of Physiology* 257: R259-R264, 1989.

9. Bouissou, P., J. P. Richalet, C. Dubray, M. Lartigue, J. C. Aldigier, HabriouxG., and F. X. Galen. Effect of beta-adrenergic receptors blockade on auricular natriuretic factor, aldosterone and renine blood activity during physical exercise. [French]. *Archives des Maladies du Coeur et des Vaisseaux* 82: 1241-1243, 1989.

10. Brooks, S., M. E. Nevill, L. Meleagros, H. K. Lakomy, G. M. Hall, and S. R. Bloom. The hormonal responses to repetitive brief maximal exercise in humans. *European Journal of Applied Physiology & Occupational Physiology* 60: 144-148, 1990.

11. Brown, S. P., J. M. Clemons, Q. He, and S. Lui. Effects of resistance exercise and cycling on recovery blood pressure. *Journal of Sports Sciences* 12: 463-468, 1994.

12. Bussieres-Chafe, L. M., P. W. Pflugfelder, A. R. Henderson, D. MacKinnon, A. W. Taylor, and W. J. Kostuk. Effect of cardiac filling pressures on the release of atrial natriuretic peptide during exercise in heart transplant recipients. *Canadian Journal of Cardiology* 10: 245-250, 1994.

13. Cable, N. T., T. Reilly, S. Winterburn, and G. Atkinson. Circadian variation in post-exertional hypotension. *Medicine and Science in Sports and Exercise* 27: s66, 1995.(Abstract)

14. Chan, J. C., C. K. Cheung, C. S. Cockram, J. A. Critchley, R. Swaminathan, L. K. Law, and M. G. Nicholls. Atrial natriuretic peptide and renin-angiotensin-aldosterone system in non-insulin-dependent diabetes mellitus. *Journal of Human Hypertension* 8: 451-456, 1994.

15. Chan, T. Y., K. S. Woo, and M. G. Nicholls. The application of nebivolol in essential hypertension: a double-blind, randomized, placebo-controlled study. *International Journal of Cardiology* 35: 387-395, 1992.

16. Cleroux, J., N. Kouame, A. Nadeau, D. Coulombe, and Y. Lacourciere. Aftereffects of exercise on regional and systemic hemodynamics in hypertension [see comments]. *Hypertension* 19: 183-191, 1992.

17. Cleroux, J., N. Kouame, A. Nadeau, D. Coulombe, and Y. Lacourciere. Baroreflex regulation of forearm vascular resistance after exercise in hypertensive and normotensive humans. *American Journal of Physiology* 263: H1523-H1531, 1992.

18. Coats, A. J., J. Conway, J. E. Isea, G. Pannarale, P. Sleight, and V. K. Somers. Systemic and forearm vascular resistance changes after upright bicycle exercise in man. *Journal of Physiology* 413: 289-298, 1989.

19. Coats, A. J. and M. Piepoli. Aftereffects of exercise [letter; comment]. *Hypertension* 20: 851-852, 1992.

20. Collins, H. L. and S. E. DiCarlo. Attenuation of postexertional hypotension by cardiac afferent blockade. *American Journal of Physiology* 265: H1179-H1183, 1993.

21. Collins, M. A., K. J. Cureton, D. W. Hill, and C. A. Ray. Relation of plasma volume change to intensity of weight lifting. *Medicine and Science in Sports and Exercise* 21: 178-185, 1989.

22. Convertino, V. A. and W. C. Adams. Enhanced vagal baroreceptor response during 24h after acute exercise. *American Journal of Physiology* 260: R570-R575, 1991.

23. Davis, A. D. Atrial Natriuretic Factor. *Advanced Pediatrics* 36: 137-150, 1989.

24. De Paoli Vitali, E., F. Malacarne, M. Vedovato, R. Cavallini, B. Bagni, and P. Gilli. Atrial natriuretic peptide and urinary sodium balance during physical exercise. *Nephron* 57: 60-63, 1991.

25. deBold, A. J. Atrial natriuretic factor: a hormone produced by the heart. *Science* 230: 767-770, 1985.

26. deBold, A. J., H. B. Borenstein, A. T. Veress, and H. Sonnenberg. A rapid and potent natriuretic response to intravenous injection of atrial myocardial extracts in rats. *Life Science* 28: 89-94, 1981.

27. Deray, G., I. Berlin, G. Maistre, F. Martinez, S. Legrand, A. Carayon, A. Puech, F. Masson, J. C. Legrand, and et al. Beta-adrenoceptor blockade potentiates exercise-induced release of atrial natriuretic peptide. *European Journal of Clinical Pharmacology* 38: 363-366, 1990.

28. Espiner, E. A. The effects of stress on salt and water balance. [Review]. *Baillieres Clinical Endocrinology & Metabolism* 1: 375-390, 1987.

29. Espiner, E. A. Physiology of natriuretic peptides. *Journal of Internal Medicine* 235: 527-541, 1994.

30. Espiner, E. A. and M. G. Nicholls. Human atrial natriuretic peptide. *Clinical Endocrinology* 26: 637-650, 1987.

31. Espiner, E. A., M. G. Nicholls, T. G. Yandle, I. G. Crozier, R. C. Cuneo, McCormickD., and H. Ikram. Studies on the secretion, metabolism and action of atrial natriuretic peptide in man. *Journal of Hypertension - Supplement* 4: S85-S91, 1986.

32. Fitzgerald, W. Labile hypertension and jogging: new diagnostic tool or spurious discovery? *British Medical Journal Clinical Research Ed.* 282: 542-544, 1981.

33. Floras, J. S. and B. L. Senn. Absence of post exercise hypotension and sympathoinhibition in normal subjects: additional evidence for increased sympathetic outflow in borderline hypertension. *Canadian Journal of Cardiology* 7: 253-258, 1991.

34. Floras, J. S., C. A. Sinkey, P. E. Aylward, D. R. Seals, P. N. Thoren, and A. L. Mark. Postexercise hypotension and sympathoinhibition in borderline hypertensive men. *Hypertension* 14: 28-35, 1989.

35. Floras, J. S. and J. Wesche. Haemodynamic contributions to post-exercise hypotension in young adults with hypertension and rapid resting heart rates. *Journal of Human Hypertension* 6: 265-269, 1992.

36. Franklin, P. J., D. J. Green, and N. T. Cable. The influence of thermoregulatory mechanisms on post-exercise hypotension in humans. *Journal of Physiology* 470 231-241, 1993.

37. Freund, B. J., J. R. Claybaugh, M. S. Dice, and G. M. Hashiro. Hormonal and vascular fluid responses to maximal exercise in trained and untrained males. *Journal of Applied Physiology* 63(2): 669-675, 1987.

38. Freund, B. J., J. R. Claybaugh, G. M. Hashiro, M. Buono, and S. Chrisney. Exaggerated ANF response to exercise in middle-aged vs. young runners. *Journal of Applied Physiology* 69: 1607-1614, 1990.

39. Freund, B. J., J. R. Claybaugh, G. M. Hashiro, and M. S. Dice. Hormonal and renal responses to water drinking in moderately trained and untrained humans. *American Journal of Physiology* 254: R417-R423, 1988.

40. Freund, B. J., E. M. Shizuru, G. M. Hashiro, and J. R. Claybaugh. Hormonal, electrolyte, and renal responses to exercise are intensity dependent. *Journal of Applied Physiology* 70: 900-906, 1991.

41. Freund, B. J., C. E. Wade, and J. R. Claybaugh. Effects of exercise on atrial natriuretic factor. Release mechanisms and implications for fluid homeostasis [published erratum appears in Sports Med 1989 Jun;7(6):following Table of Contents]. [Review]. *Sports Medicine* 6: 364-377, 1988.

42. Fyhrquist, F., I. Tikkanen, K. J. Totterman, M. Hynynen, and T. Tikkanen. Plasma atrial natriuretic peptide in health and disease. *European Heart Journal* 8 Suppl B: 117-122, 1987.

43. Gledhill, N., D. Cox, and R. Jamnik. Endurance athletes' stroke volume does not plateau: major advantage is diastolic function. *Medicine & Science in Sports & Exercise* 26: 1116-1121, 1994.

44. Goetz, K. L. Physiology and pathophysiology of atrial peptides. *American Journal of Physiology (endocrinology and metabolism 17)* 254: E1-E15, 1988.

45. Goodman, J. M., A. G. Logan, P. R. McLaughlin, A. Laprade, and P. P. Liu. Atrial natriuretic peptide during acute and prolonged exercise in well-trained men. *International Journal of Sports Medicine* 14: 185-190, 1993.

46. Guyton, A. C. and J. E. Hall. *Textbook of Medical Physiology*. Philadelphia, PA: W.B. Saunders, 1996, p. i-1148.

47. Hagberg, J. M., S. J. Montain, and W. H. Martin. Blood pressure and hemodynamic responses after exercise in older hypertensives. *Journal of Applied Physiology* 63: 270-276, 1987.

48. Hallen, J., L. Gullestad, and O. M. Sejersted. K+ shifts of skeletal muscle during stepwise bicycle exercise with and without β-adrenoreceptor blockade. *Journal of Physiology* 477: 149-159, 1994.

49. Hannum, S. M. and F. W. Kasch. Acute postexercise blood pressure response of hypertensive and normotensive men. *Scandanavian Journal of Sports Science* 3: 11-15, 1981.

