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Changes in hormone excretion in swimmers over the course of a training season

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CHANGES IN HORMONE EXCRETION IN SWIMMERS OVER THE COURSE OF A TRAINING SEASON

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ABSTRACT

Changes in urinary hormone excretion were measured during a training season for 24 members of the University of Hawaii Men's Swim Team. Each month, on a training day and a rest day, epinephrine, metanephrine, norepinephrine, and normetanephrine levels were obtained, and the results were compared to data from 12 undergraduate controls. In addition, these results were compared to the distance trained, and preceived stress to obtain possible relationships between the various parameters.

For the training day, norepinephrine, normetanephrine, epinephrine, and metanephrine excretion decreased significantly from September through November (5.51 ± 0.32 to 1.89 ± 0.11 μg/hr, 17.43 ± 0.87 to 7.14 ± 0.46 μg/hr, 1.91 ± 0.23 to 0.87 ± 0.09 μg/hr, and 6.32 ± 0.37 to 2.69 ± 0.18 μg/hr) ($p < .05$). November levels were also significantly lower than control levels ($p < .01$). Norepinephrine, normetanephrine, epinephrine, and metanephrine then increased with maximum excretion levels in February: 9.18 ± 0.56 μg/hr, 35.37 ± 2.70 μg/hr, 3.13 ± 0.27 μg/hr, and 10.07 ± 0.79 μg/hr, respectively ($p < .01$ versus controls).

For the rest day, norepinephrine, epinephrine, normetanephrine, and metanephrine excretion decreased through November with minimum levels of 1.31 ± 0.11 μg/hr, 0.48 ± 0.03 μg/hr, 12.46 ± 0.69 μg/hr, and 4.83 ± 0.23 μg/hr, respectively. November levels were also significantly less than control levels ($p < .01$). Hormone levels then returned to resting levels by January and were similar to control values ($p > .05$).

This experiment also found that training appeared to decrease some of the stress of exams ($p < .01$). Further, stress testing showed that the frequency of hassles was related to norepinephrine excretion in swimmers ($p < .05$), and the intensity of hassles was related to excretion of epinephrine and norepinephrine in controls ($p < .05$).

Thus, it was found that norepinephrine excretion was influenced primarily by

exercise and epinephrine excretion was influenced by the added stresses of school and exercise. Further, it was found that several variables effected hormone excretion.

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Preface

The purpose of this study is to investigate the change in catecholamine levels over the course of a training season in collegiate swimmers. Swimmers were chosen because there are no reports in the literature that look at the response to stress in actively training swimmers. Additionally, there are very few studies which use athletes trained at the intensity of collegiate swimmers (27, 64, 156). Thus, one of the first requirements of the study was to obtain data on collegiate swimmers training at elite levels.

The study was designed to determine the long term changes in hormone secretion patterns when the intensity of training was continually increased. There are no reports of studies on athletes training for more than four months duration (287). Since most elite athletes train for much longer periods of time than four months, the first objective was to develop a research protocol that would result in information on catecholamine production over an extended period of time.

A second objective was to test for a relationship between a simple psychological measure and the results obtained from physiological measurements. Since there are no reports about the psychological changes in elite athletes during a training season, a third objective was to determine if there was any correlation between psychological and physiological changes.

A fourth objective was to evaluate whether a testing day could be broken into time periods and then assess if there was a particular time period of the day when there was more or less change due to stress. Although a few reports have described the variation in secretion in sedentary subjects with time of day (86, 104,183), none have looked at this variation in elite athletes.

A fifth objective was to determine what variable or variables correlated with hormone secretion. Was it distance trained, psychological stress, time of day, or some other factor? Again, no one has reported attempting to determine the relationship of catecholamines to other variables in elite athletes.

The last objective of this study was to determine whether any observed changes in catecholamine output were due to changes in production or to changes in metabolism. By measuring the metabolites of norepinephrine and epinephrine, it was anticipated that the factors responsible for changes in hormone excretion could be determined.

Thus, this research sought to test three main hypotheses. First: there is a change in catecholamine production in swimmers throughout the training season. Second: this change could be correlated to changes in psychological stress evaluations and to the amount of distance trained. Finally: the change in catecholamine production could be directly correlated to a change in catecholamine metabolite production.

Chapter 1. **Introduction**

All animals are exposed to varying degrees of stress. However, the way that a particular stress effects a subject depends not only on the frequency and intensity of the stress, but also on the subject being stressed. Further, responses to stress can be wide ranging and encompass an array of responses from intense sympathetic stimulation to no apparent response. In addition, the type of stress applied to the subject can be of more than one type. Examples include physical, emotional, and mental forms of stress. To further compound the problem stress can also be acute or chronic. Thus, to record and analyze a subject's stress can be a very complicated process.

In order to begin to perform studies on stress, most researchers limit their investigation to only one or at most a very fewparameters. Further, these researchers are forced to use rigorous protocols that limit the amount of variability in their experiment. Most studies use only a few indicators, like certain hormones, to quantify results. In particular, catecholamines have been used with increasing frequency to look at both acute and chronic changes caused by stress. Specifically, plasma catecholamine levels are used in experiments where the collection period is only a few hours and urinary catecholamines levels are generally used when the experiment calls for longer term stress monitoring. This study monitored stress over a 24 hour period utilizing urinary catecholamines. This method was chosen to enable us to a compile a complete data base.

The central question that was addressed in this thesis was: What are the changes in stress hormone production assocated with chronic, intense, physical training and how does this relate to selected physical and psychological parameters. This is an important question because very little is known regarding the relationship of long term training to stress hormone production in athletes who compete and train at very intense levels.

Chapter 2. **Background**

Research in catecholamines and their effects on the body has been on going for many years. As early as the eighteenth century, scientists were studying the actions of catecholamines. In 1895, Oliver performed one of the first experiments in catecholamine research by taking extracts from the adrenal medulla and injecting them into subjects. He observed an increase in blood pressure and concluded that something in the adrenal medulla could effect a change in blood pressure (264). At about the same time, John Abel was able to isolate epinephrine and two years later in 1897, Elliot, following the work of his professor, Langley, determined the relationship of epinephrine to the nervous and cardiovascular systems (264, 265).

For the next 35 years, catecholamine research continued, but it was not until 1932 that Walter Cannon observed that stress led to an increase in stomach contractions and discovered that this was due to sympathetic nerve stimulation. Using this finding and others, Cannon came to the conclusion that the adrenal medulla was the key to the " flight or fight" reaction seen during acute stress reactions that he and de la Pan had first begun to study 24 years earlier (264, 265).

Building on Cannon's research, Hans Selye determined, through the use of animal models, that chronic stress could modify the adrenal glands by increasing their size (264). Further, Selye postulated that there were 3 phases to an animal's response to stress (265). The first component was the alarm phase which Cannon called the " flight or fight" response. This response included an increase in heart rate and blood pressure, vasoconstriction, and pupil dilation. The second component of an animal's stress response was the adaptation phase (265). During this phase the animal showed a decreased response to the same stress. Further, the stress event would have to be longer and more intense to elicit a maximal response. With constant stress, this phase continued until the animal entered the third phase: exhaustion (265). At this point the animal was unable to elicit a maximal response to stress despite increased intensity and duration of the stress stimulus.

Up until this time, experimenters were working entirely with epinephrine. In 1946, however, Von Euler was able to isolate norepinephrine and demonstrate that norepinephrine was the neurotransmitter commonly released from sympathetic nerve endings (264,265). Additionally, along with isolating norepinephrine from sympathetic nerves, Von Euler found that there was an increase in urinary output of norepinephrine with stress (264,265, 270). Both of these findings opened new areas of stress research by showing that there was more than one hormone involved in response to stress.

Using the work of others, Coupland made an important discovery regarding the interactions of the adrenal cortex and the adrenal medulla. He suggested that the adrenal medulla could be controlled by the production of hormones in the adrenal cortex . To support this concept, Coupland reported that epinephrine production depended, among other things, on the adrenal cortex glucocorticoids (264). He was the first investigator to suggest that the relationship of catecholamines and stress was a complicated process, dependent on several different variables.

In 1951, in separate studies, both Lund and Von Euler quantified the amount of catecholamines eliminated in the urine, giving researchers base levels for these hormones (187, 270). A year later, Von Euler investigated urinary excretion of catecholamines in subjects exposed to exercise and found an increased excretion with exercise. This was one of the first studies to examine the relationship of exercise to stress hormone production and show that exercise increased the level of stress hormone production (269).

By the end of the 1950's, many researchers were beginning to study in greater detail some of the findings of Coupland and Von Euler. It was not until 1959, however, that the next step in catecholamine research was taken. Prior to 1959, most studies were directed towards the mechanisms of epinephrine and norepinephrine release and their subsequent effect on the subject. Axelrod, however, initiated exploration into what happened to the catecholamines after their initial release. He was one of the first to investigate the metabolism of epinephrine. This led to the discovery that epinephrine is metabolized very rapidly in the body and that it has a half life of less than a minute in the circulation (12).

By the early 1960's, research on catecholamines and stress had rapidly accelerated. Some of the more significant experiments included: Haggendahl in 1963 on conjugated epinephrine and norepinephrine (126); Carlson in 1963 on the effect of liver catechol-o-methyltransferase (COMT) on circulating catecholamines (45); and Axelrod and Kopin in 1969 establishing the actions and metabolism of norepinephrine once released from the sympathetic nerve endings (11).

The early 1970's provided further advances in the research on epinephrine and norepinephrine and their relation to stress. For example, in 1971 Kotchen studied the appearance in the blood of norepinephrine and epinephrine in response to graded exercise. This led to the discovery that epinephrine and norepinephrine responded differently to different exercise intensity levels (107, 157). He found that norepinephrine excretion began to increase at exercise levels of approximately 60% of maximum intensity. Epinephrine, however, did not begin to increase until exercise intensity approached 80% of maximum intensity. In 1971, Taylor was the first to compare catecholamine excretion levels in sedentary subjects to those of trained athletes. He found that at the same relative intensity of exercise, sedentary subjects excreted larger amounts of epinephrine and norepinephrine (268).

Also in 1971, Frankenhaeuser was the first to elaborate on changes in epinephrine and norepinephrine appearance in the blood based on different stress events.

She found that with mild forms of mental stress, epinephrine showed a significant increase in blood levels while norepinephrine showed no change. She also discovered that norepinephrine increased at work levels of approximately 60% of maximum, while epinephrine levels did not increase until the exercise intensity approached 80% of maximum. Finally, she identified that epinephrine increased with increasing mental or emotional stresse, while norepinephrine showed no change until the subject was undergoing extreme mental or emotional stress (104). These important findings have since been confirmed by other authors.

Kotchen et al. examined changes in epinephrine and norepinephrine in 6 subjects exercising at various intensity levels. They found that norepinephrine showed a significant elevation from resting levels at 70% VO2 max. They also found that epinephrine showed no significant increase compared to resting levels unless the subject was exercising at maximal intensity (167). Dimsdale and Moss also found that norepinephrine increases are more closely related to increases in exercise than are increases in epinephrine. They reported that epinephrine levels doubled during public speaking while norepinephrine levels did not significantly change. Thus, they concluded that norepinephrine and epinephrine levels could be modified by different stimuli (75). Additional studies include those of Christensen (1983), Lehmann (1984), Gillberg (1986), and Berger (1987) which show that at low levels of exercise, norepinephrine increases and epinephrine does not increase, and at low levels of mental or emotional stress epinephrine increases while norepinephrine does not increase. These and other studies also indicate that during maximal levels of exercise or emotional/mental stress, there are increases in both hormone levels (22,,52, 104, 116, 180).

By the end of the 1970's, many different aspects of catecholamines and stress had been studied including: the finding that training decreased the levels of epinephrine and norepinephrine in subjects tested at the same relative level of exercise intensity

(Cronan 1974); that given a constant exercise intensity, changes in hormone levels occurred within 3 weeks (Winder 1978); that swimmers had the same changes in epinephrine and norepinephrine during changes in exercise intensity as runners and subjects using bicycle ergometers (Hickson 1979, and Galbo 1979); and use of liquid chromatography was an extremely rapid and accurate method of measuring catecholamine levels (Hjemdahl 1979).

During the 1980's, there have been further advances in catecholamine and stress research, most notable among these was the introduction of the Hassles test to better quantify stress (Kanner et al., 1981). On the other hand, there is still much that has not been done. In particular, despite all of the previous research, there is still a void of information regarding the changes in stress that athletes undergoing intense physical training experience. The purpose of this research, therefore, is to investigate how intense physical training impacts stress levels in swimmers.

Before considering the objectives of this study, however, a general review of the biochemistry and characteristic findings regarding catecholamines needs to discussed. This review will help develop a fundamental understanding of epinephrine and norepinephrine.

Catecholamine production starts with the amino acid tyrosine. Tyrosine is a nonessential amino acid that can either be absorbed from the gut, produced in the body from methionine or synthesized directly. The adult intake of tyrosine is estimated at 4 times the recommended daily requirement of 1.12 g/d and there can be a 2 fold increase or decrease with no change in catecholamine levels (65, 263). Once taken into the body, tyrosine is actively transported across the brush border of the small intestine. From here it is transported into catecholamine producing neurons and the adrenal medulla. At these sites tyrosine goes through a number of steps to produce epinephrine and norepinephrine, the precise pathway of which can be seen in figure 1.

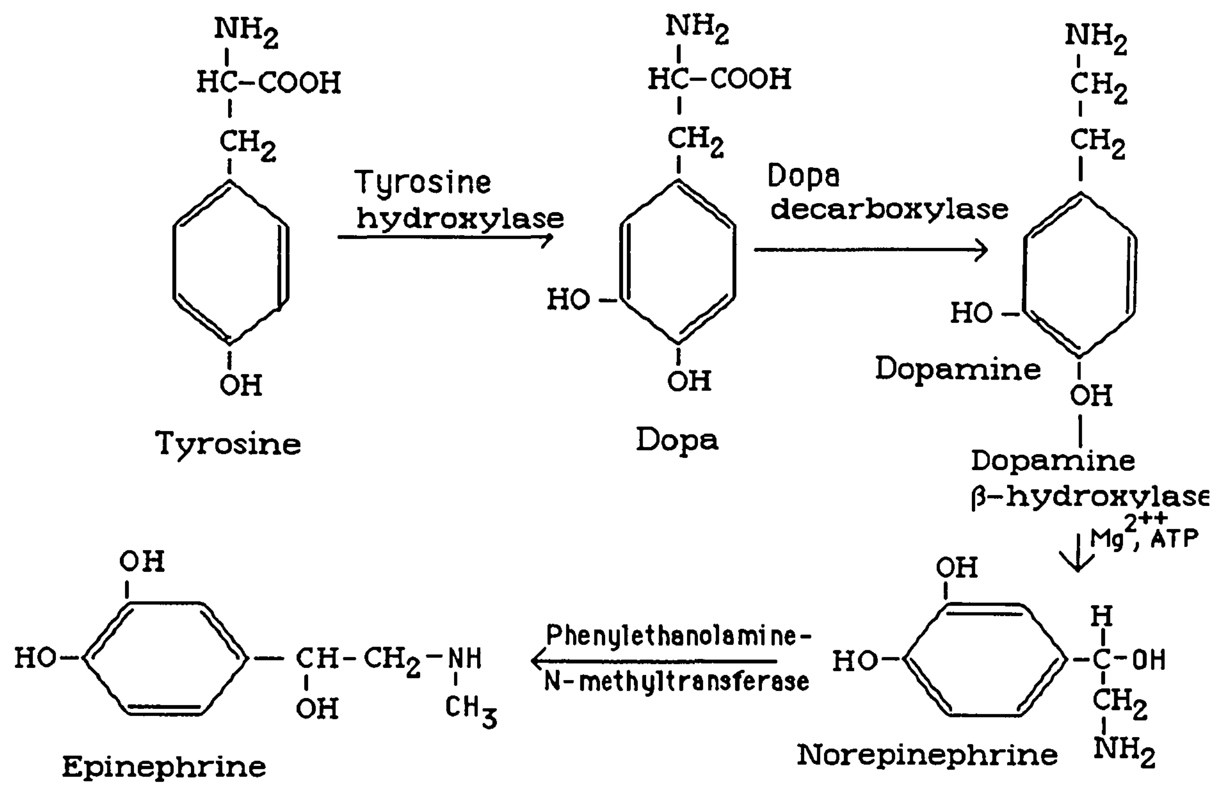

Figure 1. Catecholamine Production

The first step in the pathway is the conversion of tyrosine to l-dopa via tyrosine hydroxylase. This is the rate limiting step and is the feedback control site for the production of catecholamines (10, 11, 264). Consequently, as norepinephrine and dopamine levels rise and fall in the intraneuronal cytoplasm, tyrosine hydroxylase conversion of tyrosine to l-dopa decreases or increases (11, 264). An interesting modification to this feedback mechanism occurs with chronic stress or stimulation when there is a general increase in the resting levels of tyrosine hydroxylase (10, 264).

After the formation of l-dopa, dopamine is then rapidly produced and is the product which enters the granulation vesicles. Once inside, dopamine is rapidly converted to norepinephrine in the peripheral nervous system via dopamine ß-hydroxylase and epinephrine in the adrenal medulla via dopamine ß-hydroxylase and phenolethanolamine-N-methyltransferase (269). These hormones are then released when needed without further modification. In addition ATP and dopamine ß-hydroxylase are also released with norepinephrine. Dopamine ß-hydroxylase has also been found to have a circadian rhythm in its appearance in the blood similar to that shown by norepinephrine (264). Additionally, Frewin found that there is some variability in resting enzyme levels that relate to changes in exercise (108). Unfortunately, Perronet found that despite these findings, dopamine ß-hydroxylase is not a sensitive measure of sympathetic activity (221).

Once released, norepinephrine travels across the synaptic cleft to bind to the postsynaptic receptor and stimulate production of cAMP. Norepinephrine is then released and a majority of the hormone is recycled via a reuptake mechanism (9, 11). The remaining norepinephrine in the synaptic cleft is metabolized, either within the cleft or in the blood if it has leaked into the general circulation.

Epinephrine has a slightly different mode of action. It travels via the general circulation to its target organ where it activates cAMP. The hormone is then released and the majority metabolized; 50% of the metabolism occurs in the kidney (5). The metabolic pathways for both hormones are shown in figure 2.

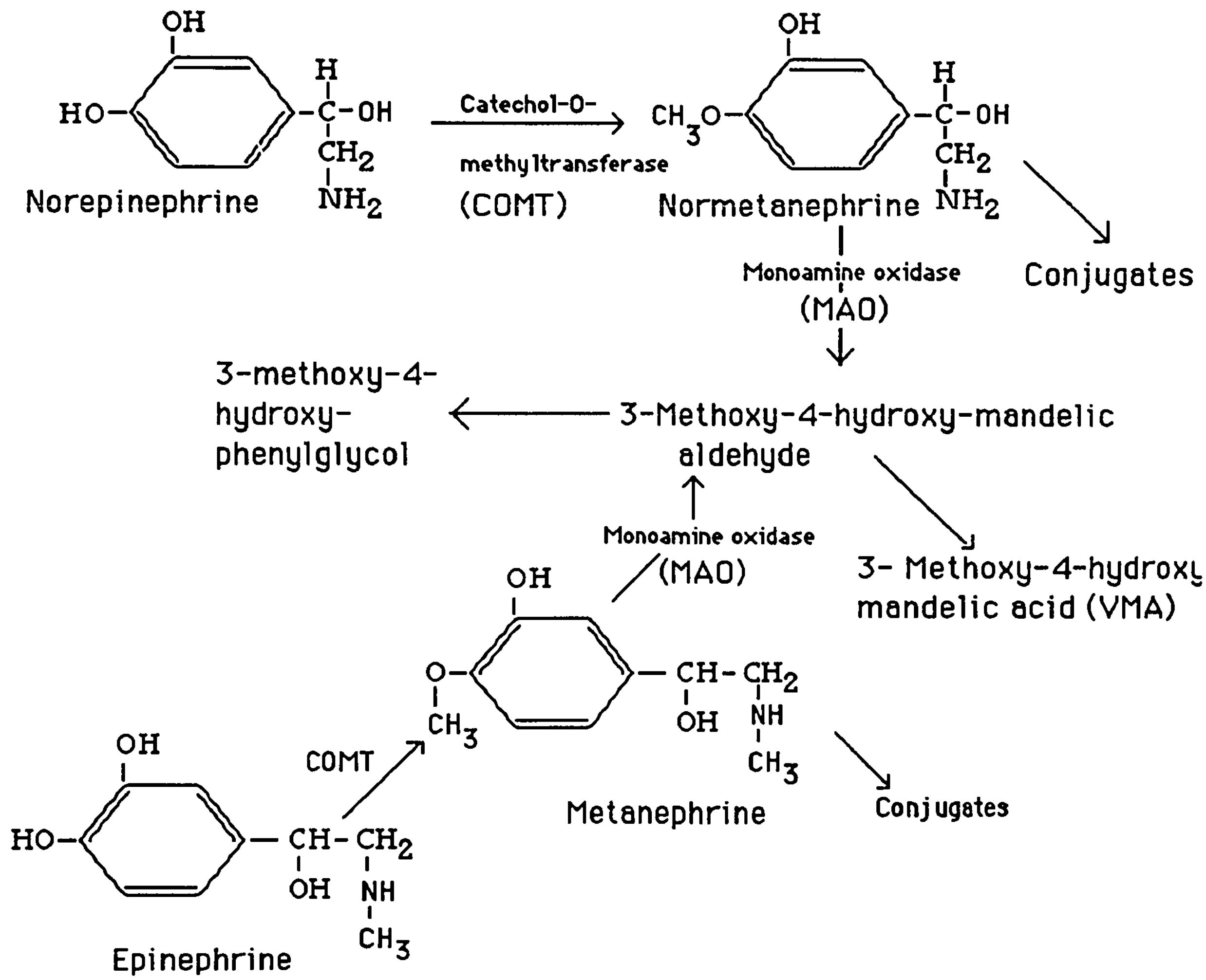

Figure 2. Catecholamine Metabolism

* MAO metabolism first of the hormones is not shown as these metabolites were not measured.

The most important enzyme in the breakdown of norepinephrine and epinephrine is catechol-o-methyltransferase (COMT). COMT is a magnesium-dependent enzyme found in most organs and tissues including: postsynaptic tissue, most capillary endothelium, and myocardial cells, but not in smooth muscle of coronary arteries (12, 29). It is also found in the brain and may serve as the barrier which prevents catecholamines from crossing into the brain from the general circulation (12, 13, 15).

Very small amounts of catecholamines are actually released in the urine unchanged, the majority are O-methylated by COMT in the liver(12). It has been found that hepatic levels of COMT change when the subject is exposed to chronic stress. COMT will decrease in concentration with chronic stress exposure of the subject (12, 264).

After epinephrine and norepinephrine have been exposed to COMT, the metabolites metanephrine and normetanephrine are produced. These metabolites are almost completely inactive, having one tenth the biological activity of their precursors (12). After these metabolites are formed, they are either conjugated and excreted, or metabolized further via monoamine oxidase (MAO). If metanephrine and normetanephrine are not conjugated, MAO acts on both to produce the same product, 3-methoxy-4- hydroxy-mandelic aldehyde. 3-methoxy-4-hydroxy-mandelic aldehyde is then metabolized to 3-Methoxy-4-hydroxy-phenylglycol or 3-methoxy-4-hydroxy-mandelic acid (VMA); the vast majority of the metabolite being VMA (189). It is important to note that VMA is the product of both norepinephrine and epinephrine and consequently is not as specific an indicator of peripheral catecholamine metabolism as the metabolites metanephrine and normetanephrine. Despite the fact that VMA is not a very specific indicator of sympathetic activity, it is a good quantitative indicator. Consequently, MAO becomes the second most important enzyme after COMT in producing VMA (12, 60).

MAO is a fairly common enzyme and is found in greatest quantities in the liver and kidney, as well as in lower amounts in red blood cells, platelets, and in most cell mitochondria (198). There are two forms of MAO: MAO A and MAO B. MAO B is found in greatest quantities in the brain, where it is more active in deaminating phenylethylamines and benzylamides than catecholamines. MAO A is found primarily in neurons and is more active in deaminating catecholamines (264, 265). MAO can be the first enzyme to metabolize epinephrine and norepinephrine. This study did not measure these metabolites since they are in small concentrations relative to those produced by

COMT. In a study by Mathew, it was discovered that resting blood levels of catecholamines and platelet levels of MAO both fluctuate directly with the amount of stress the subject is experiencing (198).