50. Hara, K. and J. S. Floras. Effects of naloxone on hemodynamics and sympathetic activity after exercise. *Journal of Applied Physiology* 73: 2028-2035, 1992.

51. Hill, D. W., M. A. Collins, K. J. Cureton, and J. J. DeMello. Blood pressure response after weight training. *Journal of Applied Sport Science Research* 3: 44-47, 1989.

52. Hoffmann, P., M. Delle, and P. Thoren. Role of opioid receptors in the long-lasting blood pressure depression after electric muscle stimulation in the hind leg of the rat. *Acta Physiologica Scandinavica* 140: 191-198, 1990.

53. Hoffmann, P., P. Friberg, D. Ely, and P. Thoren. Effect of spontaneous running on blood pressure, heart rate and cardiac dimensions in developing and established spontaneous hypertension in rats. *Acta Physiologica Scandinavica* 129: 535-542, 1987.

54. Hoffmann, P., J. O. Skarphedinsson, M. Delle, and P. Thoren. Electrical stimulation of the gastrocnemius muscle in the spontaneously hypertensive rat increases the pain threshold: role of different serotonergic receptors. *Acta Physiologica Scandinavica* 138: 125-131, 1990.

55. Hoffmann, P. and P. Thoren. Long-lasting cardiovascular depression induced by acupuncture-like stimulation of the sciatic nerve in unanaesthetized rats. Effects of arousal and type of hypertension. *Acta Physiologica Scandinavica* 127: 119-126, 1986.

56. Hoffmann, P. and P. Thoren. Electric muscle stimulation in the hind leg of the spontaneously hypertensive rat induces a long-lasting fall in blood pressure. *Acta Physiologica Scandinavica* 133: 211-219, 1988.

57. Holland, W. W. and S. Humerfelt. Measurement of blood-pressure: comparison of intraarterial and cuff values. *British Medical Journal* 2: 1241-1243, 1964.

58. Kaufman, F. L., R. L. Hughson, and J. P. Schaman. Effect of exercise on recovery blood pressure in normotensive and hypertensive subjects. *Medicine and Science in Sports and Exercise* 19: 17-20, 1987.

59. Kenney, M. J. and D. R. Seals. Postexercise hypotension. Key features, mechanisms, and clinical significance [see comments]. [Review]. *Hypertension* 22: 653-664, 1993.

60. Kiyonaga, A., K. Arakawa, H. Tanaka, and M. Shindo. Blood pressure and hormonal responses to aerobic exercise. *Hypertension* 7: 125-131, 1985.

61. Kroeker, E. J. and E. H. Wood. Comparison of simultaneously recorded central and peripheral arterial pressure pulses during rest, exercise and tilted position in man. *Circulation Research* 3: 623-632, 1955.

62. Landry, J. F., J. P. Despres, D. Prud'homme, B. Lamarche, A. Tremblay, A. Nadeau, and C. Bouchard. A study of some potential correlates of the hypotensive effects of prolonged submaximal exercise in normotensive men. *Canadian Journal of Physiology & Pharmacology* 70: 53-59, 1992.

63. Lentini, A. C. The blood pressure response to weightlifting, isometric and dynamic exercise in young healthy males. i-180, 1992.(Thesis)

64. Lentini, A. C., R. S. McKelvie, N. McCartney, C. W. Tomlinson, and J. D. MacDougall. Left ventricular response in healthy young men during heavy-intensity weight-lifting exercise. *Journal of Applied Physiology* 75(6): 2703-2710, 1993.

65. MacDonald, J. R., S. A. Interisano, J. D. MacDougall, and E. V. Younglai. The effects of resistance exercise on the secretion of atrial natriuretic peptide. *Medicine & Science in Sports & Exercise* 27: S1311995.(Abstract)

66. MacDougall, J. D. Blood pressure responses to resistive, static and dynamic exercise. In: *Cardiovascular Response to Exercise*, edited by G. F. Fletcher. Mount Kisco, NY: Futura Publishing Company Inc. 1994, p. 155-173.

67. MacDougall, J. D., R. S. McKelvie, D. E. Moroz, D. G. Sale, N. McCartney, and F. Buick. Factors affecting blood pressure during heavy weight lifting and static conditions. *Journal of Applied Physiology* 73(4): 1590-1597, 1992.

68. MacDougall, J. D., D. Tuxen, D. G. Sale, J. R. Moroz, and J. R. Sutton. Arterial blood pressure response to heavy exercise. *Journal of Applied Physiology* 58: 785-790, 1985.

69. Mannix, E. T., P. Palange, G. R. Aronoff, F. Manfredi, and M. O. Farber. Atrial natriuretic peptide and the renin-aldosterone axis during exercise in man. *Medicine & Science in Sports & Exercise* 22: 785-789, 1990.

70. Medbo, J. I. and O. M. Sejersted. Plasma potassium changes with high intensity exercise. *Journal of Physiology* 421: 105-122, 1990.

71. Michel, J. B. and J. F. Arnal. [Atrial natriuretic factor. Current data and future perspectives]. [Review] [French]. *Archives des Maladies du Coeur et des Vaisseaux* 83: 2111-2121, 1990.

72. Mooney, S. and V. B. Unnithan. *Post exercise hypotension in elite female athletes*. 1995, (UnPub)

73. Muller, D., C. Schulze, H. Baumeister, F. Buck, and D. Richter. Rat insulin-degrading enzyme: cleavage pattern of the natriuretic peptide hormones ANP, BNP, and CNP revealed by HPLC and mass spectrometry [published erratum appears in Biochemistry 1993 Apr 13;32(14):3830]. *Biochemistry* 31: 11138-11143, 1992.

74. Needleman, P., E. H. Blaine, J. E. Greenwald, L. M. Marshall, C. B. Saper, P. T. Stockmann, and H. E. Tolunay. The biochemical pharmacology of atrial peptides. *Annual Review of Pharmacology and Toxicology* 29: 23-54, 1989.

75. Novosadova, J. The changes in hematocrit, hemoglobin, plasma volume an proteins during and after different types of exercise. *European Journal of Applied Physiology & Occupational Physiology* 36: 223-230, 1977.

76. O'Connor, P. J., C. X. Bryant, J. P. Veltri, and S. M. Gebhardt. State anxiety and ambulatory blood pressure following resistance exercise in females. *Medicine & Science in Sports & Exercise* 25: 516-521, 1993.

77. Overton, J. M., M. J. Joyner, and C. M. Tipton. Reductions in blood pressure after acute exercise by hypertensive rats. *Journal of Applied Physiology* 64: 748-752, 1988.

78. Paulev, P. E., R. Jordal, O. Kristensen, and J. Ladefoged. Therapeutic effect of exercise on hypertension. *European Journal of Applied Physiology & Occupational Physiology* 53: 180-185, 1984.

79. Perrault, H., M. Cantin, G. Thibault, G. R. Brisson, G. Brisson, and M. Beland. Plasma atrial natriuretic peptide during brief upright and supine exercise in humans. *Journal of Applied Physiology* 66(5): 2159-2167, 1989.

80. Perrault, H., M. Cantin, G. Thibault, G. R. Brisson, G. Brisson, and M. Beland. Plasma atriopeptin response to prolonged cycling in humans. *Journal of Applied Physiology* 70: 979-987, 1991.

81. Perrault, H., B. Melin, C. Jimenez, G. Dureau, P. Dureau, A. M. Allevard, J. M. Cottet-Emard, G. Gauquelin, and C. Gharib. Fluid-regulating and sympathoadrenal hormonal responses to peak exercise following cardiac transplantation. *Journal of Applied Physiology* 76: 230-235, 1994.

82. Perrault, H., J. Miro, A. Davignon, M. Beland, B. Armstrong, G. Thibault, M. Cantin, and C. Chartrand. Decreased plasma atriopeptin response to volume-overloading maneuvers and exercise after atriopulmonary anastomosis of Fontan. *American Journal of Cardiology* 69: 1325-1328, 1992.

83. Pescatello, L. S., A. E. Fargo, C. N. Leach,Jr., and H. H. Scherzer. Short-term effect of dynamic exercise on arterial blood pressure [see comments]. *Circulation* 83: 1557-1561, 1991.

84. Piepoli, M. and A. J. Coats. Postexercise hypotension [letter; comment]. *Hypertension* 23: 677-678, 1994.

85. Piepoli, M., A. J. Coats, S. Adamopoulos, L. Bernardi, Y. H. Feng, J. Conway, and P. Sleight. Persistent peripheral vasodilation and sympathetic activity in hypotension after maximal exercise. *Journal of Applied Physiology* 75: 1807-1814, 1993.

86. Piepoli, M., J. E. Isea, G. Pannarale, S. Adamopoulos, P. Sleight, and A. J. Coats. Load dependence of changes in forearm and peripheral vascular resistance after acute leg exercise in man. *Journal of Physiology* 478: 357-362, 1994.

87. Ploutz-Snyder, L. L., V. A. Convertino, and G. A. Dudley. Resistance exercise-induced fluid shifts: change in active muscle size and plasma volume. *American Journal of Physiology* 269: R536-R543, 1995.