The last segment of catecholamine inactivation that has been reported is the conjugation of epinephrine and norepinephrine. There are two known methods of conjugating catecholamines, either through glucuronide or sulfate. In man sulfoconjugation is the usual pathway by which catecholamines are conjugated (5, 24, 70, 85, 126). In the plasma, approximately 80% of the norepinephrine and 85% of epinephrine is conjugated. In red blood cells, however, only 40% of the norepinephrine is conjugated and it has been suggested that red blood cells might actually act as a free norepinephrine reserve (54, 70). The actual mechanism of sulfoconjugation of norepinephrine and epinephrine involves the enzyme phenolsulfotransferase (PST) and the sulfur donor phosphoadenosine phosphosulfate (PAPS). PST is found primarily in plasma and cerebrospinal fluid and acts by adding one sulfur to the benzene ring of epinephrine and norepinephrine (170). Additionally, like MAO, there are actually two forms of PST. The first is the P-form which has a high affinity for phenols. The second type is the M-form which has a high affinity for monoamines (264).

Despite the different affinities of the PST isomers, however, sulfoconjugation is a relatively slow process and is probably concentration dependent (231). This is further supported by the finding that chronic stress leads to increased absolute levels of conjugated catecholamines (70). Acute stress, however, did not affect conjugated catecholamine levels, while the absolute amount of unconjugated catecholamines increased in response to the stressing event (67). Consequently, de Champlain suggested that conjugated catecholamines are a better indicator of chronic stress.

In addition to this brief review of the biochemistry of epinephrine and norepinephrine, other basic information regarding these hormones needs to be presented. Thus, this review will help explain their mechanism of action as well as identifying differences between known findings and the changes found in this study.

Epinephrine and norepinephrine are responsible for different aspects of the sympathetic response to stress. Epinephrine affects heart rate, arteriolar dilation in the heart and skeletal muscle, glucose mobilization, and gut immobilization. Small amounts of epinephrine result in behavioral and EEG arousal, while large amounts lead to sedation (104, 192, 221). Norepinephrine, on the other hand, affects coronary vessel dilation, changes in systolic and diastolic pressure, and vasoconstriction (104, 239). Both hormones cause increased oxygen consumption, fat mobilization, and increase free fatty acids in the plasma (104).

Although epinephrine and norepinephrine are very similar in many respects, they represent different forms of stress. Norepinephrine has been found to correlate with physical stress, while epinephrine has been found to be a good indicator of the psychological stress the subject is experiencing (3, 78, 129, 148, 264). For example, Dimsdale found that norepinephrine increased 3 fold with moderate exercise while epinephrine did not show a significant increase. On the other hand, epinephrine showed a two fold increase with public speaking, while norepinephrine did not increase significantly (78).

The increase in norepinephrine derives from sympathetic nerve endings in vascular beds in the areas of vasoconstriction in the periphery of the body and muscle tissue (52, 115, 222). Approximately 30 nmol/min must appear in the blood to keep plasma norepinephrine levels at 20 nmol/l (44, 52). Thus, in order to obtain an increase in plasma norepinephrine there has to be an increase in nerve impulse flow(125, 293). Because a large part of the norepinephrine released during stimulation is metabolized, new formation of norepinephrine is the most important mechanism for meeting the increased demands of physical stress (11, 272).

On the other hand, epinephrine is produced primarily in the adrenal medulla where it is constantly released. To obtain an increased level, there must be an increase in epinephrine production (104). Like norepinephrine,new formation of epinephrine increases during stress (11, 50).

In addition to epinephrine and norepinephrine response to the different types of stress, there is also a different pattern of increase when there is an increase in stress levels. During stress due to exercise, norepinephrine levels show a constant increase with the increasing intensity until the subject approaches exercise intensity levels of 60-70% VO2max. At this point there is a log increase in norepinephrine levels (14, 16, 268). Epinephrine, however, shows almost no increase with increases in exercise intensity until exercise levels are higher than 60% VO2max. At this point epinephrine levels increase directly with the increasing levels of exercise (92, 131, 268). When the stress is mental or emotional, epinephrine shows a significant elevation early in the experiment. This increase is approximately linear with self-reported indices of stress intensity. Norepinephrine, however, does not show any changes until much later in the experiment. At the point where mental stress is near maximal, norepinephrine shows significant, logarithmic increases (21, 268).

There have been many studies that have reported baseline levels for these hormones (2, 8, 18, 26, 39, 85, 116, 137, 138, 148, 152, 255). For plasma, norepinephrine concentrations range from 100-300 pg/ml and epinephrine levels range from 24-75 pg/ml(55). For urinary values, norepinephrine is excreted at a rate of 20-60 μg/day and epinephrine is excreted at a rate of 2-10 μg/day (85, 139, 142). At these plasma concentrations, epinephrine has some effect on heart rate but neither epinephrine nor norepinephrine have any other effects (55). Under resting conditions, norepinephrine has little hormonal activity and functions primarily as a neurotransmitter. This is because norepinephrine, which is only one tenth as effective as epinephrine, is not secreted at a level sufficient to cause a physiological effect under resting conditions (55).

An important variable that needs to be considered whenever comparisons of the amount of hormone being secreted are made is the time of day the values are obtained since catecholamine secretion exhibits a circadian rhythm (104,183, 259). Both epinephrine and norepinephrine are lowest immediately before the subject arises. They then rise rapidly, peak about 2-3 p.m., and then gradually descend during the remainder of the day until they again reach their lowest values before the subject arises (86). Interestingly, epinephrine is far more cyclic in its appearance in the blood than norepinephrine (86).

Other variables that have been postulated to influence hormone release include: racial differences in norepinephrine release (153); different catecholamine excretion levels based on body weight (104); and age of the subject(82, 97, 98, 124, 153). For changes in norepinephrine due to differences in race and changes in catecholamine excretion based on body weight, there is no evidence that either of these variables affect catecholamine levels (104, 153). Norepinephrine and epinephrine levels are particularly sensitive to the age of the subject and increase with age for both the sedentary subject and the trained athlete (97, 98, 124, 153). Part of the reason for this was proposed by Fleg,who concluded that there might be an age associated diminished end-organ response similar in appearance to ß-blockade (83).

Still another variable to be considered is diet. There are a number of foods and drugs that influence catecholamine levels. These include: cocoa, coffee, tea, B-vitamins, bananas, aspirin, and certain antibiotics (47, 68, 95). Caffeine in any form has been shown to increase plasma epinephrine levels and decrease plasma norepinephrine levels (88, 94, 174, 277). Additionally, diet type also plays a role in catecholamine release. While overeating does not affect epinephrine and norepinephrine levels, "carbohydrate loading", which is done by dramatically increasing carbohydrate intake, will lead to decreases in both hormones relative to controls after the same amount of exercise (110, 172). Further, in individuals who are fasting, there are increases in resting norepinephrine and epinephrine levels, which continues during exercise relative to controls (173, 218, 274). Unfortunately, there is also a marked decrease in performance time relative to controls.

Secretion of norepinephrine and epinephrine is reflected in the amounts of their metabolites excreted in the urine. The resting urinary output levels for the metabolites metanephrine and normetanephrine are 180 ± 20 μg/day and 330 ± 18 μg/day. Conjugation occurs in 56 ± 6% of the metanephrine and 87 ±1% of the normetanephrine. (41, 166, 210, 235, 247).

There are several reasons why urinary excretion measurements of catecholamines are preferrable to plasma values as indicators of stress response. While the mean values for both norepinephrine and epinephrine for a group of subjects are reproducible week to week for both plasma and urinary values, this is not the case when comparing week to week results for single subjects. Repeated measures of plasma levels for a single subject on a weekly basis have shown there is a large variability between samples that can only be compensated for by using a large number of individuals. Urinary excretions are less variable and allow single-subject week to week comparisons (220, 252). In addition, while urinary collection is noninvasive and simple, it is essential that plasma collection be taken specifically from an artery and not a vein (23, 51, 137). Since there is a 45% clearance of catecholamines by peripheral tissue, this results in inaccurate predictions of the amount of catecholamines in the blood (51, 137). Finally, plasma catecholamine levels are more indicative of very acute reactions to stress, while urinary levels are a better indication of what is happening to the subject on a daily basis (264, 265). As mentioned earlier, this makes individual comparisons more difficult and does not give an accurate indication of the stress the subject is undergoing during the course of the day.

From this brief review of the catecholamine literature, it ishould be apparent that the relationship of catecholamines to stress is a complicated interaction. It is also evident that there is a large area of research that has not been considered at any level. Consequently, this project will look at one of those unstudied areas while still taking into account the many variables involved in catecholamine research.

Chapter 3. Materials and Methods

Subject Populations

The subjects chosen for this research were all undergraduates at the University of Hawaii. The experimental group comprised male swimmers who were competing for the men's varsity swim team from early September through the middle of March. Each swimmer was actively training and progressively increased his monthly training distance until mid-January. At this time the swimmers began to rest for their first big swim meets and there was a decrease in training distance (Figure 3). At the same time, the intensity of the workouts was also increased so that by mid-January workouts were not only longer but also at near maximal intensity. Unlike distance, however, the intensity of the workouts actually increased, so that by the end of the season, swimmers were training at maximum effort and producing practice times that were equal to or better than previous meet times.

During the training season, the actual distance and training performance of each swimmer was monitored closely by the coach to try and ensure optimum preformance. For this study, swimmers were categorized into two major groups, distance swimmers and non-distance swimmers. A distance swimmer was defined as anyone who competed primarily in races longer than 200 yards. A non-distance swimmer was anyone who competed primarily in races of 200 yards or less (Table 1). As part of the protocol, attendance was monitored and all swimmers who participated in the study attended at least 95% of the required practices.

Finally, swimmers who participated during the first year of the experiment made up the nucleus of swimmers used during the second and third year of the experiment. This was to insure continuity and to study changes not only within a year but also between years. Unfortunately it was impossible to get the same controls, so these were changed each year.

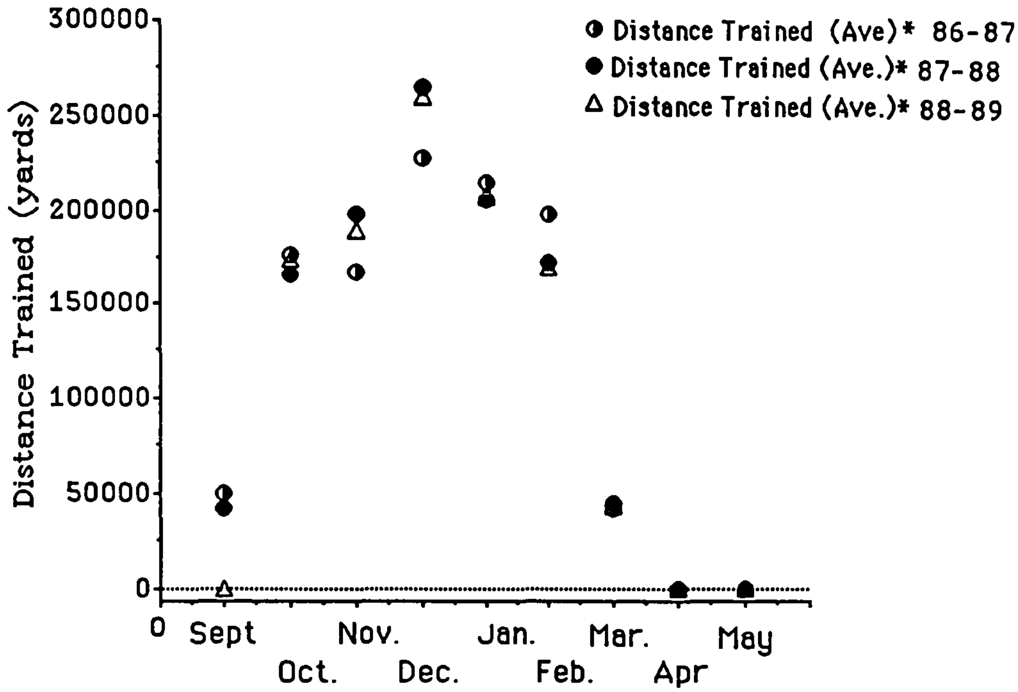

Figure 3. Training Distance versus Month

*Average distance trained each month. Individual swimmers may have different values.

Table 1.

Subject and Swimming Classification

Subject	Category
J.A.	Non-Distance
C.B.	Non-Distance
K.B.	Distance
F.B.	Distance
C.C.	Distance
G.F.	Non-Distance
C.H.	Distance
K.J.	Non-Distance
G.R.	Non-Distance
S.R.	Non-Distance
M.M.	Non-Distance
H.R.	Distance
N.S.	Distance
G.S.	Distance
M.T.	Non-Distance
D.T.	Distance
O.V.	Distance
G.H.	Non-Distance
G.W.	Distance
R.Y.	Non-Distance
J.Y.	Non-Distance
G.R.	Distance

The control group was also chosen from undergraduates at the University of Hawaii and comprised males from various biomedical classes. No special criteria were used to select this group except that the volunteers could not be involved in any structured, strenuous activity. This was to insure that the subjects truly represented average college students. Thus, activities like surfing on weekends or participating in softball games were allowed: however, activities like competing in a collegiate sport were not allowed. Four of the volunteers were involved in a physical education swim class. These four, did not show results significantly different from the other volunteers and so their results were used. Anthropometric data for both groups was taken and is presented in Table 2.

Before the experiment, the protocol was explained to both groups and they were reminded that they were under no obligation to participate and could quit at any time during the experiment. Both groups were then asked to sign an informed consent form which explained the protocol and stated that they were volunteers who could withdraw from the experiment at anytime (Appendix 1)

Urine Collections

Once the experiment was initiated, urine samples were collected twice a month, once on a weekday and once on a weekend for each of the groups. All voided urine was collected during the sampling period. Once a sample was collected, it was refrigerated. When the subject was finished with a container, the container was frozen until collected by the researcher. During the first year, 1986-1987, the collection period was early September, after the start of the swim season, to February. This year was a trial year to determine if results collected warranted further investigation and, results from this year helped to direct the study over the course of the next two years. During the second year, 1987-1988, the collection period was early September, after the start of the swim season to early May, 2 months after the end of the swim season. Additional samples

Table 2.
Anthropometric Data for Swimmers and Controls

Subject	Weight (kg.)	Height (cm.)	Age (yr.)	Swim Years	Years of Collage Complete	Heart Rate (bpm)
SWIMMERS N=24	86.03 ± 4.03	173.83 ± 9.63	21.4 ± .8	8.2 ± 1.1	2.3 ± 0.6	60 ±10
CONTROLS N=12	77.73 ± 3.13	162.38 ± 8.14	23.8 ± 1.2	---	2.4 ± 0.4	78 ±14

were taken during final exam week in December and May. Samples were also collected from the swimmers before and after a swim during the middle of the season and again for the same swim at the end of the season. During the third year,1988, samples were collected for the months September, before the start of the swim season, November, and December as well as during final exam week in December. The purpose of collecting data during this year was to confirm results obtained during the previous two years and to further elaborate on data already collected.

In order to monitor the catecholamines, samples were collected in three bottles over a 24 hour period for both a weekday and a weekend day using the following procedure. Each day was broken into 3 periods of approximately equal lengths with one bottle for each time period. Each bottle had a strip of tape identifying the subject, the number of the bottle and the collection period, as well as an area where the subjects filled in the first and last time they voided into that particular bottle. Each bottle contained 500 mg of sodium metabisulfite which acted as a preservative to retard catecholamine breakdown (184).

For the week day, the first bottle was started at 4:00 p.m. and continued till the subject went to sleep. Subjects voided prior to the start of the experiment and then collection began with the next void. The second bottle collected the subjects' overnight and first morning void. The third bottle started with the second void of the morning and continued until 4:00 p.m.. This same procedure was also followed on the weekend samples with the first bottle starting with the second morning void on Sunday. This time period was selected in order to get a 24 hour resting sample from swimmers who usually had Saturday afternoon and Monday morning workouts.

Sample Analysis

Once collection had begun, all samples were kept frozen until they were collected. The samples were then quickly thawed and volumes recorded. The actual times voided into each bottle were also recorded. This gave a record of the actual amount of time each bottle had been used. These times were then used when calculating the amount excreted to adjust the data so that the final results reflected 24 hour excretion rates. Three 25 ml. samples were then removed and acidified. The remainder of the collection was discarded. Acidification hydrolyzed the conjugated catecholamines while further insuring the stability of both catecholamines and their metabolites (3, 66, 168). This was accomplished by using an Orion pH meter read to the nearest 0.01, accurate to ±0.05, and calibrated using reference solutions of pH 1, pH 3, and pH 7 accurate to 0.0005 mol/liter.

The first samples was acidified to pH = 3 with 6M HCL and then refrozen for later catecholamine extraction. The second sample was also acidified to pH = 3 with 6M HCL and stored as a back-up to either the first or third samples. The third sample was acidified to pH = 1 with 6M HCL and stored for later catecholamine metabolite extraction (66, 168). Acidification to pH = 1 was needed, as this was the pH required in the protocol used to extract the catecholamine metabolites.

Once catecholamine extraction was ready to proceed, the frozen urine samples were quickly thawed in a boiling hot water bath and prepared for extraction. In order to insure that any changes found in the results were real and not due to an extraction error, every sample was tested in duplicate. If there was variability in the results of greater than 5%, the extraction was repeated. If the variability in the extraction results was less than 5%, the two results were combined and the mean recorded.

In order to purify norepinephrine and epinephrine, the catecholamines and internal standard were poured over a miniature cation exchange column containing multiple carboxylate sites. This allowed collection of the catecholamines and the removal of the rest of the urine sample. The columns were then rinsed with 10 ml of distilled water in order to remove nonretainable particles or cells. To remove the catecholamines from the column, dilute sulfuric acid with a volume less than the volume occupied by the resin in the column was used to protonate the carboxylate groups in the resin and release the catecholamines. Ammonium sulfate was used to wash the catecholamines off the columns and into the collection vials. Aluminum oxide was then placed in the collection vial to bind the catecholamines via their catechol group. This process was enhanced by addition of 500 µl of Tris/EDTA buffer which raised the pH to approximately 8.5, the optimum pH for the binding of catecholamines to aluminum oxide. The samples were then agitated to further enhance absorption before the supernatant was aspirated. The aluminum oxide was then rinsed with water and dried.

Epinephrine and norepinephrine were then released from the aluminum oxide using perchloric acid. This extract was then injected into the LCEC Analyzer, which employed reverse phase chromatography using ocytl sulfate as the ion-carrier. (See Appendix 2 for a more detailed description of the extraction.)

Recovery for this procedure was 54% for norepinephrine and 49% for epinephrine. Variation in random between-run samples was 1.2% for norepinephrine and 2.7% for epinephrine. There were 2 additional safeguards to insure against error in catecholamine extraction. First, by injecting new standards with every extraction batch, variations in the column and detector are controlled. Second, by using peak height ratios, the protocol insures that there is no need to calculate individual calibration curves.

In order to use the LCEC Analyzer, the instrument must be prepared for analysis. This was done by first preparing the mobile phase carrying the ions. The mobile phase was made using 18.8 gm monochloroacetic acid, 5.6 gm sodium hydroxide, and 1 gm sodium EDTA in 2 liter of HPLC grade water. This solution was adjusted to a pH of 3.0 to 3.05. To 2 liters of this solution were added 600 mg of sodium ocytl sulfate and 200 ml of HPLC grade acetonitrile. The mobile phase is then filtered through a 0.20 µm filter and degassed. (See Appendix 3 for a detailed description of preparation of all the reagents.)

The LCEC Analyzer stationary phase was a Biophase ODS 4 µm column (250 x 4 mm). The liquid chromatograph is a BAS LC-304 and the detector is a BAS LC-4A/LC-17, using a TL-5 glassy carbon electrode with an applied potential of 650 mV vs. Ag/AgCl. Flow rate was 15 ml/min; injected amount was 50-100 µl; head pressure for the system did not exceed 3500 psi; temperature was 30°C; background noise was 5-10 nA ; and the baseline for the system was flat.

Results were recorded on chart paper using a strip recorder. The speed for the system was 0.2 inches/minutes and the sensitivity was either 0-50, 0-100, or 0-200 nAmps, depending on the concentration of epinephrine and norepinephrine in the extract. In order to analyze the strip chart, standards with known amounts of norepinephrine and epinephrine were injected and the results recorded prior to the injection of the unknowns.

Four standards labeled 10, 20, 30, and 40 were used with the following increases in concentration of norepinephrine and epinephrine respectively: 12, 24, 36, and 48 nanograms/milliliter and 4, 8, 12, and 16 nanograms/ milliliter. Each catecholamine standard also had an internal standard so upon completion of injection the peak-height ratio of norepinephrine or epinephrine to internal standard was recorded for each of the concentrations. Following this procedure, the peak-height ratio vs. known concentration of catecholamine was graphed. The slope of this graph was then calculated and was used to calculate the amount of unknown based on the catecholamine to internal standard ratio (Figure 4). (Note: In all catecholamine standards, the internal standard concentration was actually half the concentration used in calculating the unknowns. Consequently, the internal standard value obtained from the extraction of the standards was doubled to make the ratios equal.) Once the standards were injected, unknown samples were run.

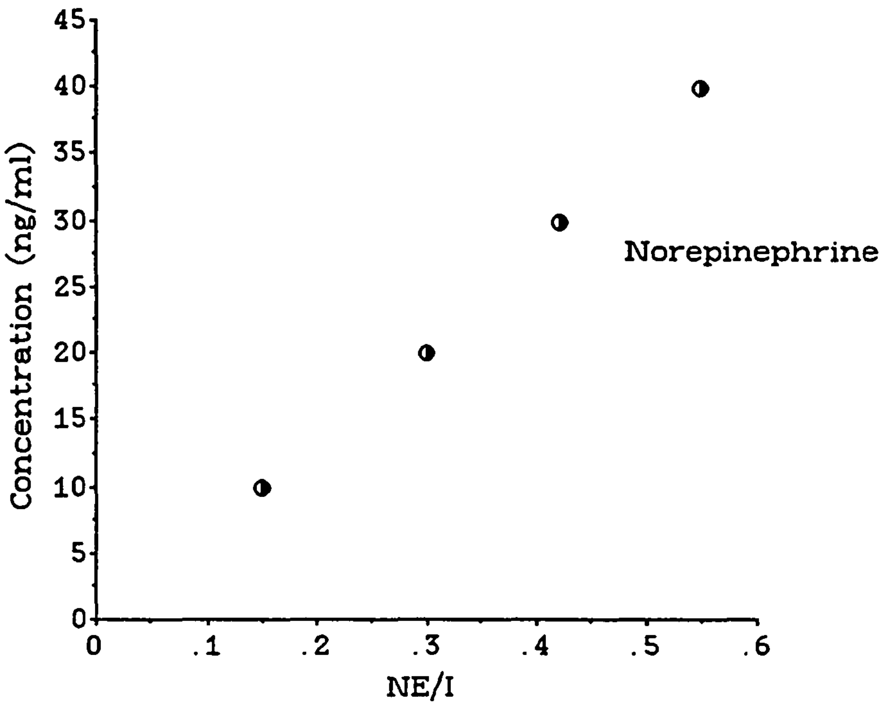

Figure 2. Calibration Curve of Norepinephrine

The hormones were then calculated using the curves determined by the standards, and the results were recorded.

After completion of extraction of the catecholamines, the metabolites metanephrine and normetanephrine were then extracted. The frozen urine samples were once again quickly thawed in a hot water bath and prepared for extraction. In order to insure that any changes found in the results were real and not due to an extraction error, every sample was preformed in duplicate. If there was variability in the results of greater than 5%, the extraction was retested. If the variability in the extraction results was less than 5%, then the two results were combined and the mean recorded.

In order to purify the metanephrine and normetanephrine, 2.0 ml aliquots of the pH 1 sample were combined with an internal standard and boiled for 30 minutes to completely hydrolyze the metabolites. The hydrolyzed urines were then diluted with ammonium pentaborate and poured over a cation exchange column. This column acts by binding amines found in the urine. The metabolites are released from the column using ammonium hydroxide and are bound to a second, strongly anionic column which is placed directly below the first column. This second column separates the metabolites from nonphenolic amines and more hydrophobic phenolic compounds. The metabolites are then released from the second column using an elution buffer and are captured in a test tube where they are combined with acetic acid. This final solution is then ready for extraction. (See Appendix 2 for more detailed instructions.)

Recovery for this procedure was 76% for normetanephrine and 72% for metanephrine. Variation in random between-run samples was 6.7% for metanephrine and 3.6% for normetanephrine. Three further controls against error are incorporated. First, as with the catecholamines, calculation of metanephrine and normetanephrine are based on ratios of hormone to internal standard so that absolute values are not required. Second a control with a known amount of metabolite is also extracted to insure there is no error in the extraction procedure. Lastly, a test kit was used to insure proper equilibration of the mobile phase .

In order to extract the metabolites, the mobile phase had to be made first and the system allowed to equilibrate at least 24 hours. The mobile phase was made using KH_2PO_4, glass distilled water, sodium hydroxide, and HPLC grade acetonitrile. This mixture was filtered through a 0.2 μm filter and was stable at room temperature for at least 1 week. (See appendix 3 for a detailed description of preparation of all the reagents.)

The LCEC Analyzer stationary phase was a Bio-Rad clinical cation-exchange column. The Liquid chromatograph is a BAS LC-304 and the detector is a BAS LC-4A/LC-17, using a TL-5 glassy carbon electrode with an applied potential of 730 mV vs. Ag/AgCl. Flow rate was 1.5 ml/min; injected amount was 50-100 μl; head pressure for the system did not exceed 2200 psi; temperature was 45°C; background noise was 5-10 nA; and the baseline for the system was flat.

Results were recorded on chart paper using a strip recorder. The speed for the system was 0.2 inches/minutes and the sensitivity was either 0-10, 0-20, or 0-50 nAmps depending on the concentration of metanephrine and normetanephrine in the extract. In order to analyze the strip chart, one standard with known amounts of metanephrine and normetanephrine were injected and the results recorded prior to the injection of the unknowns.

In order to calculate the amount of metanephrine and normetanephrine in the solution, the peak heights for metanephrine and normetanephrine where divided by the peak height for the internal standard. This gave a ratio for a known concentration of metanephrine and normetanephrine. The concentrations of unknown metanephrine and normetanephrine were then calculated by dividing these metabolites by the internal standard and then extrapolating to get the answer.

Ancillary Measurements

Besides collecting data on catecholamines and their metabolites, it was also necessary to take numerous surveys in order to minimize as many variables as possible. Some of the variables known to affect catecholamine levels include: external environment, tobacco, caffeine, drugs, excess carbohydrates, low sodium, decreased plasma volume, time of day, age, anxiety and psychological stress, posture, exercise, physical condition, and certain illneses (106). These variables were monitored by use of a modified Hassles test, diet history, and a survey of what was happening in the subjects life at the time of the test. These forms are included in Appendix 1. All forms were individually administered to the subjects and the time that each subject spent completing a form was fairly uniform for all subjects completing that form.

Resting lactic acid levels were also monitored to see if there was any relationship between resting lactic acid production and changes in catecholamine levels. Samples for lactic acid analysis were collected using the following procedure. Swimmers arrived at the pool in the morning, either before morning practice or right after waking, and rested for 15 minutes by sitting quietly. Blood samples were then obtained by cleaning any finger with an alcohol swab, lancing the finger with a disposable lancet, and collecting approximately 100 μl of blood in a capillary tube containing heparin. From this tube 50 μl of blood was mixed with 50 μl of buffer and 50 μl of this mixture was then injected into a lactate analyzer. The analyzer had been calibrated to read to within 0.1 mMol/l of a 5 mMol/l standard and within 0.4 mMol/l of a 15 mMol/l standard. During the testing of the samples obtained, the machine was rechecked after every other injection and recalibrated if the pH fell out of the expected range given above.

Data Analysis

Results for the hormones and their metabolites are presented as the amount of hormone excreted. The amount excreted was calculated by multiplying the volume of a sample by the concentration of the hormone in that sample and dividing by the time period over which the samples was collected. Statistical analysis was done on the data using a statistical package called StatView SE+Graphics and run on a MacIntosh SE. Students t-test was used in single measurement comparisons and a Scheffe F-test was used for comparison of repeat measurements. Multiple regression, ANOVA, and correlation coefficient calculations were also preformed on the data.

Chapter 4. **Individual Collection Periods**

Results

Use of Individual versus Summed Results

The first part of the study was to examine the effect of training on hormone excretion during the course of a training season. In almost all cases, there was no significant difference when comparing the average of a particular month taken over three years to the average for that month in any particular year ($p > .05$). For example, compare the average value of norepinephrine that is excreted from 4:00 p.m. to bed on a work day, taken over 3 years, to each of the individual yearly values for the month of November. No significant difference is seen between the three year average for November, and any of the individual years ($t = 1.14$, $p > .05$). Consequently, all results will be presented as sums over three years. For those hormone levels inwhich there is a signifcant difference between summed data and individual years, $p < .05$, the data is presented in a separate table and is not used to calculate the average for that month.

Month-By-Month Comparison of Swimmers to Controls

Table 3 presents the values averaged over three years for norepinephrine, epinephrine, normetanephrine, and metanephrine taken during the time period 4:00 to bed on the work day. In comparing individual months to the mean for that month, the September 1988 norepinephrine value was significantly lower than the average norepinephrine value obtained from averaging 1986 and 1987 values (table 4). Similarly, the normetanephrine level obtained in 1988 was significantly lower than that obtained in 1987 ($p < .01$, table 4). In comparing changes from month to month with in the swim category, there are multiple significant differences ($p < .05$). These differences are seen in Table 5, which shows the significant differences between a particular month and all other months. Norepinephrine and normetanephrine were

Table 3. Comparison of Hormone Averages for Samples Collected from 4:00 p.m. to bed on a work day.

	Norepinephrine (µg/hr) Swim	Norepinephrine (µg/hr) Control	Epinephrine (µg/hr) Swim	Epinephrine (µg/hr) Control	Normetanephrine (ug/hr) Swim	Normetanephrine (ug/hr) Control	Metanephrine (µg/hr) Swim	Metanephrine (µg/hr) Control
Sep[1]	9.21 ±0.67 20	3.01 ±0.10 24	2.03 ±0.11 20	1.96 ±0.09 24	23.78 ±1.99 28	14.85 ±0.50 24	6.15 ±0.48 28	6.08 ±0.34 24
Oct.	3.20 ±0.21 36	---	1.47 ±0.09 36	---	13.83 ±1.48 28	---	4.38 ±0.38 28	---
Nov.	2.04 ±0.09 38	3.20 ±0.11 24	1.15 ±0.04 38	1.90 ±0.05 24	8.16 ±0.46 28	14.82 ±0.47 24	3.89 ±0.31 28	6.01 ±0.56 24
Dec.	3.81 ±0.29 37	3.19 ±0.09 24	1.63 ±0.12 37	3.35 ±0.11 24	15.18 ±0.96 28	14.79 ±0.93 24	6.08 ±0.59 28	9.09 ±0.45 24
Jan.	7.32 ±0.52 38	---	3.98 ±0.15 38	---	22.13 ±1.87 28	---	12.54 ±0.87 28	---
Feb.	11.92 ±0.72 38	3.13. ±0.08 24	5.95 ±0.38 38	1.93 ±0.06 24	46.31 ±2.10 28	14.83 ±0.51 24	16.15 ±0.98 28	6.12 ±0.38 24
Mar.	5.78 ±0.31 37	3.09 ±0.09 24	2.06 ±0.09 37	1.89 ±0.08 24	20.09 ±0.62 28	15.03 ±0.42 24	6.19 ±0.42 28	6.08 ±0.61 24
Apr.	3.02 ±0.09 38	3.07 ±0.08 24	1.90 ±0.09 38	1.94 ±0.08 24	14.87 ±0.60 28	14.88 ±0.73 24	6.09 ±0.48 28	6.03 ±0.31 24
May	3.14 ±0.08 38	3.09 ±0.10 24	1.88 ±0.07 38	1.87 ±0.06 24	14.99 ±0.58 28	14.93 ±0.56 24	6.07 ±0.53 28	6.12 ±0.56 24

The enteries in each cell of the table are, from top to bottom: the value, the standard error, and the number of subjects.

1: September 1988, was not included as these samples were collected before the start of the training season and the other values were collected once the season had started.

Table 4. Average Hormone Values for September for Samples Collected from 4:00 p.m. to bed during a work day.

	September 1988 Average	September 1986, 1987 Combined Average
Norepinephrine	3.16 ± 0.16*	9.21 ± 0.67

* $p < .01$, F-test

N=10 for 1988
N=28 for 1986-7 average

	September 1988 Average	September 1987 Average
Normetanephrine	12.92 ± 0.63*	23.78 ± 1.99

* $p < 0.01$, t-test

N=12 for 1988
N=12 for 1987

Table 5. Sheffe F-test in Swimmer Group, 4:00 p.m. to bed On a Work Day

Norepinephrine/Normetanephrine

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	●	●	●					
January	●	●	●	●				
February	0	●	●	●	●			
March	●	●	●	0	●	●		
April	●	0	●	0	●	●	0	
May	●	0	●	0	●	●	0	0

Epinephrine/Metanephrine

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	0	●	●					
January	●	●	●	●				
February	●	●	●	●	●			
March	0	●	●	0	●	●		
April	0	●	●	0	●	●	0	
May	0	●	●	0	●	●	0	0

● $P < .05$
0 $P > .05$

combined into one category and epinephrine and metanephrine were combined into another because the significant differences between months were the same for both hormone and metabolite.

In comparing changes month to month for the control category, there were no significant differences except in December, when the epinephrine values were significantly higher from the other epinephrine monthly values (Table 3).

Comparing swimmers to controls gave the following results. For norepinephrine and normetanephrine: swim levels collected during September 1988 were not significantly different from control values ($p > .05$). September 1986 and 1987 showed swimmers with higher levels than controls ($p < .05$). October, April, and May showed no differences between swimmers and controls ($p < .05$). Swimmer levels for November were significantly less than controls ($p < .01$), and February ($p < .01$) January, and March ($p < .05$) showed swimmers with significantly higher values.

For epinephrine and metanephrine: September, March, April, and May were not different between the two groups ($p > .05$). Swim levels for October, November and December were significantly less than controls ($p < .05$). January and February showed swimmers with significantly higher values versus controls($p < .01$). These results are summarized in Table 5.

Table 6 represents the average values summed over three years for norepinephrine, epinephrine, normetanephrine, and metanephrine taken during the time the subject was asleep up to and including the first void of the day on the work day.

In comparing individual months to the mean for that month, the norepinephrine values for December 1988 are significantly lower compared to 1986 and 1987 values in swimmers ($p < .05$) (Table 7). Similarly, the swimmer normetanephrine value for December 1988 is significantly lower than that for December 1987. The discrepancy between these months, however, may be related to the fact that 1986 and 1987 values

Table 6. Average Hormone Values for Samples Collected Overnight and first void in the morning on a work day

	Norepinephrine (µg/hr) Swim	Norepinephrine (µg/hr) Control	Epinephrine (µg/hr) Swim	Epinephrine (µg/hr) Control	Normetanephrine (ug/hr) Swim	Normetanephrine (ug/hr) Control	Metanephrine (µg/hr) Swim	Metanephrine (µg/hr) Control
Sep	3.11 ±0.37 38	2.67 ±0.19 24	1.38 ±0.08 38	1.39 ± 0.10 24	11.02 ±0.95 28	11.63 ±0.96 24	4.21 ±0.29 28	4.26 ±0.27 24
Oct.	1.86 ±0.12 38	---	0.88 ±0.04 38	---	8.08 ±0.66 28	---	3.06 ±0.26 28	---
Nov.	1.44 ±0.13 37	2.58 ±0.13 24	0.46 ± 0.02 37	1.30 ±0.13 24	6.25 ±0.49 28	11.38 ±0.95 24	2.08 ±0.16 28	4.24 ±0.31 24
Dec.[1]	2.34 ±0.27 20	2.79 ±0.19 24	0.98 ±0.03 20	1.38 ±0.09 24	9.29 ±0.82 28	11.98 ±1.03 24	3.07 ±0.32 28	4.24 ±0.33 24
Jan.	3.75 ±0.29 38	---	1.73 ± 0.11 38	---	15.83 ±1.25 28	---	6.04 ±0.56 28	---
Feb.	4.23 ±0.23 38	2.63 ±0.18 24	2.46 ± 0.20 38	1.24 ± 0.11 24	19.55 ±1.68 28	11.69 ±0.78 24	10.92 ±1.08 28	4.13 ±0.34 24
Mar.	2.78 ±0.17 38	2.56 ±0.16 24	1.25 ± 0.06 38	1.30 ±0.14 24	11.59 ±0.89 28	11.55 ±0.59 24	4.17 ±0.23 28	4.19 ±0.53 24
Apr.	2.61 ±0.15 37	2.49 ±0.13 24	1.28 ± 0.10 37	1.18 ±0.09 24	11.72 ±0.68 28	11.78 ±0.81 24	4.24 ±0.21 28	4.26 ±0.58 24
May	2.73 0.24 38	2.70 ±0.19 24	1.26 ± 0.07 38	1.21 ± 0.10 24	11.65 ±0.78 28	11.70 ±0.74 24	4.20 ±0.48 28	4.25 ±0.51 24

The enteries in each cell of the table are, from top to bottom: the value, the standard error, and the number of subjects.

1: December 1988 values are not included making N for this month 20.

Table 7. Average Hormone Value for December for Samples Collected Overnight and First Void in the Morning on a Work Day

	December 1988 Average	December 1986, 1987 Combined Average
Norepinephrine	1.69 ± 0.12*	2.34 ± 0.27

* $p < .01$, F-test

N=10 for 1988
N=28 for 1986-7 average

	December 1988 Average	December 1987 Average
Normetanephrine	7.76 ± 0.32*	9.29 ± 0.82

* $p < .01$, t-test

N=12 for 1988
N=12 for 1987

Table 8. Sheffe F-test in Swimmer Group, Bed and 1st Void On a Work Day

Norepinephrine/Normetanephrine

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	●	0	●					
January	●	●	●	●				
February	●	●	●	●	●			
March	●	●	●	●	0	●		
April	●	●	●	●	●	●	●	
May	●	●	●	●	●	●	●	0

Epinephrine/Metanephrine

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	0	●	●					
January	●	●	●	●				
February	●	●	●	●	●			
March	●	●	●	0	0	●		
April	●	●	●	0	0	●	0	
May	●	●	●	0	0	●	0	0

● P $<$ .05
0 P $>$ .05

were collected while the subject was training. 1988 values were collected when the swimmers were studying for finals and had not been training for approximately 4-5 days. In comparing changes from month to month within the swim category, there are multiple significant differences ($p < .05$), and these are seen in table 8. There are no significant differences for the control groups on a month to month basis.

Comparing swimmers to controls gives the following results. For norepinephrine and normetanephrine: There is no significant difference between swimmers and controls for September, March, April, and May values ($p > .05$); swimmers have significantly lower values during October, December ($p < .05$) and November ($p < .01$) ; while January ($P<0.05$), and February ($P<0.01$) show swimmers having significantly higher values.

For epinephrine and metanephrine: September, April, and May have values that are not significantly different between the two groups($p > .05$); Swim values for October, December ($p < .05$) and November ($p < .01$) are significantly lower than controls; while January($p < .05$) and February ($p < .01$) swim levels are significantly higher than controls. Results are summarized in Table 8.

Table 9 presents the values average over three years for norepinephrine, epinephrine, normetanephrine, and metanephrine taken from the second void of the morning until 4:00 p.m. on the work day. In comparing individual months to the mean taken over three years for that month, the norepinephrine levels are lower in December of 1988 compared to the mean of the other two years ($p < .05$) (Table 10). Similarly, normetanephrine levels are significantly lower in December of 1988 compared to December of 1987 ($P<0.05$) (Table 10). Comparing changes from month to month within the swim category, there are multiple significant differences ($p < .05$). These differences are seen in Table 11. There are no significant differences for the control groups on a month to month basis.

Table 9. Average Hormone Value for Samples Collected from Second Void of the Day Until 4:00 p.m.

	Norepinephrine (µg/hr)		Epinephrine (µg/hr)		Normetanephrine (ug/hr)		Metanephrine (µg/hr)	
	Swim	Control	Swim	Control	Swim	Control	Swim	Control
Sep	4.43 ±0.32 38	3.89 ±0.35 24	2.36 ±0.21 38	2.32 ±0.13 24	16.25 ±1.03 28	16.39 ±0.61 24	7.12 ±0.47 28	7.19 ±0.57 24
Oct.	2.87 ±0.16 38	---	1.90 ±0.08 38	---	10.06 ±0.43 28	---	5.68 ±0.31 28	---
Nov.	1.97 ±0.11 38	3.94 ±0.23 24	1.27 ±0.04 38	2.32 ±0.17 24	6.74 ±0.46 28	16.17 ±0.63 24	3.36 ±0.19 28	7.38 ±0.46 24
Dec.[1]	3.02 ±0.17 20	4.01 ±0.24 24	2.18 ±0.11 20	2.29 ±0.13 24	9.24 ±0.51 28	16.23 ±0.72 24	6.28 ±0.34 28	7.13 ±0.31 24
Jan.	6.68 ±0.23 38	---	4.64 ±0.12 38	---	25.23 ±1.23 28	---	12.08 ±0.51 28	---
Feb.	11.13 ±0.36 37	3.88 ±0.23 24	5.86 ±0.31 37	2.27 ±0.16 24	40.95 ±2.65 28	16.26 ±0.58 24	16.01 ±0.92 28	7.16 ±0.42 24
Mar.	5.06 ±0.32 38	4.03 ±0.29 24	2.46 ±0.12 38	2.43 ±0.18 24	20.83 ±1.03 28	16.30 ±0.40 24	7.14 ±0.39 28	7.20 ±0.35 24
Apr.	4.02 ±0.28 38	4.06 ±0.24; 24	2.36 ±0.12 38	2.30 ±0.12 24	16.34 ±0.87 28	16.33 ±0.49 24	7.10 ±0.44 28	7.14 ±0.32 24
May	4.10 ±0.19 37	3.99 ±0.24 24	2.31 ±0.14 37	2.39 ±0.18 24	16.24 ±0.78 28	16.78 ±0.87 24	7.09 ±0.41 28	7.06 ±0.27 24

The enteries in each cell of the table are, from top to bottom: the value, the standard error, and the number of subjects.

1: December 1988 values are not included making N for this month 20.

Table 10. Average Hormone Values for December for Samples Collected from Second Void of the Day until 4:00 p.m. on a Work Day

	December 1988 Average	December 1986, 1987 Combined Average
Norepinephrine	1.27 ± 0.09 *	3.02 ± 0.17

* $p < .01$, F-test

N=10 for 1988
N=28 for 1986–7 average

	December 1988 Average	December 1987 Average
Normetanephrine	6.88 ± 0.42 *	9.24 ± 0.51

* $p < .01$, t-test

N=12 for 1988
N=12 for 1987

Table 11. Sheffe F-test in Swimmer Group, 2nd Void to 4:00 pm On a Work Day

Norepinephrine/Normetanephrine

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	●	●	●					
January	●	●	●	●				
February	●	●	●	●	●			
March	●	●	●	●	●	●		
April	●	●	●	●	0	●	●	
May	●	●	●	●	0	●	●	0

Epinephrine/Metanephrine

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	●	0	●					
January	●	●	●	●				
February	●	●	●	●	●			
March	●	●	●	●	●	●		
April	0	●	●	●	●	●	●	
May	0	●	●	●	●	●	●	0

● P < .05
0 P > .05

Comparing swimmers to controls gives the following results. For norepinephrine and normetanephrine: There is no significant difference in hormone levels during September, April, and May between the two groups ($p > .05$); swim levels in October, December ($p < .05$) and November ($p < .01$) are significantly lower than control levels; and January, February ($p < .01$) and March ($p < .05$) swim levels are significantly higher than control levels.

For epinephrine and metanephrine: September, March, April, and May have values that are not significantly different between the two groups($p > .05$); swim levels for October, December ($p < .05$), and November ($p < .01$) are significantly lower than controls; and January, February ($p < .01$) swim levels are significantly higher than control values.

Table 12 presents the values averaged over three years for norepinephrine, epinephrine, normetanephrine, and metanephrine taken from the second void of the morning until 4:00 p.m. on the rest day. In comparing individual months to the mean taken over three years for that month, there are no significant differences. Comparing changes from month to month within the swim category, there are multiple significant differences ($p < .05$). These differences are seen in Table 13. There are no significant differences for the control groups on a month to month basis.

Comparing swimmers to controls gives the following results. For norepinephrine and normetanephrine: There is no significant difference for September, February, March, April, and May values between the two groups ($p > .05$); and swim values for October, December, January ($p < .05$), and November ($p < .01$) are significantly lower than control levels.

For epinephrine and metanephrine: September, December, February, March, April, and May have values that are not significantly different between the two groups ($p > .05$); swim levels for October ($p < .05$), and November ($p < .01$) are significantly

Table 12. Average Hormone Values for Samples Collected from Second Void of the Day until 4:00 p.m. on a Rest Day

	Norepinephrine (μg/hr)		Epinephrine (μg/hr)		Normetanephrine (ug/hr)		Metanephrine (μg/hr)	
	Swim	Control	Swim	Control	Swim	Control	Swim	Control
Sept	3.69 ±0.24 38	3.76 ±0.23 24	1.79 ±0.12 38	1.91 ±0.13 24	14.64 ±0.96 28	12.69 ±1.03 24	6.26 ±0.49 28	6.01 ±0.46 24
Oct.	3.10 ±0.24 38	---	1.26 ±0.11 38	---	12.07 ±1.03 28	---	5.48 ±0.36 28	---
Nov.	2.46 ±0.21 37	3.71 ±0.36 24	0.76 ±0.06 37	1.79 ±0.19 24	8.74 ±0.52 28	12.83 ±0.88 24	4.21 ±0.40 28	6.20 ±0.31 24
Dec.	3.24 ±0.34 38	3.69 ±0.28 24	1.36 ±0.17 38	1.84 ±0.13 24	11.48 ±0.91 28	12.85 ±1.11 24	5.98 ±0.35 28	5.98 ±0 27 24
Jan.	3.70 ±0.34 37	---	1.94 ±0.20 37	---	12.79 ±1.02 28	---	6.07 ±0.47 28	---
Feb.	3.98 ±0.56 38	3.60 ±0.20 24	1.87 ±0.14 38	1.83 ±0.17 24	23.46 ±1.15 28	12.96 ±1.16 24	5.99 ±0.39 28	6.07 ±0.35 24
Mar.	3.73 ±0.26 38	3.74 ±0.21 24	1.93 ±0.10 38	1.86 ±0.21 24	17.70 ±1.23 28	12.70 ±1.06 24	6.08 ±0.49 28	6.06 ±0.40 24
Apr.	3.70 ±0.34 38	3.83 ±0.22 24	1.84 ±0.12 38	1.90 ±0.10 24	12.88 ±1.02 28	12.99 ±1.04 24	6.01 ±0.40 28	5.96 ±0.48 24
May	3.71 ±0.44 38	3.79 ±0.30 24	1.86 ±0.18 38	1.88 ±0.16 24	12.97 ±0.88 28	12.71 ±1.23 24	5.95 ±0.47 28	5.99 ±0.38 24

The enteries in each cell are, form top to bottom: the value the standard error, and the number of subjects

Table 13. Sheffe F-test in Swimmer Group, 2nd Void to 4:00 pm
On a Rest Day

Norepinephrine/Normetanephrine

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	●	0	●					
January	●	●	●	●				
February	0	●	●	●	0			
March	0	●	●	●	0	0		
April	0	●	●	●	0	0	0	
May	0	●	●	●	0	0	0	0

Epinephrine/Metanephrine

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	●	●	●					
January	●	●	●	●				
February	0	●	●	0	0			
March	0	●	●	0	0	0		
April	0	●	●	0	0	0	0	
May	0	●	●	0	0	0	0	0

● $P < .05$
0 $P > .05$

Table 14. Average Hormone Values for Samples Collected from 4:00 p.m. until Bed on a Rest Day

	Norepinephrine (µg/hr)		Epinephrine (µg/hr)		Normetanephrine (ug/hr)		Metanephrine (µg/hr)	
	Swim	Control	Swim	Control	Swim	Control	Swim	Control
Sept	2.74 ±0.13 38	2.33 ±0.16 24	1.43 ±0.12 38	1.36 ±0.18 24	13.97 ±1.01 28	13.56 ±0.99 24	4.98 ±0.41 28	5.06 ±0.46 24
Oct.	1.49 ±0.13 38	---	0.89 ±0.09 38	---	12.32 ±0.98 28	---	3.09 ±0.23 28	---
Nov.	0.74 ±0.09 38	2.44 ±0.28 24	0.46 ±0.04 38	1.39 ±0.19 24	9.55 ±0.56 28	13.64 ±0.94 24	1.98 ±0.15 28	4.88 ±0.42 24
Dec.	2.29 ±0.21 38	4.33 ±0.32 24	1.66 ±0.10 38	1.45 ±0.20 24	12.88 ±1.02 28	13.56 ±1.00 24	5.26 ±0.35 28	5.04 ±0.43
Jan.	2.68 ±0.23 38	---	1.44 ±0.13 38	---	14.98 ±1.11 28	---	4.99 ±0.43 28	---
Feb.	2.56 ±0.14 38	2.57 ±0.16 24	1.49 ±0.09 38	1.36 ±0.08 24	16.74 ±1.23 28	13.87 ±0.95 24	4.87 ±0.38 28	4.88 ±0.47 24
Mar.	2.48 ±0.21 38	2.49 ±0.19 24	1.32 ±0.20 38	1.39 ±0.12 24	13.90 ±0.89 28	13.72 ±0.85 24	5.01 ±0.46 28	4.93 ±0.31 24
Apr.	2.47 ±0.15 38	2.51 ±0.24 24	1.36 ±0.10 38	1.27 ±0.11 24	13.81 ±0.97 28	13.66 ±1.03 24	4.89 ±0.34 28	4.86 ±0.36 24
May	2.43 ±0.18 38	2.48 ±0.16 24	1.40 ±0.17 38	1.38 ±0.28 24	13.84 ±0.88 28	13.79 ±1.05 24	4.83 ±0.39 28	4.87 ±0.28 24

The enteries in each cell are, form top to bottom: the value the standard error, and the number of subjects

Table 15. Sheffe F-test in Swimmer Group, 4:00 p.m. till bed On a Rest Day

Norepinephrine/Normetanephrine

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	0	0	●					
January	0	●	●	0				
February	0	●	●	0	0			
March	0	●	●	0	0	0		
April	0	●	●	0	0	0	0	
May	0	●	●	0	0	0	0	0

Epinephrine/Metanephrine

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	0	●	●					
January	0	●	●	0				
February	0	●	●	0	0			
March	0	●	●	0	0	0		
April	0	●	●	0	0	0	0	
May	0	●	●	0	0	0	0	0

● $P < .05$
0 $P > .05$

lower than controls; and swim levels in January ($p < .05$) are significantly higher than controls.