88. Poliner, L. R., G. J. Dehmer, S. E. Lewis, R. W. Parkey, C. G. Blomqvist, and J. T. Willerson. Left Ventricular Performance in Normal Subjects: Comparison of the Responses to Exercise in the Upright and Supine Positions. *Circulation* 62: 528-534, 1980.

89. Ray, C. A., M. D. Delp, and D. K. Hartle. Interactive effect of body posture on exercise-induced atrial natriuretic peptide release. *American Journal of Physiology* 258: E775-E779, 1990.

90. Ray, S. G., M. Pye, K. G. Oldroyd, J. Christie, D. T. Connelly, D. B. Northridge, I. Ford, J. J. Morton, H. J. Dargie, and S. M. Cobbe. Early treatment with captopril after acute myocardial infarction. *British Heart Journal* 69: 215-222, 1993.

91. Richards, A. M., G. Tonolo, J. G. Cleland, G. D. McIntyre, B. J. Leckie, H. J. Dargie, and J. I. Robertson. Plasma atrial natriuretic peptide concentrations during exercise in sodium replete and deplete normal man. *Clinical Science* 72: 159-164, 1987.

92. Robinson, T. E., D. Y. Sue, A. Huszczuk, D. Weiler-Ravell, and J. E. Hansen. Intra-arterial and cuff blood pressure responses during incremental cycle ergometry. *Medicine and Science in Sports and Exercise* 20: 142-149, 1988.

93. Rogers, P. J. G. M. Tyce, K. R. Bailey, and A. A. Bove. Exercise-induced increases in atrial natriuretic factor are attenuated by endurance training. *Journal of the American College of Cardiology* 18: 1236-1241, 1991.

94. Saito, Y., K. Nakao, and K. Nishimura. Clinical application of atrial natriuretic peptide in patients with congestive heart failure: beneficial effects on left ventricular function. *Circulation* 76: 1151987.

95. Saito, Y., K. Nakao, A. Sugawara, K. Nishimura, M. Sakamoto, N. Morii, H. Itoh, S. Shiono, T. Kuriyama, and et al. Atrial natriuretic polypeptide during exercise in healthy man. *Acta Endocrinologica* 116: 59-65, 1987.

96. Seals, D. R. and J. M. Hagberg. The effect of exercise training on human hypertension: a review. *Medicine and Science in Sports and Exercise* 16: 207-215, 1984.

97. Shyu, B. C., S. A. Andersson, and P. Thoren. Circulatory depression following low frequency stimulation of the sciatic nerve in anesthetized rats. *Acta Physiologica Scandinavica* 121: 97-102, 1984.

98. Somers, V. K., J. Conway, A. J. Coats, J. Isea, and P. Sleight. Postexercise hypotension is not sustained in normal and hypertensive humans. *Hypertension* 18: 211-215, 1991.

99. Somers, V. K., J. Conway, M. LeWinter, and P. Sleight. The role of baroreflex sensitivity in post-exercise hypotension. *Journal of Hypertension - Supplement* 3 Suppl 3: S129-S130, 1985.

100. Steingart, R. M., J. Wexler, S. Slagle, and J. Scheuer. Radionuclide ventriculographic responses to graded supine and upright exercise: critical role of the Frank-Starling mechanism at submaximal exercise. *American Journal of Cardiology* 53: 1671-1677, 1984.

101. Seuss, Dr. *Green Eggs and Ham.* New York: Random House, Inc. 1960.

102. Tanaka, H., M. Shindo, J. Gutkowska, A. Kinoshita, H. Urata, and M. Ikeda. Effect of acute exercise on plasma immunoreactive-atrial natriuretic factor. *Life Sciences* 39: 1685-1693, 1986.

103. Taylor-Tolbert, N. S., D. R. Dengel, M. D. Brown, S. D. McCole, R. J. Zimet, R. E. Pratley, and J. M. Hagberg. Ambulatory blood pressure following acute exercise in older men with essential hypertension. *in submission to Hypertension* 1995.

104. Tipton, C. M., R. D. Matthes, K. D. Marcus, K. A. Rowlett, and J. R. Leininger. Influences of exercise intensity, age, and medication on resting systolic blood pressure of SHR populations. *Journal of Applied Physiology: Respiratory, Environmental & Exercise Physiology* 55: 1305-1310, 1983.

105. Tipton, C. M., S. McMahon, E. M. Youmans, J. M. Overton, J. G. Edwards, E. B. Pepin, and C. Lauber. Response of hypertensive rats to acute and chronic conditions of static exercise. *American Journal of Physiology* 254: H592-H598, 1988.

106. Tipton, C. M., L. A. Sebastian, J. M. Overton, C. R. Woodman, and S. B. Williams. Chronic exercise and its hemodynamic influences on resting blood pressure of hypertensive rats. *Journal of Applied Physiology* 71: 2206-2210, 1991.

107. Urata, H., Y. Tanabe, A. Kiyonaga, M. Ikeda, H. Tanaka, M. Shindo, and K. Arakawa. Antihypertensive and volume-depleting effects of mild exercise on essential hypertension. *Hypertension* 9: 245-252, 1987.

108. Vollmer-Larsen, B., A. Vollmer-Larsen, O. G. Larsen, L. Breum, and J. Larsen. Atrial natriuretic factor during exercise in male endurance athletes: effect of training. *Clinical Physiology* 9: 449-456, 1989.

109. Webster, J., C. T. Dollery, and C. N. Hensby. Circulating prostacyclin concentrations may be increased by bendrofluazide in patients with essential hypertension. *Clinical Science* 59 Suppl 6: 125s-128s, 1980.

110. Wiecek, E. M., N. McCartney, and R. S. McKelvie. Comparison of direct and indirect measures of systemic arterial pressure during weightliftng in coronary artery disease. *American Journal of Cardiology* 66: 1065-1069, 1990.

111. Wilcox, R. G., T. Bennett, A. M. Brown, and I. A. Macdonald. Is exercise good for high blood pressure? *British Medical Journal Clinical Research Ed.* 285: 767-769, 1982.

112. Wilcox, R. G., T. Bennett, I. A. Macdonald, F. Broughton Pipkin, and P. H. Baylis. Post-exercise hypotension: the effects of epanolol or atenolol on some hormonal and cardiovascular variables in hypertensive men. *British Journal of Clinical Pharmacology* 24: 151-162, 1987.

113. Wilkins, M. R., J. A. Wood, D. Adu, C. J. Lote, M. J. Kendall, and J. Michael. Change in plasma immunoreactive atrial natriuretic peptide during sequential ultrafiltration and haemodialysis. *Clinical Science* 71: 157-160, 1986.

114. Yandle, T. G. Biochemistry of natriuretic peptides. *Journal of Internal Medicine* 235: 561-576, 1994.

115. Yandle, T. G., A. M. Richards, and M. G. Nicholls. Metabolic clearance rate and plasma half life of alpha-human atrial natriuretic peptide in man. *Life Science* 38: 1827-1833, 1986.

116. Yao, T., S. Andersson, and P. Thoren. Long-lasting cardiovascular depressor response following sciatic stimulation in spontaneously hypertensive rats. Evidence for the involvement of central endorphin and serotonin systems. *Brain Research* 244: 295-303, 1982.

117. Yao, T., S. Andersson, and P. Thoren. Long-lasting cardiovascular depression induced by acupuncture-like stimulation of the sciatic nerve in unanaesthetized spontaneously hypertensive rats. *Brain Research* 240: 77-85, 1982.

Appendix A

Subject Characteristics

Subject Characteristics

Subject	Age (yrs)	Weight (kg)	Height (cm)	1RM (kg)	$VO_{2\ Max}$ ($ml \cdot kg^{-1}$)
1	22	70	178	140.00	58.05
2	22	80	175	125.00	47.56
3	23	93	185	110.00	43.64
4	22	74	175	142.00	52.45
5	22	67	173	99.00	58.37
6	28	78	182	97.50	55.22
7	25	73	175	103.00	37.72
8	30	68	170	102.50	56.76
9	25	71	178	132.50	62.48
10	25	81	183	110.00	62.60
11	25	79	172	103.75	58.45
12	24	65	170	93.75	47.59
13	23	66	168	95.00	59.90
MEAN	24.3	74.2	175.7	111.8	53.9
STDEV	2.46	7.87	5.30	17.13	7.65

Appendix B

Consent Form

Consent Form

Stimulus for Atrial Natriuretic Peptide Secretion: Pressure or Distension

INVESTIGATORS	ADDRESSES	TELEPHONE#
Dr. J.D.MacDougall, PhD	Dept. of Kinesiology	x 24647
Dr. N. McCartney, PhD	Dept. of Kinesiology	x 24469
Dr. M.A. Tarnopolsky, MD,PhD	Dept. of Kinesiology	x 23591
Dr. R.S. McKelvie, MD	Dept. of Cardiology	
Mr. J.R. MacDonald	Dept. of Kinesiology	x 23596
Ms. K.M. Smith	Dept. of Kinesiology	x 23596

Purpose:

Through the uncoupling of atrial distension and pressure, we hope to determine the mechanism for Atrial Natriuretic Peptide secretion. Previous research has shown that a combination of pressure and distension of the atria causes secretion of this hormone, although these studies have been unable to distinguish between the two factors. Resistance exercise which incorporates a Valsalva manoeuvre (the exhalation against a closed glottis) will produce an increase in pressure without a concomitant increase in volume (distension) and will allow us to evaluate the effects of increased pressure. Conversely, endurance exercise (cycle ergometry) will elicit an increase in volume (distension) while moderating pressure at low levels. Through the measurement of blood pressure and blood collection we will attempt to determine if the actual release mechanism of Atrial Natriuretic Peptide is a pressure response or a volume (distension) response.