Table 14 presents the values averaged over three years for norepinephrine, epinephrine, normetanephrine, and metanephrine taken from 4:00 p.m. till bed on the rest day. In comparing individual months to the mean taken over three years for that month, there are no significant differences. Comparing changes from month to month with in the swim category, there are multiple significant differences ($p < .05$). These differences are seen in table 15. There are no significant differences for the control groups on a month to month basis.

Comparing swimmers to controls gives the following results. For norepinephrine and normetanephrine: There is no significant difference between September, December, January, February, March, April, and May values for the two groups ($p > .05$); and swim levels in October ($p < .05$), and November ($p < .01$) are significantly lower than those of controls.

For epinephrine and metanephrine: September, December, January, February, March, April, and May have values that are not significantly different between the two groups ($p > .05$); and swim levels for October ($p < .05$), and November ($p < .01$) are significantly lower than those for controls.

Table 16 presents the values averaged over three years for norepinephrine, epinephrine, normetanephrine, and metanephrine taken from the time the subject goes to bed through the first void of the morning. In comparing individual months to the mean taken over three years for that month, there are no significant differences. Comparing changes from month to month within the swim category, there are multiple significant differences ($p < .05$). These differences are seen in Table 17. There are no significant differences for the control groups on a month to month basis.

Comparing swimmers to controls gives the following results. For

Table 16. Average Hormone Values for Samples Collected Overnight and First Void in the Morning on a Rest Day

	Norepinephrine (µg/hr) Swim	Norepinephrine (µg/hr) Control	Epinephrine (µg/hr) Swim	Epinephrine (µg/hr) Control	Normetanephrine (ug/hr) Swim	Normetanephrine (ug/hr) Control	Metanephrine (µg/hr) Swim	Metanephrine (µg/hr) Control
Sept	1.86 ±0.16 38	1.91 ±0.14 24	0.96 ±0.07 38	0.93 ±0.05 24	11.74 ±1.14 28	10.16 ±1.01 24	3.39 ±0.24 28	3.47 ±0.28 24
Oct.	1.39 ±0.14 37	---	0.69 ±0.03 37	---	9.67 ±0.87 28	---	2.94 ±0.23 28	---
Nov.	0.83 ±0.05 37	1.97 ±0.18 24	0.37 ±0.02 37	0.96 ±0.08 24	6.78 ±0.45 28	10.58 ±0.99 24	2.02 ±0.14 28	3.43 ±0.26 24
Dec.	1.38 ±0.11 38	1.92 ±0.13 24	0.51 ±0.03 38	0.88 ±0.07 24	9.11 ±0.81 28	10.79 ±0.84 24	3.07 ±0.26 28	3.41 ±0.29 24
Jan.	1.87 ±0.10 38	---	1.05 ±0.08 38	---	10.23 ±1.03 28	---	3.48 ±0.17 28	---
Feb.	1.96 ±0.14 38	2.01 ±0.14 24	0.87 ±0.05 38	0.99 ±0.06 24	18.75 ±1.12 28	10.28 ±1.03 24	3.31 ±0.28 28	3.29 ±0.22 24
Mar.	1.90 ±0.18 38	2.03 ±0.16 24	0.92 ±0.08 38	0.87 ±0.08 24	13.79 ±1.10 28	10.41 ±0.96 24	3.36 ±0.21 28	3.48 ±0.31 24
Apr.	1.87 ±0.13 38	1.89 ±0.14 24	0.86 ±0.07 38	0.91 ±0.04 24	10.27 ±0.98 28	10.67 ±1.02 24	3.46 ±0.32 28	3.35 +0.38 24
May	1.99 ±0.09 37	2.00 ±0.17 24	0.91 ±0.09 37	0.90 ±0.06 24	10.16 ±0.89 28	10.25 ±0.84 24	3.34 ±0.19 28	3.28 ±0.23 24

The enteries in each cell are, form top to bottom: the value the standard error, and the number of subjects

Table 17. Sheffe F-test in Swimmer Group, Bed and 1st Void On a Rest Day

Norepinephrine/Normetanephrine

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	●	0	●					
January	0	●	●	●				
February	0	●	●	●	0			
March	0	●	●	●	0	0		
April	0	●	●	●	0	0	0	
May	0	●	●	●	0	0	0	0

Epinephrine/Metanephrine

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	0	●	●					
January	0	0	●	●				
February	0	0	●	●	0			
March	0	0	●	●	0	0		
April	0	0	●	●	0	0	0	
May	0	0	●	●	0	0	0	0

● P < .05
0 P > .05

norepinephrine and normetanephrine: There is no significant difference between September, January, February, March, April, and May values for the two groups ($p > .05$); and swim levels for October, December ($p < .05$), and November ($p < .01$) are significantly lower than those for controls.

For epinephrine and metanephrine: September, December, January, February, March, April, and May have values that are not significantly different from control levels ($p > .05$); and swim levels for October ($p < .05$), and November ($p < .01$) are significantly lower than those of controls.

Discussion

The first part of this study was concerned with the interaction of training and hormone excretion. Specifically, the hypothesis was tested that training would decrease the excretion of catecholamines and their metabolites from month to month within the swimmer group. Further, it was proposed that there would be a significant difference between swimmers and controls when comparing samples collected during various times of the day. Before discussing this, however, the differences in catecholamine excretion during September need to be analyzed.

Hormone Excretion During September

The results for September, presented in Tables 3 and 4, show that there was a significant difference between the first two years of the study and the last year in the excretion of norepinephrine and normetanephrine. This difference is the result of starting the last year of the experiment before the start of the swimming season. In the previous two years, sample collection did not start until after one week of training. Consequently, it is apparent that the initial effects of exercise on norepinephrine and normetanephrine excretion are rapid and occur within the first week of training.

The results in Table 3 also show that there is a three-fold increase in norepinephrine and normetanephrine excretion compared to controls. This finding is unique, as no other studies have reported increases of this magnitude (222, 286, 287). In separate studies, both Peronnet and Winder found that norepinephrine excretion in exercising subjects only doubled relative to controls (222, 287). One reason is this study is the first to look at the effects of training on hormone excretion by splitting the 24 hour sampling interval into 3 collection periods. This division allows for precise detection of changes in catecholamine excretion do to specific events that nondivided collection protocols can not provide. Consequently, the larger increase in norepinephrine and normetanephrine excretion shown in this experiment could be related to a more precise sampling protocol.

This study also shows, however, that summing norepinephrine and normetanephrine excretion over 24 hours results in a three-fold increase in swimmers' excretion of these hormones during a work day compared to samples taken either from the same group during a rest day or control samples taken on either day (Table 18). One reason is that these samples were collected over a time period when the swimmers were actually training and so will reflect an increase in hormone levels due to physical exertion. This does not completely explain the magnitude of this increase, however, as other studies have collected samples during and after exercise at the start of a training period and do not show these large increases (37, 66, 93, 121, 132, 163, 286). An additional reason is suggested by the research of Guezennec, who compared runners and swimmers and found that, at the same intensity of exercise, swimmers had significantly higher catecholamine levels compared to runners ($p < .05$) (121). It is likely that the reason for the larger elevations in hormones of swimmers are two-fold. First, these samples were collected over 24 hours with inclusion of the training period; and second, swimming may elicit higher catecholamine excretion than other exercises.

Another reason for increased excretion of catecholamines in swimmers is that during the first weeks of training, swimmers are often mechanically inefficient and not physically fit relative to their intensity of training . The combination of these two limitations could then make swimming values significantly higher compared to other groups of athletes. While all athletes have the physical stress of starting a training season in relatively poor physical fitness, swimmers also have to contend with the stress of being mechanically inefficient due to lack of flexibility, strength, and practice. Thus, it typically takes the average swimmer, who has not been swimming for a month, at least two weeks to regain the stroke mechanics necessary for competitive swimming.

While the swimmer is regaining proper stroke mechanics, norepinephrine excretion would be elevated compared to controls due to the increased physical stress the swimmer is undergoing. Further, comparing norepinephrine and normetanephrine values for October and November (Table 3) to control values, it could be predicted that swimmers who have stopped training take at least one to two months to develop sufficient stroke mechanics to return norepinephrine and normetanephrine levels to those of controls.

Changes in Catecholamine Excretion through December

Another important finding from this study is that swimmers show a steady, significant decrease in hormone excretion. As was mentioned earlier, one reason for this decrease is an increase in swimming efficiency producing less stress on the swimmers. This mechanism, however, would only explain a return to control values. The continued decrease in hormone levels indicates the occurrence of additional processes.

Two mechanisms could explain the decrease in hormone levels. Either there is a decrease in the production of catecholamines leading to a decrease in excretion of both hormones and metabolites, or there is an increase in the metabolism of the catecholamines leading to a decrease in norepinephrine and epinephrine excretion and an increase in the excretion of their metabolites. As Tables 3, 6, 9, 12, 14, and 16 have shown, both hormones and metabolites decrease suggesting there is a decrease in catecholamine production. The mechanism for this decrease is the following: constant exposure to high circulating hormone levels leads to negative feedback of the amount of catecholamine produced. There is some controversy in the literature, however, regarding the effect decreased catecholamine production has on receptor density and circulating half life of the catecholamines. Some studies have found that there is an increase in receptor density (40, 180, 185), while others have found that there appears to be some increase in the circulating half life of the hormone (79, 262).

One study that found an increase in the number of receptors was Butler et al.. They assayed changes in lymphocyte receptors and concluded that the density of receptors was inversely proportional to the concentration of urinary and plasma norepinephrine (41). In addition, Lehmann found that the amount of ß-adrenergic receptors on polymorphonuclear leukocytes increased with training (180). Lockette found, however, that a-receptors did not change with exercise (185), and no studies have shown changes in cardiac or respiratory receptors. Similarly, while some reports have indicated that catecholamine appearance in the blood may be elevated with exercise, there is very little evidence yet to suggest that this has any physiological significance (46, 64).

In either case, this experiment found that the length of time required for cessation of changes in the excretion of catecholamines is much longer than previously reported (48, 64, 131, 287). Winder found that changes in the excretion of hormones occur within the first three to six weeks (287), a finding that has been supported by other researchers (48, 64, 222). This experiment, however, showed that catecholamine levels decreased for four to five months before returning to control levels. This difference in adaptation time could be related to the intensity and duration of exercise demanded in this experiment, or that this experiment increased the intensity of the training on a daily basis. Previous to this experiment, no study had utilized the intense physical demands required in this experiment (48, 64, 222, 287). Further, no previous study manipulated the intensity of exercise on a daily basis. Consequently, either one or both of these factors could lead to an increase in the time period required for cessation of changes in catecholamine excretion.

Changes in Catecholamine Excretion from January through May

In looking at the differences between each of the months for all four hormones, it can be seen that there is a decrease in hormone excretion until December, at which time there is a reversal, with hormone production peaking in February and returning to control levels in April and May. As was mentioned earlier, the reason for the decrease in hormone levels is probably increased physical fitness and stroke efficiency, with a consequent decrease in hormone production. Hormone excretion, however, starts to rise in December despite a continued increase in the amount of distance trained.

A partial explanation for the observed increase is that there may be a net decrease in the amount of stress on the swimmers. Swimmers are not in school during this period of time and tend to do nothing more than swim, eat, and sleep. Consequently, they are actually better able to rest and recuperate than when attending classes. Further, as the distance trained starts to decrease in January and February, practices become less stressful and hormone levels tend to return to resting values. This does not mean that the swimmers are becoming less fit or are less efficient at swimming, but rather that the body is returning to its equilibrium level. The reason for the overshoot in February and March is because this is the time when swimmers undergo a process known as "tapering". Tapering is the term applied to training which is of high intensity and low distance. Swimmers respond to a taper by increasing net norepinephrine excretion.

Process of Hormone Changes during a Training Season

Summarizing the above discussion, a possible reason for the changes in the amount of hormones excreted during the training season could be as follows. There are three components to swim training: intensity of a workout, the amount of distance swum during that workout, and the physical fitness and ability of the swimmer to complete the workout. During the first half of the season practices are long and demanding and there is a decrease in hormone production as the athlete increases fitness and swimming efficiency. During the second half of the season, however, the distance swum decreases markedly. At the same time, there is an increase in intensity. The overall picture, however, is less stressful than earlier in the year, because the swimmers are fit and swimming efficiently. Thus, hormone levels return to pretraining values. Continued rest leads to hormone levels rising above resting values because there is not a constant elevation of hormones and thus no negative feedback. Hormone levels then return to resting values as the swimmer stops training.

Kjaer et al. offer a mechanism for the elevated hormone response in February and March (160). In their work, Kjaer et. al. found that long-term training lead to an increase in the responsiveness of the adrenal medulla to exercise (160). This increase in sensitivity was gradual in onset, but did not disappear within 24 hours as has been reported for changes in receptor density (40, 41). Further, this change continued weeks after exercise had been halted. Extrapolating these findings to the present experiment, it could be concluded that the swimmers also developed an increase in sensitivity to exercise. The technique of tapering utilizes both the increased sensitivity, and the longevity of changes to produce increased levels of catecholamines despite diminished training levels.

Comparison of Individual Collection Periods

In analyzing each collection period during the work day, similar results are observed (Tables 3-11). The only difference in excretion patterns being the following. For the overnight period, there is a significant increase in hormone excretion during December compared to the 4:00 p.m. to bed sample. Hormone levels are still significantly lower, however, than resting levels. Similarly, the period from the second void until 4:00 p.m., shows a significant increase during November compared to the 4:00 p.m. to bed sample, but is still less than resting levels. In both cases it could be that hormones are not being excreted at the same amount as they are during the first sample period.

Swimmers versus Controls

Comparing swimmers to controls for each of the periods on the work day confirmed that swimmers had a relative decrease in hormone production with training. This is only true, however, if it is recognized that swimmers are actually starting from a higher baseline due to the initial increase in stress observed at the beginning of the season. It can then be seen that swimmers show continual, significant decreases while controls remain unchanged (Table 6, 10, 14). If, however, swimmers and control subjects are considered to be starting from the same base, then it is apparent that swimmers do not show a significant difference in excretion relative to controls until mid-October.

Excretion of Epinephrine during December in Controls

In comparing the monthly values in the control group, there are no significant differences for a particular hormone except epinephrine excretion in December during the 4:00 p.m. to bed sample (Table 3). The significance of this finding lies in the fact that this sample was taken during exam week. Thus, the increase would be expected to relate to an increase in emotional stress. Swimmers, however, do not appear to show this increase. Despite showing a general increase in all hormone excretion patterns in December, there appears to be no difference between December epinephrine values taken during exam week and those taken at other times (Tables 3, 6, 9). Consequently, it might be that this increase does not occur in swimmers and would then lend support to the idea that some physical exercise reduces anxiety (33, 92, 252).

Changes in Norepinephrine During December in Swimmers

Another finding in this study is that norepinephrine samples excreted overnight, and from the second void until 4:00 p.m. on the work day during exam week of the third year are significantly lower than those taken during the two previous years (Tables 7, 10). However, the December data for the previous two years were not collected during exam week. During exam week, the swimmers were not swimming as hard this week relative to the rest of the month. That the levels were decreased and not elevated indicates that more than one week is required for the body to respond to changes in chronic physical stress.

Changes in Hormones during the Rest Days

Another unique aspect of this study is the use of both work and rest days. This allows a comparison between the two time periods in order to look at the direct effects of training on hormone output. In swimmers, for all three rest day samples, there is a significant drop in rest day hormones from September through November. Additionally, unlike the work day values, the September value is similar to the control value. All decreases in hormones in swimmers are significant relative to their initial values and to control samples (Tables 16, 18, 20). Further, the 4:00 p.m. to bed collection period is unique in that as early as December, values return to resting levels while the other two periods do not return to resting levels until January. From January through the end of the year, there is no significant difference between rest day levels and control levels, and none of these samples show the excess hormone excretion observed in February and March during the week day. This indicates that training initially effects hormone excretion during both rest and work days but not to the same extent. The influence exercising during the week has on hormone excretion during the rest day diminishes over three to four months with hormone excretion returning to control values by January.

These findings also support to the theory the large excretion of hormones seen in September, February, and March are directly due to training. Further, they support the proposal that the large increase in hormone excretion during February and March is due to long term physiologic changes which make the trained subject more sensitive to exercise. On the rest days in February and March, swimmers do not show increases in hormone excretion because they are not exercising, and the diminished amount of exercise during the week has no effect on hormone excretion during the rest day.

Swimmers are, however, sensitive to exercise and during the work days this is evident by markedly elevated hormone excretion.

Chapter 5. Summed Time Periods

Results

By combining the results into resting and working days, it becomes easier to look at the effects of swimming and school on the subjects. The daily excretion rates for each day were calculated by summing the total amount of hormone excreted in that day and then dividing by the actual time peiod over which the sample was collected (Figures 5-8). The swimmers results for September and December of 1988 were not included because these values were significantly different from previous years (see previous results section). In looking at the different months within the control group, there are no significant differences ($p > .05$) between any of the months for any hormone category for either resting or working days. The only exception is the epinephrine value for the December working day. This value is significantly greater than any of the other monthly epinephrine value ($p < .05$).

Work vs. Rest Days

In studying the different months within the swimmer group, there are many significant differences between these months for a particular hormone category for both work and rest days. These differences are presented in Tables 18-21. These tables are for each of the hormones and show only relationships between a particular month and the other months that are significantly different ($p < .05$).

Comparing swim and control work days to each other as well as to the rest days gives the following results. For norepinephrine; September: Swim work day values were significantly greater than Swim rest day values ($p < .05$). Swim rest day, Control work day, and Control rest day values were all not significantly different from each other ($p > .05$); October: Swim work days were significantly greater than Swim rest days ($P<0.01$); November: Control work day values were significantly greater than Control rest day values ($p < .05$). Control rest day values were significantly greater

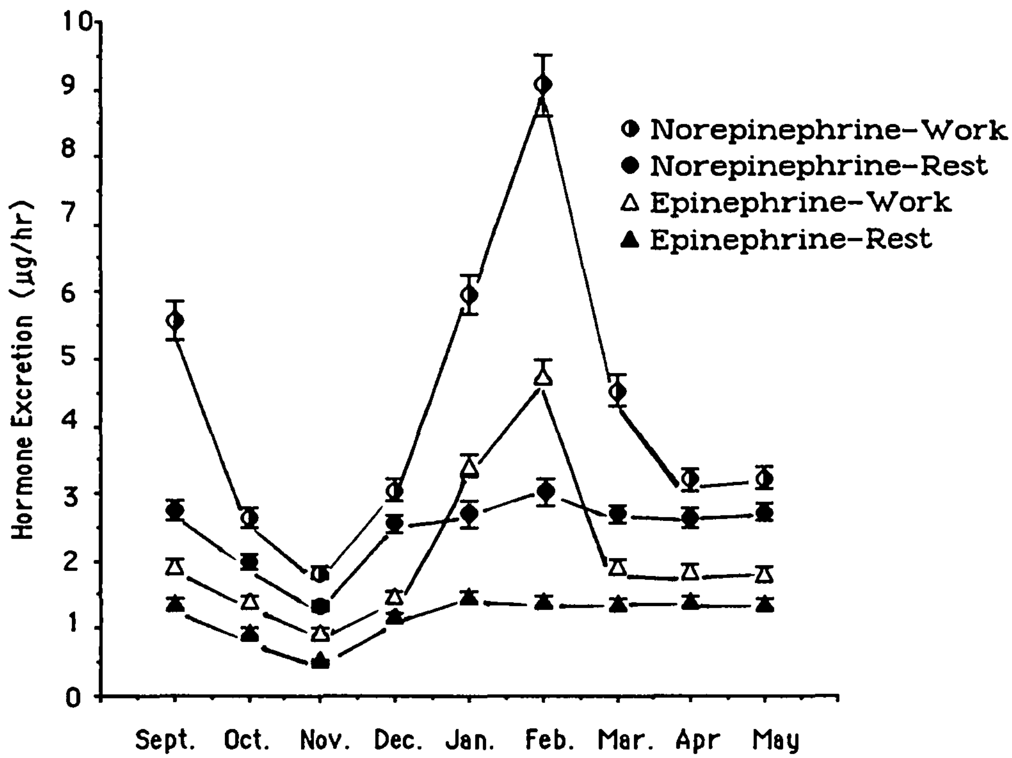

Figure 5. Comparison of Work to Rest Day Excretion of Epinephrine and Norepinephrine by Swimmers

Error Bar Represents Standard Error

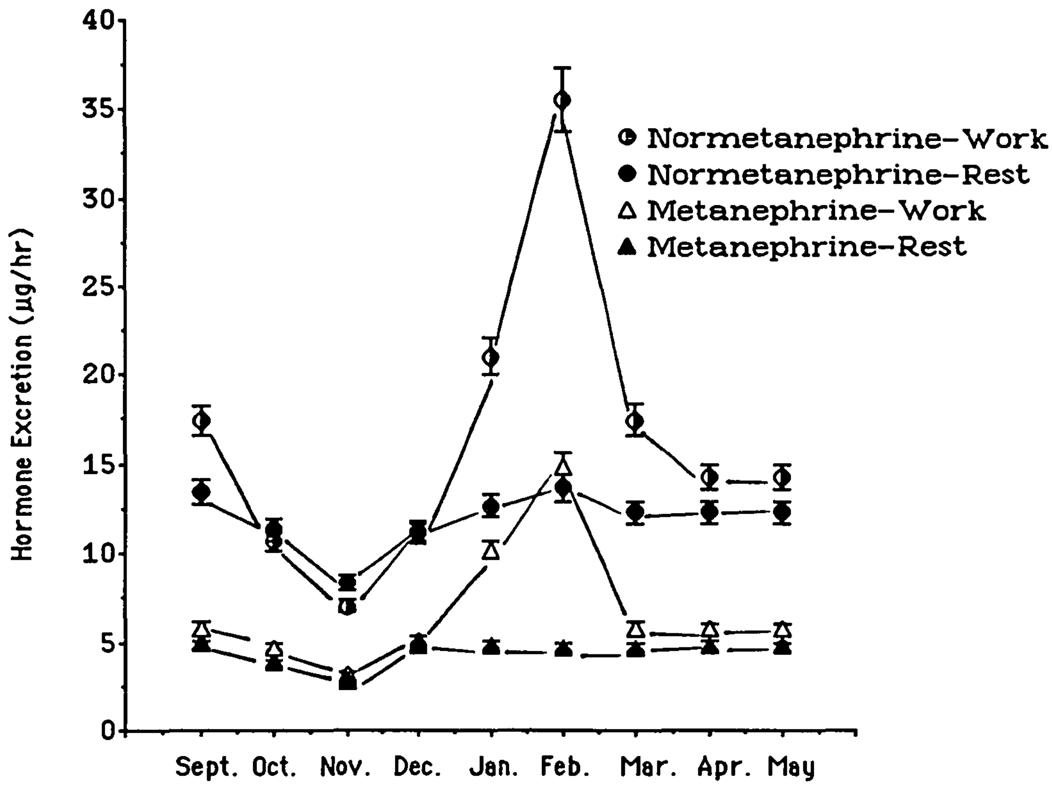

Figure 6. Comparison of Work to Rest Day Excretion of Metanephrine and Normetanephrine by Swimmers

Error Bar Represents Standard Error

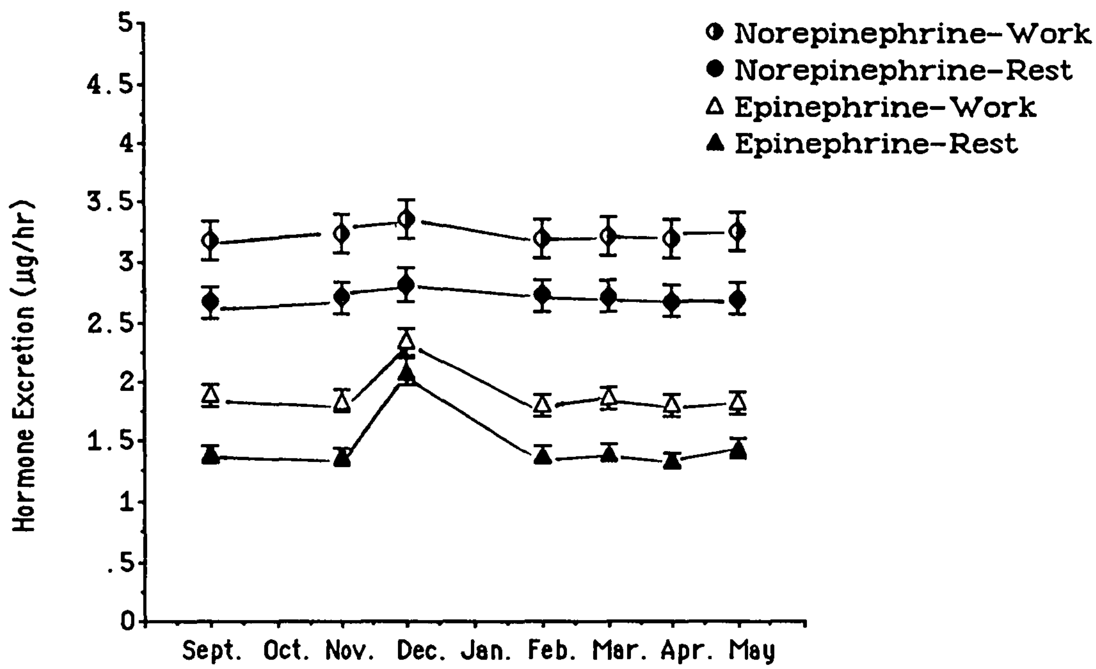

Figure 7. Comparison of Work to Rest Day Excretion of Epinephrine and Norepinephrine by Controls

Error Bar Represents Standard Error

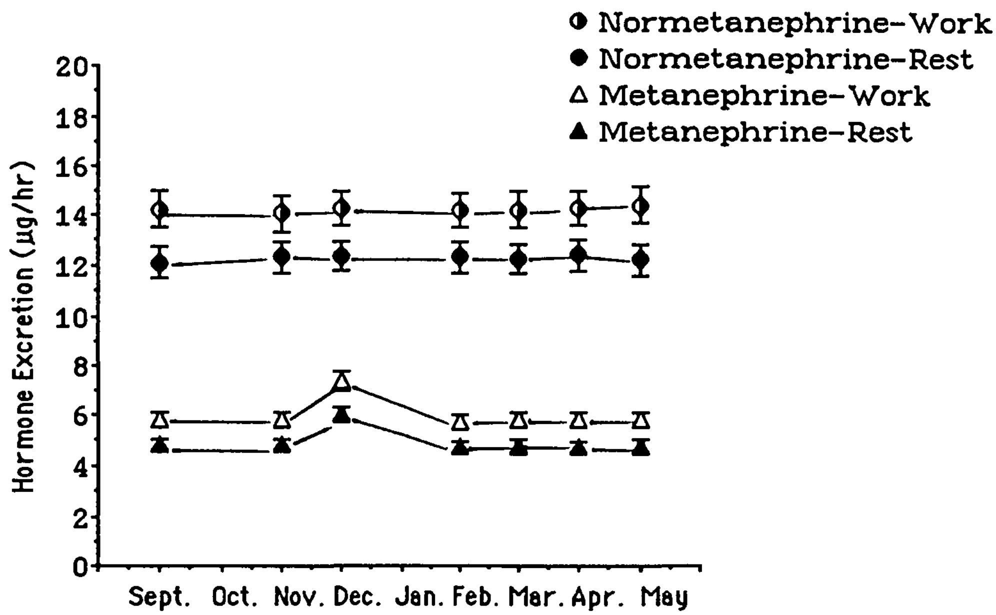

Figure 8. Comparison of Work to Rest Day Excretion of Metanephrine and Normetanephrine by Controls

Error Bar Represents Standard Error

Table 18. Scheffe F-test for Norepinephrine Excretion in Swimmers During Work and Rest Days

Norepinephrine Work Day

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	●	0	●					
January	●	●	●	●				
February	●	●	●	●	●			
March	●	●	●	●	0	●		
April	●	●	●	●	0	●	0	
May	●	●	●	●	0	●	0	0

Norepinephrine Rest Day

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	●	0	●					
January	●	●	●	●				
February	0	●	●	●	0			
March	0	●	●	●	0	0		
April	0	●	●	●	0	0	0	
May	0	●	●	●	0	0	0	0

● P < .05
0 P > .05

Table 19. Scheffe F-test for Eprinephrine Excretion in Swimmers During Work and Rest Days

Epinephrine Work Day

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	0							
November	●	0						
December	0	●	●					
January	●	●	●	●				
February	●	●	0	●	●			
March	0	●	0	●	●	●		
April	0	●	0	●	●	●	0	
May	0	●	0	●	●	●	0	0

Epinephrine Rest Day

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	0							
November	●	●						
December	0	●	●					
January	0	●	●	0				
February	0	●	●	0	0			
March	0	●	●	0	0	0		
April	0	●	●	0	0	0	0	
May	0	●	●	0	0	0	0	0

● $P < .05$
0 $P > .05$

Table 20. Scheffe F-test for Normetanephrine Excretion in Swimmers During Work and Rest Days

Normetanephrine Work Day

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	●	●	●					
January	●	0	●	●				
February	●	●	●	●	●			
March	●	0	●	●	0	●		
April	●	0	●	●	0	●	0	
May	●	0	●	●	0	●	0	0

Normetanephrine Rest Day

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	●	0	●					
January	0	●	●	●				
February	●	●	●	●	0			
March	0	●	●	●	0	0		
April	0	●	●	●	0	0	0	
May	0	●	●	●	0	0	0	0

● $P < .05$
0 $P > .05$

Table 21. Scheffe F-test for Metanephrine Excretion in Swimmers During Work and Rest Days

Metanephrine Work Day

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	●	●	●					
January	0	●	●	●				
February	●	●	●	●	●			
March	0	●	●	●	●	●		
April	0	●	●	●	●	●	0	
May	0	●	●	●	●	●	0	0

Metanephrine Rest Day

	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.
October	●							
November	●	●						
December	●	●	●					
January	●	●	●	●				
February	●	●	●	●	0			
March	0	●	●	0	0	0		
April	0	●	●	0	0	0	0	
May	0	●	●	0	0	0	0	0

● P $<$ .05
0 P $>$ .05

than Swim work days values ($p < .01$), and these were significantly greater than Swim rest day values ($p < .05$); December: Control work and rest day values were not significantly different ($p > .05$), however, Swim work day values were significantly less than Control work day values ($p < .05$), yet not significantly different than Control rest day values ($p > .05$). All three values were significantly greater than Swim rest day values ($p < .01$); January: Swim work day values were significantly greater than Swim rest day values; February: Swim work day values are significantly greater than Control work day values ($p < .01$). Control work day values are not significantly different than Control rest day values ($p > .05$), which are significantly greater than Swim rest day values ($p < .05$); March, April and May: Swim and Control work day values are similar and are significantly different than Swim and Control rest day values ($p < .05$).

Comparing swim and control work days to each other as well as to the rest days gives the following results. For epinephrine; September: Swim work day values were significantly greater than Swim rest day values ($p < .05$). Swim rest day, Control work day, and Control rest day values were all not significantly different from each other ($p > .05$); October: Swim work days were not significantly greater than Swim rest days ($p > .05$); November: Control work day values were not significantly greater than Control rest day values ($p > .05$). Control rest day values are significantly greater than Swim work days values($p < .01$), which were significantly greater than Swim rest days values ($P<0.05$); December: Control work and rest day values were significantly different ($p < .05$), however, Control work day, Swim work day, and Control rest day values were all similar ($p > .05$); January: Swim work day values were significantly greater than Swim rest day values; February: Swim work day values are significantly greater than Swim rest day values ($p < .01$). Swim rest day values are significantly different than Control work and rest day values ($p < .05$), which are not significantly different ($p > .05$); March, April and May: Swim and Control values for both work and rest days are all similar ($p > .05$).

Comparing swim and control work days to each other as well as to the rest days gives the following results. For normetanephrine; September: Swim work day values were significantly greater than Swim rest day values ($p < .05$). Swim rest day, Control work day, and Control rest day values were all not significantly different from each other ($p > .05$); October: Swim work days were significantly greater than Swim rest days ($p < .01$); November: Control work day values were significantly greater than Control rest day values ($p < .05$). Control rest day values were significantly greater than Swim work days values($p < .01$), and these were significantly greater than Swim rest days values ($p < .05$); December: Control work day values were significantly different from Control rest day values ($p < .05$), however, Control rest day values were not significantly different from Swim work day values ($p > .05$). All three values were significantly greater than Swim rest day values ($p < .01$); January: Swim work day values were significantly greater than Swim rest day values; February: Swim work day values are significantly greater than Swim rest day values ($p < .01$). Swim rest day values are not significantly different than Control work day values ($p > .05$), which are significantly greater than Control rest day values($p < .05$); March, April and May: Swim and Control work day values are similar and are significantly different than Swim and Control rest day values ($p < .05$).

Comparing swim and control work days to each other as well as to the rest days gives the following results. For metanephrine; September: Swim work day values were not significantly greater than Control work day values ($p > .05$). Control work day values were significantly greater than Swim rest day values ($p < .05$), which were not significantly different from Control rest day values ($p > .05$); October: Swim work days were not significantly greater than Swim rest days ($p > .05$); November: Control work day values were significantly greater than Control rest day values ($p < .05$). Control rest day values are significantly greater than Swim work days values($p < .01$), which were significantly greater than Swim rest days values ($p < .05$); December: Control work and rest day values were significantly different ($p < .05$), however, Control work day, Swim work day, and Control rest day values were all similar($p > .05$); January: Swim work day values were significantly greater than Swim rest day values; February: Swim work day values are significantly greater than Swim rest day values ($p < .01$). Swim rest day values are significantly greater than Control work values ($p < .05$), and Control work day values are greater than Control rest day values ($p < .05$); March, April and May: Swim and Control values for both work and rest days are all similar ($p > .05$).

Interrelationship of Hormones

In order to see if there is any relationship between each of the hormones, a correlation analysis was performed. Results are shown in Tables 22 and 23. For swimmers, norepinephrine values show a strong correlation with each of the other hormones except epinephrine. In fact, there is only a slight correlation between epinephrine excretion during work days and norepinephrine excretion. For swimmers epinephrine values, there is a strong relationship between epinephrine and metanephrine, with weaker relationships to the other hormones. For normetanephrine and metanephrine in swimmers, there are strong correlations to norepinephrine and epinephrine, respectively.

For control subjects, norepinephrine is strongly correlated to normetanephrine, but weakly negatively correlated to epinephrine values. For epinephrine, there is a strong correlation to metanephrine, with weaker or negative correlations to other hormones. Normetanephrine and metanephrine are strongly correlated to norepinephrine and epinephrine, respectively.

Table 22. Correlation of Work Days to Rest Days for All Collected Hormones in Swimmers

		Norepinephrine Work Day	Norepinephrine Rest Day	Epinephrine Work Day	Epinephrine Rest Day	Normetanephrine Work Day	Normetanephrine Rest Day	Metanephrine Work Day	Metanephrine Rest Day
Norepinephrine	Work Day	1.0 +							
	Rest Day	.82 +	1.0 +						
Epinephrine	Work Day	.30	.48	1.0 +					
	Rest Day	.70 *	.87 +	.40	1.0 +				
Normetaneph.	Work Day	.91 +	.58	.83 +	.47	1.0 +			
	Rest Day	.92 +	.89 +	.73 *	.81 +	.81 *	1.0+		
Metanephrine	Work Day	.90 +	.87 *	.82 +	.86 +	.82 +	.95 +	1.0 +	
	Rest Day	.77 *	.75 *	.74 *	.91 +	.68 *	.86 +	.91 +	1.0 +

* $p < .05$

+ $p < .01$

Table 23. Correlation of Work Days to Rest Days for All Collected Hormones in Controls

		Norepinephrine		Epinephrine		Normetanephrine		Metanephrine	
		Work Day	Rest Day	Work Day	Rest Day	Work Day	Rest Day	Work Day	Rest Day
Norepinephrine	Work Day	1.0 +							
	Rest Day	.95 +	1.0 +						
Epinephrine	Work Day	.47	.33	1.0 +					
	Rest Day	.81 *	.52	.37	1.0 +				
Normetaneph.	Work Day	.82 +	.28	.32	.18	1.0 +			
	Rest Day	.62	.92 +	.57	.39	.05	1.0 +		
Metanephrine	Work Day	.07	.24	.96 *	.47	.32	.06	1.0 +	
	Rest Day	.41	.24	.76	.89 +	.65	.64	.18	1.0 +

+ $p < .01$

* $p < .05$

Training and Diurnal Excretion Patterns

The effects of training on the diurnal secretion patterns for norepinephrine and epinephrine for both the work and rest day can be seen in Figures 9-12. For norepinephrine there is definitely a change in diurnal secretion for the work day. In September the peak excretion shifts from the second void until 4:00 p.m. sample to the 4:00 p.m. to bed sample. In November there is no significant difference between either the 4:00 p.m. to bed sample or the overnight sample ($p > .05$), and these are only slightly less than the second void until 4:00 p.m. sample. Only in April does the swimmer peak mimic the control peak. The diurnal secretion of norepinephrine during the rest day is not different from the control pattern, except the second void until 4:00 p.m. sample is not significantly different 4:00 p.m. to bed sample in November ($p > .05$) like the control profile.

For epinephrine, the work day samples are very similar to the diurnal pattern of secretion shown for the control samples, except in September where the 4:00 p.m. to bed sample shows no difference from the overnight sample ($p > .05$). The diurnal secretion of epinephrine during the rest day is not different from the control pattern except the second void until 4:00 p.m. sample is not significantly different 4:00 p.m. to bed sample during November ($p > .05$) like the control profile.

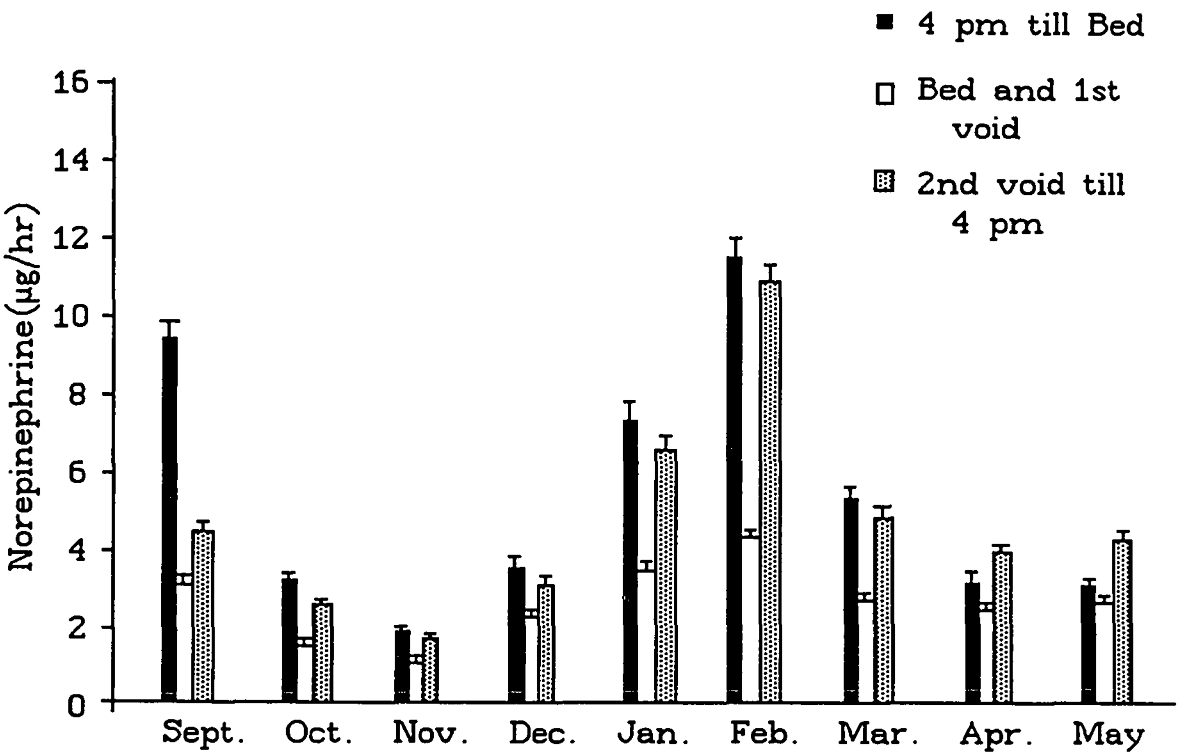

Figure 9. Shift in Peak Excretion for Norepinephrine in Swimmers and Controls for a Workday

Error Bars Represent Standard Error

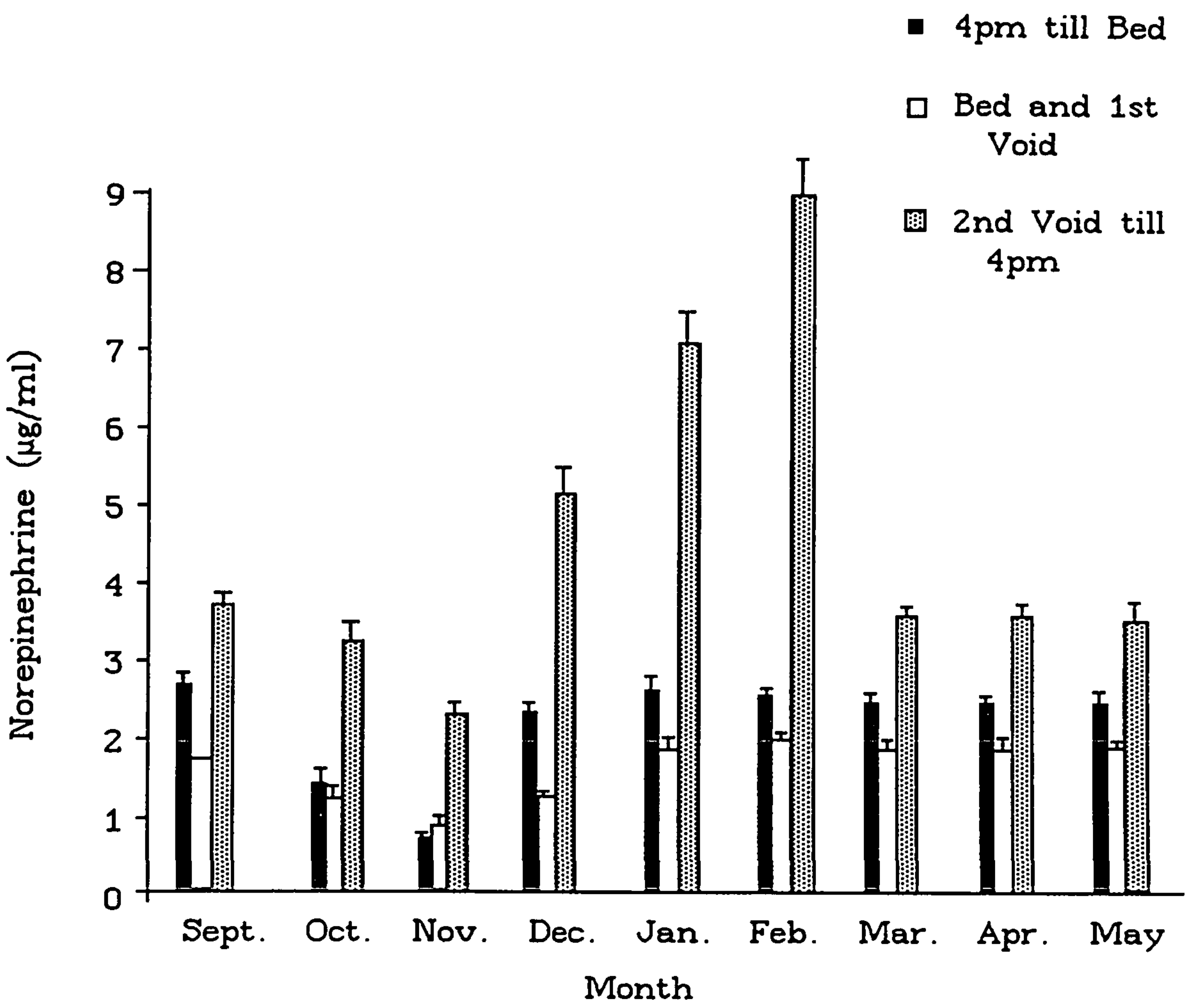

Figure 10. Shift in Peak Excretion for Norepinephrine in Swimmers and Controls During a Restday