Procedure:

A) Preliminary Testing

Subjects will be required to perform a maximal oxygen uptake test on a cycle ergometer in order to determine their percent maximum values for testing workloads. Additionally, unilateral 1 RM for the leg press will be found in order to determine the appropriate resistance settings.

B) Resistance Exercise

Subjects will report to the laboratory where they will undergo catheterization of the brachial artery with a pressure transducer and blood sampling line. Additionally, an esophogeal pressure transducer will be introduced through the nasal passage in order to evaluate intrathoracic pressures. V5 reference electrodes will be placed on the chest and the signal will be coupled to a counting device to record the number of cardiac cycles. Upon completion of these procedures, subjects will complete unilateral leg press at 65% unilateral 1 RM for a duration of 15 minutes using the contralateral limb when extreme fatigue occurs. Blood (approx. 10 ml) will be taken at rest, 7.5 and 15 minutes into exercise and 2, 4, 6, 8, 10, 15, 30, 45 and 60 minutes post exercise. Concomitant summed heart cycles will be recorded at each time point.

C) Endurance Exercise

One week later, subjects will undergo a bout of endurance exercise. The same catheterization and electrode placement procedures described above will be employed. Additionally, subjects will undergo oxygen uptake assessment to ensure accurate percentage of maximal values. Participants will then be required to cycle at a power output approximating 65% of maximum. During the exercise session, blood will be sampled at the number of cardiac cycles completed which will correspond to measures taken during the resistance exercise. (i.e. if during the resistance exercise, blood was drawn at 5 minutes, which corresponded to 800 cardiac cycles, the endurance session would collect blood at a time point corresponding to 800 cardiac cycles.)

D) Urine Collection:

Subjects will be required to perform urine collection for 24 hours on each of the test days and a control day for analysis of sodium and creatinine excretion.

Potential Risks:

Exercise may cause slight muscle strains and as with all exercise, there is a very slight risk of having a heart attack or collapsing. A supervised, adequate warm-up should alleviate the complication of muscle strains.

The catheter inserted for blood pressure and sampling may cause slight bruising, but this will disappear within a few days. The catheter also imposes a risk of a blood clot to the hand. This could result in severe, permanent damage to the hand, including the loss of a finger. A published survey of complications from arterial catheterization found a one in one thousand (1/1000) chance of a blood clot developing when the catheter was left in place for twenty-four hours. When this complication

occurred, there was always complete resolution of the blood clot without residual damage. In this laboratory's experience, when the catheter has been in place for only a few hours, there has not been any complication related to a blood clot. The risk of a blood clot is minimized by the short duration that the catheter will be in place. A slight risk of infection related to the catheterization of the artery also exists. This could result in a generalized infection of the body. However, this is only a very small potential risk as a recent survey did not find evidence of infection nor have any of the previous subjects in this laboratory suffered this complication. The esophageal catheter will not cause any pain, but may trigger a "gag reflex". This will pose no risks to the subject. Emergency equipment is available at all times in the laboratory and a physician will be present should any such complication arise. If any problems occur after the test is completed, a contact number of a physician will be provided.

Withdrawal:

Subjects will be free to withdraw at any point during the study without repercussion. Withdrawing subjects will be permitted to view their collected data to date, after which point, that data will be destroyed.

Confidentiality:

The data will be stored inside a locked filing cabinet within a locked office located in the Human Performance Laboratory. Only the listed investigators will have access to this data. Collected data will be used in the preparation of scientific manuscripts. Subjects will in no way be identified in resulting publications or presentations.

Remuneration:

Subjects will be compensated $100.00 for their time commitment to this study.

Having read the above information, I consent to participate in all aspects of the study. I am aware that I am able to withdrawal at any time without repercussion.

_____ (signature) _____ (date)

_____ (witness) _____ (date)

Appendix C

Raw Data

(i) Exercise Time

	Time (min)	
Subject	Resistance	Endurance
1	15.25	12.87
2	15.25	14.45
3	15.25	12.03
4	15.25	
5	15.25	14.82
6	15.25	14.00
7	15.25	15.13
8	15.25	11.33
9	15.25	13.78
10	15.25	14.15
11	15.25	13.48
12	15.25	15.20
13	15.25	14.53
MEAN	15.25	13.78
STDEV	0.00	1.16

(ii) Atrial Natriuretic Peptide ($pg \cdot ml^{-1}$)

	Resistance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
8	3.24	3.71	2.96	2.66	3.40	0.57	3.34	2.57		1.49	3.46	
9	4.34	7.36	6.3	5.43	10.23	5.40	6.12	4.40	3.24	5.90	1.18	2.08
10	3.18	7.05	6.74	11.04	10.83	7.89	7.39	4.24	4.21	3.90	3.87	3.56
11	1.57	2.87	2.91	3.56		3.84	3.78	3.02	2.51	3.18	1.47	4.24
12	6.02	6.08	4.24	5.12	4.15	4.12	4.37	4.71	5.15	4.06	3.4	4.52
13	8.3	2.24	5.05	4.18	4.43	3.21	3.99	7.74	5.68	4.84	0.81	6.68
MEAN	4.44	4.89	4.70	5.33	6.61	4.17	4.83	4.45	4.16	3.89	2.37	4.22
STDEV	2.39	2.22	1.63	2.98	3.61	2.42	1.58	1.82	1.31	1.50	1.35	1.67

	Endurance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
8		9.73	5.71	10.48	10.26	9.42	9.98	8.42	8.42	6.77	7.58	5.4
9	8.24	3.24	2.47	1.87	2.99	2.18	3.62	3.21	1.70	6.86	5.21	5.52
10	5.02	12.79	15.69	31.73	10.8	17.94	10.26	11.04	7.24	6.99	4.52	3.81
11	2.84	1.83	5.18	5.52	2.78	4.21	2.86	3.34	3.56	3.37	2.03	4.77
12	4.8	4.52	4.46	3.78	3.93	4.06	4.24	4.84	4.15	4.21	2.02	0.95
13	4.24	5.05	2.73	3.81	1.87	4.43	3.11	4.06	5.05	4.87	4.24	9.24
MEAN	5.03	6.20	6.04	9.53	5.44	7.04	5.68	5.82	5.02	5.51	4.27	4.95
STDEV	1.98	4.19	4.9	11.26	4.00	5.86	3.48	3.20	2.47	1.57	2.10	2.69

(iii) Peak Systolic Blood Pressure (mmHg)

	Resistance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	193	305	323	283	147	167	163	162	171	149	172	163
2	186	300	290	236	170	117	129	121	110	121	101	117
3	162	229	242	232	163	160	142	138	149	131	143	141
4	157	256	276	296	170	158	150	162	173	148	126	137
5	168	243	265	248	184	164	156	159	151	155	158	163
6	151	207	219	206	165	153	158	145	152	145	142	150
7	169	259	253	270	201	202	187	178	166	155	167	151
8	138	254	234	249	169	145	149	146	136	123	139	134
9	189	376	379	371	239	205	186	178	174	172	162	164
10	196	259	280	315	188	167	181	159	154	151	151	159
11	167	269	284	274	225	197	189	169	159	140	164	147
12	179	235	241	227	167	175	170	162	167	161	157	169
13	157	240	206	235	169	174	153	153	142	148	135	141
MEAN	170.15	264	268.62	264.77	181.31	168.00	162.54	156.31	154.15	146.08	147.46	148.92
STDEV	17.57	42.91	45.94	44.18	26.17	24.13	18.9	15.92	17.86	14.49	19.53	14.85

	Endurance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	188	282	251	231	199	180	169	173	165	174	186	179
2	203	281	131	236	208	178	192	180	155	151	143	152
3	152	207	193	177	148	137	136	126	127	115	120	129
4	177	244	254	225	193	178	164	151	156	154	146	155
5	181	273	246	222	175	181	169	168	159	168	173	182
6	152	225	218	215	167	146	144	143	107	143	143	149
7	147	176	190	175	144	154	153	161	144	138	144	144
8	146	260	257	231	164	150	142	130	133	134	137	145
9	196	293	252	240	211	181	164	157	151	144	149	141
10	183	289	233	228	184	148	140	138	143	145	152	158
11	149	269	234	229	170	160	143	151	156	153	159	169
12	186	253	233	225	179	159	155	182	160	165	176	174
13	182	225	239	191	155	149	152	151	156	147	147	147
MEAN	172.46	252.08	225.46	217.31	176.69	161.62	155.62	154.69	147.08	148.54	151.92	155.69
STDEV	20.3	35.25	35.65	21.88	21.69	15.87	15.68	17.87	16.28	15.46	17.72	15.99

(iv) Peak Diastolic Blood Pressure (mmHg)