Error Bars Represent Standard Error

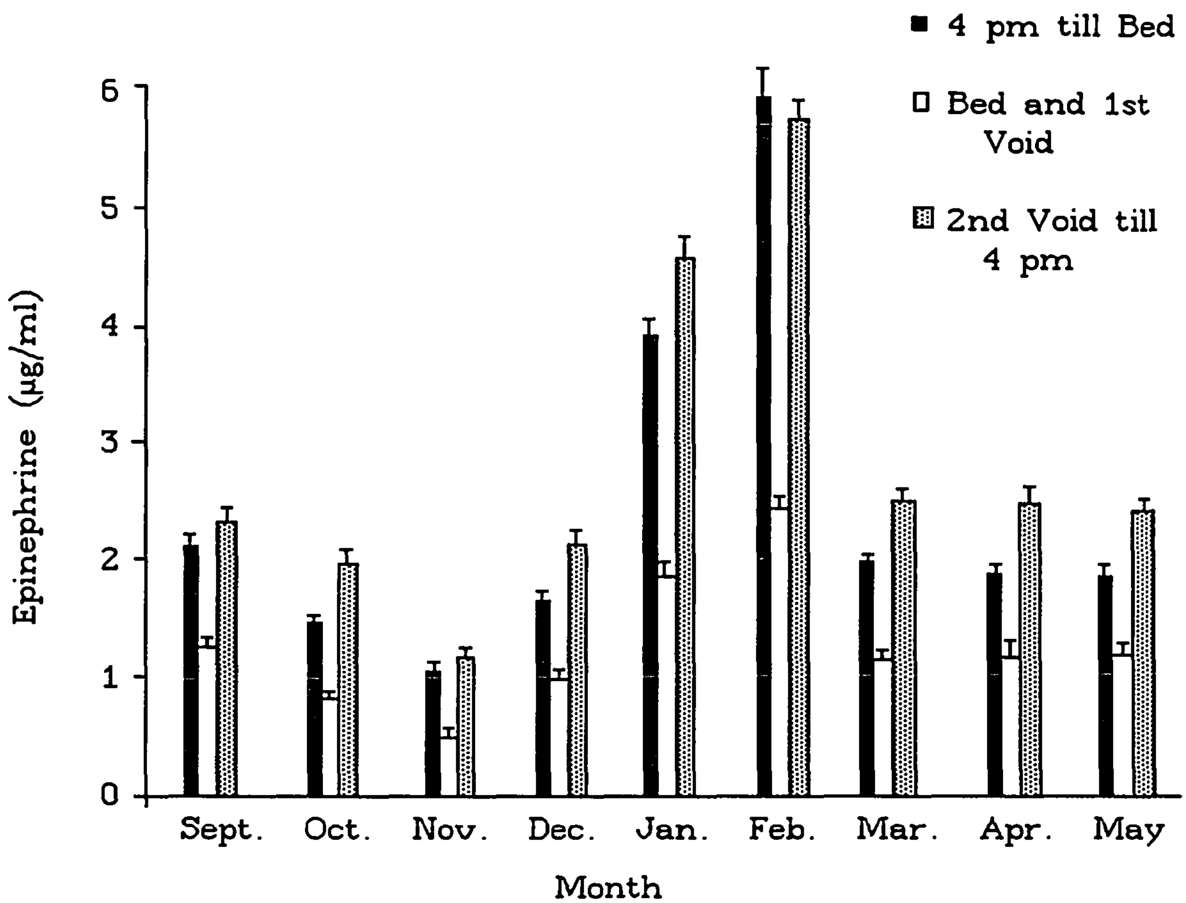

Figure 11. Shift in Peak Excretion for Epinephrine in Swimmers and Controls for a Workday

Error Bars Represent Standard Error

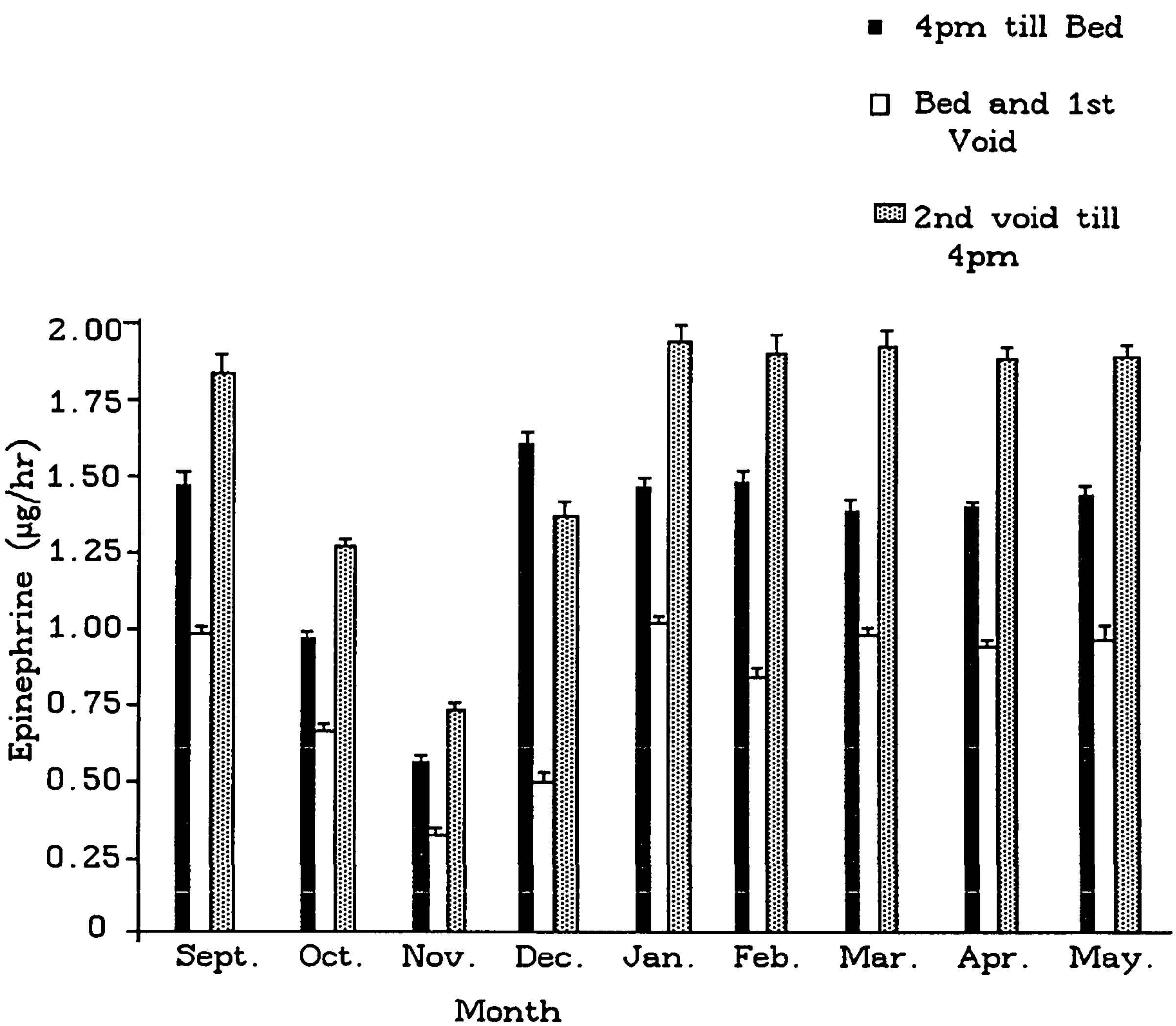

Figure 12. Shift in Peak Excretion for Epinephrine in Swimmers and Controls for a Restday

Error Bars Represent Standard Error

Discussion

Combining the results into working and resting days allows an accurate understanding of the influences of school and swimming on the subject. As would be expected, hormone levels for the entire day reflect the individual time periods in that day. Thus in the work days, there is an elevated level of hormone excretion during September which then decreases through November, before reversing and peaking in February and then returning to base levels by April and May. For the rest days, there is a decrease from a baseline level in September to a low in November, and then a return to pretraining levels by December. Some of the subtle changes seen by looking at the individual bottles are no longer apparent. Combining the results into work and rest days does give a better overall summary of changes that are taking place on a monthly basis.

Work versus Rest Day

Two facts become readily apparent by summarizing data. First, swimmers show the same pattern of change that is found by looking at individual time periods for both resting and work days. Second, there is a difference between swimmers and controls for both resting and working days, similar to that found by comparing individual time periods within each of the days. One additional finding, however, is that it is easier to compare the influence of school and swimming on swimmers.

Results obtained during September, before swimming started, should show differences that are primarily related to school days versus non-school days. For norepinephrine and epinephrine excretion, there is no significant difference between school days and non-school days ($p > .05$). Further, there is no significant difference between school day and non-school day excretion of either hormone metabolite ($p > .05$). In addition, controls showed similar results. These results indicate there is no difference between school day and non-school day catecholamine excretion levels for students as a group. Consequently, it can be concluded that school either has little effect on catecholamine excretion or that school, or some other stress event, has the same effect on students for both work and rest days.

The most likely explanation for the lack of difference between days is that school has a similar effect on students during both school days and non-school days. There are several facts which support this hypothesis. First, there were no stress events, like exams or swim meets, occurring during the collection periods. This was done intentionally in order to minimize the variability that would have been introduced by having subjects undergo stress events of varying degrees of intensity and importance. The exceptions to this have already been noted, and it is very apparent that testing is a mental stress that does effect epinephrine levels (Figure 5,7). Second, school had been in session for almost a month when the first samples where collected. Again, this was done to minimize the possible variation that could arise from different subjects responding differently to new school classes. Third, all but four of the subjects were sophomores or older. This was done to try and minimize the tremendous stress involved in starting college and the additional stress associated with starting school in a different state. Fourth, there were no differences in activity between school days and non-school days. Only two subjects went to the beach during the testing period, and both did so everyday so that neither showed a difference between working and resting days. Further, no control subject participated in any extracurricular activity during any testing period. Finally, all but four subjects lived on campus, so that to some extent the influences of school were always present. Thus, it is probable that school has some influence on catecholamine excretion. However, the actual influence school exerts appears to be diffuse and affects students equally during both school and non-school days. This finding has important implications for swimmers. Specifically, any differences between work and rest days must be directly related to the impact of swimming on hormone excretion.

Changes in Catecholamine Excretion during the Training Season

For norepinephrine, there is a significant difference in hormone excretion between rest and work days from September (once swimming started) through February ($p < .01$) (Figure 5-8). This result is also seen for normetanephrine and indicates that swimming has a similar effect on both hormone and metabolite excretion. In comparison, control results show no significant differences between work and rest days ($p > .05$). These results indicate that swimming is the cause of the change in norepinephrine and normetanephrine excretion, because this is the only stress event that was notably different between swimmers and controls.

Another finding is that norepinephrine and normetanephrine excretion levels show a significant drop through November ($p < .05$), start rising in December, show a significant increase and peak in February ($p < .05$), and then return to non-swimming levels in March for the work day. This is in contrast to the rest day, which shows a significant drop through November ($p < .05$), starts rising in December, but then remains at September (1988) levels for January through May.

For epinephrine, there is no significant decrease in excretion values between months until November (Figure 5). This result is also seen for metanephrine excretion and indicates that hormone and metabolite are being similarly influenced by swimming. In contrast, control groups show no differences between work days and rest days ($p > .05$). A couple of conclusions can be made based on these results.

First, swimming does not have an effect on epinephrine or metanephrine excretion until November. This is shown in Figures 6 and 8 and supports the hypothesis that the stress of school is an overriding influence on epinephrine excretion, counteracting any action swimming might have on hormone excretion. Despite the fact that swimming training levels and intensity increased from September through October, epinephrine and metanephrine excretion did not change significantly until November.

This indicates that there is some other stress event that is having a larger affect on swimmers than swimming. As school is the largest stress event influencing swimmers, other than swimming, it can be concluded that school has a larger influence on epinephrine and metanephrine excretion than swimming for the months of September and October.

Second, swimming does decreases the stress of school on swimmers significantly in November. This is also seen in Figures 5 and 6 and indicates that during the month of November, the influence swimming has on epinephrine and metanephrine excretion overcomes that due to school. This conclusion is supported by a couple of findings. Swim training and intensity continue to increase through November (Figure 3). In addition, there is no change in the stress school exerts on the swimmers as evidenced by the fact that controls show no changes in hormone secretion in November (Figures 7,8). Thus, swimming does exert an effect on epinephrine and metanephrine excretion in swimmers.

Finally, epinephrine and metanephrine excretion levels show a significant drop in November ($p < .05$), start rising in December, show a significant increase and peak in February ($p < .05$), and then return to non-swimming levels in March for the work day. This is in contrast to the rest day, which shows a significant drop in in November ($p < .05$), with a return to resting values in December which is sustained through May.

From these findings a few conclusion can be reached. First, it is readily apparent that epinephrine and norepinephrine continued to change well after 6 to 7 weeks of training. This is in conflict with most studies, which show most changes being complete by 7 weeks (28, 32, 37, 48, 64, 178, 222, 226, 286). This difference in results, however, can be explained by looking at the materials and methods of each of the papers. One difference between studies is the degree of intensity at which the subjects were trained. Either there was no adjustment for increased fitness (32), there was some adjustment but not on a daily basis like this study (37, 48, 64, 131, 286), or the protocol was not intense enough to elicit a response (222). For example, Winder et al. found that changes in hormone excretion took about 6 weeks (287). In the discussion, however, they conclude that if a training protocol based on constant evaluation of the fitness of the subject were used, their results would be different. Consequently, the swimmers in this study are not undergoing the same training protocols as in the other studies and would be expected to show different results.

There is an additional series of studies which suggest there may be no difference in hormone excretion patterns between trained and untrained subjects (28, 178, 226). As can be seen in Figures 5 through 8, this study does not support those findings. An explanation for the difference between reports is apparent, however, if the subjects used in each study are examined. This study showed a significant decrease in heart rate in swimmers from September to December. It also showed a significant difference in resting heart rate between swimmers and controls after training (Table 2). These results would be expected and represent an increase in cardiovascular fitness of the swimmers. In comparison, those reports which showed no difference in hormone excretion between swimmers and controls showed no differences in resting heart rate between groups after training. In two studies controls actually had lower resting heart rates when they were compared to the athletes (28,178). Thus, it is not surprising that no differences in hormone excretion were found between the groups.

Finally, swimmers and control subjects do respond differently to acute stress events. Table 24 compares epinephrine excretion levels for swimmers and controls during November and final exam week in December of 1988. As can be seen, swimmers show no significant differences in hormone excretion between November and December for either hormone. Controls, however, show an increase in epinephrine excretion that is significantly different when compared to November values.

Table 24. Comparison of Epinephrine values from November and Exam Week in Swimmers and Controls

Epinephrine

	November 1988 (μg/day)	Final Exams 1988 (December) (μg/day)
Swimmers	33.60 ± 2.32* N=12	32.60 ± 2.09* N=12
Controls	43.12 ± 3.07 N=12	55.20 ± 3.60# N=12

*: P < .01: Swimmers vs. Controls within the month
#: P < .05: Controls vs. Controls

Catecholamine Response to Stress

Another conclusion that can be made by comparing work to rest days is that there is a definite difference between how norepinephrine and epinephrine are initially produced in response to the stresses of school and swimming. Norepinephrine is primarily related to physical stress and epinephrine is related primarily to emotional stress. Consequently, the norepinephrine levels produced by the swimmers should be an indication of the physical stress they are undergoing. Similarly, epinephrine levels will indicate the mental and emotional stress the swimmer undergoes due to swimming and school. Thus, at the beginning of the season swimmers find training physically demanding and respond by increasing norepinephrine and normetanephrine excretion. While it is probable that they also find training emotionally and mentally stressful, there is no initial change in epinephrine or metanephrine excretion. This is most likely a result of the larger influence that school has on epinephrine and metanephrine excretion when compared to swim training.

As the season progresses, swimmers find practices less stressful physically, despite increased intensity and distance trained. In addition, swimmers show a decrease in epinephrine and metanephrine output, indicating a decreased stress due to training and school. Epinephrine values are also lower in swimmers compared to controls during finals week, indicating exams may be less emotionally stressful to the swimmers.

By December, however, swimming once again starts to become both physically and emotionally stressful and epinephrine and norepinephrine show similar responses. This is evidenced by the fact that despite being out of school in December and January, both epinephrine and norepinephrine show increases in excretion. Further, this increase in hormone excretion was associated with a change in the type of training, switching from a quantity-orientated workout to a quality-orientated workout. The change in hormone excretion was probably not related to an increase in extracurricular activity, because this remained constant not only during December and January but throughout the training season.

This increase in hormone excretion continues to a peak in hormone output in February. Again, this increase in hormone excretion occurs despite a decrease in the distance trained. With the end of the swimming season, swimming no longer has an effect on the swimmers, and hormone levels reflect those of sedentary subjects by April.

Correlation of Catecholamines to Each Other in Swimmer Samples

Another comparison that can be made is to look at the correlation of each of the hormones to each other for both working and resting days. For swimmers, norepinephrine is strongly correlated to normetanephrine, while epinephrine is strongly correlated to metanephrine for both working and resting days (Table 22). This is expected and matches results of Linnolia, who found that changes in norepinephrine had a correlation value r of 0.92 when compared to changes in exercise(184).

It is interesting to note some of the other correlations. In particular, the work and rest values of norepinephrine are strongly correlated to each other. This could be explained if norepinephrine is being influenced by a single factor that effects hormone excretion both during work and rest days. By considering the results previously discussed, it is possible that swimming is influencing norepinephrine. In comparison, working levels of epinephrine do not show strong correlations to resting values. This suggests that this hormone may not be as tightly controlled by one external force. It is apparent that swimming tends to decrease epinephrine excretion, evidenced by the eventual decrease in epinephrine in November. In contrast, school tends to keep epinephrine levels elevated. Thus, although school does have an effect on epinephrine values, there is also an opposing effect due to swimming so that the correlation between work and rest days is not as strong.

Correlation of Catecholamines to Each Other in Control Samples

Control subjects show slightly different results. Norepinephrine and normetanephrine are still strongly correlated to each other, as are epinephrine and metanephrine. However, some of the other correlations are different from swimmers. For example, norepinephrine now has an inverse correlation to epinephrine excretion. This would indicate that subjects are not undergoing physical and emotional stress at the same time. Thus, if the subjects are exercising more, as seen by a relative increase in norepinephrine, they are less stressed by studying, evidenced by a relative decrease in epinephrine, and vice versa. Also, epinephrine excretion during the work day is inversely correlated to epinephrine excretion during the rest day. This result indicates that epinephrine excretion was not constant through both the week and the weekend. The reason for this is unclear and additional data not collected during this study would be needed to clarify it.

Training versus Diurnal Excretion of Catecholamines

The last part of this section looks at the effects of training on the diurnal excretion of norepinephrine and epinephrine. As is seen in Figure 9, swimming leads to increased norepinephrine excretion during the end of the day. This is in direct contrast to norepinephrine excretion on the rest day and to norepinephrine excretion by control subjects (Tables 12, 14, 16). In both of these latter instances, the peak in norepinephrine excretion is during the middle of the day which confirms most studies that also indicate that peak norepinephrine occurs during the middle of the day (86, 104, 183, 259). The reason for this shift in the peak of norepinephrine excretion, however, is due to the simple fact that the four p.m. to bed bottle is the one that is used during and after swimming practice. Further, when the swimmers stop training in April, the large amounts of norepinephrine excreted in the four p.m. to bed bottle also stop, and the largest amount of norepinephrine is that excreted during the middle of the day. Excretion of norepinephrine during the rest day showed peaks during the middle of the day for every month except November. During November, the second largest amount of norepinephrine excretion occurred during the overnight sample. There are at least two possible reasons for this relative increase in the amount of excretion during the overnight period.

The first possibility for the change in the excretion pattern could be due to an increase in stress during this time period. Although an increase in physical stress is unlikely, it is possible that there was such a high level of emotional stress that both norepinephrine and epinephrine would be increased above regular levels. This is not the case, however, as epinephrine excretion during this time period does not show the same pattern as norepinephrine excretion. Another possible explanation for the change in the excretion pattern of norepinephrine would be a marked decrease in physical activity during the end of the day. Unfortunately, none of the swimmers reported making a conscious effort to decrease their normal physical activity. Thus, it is unclear as to why there was a change in the pattern of norepinephrine excretion during November.

Peak levels of epinephrine excretion were also influenced by swimming. During the work day, the peak in epinephrine excretion was during the midday bottle for every month but February (Figure 11). The simplest explanation for this is that there was a dramatic increase in the amount of stress the swimmers were experiencing during the end of the day. This explanation gains support from the fact that this is the time of the year when the swimmers "taper". As noted, tapering is extremely emotionally stressful. Thus, it is not surprising that there is a large increase in epinephrine excretion. Further, the finding that this change in the excretion of epinephrine did not occur during the rest day also supports the theory that the taper leads to a markedly increased amount of epinephrine excretion.

Finally, epinephrine excretion during the rest day was highest during the middle of the month for every month except December. It is important to remember that the December results were collected during studying for finals. Thus, it is possible that there was a large increase in epinephrine excretion secondary to studying for exams. Further, this idea is supported by the fact that several studies have shown that studying will increase epinephrine excretion (104, 183, 259). Consequently, it is likely that an increase in studying was the cause for the change in epinephrine excretion during December.

Chapter 6. **Factors Influencing Hormone Excretion**

Results

Distance Trained vs. Hormone Excretion

In order to try and develop an understanding of the factors that influence swimming performance, various variables were looked at and compared to the excretion of epinephrine and norepinephrine and their metabolites. Figures 13 through 16 represent the regression analysis of the distance trained versus the hormone and day collected. As can be seen, only epinephrine and metanephrine values collected during the rest days have even a slight relationship to the distance trained. When the samples are broken into individual bottles, however, there are stronger correlations to distance trained. Tables 25 and 26 show the correlations between catecholamines and the mileage trained for each month.

Hassles Test vs. Hormone Excretion

Another means of determining some of the variables that influence swimmers is to look at the effects of psychological stress on swimmers. Figures 17 and 18 show the correlations between the intensity of hassles and frequency of hassles and the training month using a Hassles scale. As can be seen, the frequency of hassles is slightly correlated to the month in swimmers, while the intensity of hassles is slightly correlated to the month for control subjects. Comparing control hassles frequency scores to swimmer frequency scores, it was found that there was no significant difference ($p > .05$). Comparing control hassles intensity scores to swimmer hassles intensity scores, however, showed that controls have significantly higher scores ($p < .01$).

The correlation of frequency and intensity of hassle to each of the hormones for both working and resting days was also calculated. Tables 27 and 28 show the various correlations for each of the hormones compared to the frequency and intensity of hassles.

Table 25. Correlation of Norepinephrine Excretion and Distance Trained, Month by Month

	Work Day			Rest Day		
	4pm-Bed	Bed-1st Void	2nd Void till 4pm	2nd Void till 4pm	4pm-Bed	Bed-1st Void
Sept.	.49 * 20	.45 * 38	.17 38	.14 38	.37 38	.48 * 38
Oct.	.07 36	.19 38	.09 38	.28 38	.24 38	.36 37
Nov.	.42 * 38	.17 37	.43 * 38	.42 * 37	.29 38	.14 37
Dec.	.63 * 37	.57* 20	.73 * 20	.40 * 38	.30 38	.05 38
Jan.	.05 38	.22 38	.03 38	.20 37	.36 38	.21 38
Feb.	.31 38	.05 38	.73 * 37	.37 38	.36 38	.31 38
Mar.	.01 37	.06 38	.57 * 38	.02 38	.18 38	.22 38
Apr.	.07 38	.34 37	.14 38	.24 38	.24 38	.24 38
May	.30 38	.17 38	.11 37	.27 38	.34 38	.21 37

*: $P < .05$

The first number in each cell is the correlation value, the second is the N.

Table 26. Correlation of Epinephrine Excretion and Distance Trained, Month by Month

	Work Day			Rest Day		
	4pm-Bed	Bed-1st Void	2nd Void till 4pm	2nd Void till 4pm	4pm-Bed	Bed-1st Void
Sept.	.61* 20	.24 38	.01 38	.34 38	.01 38	.24 38
Oct.	.51* 36	.26 38	.13 38	.03 38	.06 38	.38 37
Nov.	.16 38	.23 37	.47* 38	.63* 37	.27 38	.26 37
Dec.	.41* 37	.31 20	.41* 20	.03 38	.29 38	.67* 38
Jan.	.36 38	.33 38	.67* 38	.22 37	.30 38	.07 38
Feb.	.11 38	.13 38	.14 37	.07 38	.34 38	.20 38
Mar.	.01 37	.15 38	.11 38	.18 38	.32 38	.15 38
Apr.	.17 38	.17 37	.19 38	.22 38	.20 38	.05 38
May	.06 38	.08 38	.13 37	.31 38	.01 38	.19 37

*: $P < .05$

The first number in each cell is the correlation value, the second is the N.

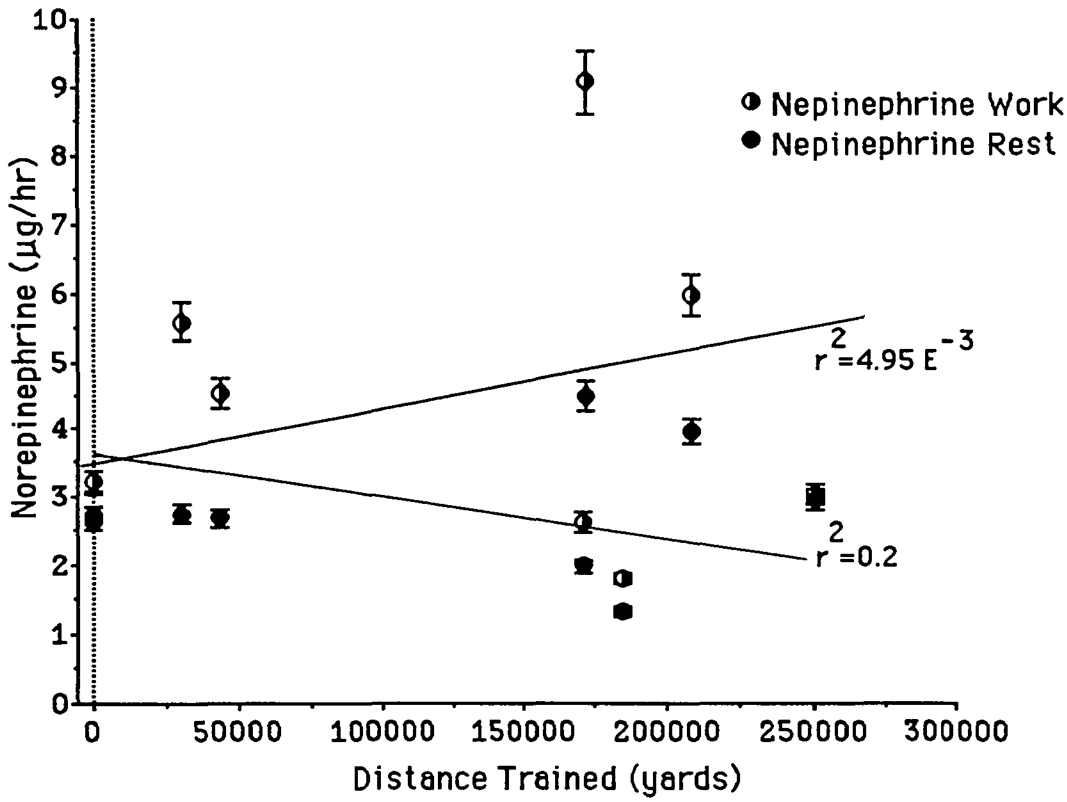

Figure 13. Correlation of Mileage to Norepinephrine for Work and Rest Days

Error Bar Represents Standard Error

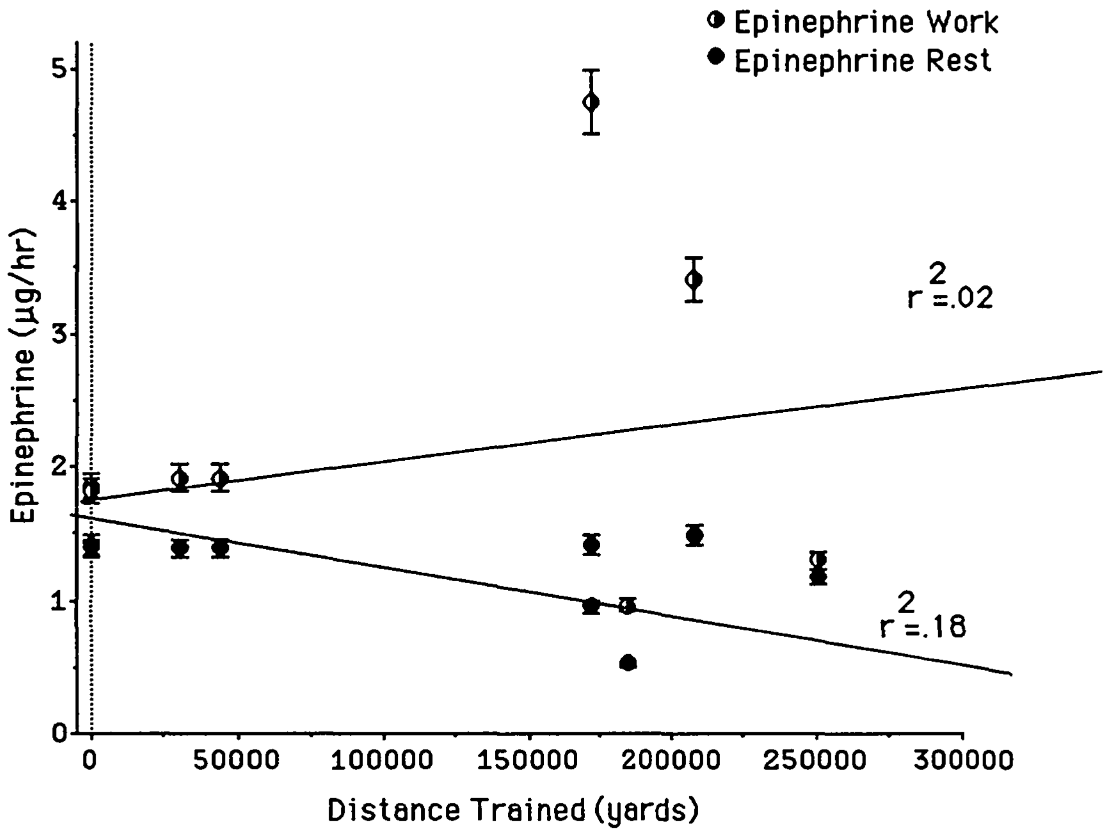

Figure 14. Correlation of Mileage to Epinephrine for Work and Rest Days

Error Bar Represents Standard Error

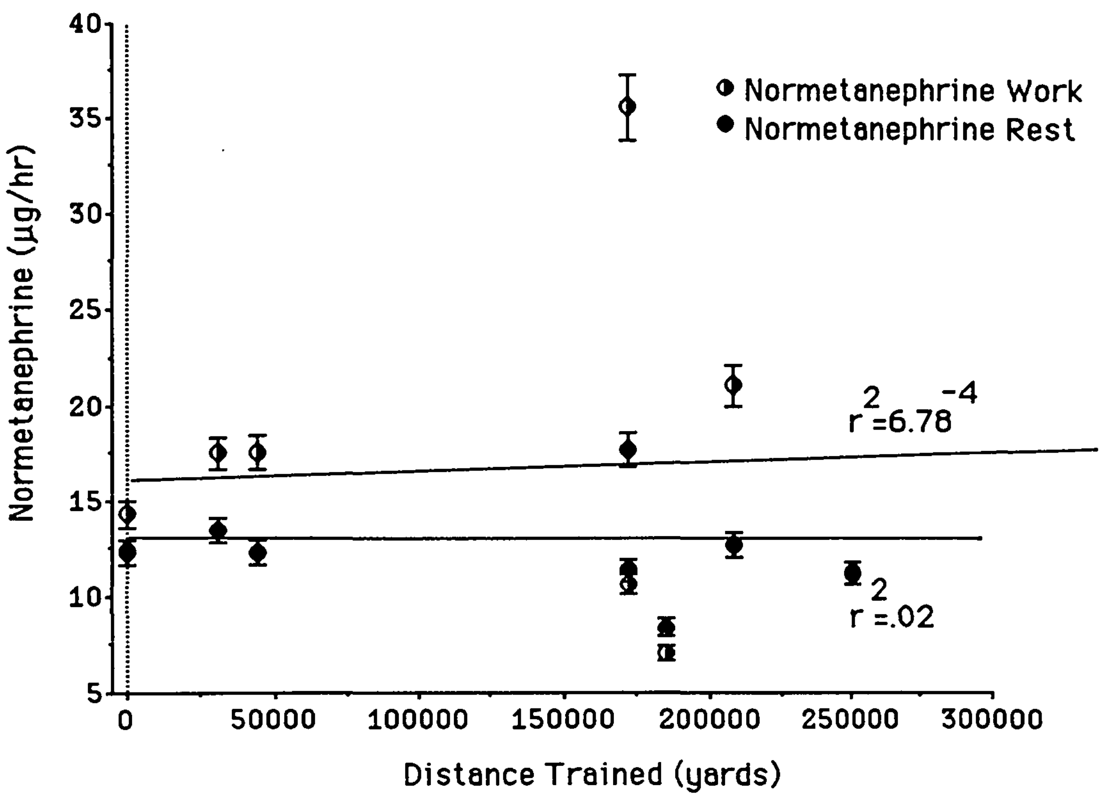

Figure 15. Correlation of Mileage to Normetanephrine for Work and Rest Days

Error Bar Represents Standard Error

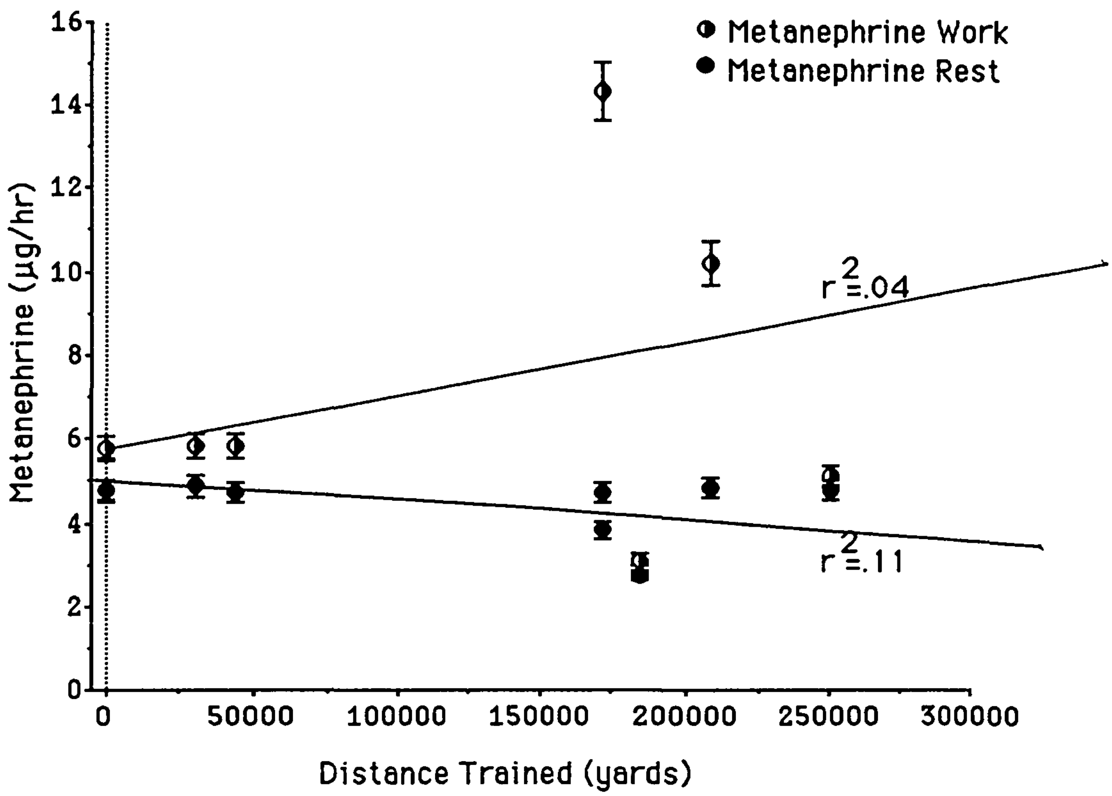

Figure 16. Correlation of Mileage to Metanephrine for Work and Rest Days

Error Bar Represents Standard Error

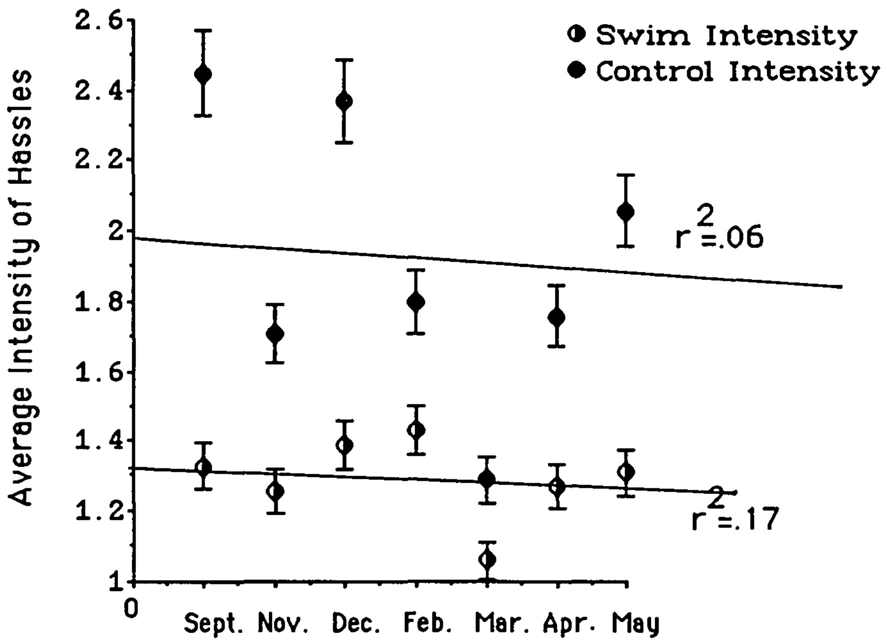

Figure 17. Hassles Intensity versus Month for Swimmers and Controls

N equals 24 for both Control and Swimmer Samples
Error Bar Represents Standard Error

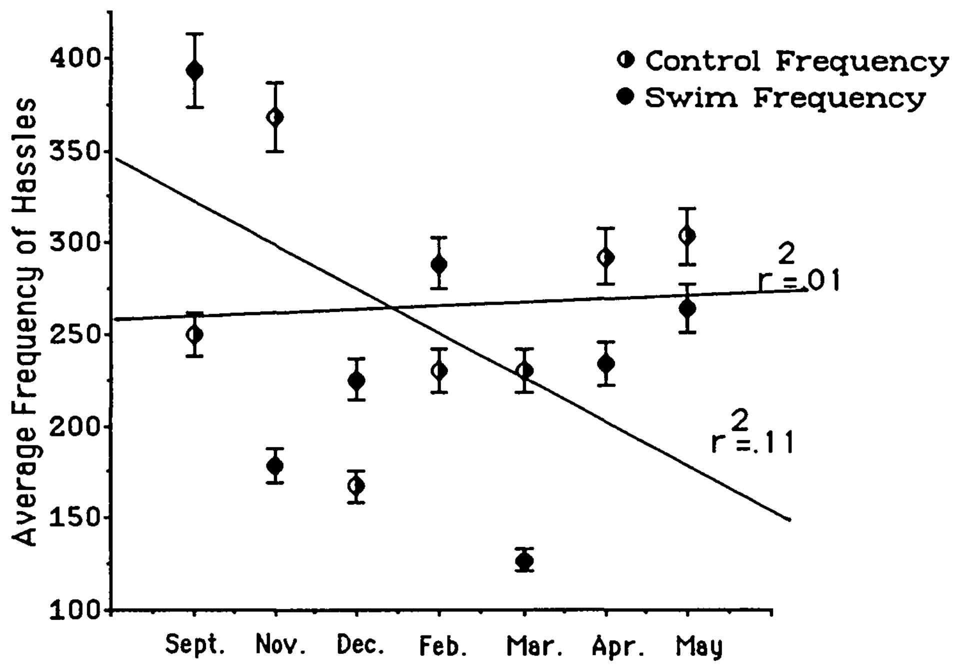

Figure 18. Hassles Frequency versus Month for Swimmers and Controls

N equals 24 for both Control and Swimmers Samples
Error Bar Represents Standard Error

Table 27. Correlation between Hormone Excretion and Hassles Score in Swimmers

	Norepinephrine		Epinephrine		Normetanephrine		Metanephrine	
	Work	Rest	Work	Rest	Work	Rest	Work	Rest
Frequency of Hassles	.61 *	.36 +	.33 +	.33 +	.54 *	.32 +	.43 +	.32 +
Intensity of Hassles	.22	.01	.60 *	.16	.29	.01	.51 *	.26

*:P < .01
+:P < .05

Table 28. Correlation between Hormone Secretion and Hassles Score in Controls

	Norepinephrine		Epinephrine		Normetanephrine		Metanephrine	
	Work	Rest	Work	Rest	Work	Rest	Work	Rest
Frequency of Hassle	.11	.25	.60 *	.04	.22	.15	.57 *	.06
Intensity of Hassle	.44 +	.23	.50 *	.17	.40 +	.27	.49 +	.21

*: $P < .01$
+: $P < .05$

For norepinephrine excretion in swimmers, there is a strong correlation of the frequency of hassles reported to norepinephrine excretion during the work day, and a moderate one during the rest day. Epinephrine excretion in swimmers is also moderately correlated to the frequency of hassle during the work day and rest day, and it is also strongly correlated to the intensity of hassles during the work day. For normetanephrine, the frequency of reported hassles is correlated to the excretion of the hormone on both working and resting days. Finally, metanephrine is related to both the frequency and intensity of reported hassles for the work day and the intensity of reported hassles on the rest days.

For control subjects, the results are somewhat different. Norepinephrine excretion values are correlated to the intensity of hassle reported during the rest days. Epinephrine excretion values are strongly correlated to the frequency and intensity of hassles during the work day, but show little correlation to either variable during the rest day. Normetanephrine excretion is strongly correlated to the intensity of hassles during the work day. Finally, metanephrine excretion is strongly correlated to the frequency and intensity of hassles during the work day.

Hormone Excretion Patterns

If the pattern of secretion of norepinephrine is monitored over the period from November through January, a pattern of hormone excretion develops which may be useful in predicting the type of training the swimmer underwent. Table 29 shows the predicted pattern of norepinephrine output from highest to lowest concentration for distance and non-distance training groups. In all but five cases, the predicted pattern matched the actual pattern. For these five cases, the excretion patterns were examined separately as seen in Table 30. The changes in swimming performance between midseason and the end of the season and from year to year were evaluated and are shown in Table 31. Based on norepinephrine excretion patterns, those swimmers who had

Table 29. Pattern of Largest Norepinephrine Excretion for the Months: November, December, and January

Stroke Trained	Predicted Pattern of Norepinephrine Excretion	Actual Number of swimmers conforming to prediction
Non-Distance	Jan. > Dec. > Nov.	8/11
Distance	Dec. > Nov. > Jan.	9/11

Table 30. Pattern of Norepinephrine Excretion from November through January for 5 Unique Swimmers

Subject	Predicted Pattern	Pattern Observed
C.B.	Jan. > Dec. > Nov.	Dec. > Nov. > Jan.
F.B.	Jan. > Dec. > Nov.	Dec. > Nov. > Jan.
H.R	Dec. > Nov. > Jan.	Jan. > Dec. > Nov.
D.T.	Jan. > Dec. > Nov.	Dec. > Nov. > Jan.
G.S.	Dec. > Nov. > Jan.	Jan. > Dec. > Nov.

Table 31. Event Times From 1987 through 1989

Subject	Event/Distance (yards)	1987-8 Times(sec.) Midyear	1987-8 Times(sec.) End Year	1988-9 Times (sec.) Midyear	1988-9 Times (sec.) End Year
J.A	100 Breast	64.88	61.71		
	200 Breast	142.69	138.66		
C.B.	100 Fly	54.47	51.33	53.47	51.63
	200 Fly	116.45	113.13	122.25	115.91
K.B.	200 Free	111.69	104.31	108.20	103.98
F.B.	500 Free	303.00	283.90	307.16	285.05
	100 Back	52.29	52.54	55.42	55.89
	200 Back	118.29	111.75	143.03	118.85
C.C.	50 Free	21.45	20.53	21.82	20.44
	100 Free	47.24	44.78	47.74	45.33
G.F.	100 Breast	59.10	56.08		
	200 Breast	131.81	124.17		
K.J.	50 Free	23.06	20.73	22.48	21.14
	100 Free	50.90	45.97	50.64	47.18
G.R.	50 Free	22.37	21.59	22.22	21.10
	100 Free	50.20	47.91	49.34	47.21
S.R.	50 Free	22.86	21.92		
	100 Free	49.23	49.75		
H.R.	100 Free	48.76	46.38		
	200 Free	102.31	102.32	103.98	104.33
G.S.	200 Free	102.49	98.52	104.31	100.71
	500 Free	585.61	598.34	587.13	598.78
	200 Back	119.11	118.75	121.86	115.8
M.T.	100 Breast	58.95	57.01		
	200 Breast	126.88	122.31		
D.T.	50 Free	24.43	24.69		
	100 Free	53.34	53.46		
O.V.	100 Free	48.89	46.63		
	100 Fly	52.71	50.39	52.06	50.18
	200 Fly	119.31	113.20	115.66	109.98
G.W.	100 Free	49.09	46.27	48.85	46.06
	200 Free	102.65	100.45	105.67	100.37
R.Y.	100 Back	58.41	56.26	56.14	52.67
	200 Back	131.06	119.29	131.17	123.52
J.Y.	100 Breast	70.93	60.61	63.07	60.94
	200 Breast	150.93	137.43	137.63	134.99

excretion patterns different from other swimmers in their group tended to have slower changes in time both from the middle to the end of a season and from season to season ($p < .05$).

Pre- and Post-race Excretion Patterns

Figures 18 and 20 show the net changes in hormone excretion measured by taking post race values and subtracting the pre-race levels during the middle and end of the season for the same event. Norepinephrine levels show a bigger net increase between pre- and post-race levels at the end of the season compared to the middle of the season. Epinephrine values show a large decrease in epinephrine production after a race compared to before a race in samples collected at the end of the year. This is in direct contrast to epinephrine production at the middle of the season in which there is more epinephrine produced at the end of the swim. For both epinephrine and norepinephrine production comparing midseason production to post season production of the hormone show significant differences ($p<0.01$).