	Resistance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	86	159	181	161	76	79	79	77	82	71	94	72
2	95	124	120	120	73	60	76	69	87	88	84	88
3	83	138	149	153	87	90	82	84	91	77	81	78
4	94	137	186	186	86	91	90	98	109	92	86	89
5	91	139	152	133	81	82	83	86	86	90	90	98
6	96	117	114	108	95	90	92	85	87	83	87	88
7	103	138	153	177	105	112	114	118	108	103	106	100
8	84	151	117	136	83	73	84	86	81	77	82	81
9	102	234	216	186	101	93	92	102	103	106	99	93
10	84	125	174	170	81	75	89	79	82	84	79	80
11	77	122	126	114	82	84	78	76	76	76	79	68
12	102	147	138	133	89	99	95	90	96	92	94	98
13	89	133	103	127	91	90	84	80	87	87	82	84
MEAN	91.23	143.38	148.38	146.46	86.92	86.00	87.54	86.92	90.38	86.62	87.92	85.92
STDEV	8.28	29.75	33.40	27.31	9.29	12.92	9.90	12.87	10.56	10.32	8.29	10.00

	Endurance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	94	98	94	98	87	91	96	94	95	96	93	88
2	100	100	103	101	90	90	96	91	84	81	74	73
3	89	80	80	75	72	77	85	79	77	71	74	79
4	107	114	118	110	106	107	96	98	108	105	96	96
5	87	96	98	89	82	89	88	96	99	90	99	105
6	94	95	96	95	90	91	91	88	144	90	87	89
7	88	90	92	95	85	93	86	97	90	82	86	93
8	82	103	107	98	74	76	81	76	82	78	79	87
9	91	92	85	84	93	89	98	96	93	86	93	84
10	93	82	78	77	72	67	72	77	77	70	77	75
11	80	100	92	88	81	81	84	88	89	84	85	98
12	99	108	99	96	89	87	94	94	96	94	97	95
13	97	107	97	94	78	90	88	96	87	82	82	88
MEAN	92.38	97.31	95.31	92.31	84.54	86.77	88.85	90.00	93.92	85.31	86.31	88.46
STDEV	7.44	9.82	10.80	9.65	9.60	9.79	7.43	7.90	17.41	9.82	8.77	9.21

(v) Trough Systolic Blood Pressure (mmHg)

	Resistance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	168	173	138	133	100	128	147	131	141	120	149	137
2	172	213	196	138	122	85	116	110	97	106	87	106
3	142	150	120	96	115	130	129	120	111	122	120	119
4	133	146	140	132	140	136	131	134	129	116	114	116
5	107	158	134	140	158	140	141	117	128	118	127	123
6	122	165	177	162	137	136	138	128	134	137	133	127
7	163	200	162	136	160	156	157	147	140	145	138	138
8	126	175	178	173	144	128	116	117	104	109	120	124
9	157	161	149	150	197	168	153	140	147	145	140	130
10	151	209	171	141	144	130	140	121	137	127	133	122
11	148	211	203	182	193	169	163	152	143	112	127	133
12	166	183	173	147	147	139	151	146	136	145	141	157
13	133	189	164	170	148	135	125	123	119	121	112	121
MEAN	145.23	179.46	161.92	146.15	146.54	136.92	139.00	129.69	128.15	124.85	126.23	127.15
STDEV	20.09	23.41	24.67	22.29	27.28	21.07	15.08	13.28	15.78	13.89	16.14	12.51

	Endurance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	167	245	218	199	180	153	146	146	151	156	164	168
2	172	253	112	183	178	169	172	162	137	125	121	139
3	128	165	164	145	129	115	106	107	116	106	102	105
4	145	194	224	194	153	144	129	120	122	130	128	143
5	159	218	187	158	131	135	131	131	126	141	125	125
6	134	196	199	192	154	133	129	127	94	124	130	130
7	117	152	159	148	116	115	129	112	121	127	117	132
8	131	217	206	189	152	118	118	119	108	114	97	114
9	135	240	212	192	166	136	119	119	109	118	113	122
10	138	258	188	188	123	112	102	113	99	113	103	130
11	126	215	195	175	151	135	128	128	139	132	140	133
12	153	215	199	188	159	141	123	141	138	152	163	164
13	139	192	174	165	139	130	136	113	140	133	136	124
MEAN	141.85	212.31	187.46	178.15	148.54	133.54	128.31	126.00	123.08	128.54	126.08	133.00
STDEV	16.53	32.32	29.96	18.26	20.06	16.37	17.56	15.76	17.44	14.72	21.12	17.68

(vi) Trough Diastolic Blood Pressure (mmHg)

	Resistance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	69	72	69	60	54	63	69	60	65	65	72	63
2	78	69	69	55	58	47	68	61	76	77	72	72
3	69	75	60	43	64	68	71	70	70	69	71	57
4	81	60	57	58	77	76	75	78	76	65	73	69
5	66	48	49	64	67	67	70	65	69	68	73	68
6	74	75	67	74	76	76	80	75	78	74	77	75
7	96	92	85	84	82	85	88	92	87	92	91	93
8	75	77	75	70	67	65	63	63	65	68	72	74
9	82	76	59	68	88	79	77	85	84	82	87	77
10	61	74	76	60	64	62	65	64	75	67	71	62
11	65	71	64	61	69	61	65	69	66	56	59	60
12	85	101	91	68	76	79	85	78	74	81	80	90
13	62	78	73	71	76	72	73	68	68	69	55	68
MEAN	74.08	74.46	68.77	64.31	70.62	69.23	73.00	71.38	73.31	71.77	73.31	71.38
STDEV	10.18	12.88	11.53	10.06	9.62	10.07	7.75	9.72	7.02	9.30	9.64	10.76

	Endurance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	73	73	75	69	77	74	75	78	85	83	76	80
2	78	82	76	75	72	83	78	84	73	60	58	59
3	67	50	60	58	65	66	64	70	65	61	61	61
4	87	87	95	88	79	84	75	78	82	80	84	88
5	75	59	56	59	66	59	65	71	72	75	72	75
6	82	77	79	77	82	79	79	78	128	75	75	73
7	69	73	71	67	65	72	69	72	73	73	64	72
8	73	78	77	65	65	63	62	71	67	68	60	73
9	63	63	62	60	71	67	70	72	59	73	68	77
10	62	56	52	53	45	58	54	64	52	55	53	66
11	63	61	64	69	71	63	71	79	76	76	72	66
12	76	81	78	71	75	74	68	76	81	86	86	86
13	68	76	71	66	68	79	70	61	76	73	68	72
MEAN	72.00	70.46	70.46	67.46	69.31	70.85	69.23	73.38	76.08	72.15	69.00	72.92
STDEV	7.64	11.42	11.54	9.23	9.21	8.86	6.92	6.34	18.14	9.07	9.86	8.67

(vii) Average Systolic Blood Pressure (mmHg)

	Resistance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	182	225	225	195	127	154	156	146	155	137	155	153
2	179	269	234	187	158	106	126	113	102	112	93	113
3	152	184	178	160	143	143	137	129	126	125	130	127
4	145	196	200	207	159	150	141	146	147	133	120	127
5	137	194	197	196	170	152	148	143	140	136	141	139
6	138	187	199	189	152	146	146	138	138	141	138	141
7	166	225	202	207	179	180	173	161	150	151	148	145
8	132	208	208	207	157	136	136	127	121	116	128	130
9	175	253	243	255	221	188	171	158	161	161	154	144
10	175	240	219	214	168	146	155	143	144	138	144	140
11	159	211	240	230	208	185	177	162	152	129	143	140
12	175	209	207	182	158	157	163	153	153	155	150	164
13	144	210	190	204	156	158	139	136	131	133	124	131
MEAN	158.38	216.23	210.92	202.54	165.85	153.92	151.38	142.69	140.00	135.92	136.00	138.00
STDEV	17.95	25.56	19.90	23.19	25.14	21.82	15.99	14.30	16.41	14.16	17.12	12.86

	Endurance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	175	264	232	218	188	169	159	162	159	165	174	174
2	190	267	241	211	189	173	181	170	146	141	132	145
3	138	186	180	161	141	126	120	116	121	111	108	116
4	164	218	238	211	175	160	144	136	140	142	135	148
5	170	247	221	196	154	157	154	149	145	152	151	155
6	142	213	210	202	161	139	138	135	137	132	137	137
7	135	164	173	164	130	136	138	131	133	133	132	137
8	138	238	233	209	157	134	129	124	121	125	120	127
9	171	271	233	219	188	159	145	140	132	133	134	134
10	156	277	215	207	152	131	121	126	126	126	130	145
11	135	246	217	209	162	147	137	144	147	144	152	142
12	170	234	220	207	171	150	143	152	151	159	169	168
13	158	214	192	178	149	141	145	137	149	139	142	136
MEAN	157.08	233.77	215.77	199.38	162.85	147.85	142.62	140.15	139.00	138.62	139.69	143.38
STDEV	18.06	33.96	21.88	19.37	18.59	14.89	16.13	15.23	11.90	14.58	18.23	15.68

(viii) Average Diastolic Blood Pressure (mmHg)

	Resistance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	80	111	114	101	61	73	73	68	73	68	78	68
2	86	94	91	78	68	52	71	66	81	82	80	82
3	77	97	101	87	70	76	75	77	77	73	76	70
4	88	105	113	113	82	85	83	87	89	80	79	80
5	77	85	91	91	76	75	78	78	77	78	79	79
6	81	94	94	91	83	82	85	81	81	83	81	82
7	67	113	92	91	89	82	74	61	53	55	52	48
8	79	108	95	100	74	69	75	74	73	72	78	77
9	90	127	109	107	94	86	84	93	93	93	94	83
10	77	98	102	96	70	69	73	73	78	75	75	70
11	70	71	87	83	75	71	70	72	71	63	69	64
12	92	121	109	99	83	90	91	83	85	87	88	94
13	72	101	91	97	81	81	79	75	78	78	72	76
MEAN	79.69	101.92	99.15	94.92	77.38	76.23	77.77	76.00	77.62	75.92	77.00	74.85
STDEV	7.66	14.87	9.40	9.55	9.10	9.93	6.30	8.70	9.73	10.08	9.85	11.25

	Endurance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	80	85	83	85	81	82	84	86	91	90	85	84
2	89	91	89	86	81	87	87	88	77	71	65	67
3	76	68	69	66	69	72	75	72	74	68	65	67
4	95	98	108	99	93	97	85	87	92	93	89	92
5	81	82	76	77	76	75	76	83	85	83	86	88
6	86	87	87	87	86	84	86	83	82	83	82	79
7	58	83	90	82	55	53	59	49	53	55	56	59
8	77	87	88	80	68	69	71	73	73	74	71	77
9	78	78	75	73	77	77	86	85	76	80	80	80
10	73	70	64	63	59	62	63	70	64	63	62	70
11	71	82	79	78	76	73	79	83	82	79	78	72
12	89	91	90	84	83	81	81	85	88	89	91	90
13	82	93	82	77	75	84	82	81	82	77	75	81
MEAN	79.62	84.23	83.08	79.77	75.31	76.62	78.00	78.85	78.38	77.31	75.77	77.38
STDEV	9.44	8.61	11.13	9.34	10.51	11.35	8.98	10.74	10.91	11.03	11.16	9.95

(ix) Pulse Pressure (mmHg)

	Resistance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	102	114	111	94	66	81	83	78	82	69	77	85
2	93	175	143	109	90	54	55	47	21	30	13	31
3	75	87	77	73	73	67	62	52	49	52	54	57
4	57	91	87	94	77	65	58	59	58	53	41	47
5	60	109	106	105	94	77	70	65	63	58	62	60
6	57	93	105	98	69	64	61	57	57	58	57	59
7	99	112	110	116	90	98	99	100	97	96	96	97
8	53	100	113	107	83	67	61	53	48	44	50	53
9	85	126	134	148	127	102	87	65	68	68	60	61
10	98	142	117	118	98	77	82	70	66	63	69	70
11	89	140	153	147	133	114	107	90	81	66	74	76
12	83	88	98	83	75	67	72	70	68	68	62	70
13	72	109	99	107	75	77	60	61	53	55	52	55
MEAN	78.69	114.31	111.77	107.62	88.46	77.69	73.62	66.69	62.38	60.00	59.00	63.15
STDEV	17.58	25.74	21.32	21.67	20.90	17.29	16.69	15.23	18.80	15.42	19.66	16.87

	Endurance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	95	179	149	133	107	87	75	76	68	75	89	90
2	101	176	152	125	108	86	94	82	69	70	67	78
3	62	118	111	95	72	54	45	44	47	43	43	49
4	69	120	130	112	82	63	59	49	48	49	46	56
5	89	165	145	119	78	82	78	66	60	69	65	67
6	56	126	123	115	75	55	52	52	55	49	55	58
7	77	81	83	82	75	83	79	82	80	78	76	78
8	61	151	145	129	89	65	58	51	48	51	49	50
9	93	193	158	146	111	82	59	55	56	53	54	54
10	83	207	151	144	93	69	58	56	62	63	68	75
11	64	164	138	131	86	74	58	61	65	65	74	70
12	81	143	130	123	88	69	62	67	63	70	78	78
13	76	121	110	101	74	57	63	56	67	62	67	55
MEAN	77.46	149.54	132.69	119.62	87.54	71.23	64.62	61.31	60.62	61.31	63.92	66.00
STDEV	14.45	35.57	21.43	18.65	13.67	11.99	13.24	12.47	9.68	11.21	13.76	13.17

(x) Mean Arterial Pressure (mmHg)

	Resistance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	105	142	142	125	78	95	96	90	95	87	95	91
2	107	127	117	102	86	86	85	82	92	92	83	99
3	99	122	120	108	88	96	96	94	95	90	92	89
4	96	132	137	139	103	106	103	108	109	98	93	110
5	101	115	117	115	102	99	100	99	97	95	99	98
6	100	125	124	120	105	102	105	100	101	100	100	101
7	118	138	132	137	109	117	117	118	112	114	114	111
8	95	136	119	122	92	89	95	92	89	87	93	93
9	113	163	144	142	122	112	109	113	112	112	111	100
10	104	139	137	128	95	93	97	93	97	92	94	89
11	93	135	122	117	102	97	95	94	92	80	87	83
12	120	151	138	124	106	113	115	106	108	110	108	117
13	93	130	116	124	102	101	98	95	94	93	87	91
MEAN	103.38	135.00	128.08	123.31	99.23	100.46	100.85	98.77	99.46	96.15	96.62	97.85
STDEV	9.01	12.52	10.46	11.61	11.37	9.39	8.85	10.03	8.08	10.38	9.50	9.99

	Endurance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	103	123	117	116	107	105	79	106	109	109	105	105
2	111	126	118	112	105	109	111	108	96	89	82	86
3	98	101	100	96	89	90	90	89	90	84	80	85
4	117	129	138	128	113	116	105	115	109	110	105	111
5	106	121	114	109	103	98	99	104	104	103	103	106
6	104	119	119	117	108	103	104	103	100	98	101	97
7	95	104	105	102	90	98	96	96	96	93	91	95
8	96	123	122	114	91	88	90	90	89	89	86	92
9	104	123	118	112	107	103	105	103	94	96	96	96
10	95	115	105	102	79	80	80	90	84	82	81	90
11	93	122	116	114	102	96	99	101	101	96	99	91
12	115	129	124	117	108	104	103	107	111	112	115	113
13	103	119	111	105	95	102	99	99	100	92	91	97
MEAN	103.08	119.54	115.92	111.08	99.77	99.38	96.92	100.85	98.69	96.38	95.00	97.23
STDEV	7.73	8.52	9.70	8.33	10.00	9.41	9.72	7.64	8.28	9.73	10.88	9.02

(xi) Exercise Oxygen Consumption ($ml \cdot kg^{-1} \cdot m^{-1}$)

	Resistance Trial			
Subject	Baseline	During 5	During 10	During 15
1	3.13	20.44	25.56	31.90
2	5.14	23.63	23.79	29.45
3	1.52	15.22	16.00	21.22
4	2.00	16.89	23.93	28.17
5	2.53	18.98	20.70	21.27
6	3.85	16.53	18.02	18.05
7	2.98	13.27	15.55	15.84
8	3.20	11.47	15.57	21.11
9	5.80	24.77	26.85	28.20
10	2.68	16.56	22.63	21.91
11	4.82	13.97	14.23	14.66
12	7.15	17.27	19.51	21.45
13	1.63	14.92	17.89	16.49
MEAN	3.57	17.22	20.02	22.29
STDEV	1.70	3.88	4.21	5.55

	Endurance Trial			
Subject	Baseline	During 5	During 10	During 15
1	4.74	39.53	39.47	40.13
2	4.42	30.81	32.49	32.49
3	5.30	23.29	27.49	29.08
4	3.42	28.81	30.00	35.58
5	4.74	39.43	42.66	41.87
6	2.34	33.15	34.48	36.40
7	5.74	26.68	16.43	17.01
8	2.56	38.00	40.22	38.31
9	5.96	41.74	44.54	43.33
10	6.34	39.70	39.78	42.16
11	3.76	39.31	40.31	39.88
12	4.82	32.52	32.70	32.98
13	8.64	38.73	35.61	36.22
MEAN	4.83	34.75	35.09	35.80
STDEV	1.68	5.92	7.56	7.03

(xii) Heart Rate (bpm)

	Resistance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	69	135	144	156	107	87	85	84	84	74	62	63
2	53	137	154	160	123	75	76	84	79	69	72	61
3	57	116	142	151	105	91	84	92	88	79	74	66
4	63	130	166	174	113	100	96	96	90	80	76	72
5	75	128	144	150	97	93	90	91	89	80	76	77
6	63	91	99	106	70	68	73	69	66	59	62	60
7	83	120	153	162	137	120	107	93	96	91	67	87
8	79	134	157	173	129	114	114	96	96	89	84	80
9	66	139	145	161	120	108	102	98	91	75	75	71
10	80	114	133	148	109	99	87	80	83	78	69	66
11	51	95	103	110	75	63	60	63	58	62	60	50
12	69	134	151	152	121	113	95	86	85	77	80	67
13	100	134	147	155	108	92	92	94	88	89	83	75
MEAN	69.85	123.62	141.38	150.62	108.77	94.08	89.31	86.62	84.08	77.08	72.31	68.85
STDEV	13.57	15.75	19.65	20.56	19.37	17.69	14.50	10.70	11.02	9.72	7.91	9.67

	Endurance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	58	138	147	149	97	92	78	78	80	67	62	59
2	65	136	147	149	116	96	103	75	74	70	58	52
3	59	116	133	148	101	94	96	79	80	75	71	68
4	70	136	162	171	125	111	101	99	91	77	70	64
5	65	145	151	156	114	100	93	89	85	82	82	80
6	74	128	131	137	82	73	73	74	71	72	68	68
7	84	133	143	151	122	110	101	94	88	81	85	75
8	69	161	171	171	115	112	106	98	96	91	90	81
9	70	142	153	155	112	104	95	83	86	78	73	67
10	64	139	151	160	130	108	101	92	88	73	69	61
11	63	135	134	137	85	74	67	70	70	65	59	55
12	66	150	154	156	117	104	100	81	78	74	65	64
13	98	157	166	168	123	116	106	92	90	85	82	81
MEAN	69.62	139.69	149.46	154.46	110.69	99.54	93.85	84.92	82.85	76.15	71.85	67.31
STDEV	10.84	11.86	12.37	11.14	15.06	13.65	12.86	9.62	8.07	7.30	10.16	9.63

(xiii) Rate Pressure Product (10^3)

	Resistance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	12.558	30.375	32.400	30.420	13.589	13.398	13.260	12.264	13.020	10.138	9.610	9.639
2	9.487	36.853	36.036	29.920	19.434	7.950	9.576	9.492	8.058	7.728	6.696	6.893
3	8.664	21.344	25.276	24.160	15.015	13.013	11.508	11.868	11.088	9.875	9.620	8.382
4	9.135	25.480	33.200	36.018	17.967	15.000	13.536	14.016	13.230	10.640	9.120	9.144
5	10.275	24.832	28.368	29.400	16.490	14.136	13.320	13.013	12.460	10.880	10.716	10.703
6	8.694	17.017	19.701	20.034	10.640	9.928	10.658	9.522	9.108	8.319	8.556	8.460
7	13.778	27.000	30.906	33.534	24.523	21.600	18.511	14.973	14.400	13.741	9.916	12.615
8	10.428	27.872	32.656	35.811	20.253	15.504	15.504	12.192	11.616	10.324	10.752	10.400
9	11.550	35.167	35.235	41.055	26.520	20.304	17.442	15.484	14.651	12.075	11.550	10.224
10	14.000	27.360	29.127	31.672	18.312	14.454	13.485	11.440	11.952	10.764	9.936	9.240
11	8.109	20.045	24.720	25.300	15.600	11.655	10.620	10.206	8.816	7.998	8.580	7.000
12	12.075	28.006	31.257	27.664	19.118	17.741	15.485	13.158	13.005	11.935	12.000	10.988
13	14.400	28.140	27.930	31.620	16.848	14.536	12.788	12.784	11.528	11.837	10.292	9.825
MEAN	11.01	26.88	29.75	30.51	18.02	14.56	13.51	12.34	11.76	10.48	9.80	9.50
STDEV	2.20	5.52	4.59	5.54	4.24	3.78	2.66	1.88	2.06	1.74	1.39	1.59

	Endurance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	10.150	36.432	34.104	32.482	18.236	15.548	12.402	12.636	12.720	11.055	10.788	10.266
2	12.350	36.312	35.427	31.439	21.924	16.608	18.643	12.750	10.804	9.870	7.656	7.540
3	8.142	21.576	23.940	23.828	14.241	11.844	11.520	9.164	9.680	8.325	7.668	7.888
4	11.480	29.648	38.556	36.081	21.875	17.760	14.544	13.464	12.740	10.934	9.450	9.472
5	11.050	35.815	33.371	30.576	17.556	15.700	14.322	13.261	12.325	12.464	12.382	12.400
6	10.508	27.264	27.510	27.674	13.202	10.147	10.074	9.990	9.727	9.504	9.316	9.316
7	11.340	21.812	24.739	24.764	15.860	14.960	13.938	12.314	11.704	10.773	11.220	10.275
8	9.522	38.318	39.843	35.739	18.055	15.008	13.674	12.152	11.616	11.375	10.800	10.287
9	11.970	38.482	35.649	33.945	21.056	16.536	13.775	11.620	11.352	10.374	9.782	8.978
10	9.984	38.503	32.465	33.120	19.760	14.148	12.221	11.592	11.088	9.198	8.970	8.845
11	8.505	33.210	29.078	28.633	13.770	10.878	9.179	10.080	10.290	9.360	8.968	7.810
12	11.220	35.100	33.880	32.292	20.007	15.600	14.300	12.312	11.778	11.766	10.985	10.752
13	15.484	33.598	31.872	29.904	18.327	16.356	15.370	12.604	13.410	11.815	11.644	11.016
MEAN	10.90	32.77	32.34	30.81	17.99	14.70	13.38	11.84	11.48	10.52	9.97	9.60
STDEV	1.86	5.94	4.87	3.80	2.98	2.34	2.41	1.32	1.16	1.21	1.47	1.41

(xiv) Hematocrit (%)

	Resistance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	45	46	46	48	47	48	47	45	47	43	43	42
2	42	45	47	46	46	45	47	45	44	43	40	42
3	46	47	47	48	47	48	48	46	45	42	43	44
4	48	50	50	50	50	50	48	47	47	46	45	44
5	43	45	47	47	46	46	46	45	43	43	43	44
6	44	47	47	48	45	45	47	45	45	43	43	46
7	47	50	49	51	52	51	49	48	51	49	48	48
8	44	47	48	49	47	48	48	47	45	45	43	44
9	44	43	45	47	45	46	43	43	41	40	41	41
10	42	43	43	44	43	42	43	41	40	39	39	38
11	45	45	48	47	47	48	46	44	44	45	44	44
12	49	53	53	55	53	51	52	51	50	48	47	47
13	44	44	48	47	48	48	47	44	43	45	43	44
MEAN	44.85	46.54	47.54	48.23	47.35	47.38	47.00	45.46	45.00	43.88	43.23	43.69
STDEV	2.15	2.96	2.40	2.68	2.75	2.57	2.35	2.47	3.16	2.77	2.49	2.59

	Endurance Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	44	44	45	44	44	47	45	47	45	47	43	41
2	43	43	45	43	44	44	43	43	41	40	39	41
3	44	44	47	46	45	45	47	45	44	43	43	43
4	46	48	47	48	48	47	47	46	47	46	47	45
5	43	45	45	46	45	45	46	44	43	42	43	42
6	44	46	44	46	46	43	42	43	43	42	44	43
7	50	48	49	49	48	49	48	48	46	45	46	46
8	43	47	46	45	45	45	45	44	42	42	42	40
9	40	42	40	42	41	41	41	42	40	39	40	39
10												
11	48	47	49	48	49	48	50	47	45	44	44	44
12	48	50	52	50	50	50	50	50	49	48	48	48
13	39	40	44	47	42	43	40	42	46	45	45	49
MEAN	44.29	45.25	46.00	46.17	45.50	45.58	45.29	45.04	44.21	43.58	43.67	43.42
STDEV	3.18	2.78	2.93	2.41	2.62	2.68	3.25	2.51	2.52	2.75	2.64	3.12

(xv) Right Atrial Volume (ml)

Subject	Rest	Cycle	Leg Press
1	42.77	53.74	32.51
2	39.56	50.38	31.76
MEAN	41.17	52.06	32.14
STDEV	2.27	2.38	0.53

(xvi) End Diastolic Volume (ml)

Subject	Rest	Cycle	Leg Press
1	136.12	156.86	138.96
2	139.12	154.64	142.67
MEAN	137.62	155.75	140.82
STDEV	2.12	1.57	2.62

(xvii) End Systolic Volume (ml)

Subject	Rest	Cycle	Leg Press
1	46.48	32.22	33.55
2	54.90	45.95	38.75
MEAN	50.69	39.09	36.15
STDEV	5.95	9.71	3.68

(xviii) Ejection Fraction (%)

Subject	Rest	Cycle	Leg Press
1	66.00	79.50	76.00
2	61.00	70.50	73.00
MEAN	63.50	75.00	74.50
STDEV	3.54	6.36	2.12

(xix) Stroke Volume (ml)

Subject	Rest	Cycle	Leg Press
1	89.48	124.65	105.41
2	84.22	108.69	103.92
MEAN	86.85	116.67	104.67
STDEV	3.72	11.29	1.05

(xx) Average Systolic Blood Pressure (mmHg)

	Non-Exercise Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	157.00	166.00	161.00	160.00	161.00	163.00	158.00	160.00	163.00	158.00	156.00	149.00
4	128.00	134.00	132.00	126.00	127.00	124.00	126.00	126.00	124.00	129.00	135.00	131.00
MEAN	142.50	150.00	146.50	143.00	144.00	143.50	142.00	143.00	143.50	143.50	145.50	140.00
STDEV	20.51	22.63	20.51	24.04	24.04	27.58	22.63	24.04	27.58	20.51	14.85	12.73

(xxi) Average Diastolic Blood Pressure (mmHg)

	Non-Exercise Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	68.00	70.00	70.00	70.00	73.00	73.00	72.00	72.00	70.00	67.00	67.00	68.00
4	69.00	76.00	72.00	73.00	76.00	71.00	73.00	73.00	66.00	73.00	77.00	74.00
MEAN	68.50	73.00	71.00	71.50	74.50	72.00	72.50	72.50	68.00	70.00	72.00	71.00
STDEV	0.71	4.24	1.41	2.12	2.12	1.41	0.71	0.71	2.83	4.24	7.07	4.24

(xxii) Mean Arterial Pressure (mmHg)

	Non-Exercise Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	91.00	94.00	92.00	92.00	96.00	96.00	94.00	93.00	92.00	88.00	88.00	88.00
4	88.00	95.00	92.00	90.00	92.00	89.00	91.00	90.00	85.00	91.00	96.00	93.00
MEAN	89.50	94.50	92.00	91.00	94.00	92.50	92.50	91.50	88.50	89.50	92.00	90.50
STDEV	2.12	0.71	0.00	1.41	2.83	4.95	2.12	2.12	4.95	2.12	5.66	3.54

(xxiii) Hematocrit (%)

	Non-Exercise Trial											
Subject	Baseline	During 5	During 10	During 15	1:30 Post	3 Post	5 Post	10 Post	15 Post	30 Post	45 Post	60 Post
1	47	48	44	46	45	46	46	46	46	48	44	46
4	41	42	41	41	41	42	41	42	41	42	41	42
MEAN	44	45	43	44	43	44	44	44	44	45	43	44
STDEV	4.24	4.24	2.12	3.54	2.83	2.83	3.54	2.83	3.54	4.24	2.12	2.83

Appendix D

ANOVA Summary Tables

(i) Exercise Time

1-TRIAL

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	14.00178	12	0.67686	20.68639	0.000668

(ii) Plasma αANP

1-TRIAL, 2-TIME

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	66.20393	5	59.77041	1.107637	0.340776
2	11	11.81837	55	10.33604	1.143414	0.347278
12	11	5.165792	55	4.923752	1.049158	0.418126

(iii) Peak Systolic Blood Pressure

1-TRIAL, 2-TIME

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	6935.388	12	1980.839	3.501237	0.085897
2	11	45505.39	132	412.0046	110.4487	0.00000
12	11	2026.717	132	309.38	6.550897	1.21E-08

(iv) Peak Diastolic Blood Pressure

1-TRIAL, 2-TIME

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	11582.7	12	865.2789	13.38608	0.003274
2	11	5702.031	132	110.9756	51.38094	0.00000
12	11	3624.045	132	135.7649	26.69354	1.9E-28

(v) Trough Systolic Blood Pressure

1-TRIAL, 2-TIME

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	3090.782	12	1679.351	1.840462	0.19987
2	11	13167.83	132	259.856	50.67359	0.00000
12	11	1482.034	132	271.126	5.466218	3.85E-07

(vi) Trough Diastolic Blood Pressure

1-TRIAL, 2-TIME

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	2.884615	12	538.6624	0.005355	0.942869
2	11	126.9674	132	44.8108	2.83341	0.002344
12	11	49.6049	132	45.69328	1.085606	0.377644

(vii) Average Systolic Blood Pressure

1-TRIAL, 2-TIME

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	37.38462	12	1751.537	0.021344	0.886272
2	11	26147.51	132	256.9852	101.7471	0.000000
12	11	305.5804	132	112.8544	2.70774	0.003535

(viii) Average Diastolic Blood Pressure

1-TRIAL, 2-TIME

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	1056.013	12	341.7073	3.090402	0.10421
2	11	1007.202	132	45.06527	22.34984	0.00000
12	11	391.0338	132	39.01612	10.02236	4.39E-13

(ix) Pulse Pressure

1-TRIAL, 2-TIME

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	1490.782	12	1061.233	1.404764	0.258869
2	11	17271.72	132	272.2412	63.44271	0.000000
12	11	1054.726	132	104.6169	10.0818	3.73E-13

(x) Mean Arterial Pressure

1-TRIAL, 2-TIME

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	1111.926	12	518.9055	2.14283	0.168936
2	11	3090.563	132	38.90671	79.4352	0.000000
12	11	230.5627	132	26.42818	8.724123	1.73E-11

(xi) Exercise Oxygen Consumption

1-TRIAL, 2-TIME

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	3646.247	12	49.60581	73.50443	1.84E-06
2	3	3577.742	36	13.34404	268.1153	0.000000
12	3	341.3149	36	9.210123	37.05867	4.21E-11

(xii) Heart Rate

1-TRIAL, 2-TIME

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	620.5128	12	238.7628	2.598867	0.132913
2	11	22966.1	132	84.53176	271.6861	0.000000
12	11	180.2401	132	36.67191	4.914936	2.33E-06

(xiii) Rate Pressure Product

1-TRIAL, 2-TIME

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	36.2374	12	25.71119	1.409402	0.258126
2	11	1903.516	132	8.644444	220.201	0.000000
12	11	21.46594	132	2.981055	7.200789	1.62E-09

(xiv) Hematocrit

1-TRIAL, 2-TIME

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	1	137.5035	11	5.57923	24.6456	0.000426
2	11	42.06597	121	1.773273	23.72223	0.000000
12	11	3.815972	121	1.592143	2.396752	0.010030

(xv) Right Atrial Volume

1-TRIAL

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	2	199.0825	2	1.07385	185.3914	0.005365

(xvi) End Diastolic Volume

1-TRIAL

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	2	187.3197	2	5.243117	35.72679	0.027228

(xvii) End Systolic Volume

1-TRIAL

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	2	118.2339	2	9.277117	12.74469	0.072755

(xviii) Ejection Fraction

1-TRIAL

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	2	84.5	2	4.666667	18.10714	0.052336

(xix) Stroke Volume

1-TRIAL

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	2	450.2422	2	28.17365	15.98097	0.058889

(xx) Average Systolic Blood Pressure (Non-Exercising)

1-TRIAL

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	11	12.62121	11	19.89394	0.634425	0.768705

(xxi) Average Diastolic Blood Pressure (Non-Exercising)

1-TRIAL

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	11	6.829545	11	7.375	0.92604	0.549559

(xxii) Mean Arterial Blood Pressure (Non-Exercising)

1-TRIAL

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	11	6.545455	11	10.54545	0.62069	0.779234

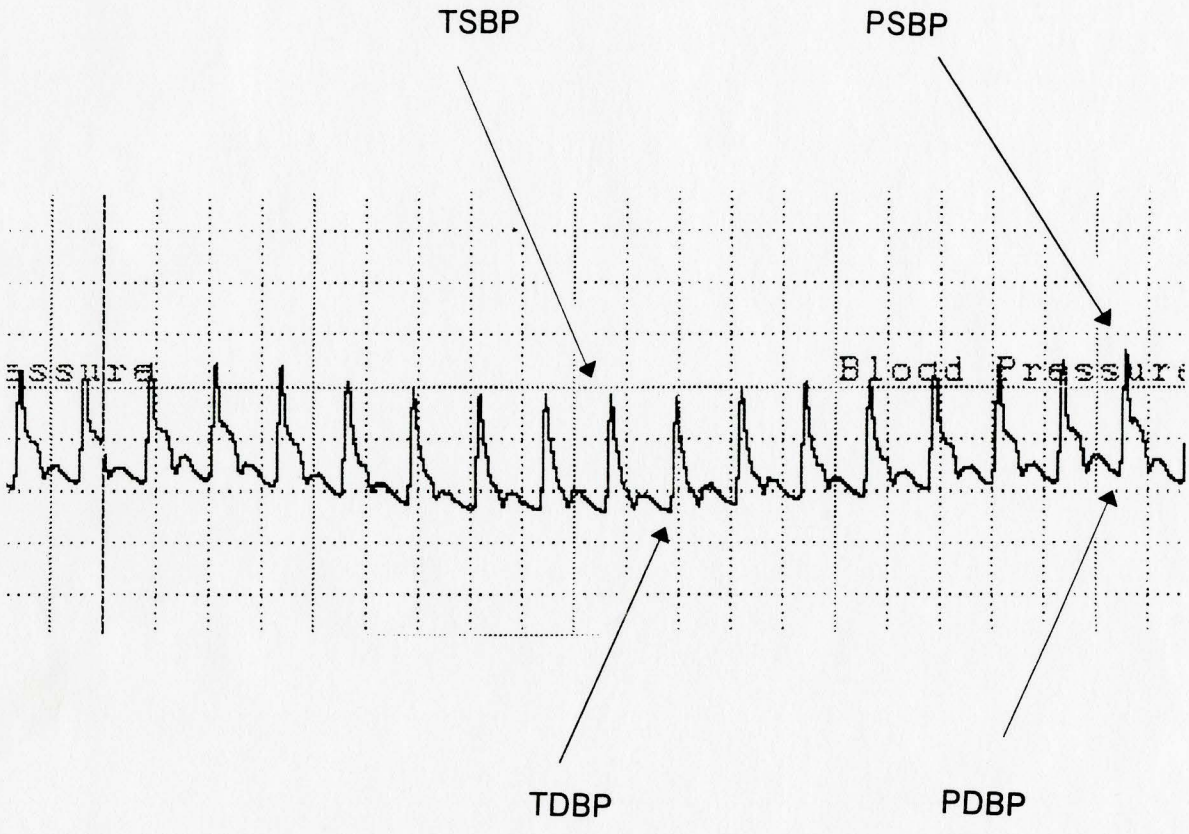
(xxiii) Hematocrit (Non-Exercising)

1-TRIAL

	df Effect	MS Effect	df Error	MS Error	F	p-level
1	11	1.314394	11	0.587121	2.23871	0.098562

Appendix E

Pressure Wave Form


TSBP
PSBP
TDBP
PDBP