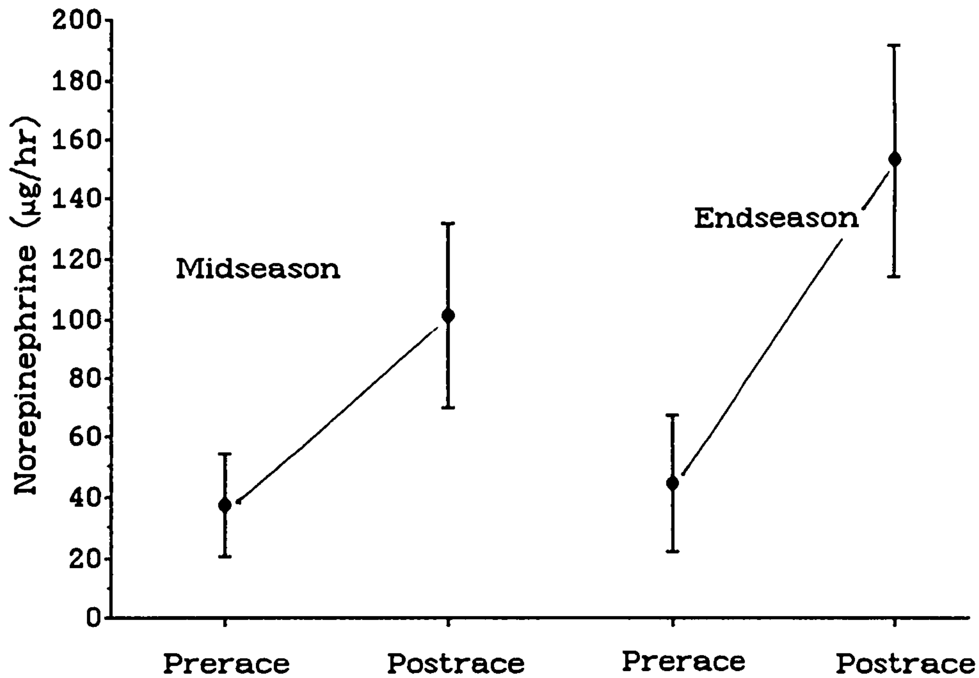

Figure 19. Pre/Post Norepinephrine Excretion Patterns During the Middle and End of the Season

N=15 for each point
Error Bar Represents Standard Error

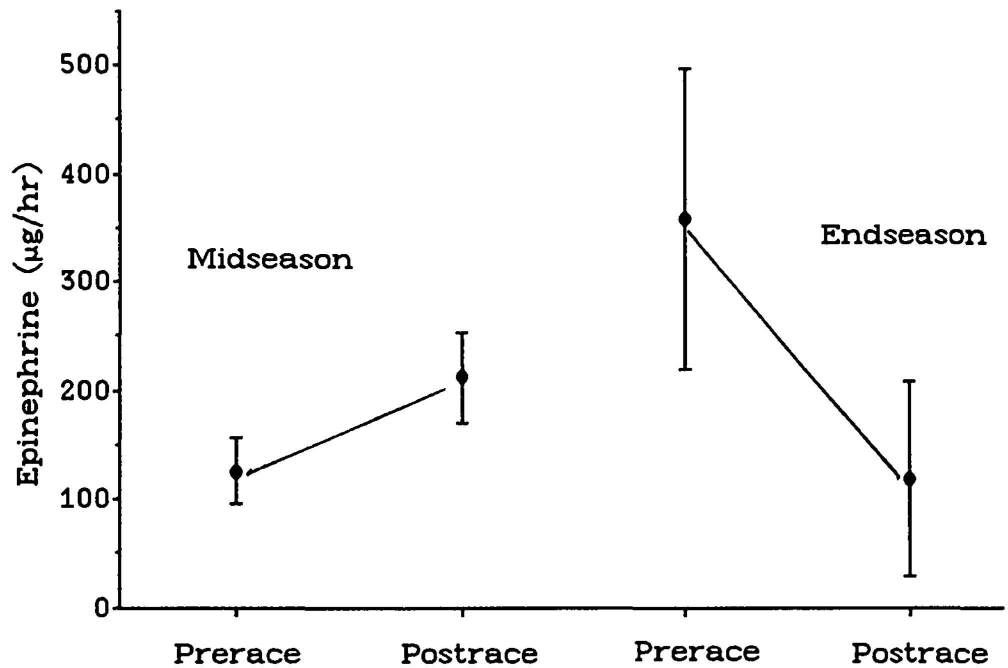

Figure 20. Pre/Post Epinephrine Excretion Patterns During the Middle and End of the Season

N=15 for each point
Error Bar Represents Standard Error

Discussion

Training versus Hormone Excretion

The final section of this report looks at some of the factors that may have an influence on catecholamine excretion. The first of these factors is the distance each swimmer trained. Although it might be expected that the amount of yardage the athlete swam and hormone excreted would be related, this is not the case. As can be seen in Figures 13-16, there is very little relationship between training distance and hormone excretion for either the work or resting day. This does not mean, however, that there is no relationship between hormone produced and training distance. If the work and rest days are broken into individual periods, many relationships become apparent (Tables 25-26). For norepinephrine, there are mild correlations between distance trained and hormones excreted during the individual collection periods for both the work and rest days (Table 25). In addition, epinephrine excretion shows weak correlations for the individual collection times during the work day (Table 30). There are no clear trends, however, during the rest day for epinephrine secretion.

A few conclusions can be drawn from these findings. First, these results show that norepinephrine is related to the distance trained. This further confirms other results already presented and gives more support to the hypothesis that swimming effects excretion of norepinephrine. A second conclusion is that epinephrine is only related to distance trained during the work day. Again, this supports earlier findings that swimming only has an effect on work day epinephrine excretion levels. Finally, it is again apparent that epinephrine and norepinephrine respond to different aspects of swimming. While the excretion of both hormones is related to the amount of training the swimmer are undergoing, only norepinephrine appears to be affected on rest days by swimming.

Psychological Stress versus Hormone Excretion

Another factor that might influence catecholamine excretion is psychological stress. In order to monitor this, a modified Hassles test was used to measure the frequency of reported hassles for swimmers and controls and the intensity of these hassles (Fig. 17,18). While there have been many reports on observed psychological changes (17, 22, 26, 104, 219, 251, 267) there are very few that use the Hassles test to quantify these changes (72, 154, 276). Despite this lack of use, however, monitoring the frequency and intensity of daily hassles has been found to be an excellent method of monitoring stress. In fact, Delongis, Kanner, and Weinberger all found in separate studies that the use of the Hassles scale was much better than the use of any other form of stress monitoring, including monitoring major life events (72, 154, 276).

In this study it was found that there was a mild correlation between the intensity of hassles reported by the control group and the month, as well as a mild correlation between the frequency of hassles reported by swimmers and the month. This is not supported by the work of Kanner, however, who found that while there is a strong correlation between the frequency of hassle when comparing one month to the next ($p < .01$), there is no correlation between the frequency of hassles and the month if all of the months are compared together (154). The Kanner results are not supported by the findings of Moore et al., and Sinyor et al., however, who independently showed that there are correlations of mood to training that can be demonstrated over the length of an experiment (162, 251). A possible reason for the difference between this experiment and Kanner's is that he used subjects that were ten to twenty years older and were not in school. Consequently, the two studies are not comparing the same subjects and so it should not be surprising that results are different.

It is better to compare the correlation for each of the hormones for both resting and working days to hassle frequency and intensity as shown in Tables 27 and 28. It becomes apparent that norepinephrine excretion in swimmers is very strongly related to the frequency of reported hassles. Epinephrine excretion in swimmers and controls during the work day is also strongly correlated with the intensity of the hassles . Thus, we have determined that both norepinephrine and epinephrine excretion are strongly related to the intensity of reported hassles during the work day. In addition, epinephrine is also strongly related to the frequency of hassles during the work day. Neither hormone show any relationship to the frequency or intensity of hassles during the rest day. These results have not been reported in other studies and may indicate differences due to differences in subjects.

Finally, if controls are compared to swimmers, there is no significant difference in the frequency of reported hassles. However, there is a significant difference in the intensity of hassle as shown in Table 32. Swimmers have a significantly lower score ($p < .01$). This result would indicate that swimmers are not are not as irritated as control subjects.

Effect of Multiple Surveys

It might be argued that there are errors inherent in using repeated surveys. Klein found that there is a 26% decline in the amount of events reported if testing is done at the beginning and end of a 20 week experiment when compared to getting reports every 5 weeks (162). However, Kanner showed that while there is some decline in the tendency to report an incident, this remains constant for both test subjects and controls so that comparisons can be made between the two groups (154).

Preformance vs. Catecholamine Excretion

A direct effect of the excretion of norepinephrine and epinephrine is how it might be related to performance. Therefore, the ability to predict performance, based on catecholamine excretion, could be very important and useful. A possible means to actually predict performance based on catecholamine secretion is presented in Table 29. This study noted that when the amount of norepinephrine was recorded from November through January and the months then placed in order from largest amount of hormone excreted to smallest, predictions could be made about the various types of training the swimmers were undertaking. In all but five cases the predicted pattern matched the type of training the swimmer was undergoing: distance or non-distance. In those five cases in which there was not a match between the type of training undergone and the predicted norepinephrine excretion pattern, the individual swam poorly relative to his best time. One swimmer who trained in the distance group but presented with a non-distance excretion pattern, did not improve his time in his distance events but did in his non-distance events. Consequently, the use of norepinephrine secretion patterns to predict performance could be a valuable tool. This idea is supported by Von Euler, who found that changes in norepinephrine could be used to predict performance (268). These results could simply be a phenomena of the coachs' training protocol. However, the present study was done under two different head coaches and indicates a possible mechanism for monitoring the appropriateness of training.

Changes in Norepinephrine Pre- and Post Swim

The last item that will be discussed is the changes in norepinephrine and epinephrine before and after a particular swim during the middle and end of the season. During the middle of the season, norepinephrine and epinephrine values reveal a marked increase indicating that there is a large amount of physical and emotional stress during and after the event. By the end of the season, this increase in norepinephrine excretion is even more dramatic. There is a dramatic decrease in epinephrine excretion in the postrace samples. These results indicate that there is even more of a physical stress on the swimmer during the end of the season and that almost all the mental stress is prior to the event. It is difficult to determine whether these changes help or hinder performance. On the one hand, high catecholamine levels will mobilize energy stores and lead to increased performance but on the other excess levels of catecholamines could cause undue mental stress and lead to a poor performance. By the very nature of the way swimmers train, these hormones will be elevated at the end of the season, so it is probable that at least some increase in hormone level is beneficial. At what point this increase becomes detrimental is unclear.

Chapter 7. **Conclusions**

It is readily apparent that epinephrine,metanephrine, norepinephrine and normetanephrine respond to different stresses. Norepinephrine responds to physical stress while epinephrine responds to mental stress. Based on this study the following conclusions can be made regarding the effects of physical exercise on catecholamine production.

After the start of a training season, swimmers show a transient increase in the amount of norepinephrine excreted. The most plausible explanation for this is due to poor physical fitness and inefficient stroke mechanics. The increase in norepinephrine excretion during the work day can be seen as early as three days after the start of training but resting samples take a month to show a change in excretion levels.

The decrease in the amount of hormones excreted is a long term process and lasts beyond the 6 weeks seen in some other studies. The reasons for this extended period of hormone change are probably due to use of athletes undergoing extreme exercise protocols which are adjusted daily to give maximum performance while swimmers may take a longer period of time to develop optimal stroke efficiency.

Another finding of this study is that there are several variables that influence catecholamine excretion including : Swim training, school, exams, and swim meets. Collecting samples during resting and working days, as well as dividing each day into three collection periods allows for the effects of these variables to be individually examined. It was found that school and swimming had very different effects on the hormone excretion of swimmers and that these two variables had greater or lesser amounts of influence depending on the time of year and what was happening with each variable. For example, the effects of swimming on epinephrine excretion were not apparent until November, however, events such as examinations had a dramatic effect on epinephrine secretion independent of the time of year they occurred. Additionally, training leads to a decrease in the amount of hormones excreted, whereas tapering can lead to an "overexcretion" of hormones. In general excretion of epinephrine is most closely related to changes in school and norepinephrine excretion is most closely related to changes in physical activity.

Another finding is that metabolite excretion patterns mimicked their hormone excretion patterns. This implies that there is a net decrease in the amount of hormone being excreted and possibly an increase in the amount of receptors. The excretion pattern of all four hormones was influenced by both physical and psychological stresses and use of Hassles testing was an excellent means of monitoring perceived stress in swimmers and controls.

Some predictions about the type of swimmer a subjects is and how effectively his training program is working may be made based on norepinephrine levels. Monitoring norepinephrine excretion levels from November through January might also allow predictions to be made about future performances and might be used to modify training to improve future performances.

Finally, excretion patterns for catecholamines differ between the beginning of the season and the end of the season when looking at pre and post secretion levels.

Thus, there are several results that are evident from this study. There are also other areas where future studies could improve upon this investigation. One of the first areas is the sample size of the study, particularly the control groups. It was very difficult to get subjects who were willing to collect 24 hour urine samples. In fact, it was necessary to pay both swimmers and controls to obtain sufficient numbers. Additionally, because of the difficulty gathering subjects, the study was unable to collect data during two of the months. Although this probably did not effect the overall results of the study, any acute changes the controls might have undergone during these months were not recorded.

Related to the problem with subject size is the type of subject used in this experiment. All subjects were sophomores or older and there were no women. Consequently, by expanding the subject base more information regarding stresses in athletes and students could be obtained and some additional questions could be answered. For example, it would be interesting to know what effect being a freshman has on hormone excretion; it would also be important to know how exercise and menstruation affect hormone excretion because this could have important implications for training and competition.

Another area that this study did not cover was the effect of changing hormone production on the various biological systems in the body. While it is implied that a decrease in catecholamines and their metabolites implies that there is a decrease in production, the effect this has on the body is unknown. Do receptors actually increase in number or remain the same? Would catecholamine receptors in the cardiovascular system respond the same as receptors on adipose cells? Thus, there are still numerous questions regarding how the changes in hormone production effect the internal milieu of the body.

Informed Consent

The study you will be participating in is one that will look at the levels of stress a college athlete undergoes during the course of a training season. In order to evaluate this, however, I need to also have values for typical undergraduates. I am looking for 15 male students, at least 7 of which are freshman, to participate in this study. You will be required to collect your urine over a 24 hour period and you will do this once during the week and once on Sunday for four collection periods running from March 1 to the first week in May. During each of the collecting periods I will also ask you to be filling our a simple stress evaluation form and a diet history form. At the end of the experiment you will be paid 25 dollars. All of your names will be kept confidential and results will only be referred to by initials. Further, your urine samples will be tested only for stress hormones (epinephrine, norepinephrine, dopamine and cortisol). Nothing else will be tested.

The procedure for this experiment is quite simple. There are three bottles which you will be filling over a 24 hour period. For each of the bottles you need to do the following: 1) Record the first time you void into the bottle: 2) Record the last time you void into the bottle; and 3) Freeze or refrigerate the bottle once you finish using it.

The first bottle should be used between 4:00 p.m. and the time you go to bed. During this time, anytime you have to urinate you will be filling this bottle. Again, you will record the first time you void into the bottle and the last time you void into the bottle.

The second bottle will be used from the time you go to bed up to and including the first morning urine sample. Thus, if you void at 11:00 and then go to bed only to wake-up an hour latter having to void again, that sample will go in the second bottle. Again, record the first and last sample times on the side of the bottle.

The third bottle will run from the second void until 4:00 p.m.. In this bottle it is important that you bring it to school and use it. It is also important that you try to make your last void as close to 4:00 p.m. as possible.

This procedure will be done once during the school week and once during the weekend. For the weekend, you will start your 24 ;hour period with the second void on Sunday. Thus, bottle one will run from the second void Sunday till 4:00 p.m.. The second bottle will go from 4:00 p.m. until bed, and the last bottle will be an overnight bottle which includes the next morning sample.

It is essential to this study that you do not skip any samples. This becomes especially important on Sunday when you might want to go to the beach. Please do not limit your activities by remember that I have to have a complete record. I know this may be inconvenient but I am only asking you to do this once a month for three months

I have read and understand the above experiment. I agree to participate freely and understand that I may quit at anytime prior to the completion of the experiment, but that I will not be paid.

____________________ Print Name

____________________ Sign Name

Evaluation of Monthly Stress Events

1. Resting HLa (1x month) ___________

2. Did you have any test in the last two weeks? _____________
   How much did you study for each? _________________
   Were you worried about them? ___________________
   How stressful were they on a scale of 1-10 ___________
   (One being no worry at all so you did not study
   and 10 being you studied as hard as you could.)

3. Did you have any meets in the last two weeks?_____________
   Did you worry about them? _____________________
   Did you get 'psyched up' for them?_________________
   Rate each meet on a scale of 1-10
   in terms of how emotional you
   got. (1 being none and 10 being
   like the meet was NCAA's.)_____________________

4. Is there any other stress that
   is effecting you? (Girlfriend
   job, etc.) ________________________________
   Rate it on a scale of 1-10 _____________________
   (One being little but
   noticeable and 10 enough
   to influence every aspect
   of your life.) _____________________________

5. How many practices did you go to in the last 2 weeks? ___
   How many were you required to attend?____________

6. What percentage of your normal
   health were you in in the last 2 weeks? ____________

7. Were you injured enough in the last 2 weeks so that you had to ease back on practices? _______
How much did you rest (1-100%)? _______________

8. Were you injured enough to miss practice? __________
How many practices did you miss (1-100%)? _______

9. Did you do a special workout due to injury? _________
Was it effective?____________________________
(One being worthless and 10 as good or better than a normal practice.)

10. Did you like the special workout? ______________
Was it better, worse, or the same as a normal workout? ______________________
Would you like to do this more often? ___________

11. Did you rest yourself this week, independent of the written workout? ___________

12. Did you rest for any meets? _________________
How many days/weeks? ____________________
Was it enough? __________________________
Are you happy with your results? ______________
(One being the worst taper and 10 the best.)

13. Do you find lactate testing stressful? ___________
(One being no problem and 10 you would never do it again.)

14. What is your self evaluation of the last 2 weeks "stress load" wise?_______________________

Sunday Activity and Diet Logs

What time did you get up?

What did you have for breakfast? (Exact amount. Everything.)

What did you do until lunch?

What did you eat or drink between breakfast and lunch?

When did you have lunch?

What did you have for lunch? (Exact amount. Everything.)

What did you do till Dinner?

What did you eat or drink between lunch and dinner?

What did you eat for dinner?(Exact amount. Everything.)

What did you do until bed?

What did you eat?

What time did you go to bed?

Did you nap during the day? How long?

Did you eat any candy, chocolate, coffee, tea, or sodas? How much

What time was your first void into bottle 1?

What time was you last void?

What time was your first void into bottle 2?

What time was you last void into bottle 2?

What time was your first void into bottle 3?

What time was your last void into bottle 3?

Name:

Weight:

Weekday Activity and Diet Log

When did you have lunch?

What did you have for lunch? (Exact amount. Everything.)

What did you do till practice?

Did you nap during the day? How long?

What did you eat or drink between lunch and dinner?

What did you eat for dinner?(Exact amount. Everything.)

What did you do until bed?

What did you eat?

What time did you go to bed?

What time did you get up?

Did you have morning practices? How much did you swim?

Did you eat before practices? What?

What did you have for breakfast? (Exact amount. Everything.)

What did you do until lunch?

What did you eat or drink between breakfast and lunch?

When did you have lunch?

What did you have for lunch? (Exact amount. Everything.)

Did you eat any candy, chocolate, coffee, tea, or sodas? How much

What time was your first void into bottle 1?

What time was you last void?

What time was your first void into bottle 2?

What time was you last void into bottle 2?

What time was your first void into bottle 3?

What time was your last void into bottle 3?

Name:

Weight:

Appendix 2. **Catecholamine Extraction**

Sample Cleanup for Catecholamines

1. Pour cation exchange resin into plastic columns. The lower portion of the column should be filled as completely as possible with air bubbles.

2. Transfer 5.0 ml of urine using a autopipet accurate to 0.2% with to a 25 ml beaker. Add 50 µl of working internals standard using a autopipet accurate to 0.2% and 15 ml of 0.1 M, pH 7 phosphate buffer using a REPIPET dispenser accurate to 1% with a reproducibility to 0.1%.

3. Pour the contents of the beaker onto the cation exchange isolation columns. Allow to drain completely and then rinse with approximately10 ml of distilled water.

4. When columns have completely drained, add 1.3 ml of 0.7 M H2SO4 using a repipet accurate to 0.2%.

5. Allow to completely drain then place a 5.0 ml reaction vial under the column and elute the catecholamines with 4.0 ml of 2 M (NH4)2SO4 using a REPIPET dispenser accurate to 1% with a reproducibility to 0.1% .

6. Place 50 mg of alumina in each vial using a piece of glass molded to hold 50 mg.

7. Add 500µl of TRIS/EDTA buffer to the reaction vial using a repipet accurate to 0.2%. Screw on cap and shake for 20 minutes.

8. Remove vials from the shaker and allow alumina to settle.

9. Remove supernatant by aspiration.

10. Wash the alumina once with distilled water. The alumina must be thoroughly agitated. Allow particles to settle and then again aspirate.

11. Add 0.5-1.0 ml of water to each sample, then transfer the slurry to a Microfilter loaded with an RC-58 membrane using a disposable pipette.

12. Place the Microfilter in a centrifuge accurate to 0.2% and spin it to dryness at 1000 x g for 30 seconds.

13. Put a clean, dry receiver tube on the Microfilter and add 200 µl of 0.1M HClO4 using a repipet accurate to 0.2%. Vortex briefly, wait a few minutes and vortex again.

14. Centrifuge the Microfilter at 1000 x g for 1 minute.

15. Inject 50-100 µl of extract into the LCEC Analyzer.

Prior to injecting the extract, however, the analyzer needs to be prepared. This is done by first preparing the mobile phase and allowing at least 24 hours for the system to equilibrate to establish stable chromatography. The detectors initial sensitivity is set to the 200 nanoamp scale and a potential of +650 millivolts vs. Ag/AgCl/3M NaCl is applied to the system. The system is then ready for extraction.

Sample Cleanup for Metabolites

1. Set pH meter calibration at 7.00 using pH 7 buffer. Adjust the pH meter slope calibration to 1.00 using pH 1 buffer.

2. Quantitatively pipette 2.0 ml of standard, control, and patient samples into labeled 16 x 150 mm tubes using a repipet accurate to 0.2%. Add 2.0 ml distilled water using a repipet accurate to 0.2% and 200 μl internal standard solution using a repipet accurate to 0.2% to each tube. Vortex tubes briefly.

3. Add 2M HCL, drop by drop to attain a pH of between 0.8 and 1.0 pH for each tube.

4. Cover all tubes with Parafilm. Place tubes in Precision hot water bath and allow 30 minutes for complete hydrolysis of metanephrines.

5. Remove tubes and allow to cool.

6. Label and prepare one prepacked Bio-Rad cation column and one anion column for each sample. Place the cation column in the front row and the anion column in the rear. Allow columns to drain.

7. To each tube add 5.0 ml ammonium pentaborate buffer using a REPIPET dispenser accurate to 1% with a reproducibility to 0.1% and 300 μl 0.5M NaOH mix using a repipet accurate to 0.2%. Check to make sure pH is between 6.0 and 7.0. If necessary, adjust with either 0.05M NaOH or 1.0 acetic acid.

8. Pour each sample into the cation exchange column

9. Rinse column with approximately 10 ml distilled water.

10. Place a polycolumn support over each anion column. Move the appropriate cation column over the anion column.

11. Pipette 8.0 ml of 2M ammonium hydroxide into each upper column using a REPIPET dispenser accurate to 1% with a reproducibility to 0.1% and allow to drain.

12. Rinse with approximately 5.0 ml distilled water

13. Replace waste reservoir with test tube rack

14. Dispense 5. ml of elution buffer into each column using a REPIPET dispenser accurate to 1% with a reproducibility to 0.1% and allow to drain.

15. Add 400 µl acetic acid to each tube using a repipet accurate to 0.2%, then vortex. The tubes may then be stored at room temperature for 1 night or for 1 week at 2-8°C.

Assay Steps

Again, in order to inject the extraction into the LCEC, the mobile phase must first be prepared and the system equilibrated at least 24 hours prior to inital extraction. The detectors inital sensitivity should be set to the 10 nanoamp. scale and a potential 730 millivolts vs. Ag/AgCl/3M NaCl is applied to the system. In addition the system needs to be tested. This is done by diluting the premade test mix fourhundred fold with elution buffer. The test mix is then injected and the performance compared to the chromatograph received with the test mix. If the run is not satisfactory, the dectector needs to be further equilibrated. Once the run is satifactory the system is ready for extraction. A urine standard is then injected and peak heights measured. For this set of extractions the concentration of normetanephrine and metanephrine in the urine standard were 1033 and 418 µg/l respectively.

Appendix 3. **Reagent Preparation**

Reagents Used During Catecholamine Extraction

1. 6 M HCL: Dilute 250 ml of distilled water with 250 ml of concentrated HCL using a 250 ml graduated cylinder accurate to 0.10%.
2. 2 M $(NH_4)_2SO_4$: Dissolve 66 grams of ammonium sulfate in 250 ml of distilled water using a 250 ml graduated cylinder accurate to 0.10%.
3. 0.7 M H_2SO_4: Dilute 4 ml concentrated sulfuric acid in 100 mldistilled water using a 100 ml graduated cylinder accurate to 0.08%.
4. EDTA/GSH stabilizing solution: Dissolve 1 gm glutathione and 5 gm Na_2EDTA into 100 ml distilled water using a 100 ml graduated cylinder accurate to 0.08%.
5. Phosphorous buffer, pH 7: Dissolve 4.32g anhydrous Na_2HPO_4, 1.19g KH_2PO_4, and 10.0 g disodium EDTA in distilled water and dilute to 1.0 liter using a 1000 ml graduated cylinder accurate to 0.30%.
6. 3 M Tris/EDTA buffer, pH 8.6: Dissolve 36.3g Trizma base into 100 ml distilled water using a 100 ml graduated cylinder accurate to 0.08%. The solution may need to be warmed and stirred for complete dissolution. Add 6M HCL until pH=8.6.
7. Acid Washed Alumina Oxide: Use as is.
8. Bio Rex 70 cation exchange resin: Resin is cleaned by washing with successive volumes of 3 M HCL, 3 M NaOH, 3 M acetic acid, and 0.1 M, pH 6.5 phosphate buffer. pH is adjusted to 6.5 during the last wash.
9. Stock Catecholamine Standard Solutions: Dissolve 36.5 mg norepinephrine HCL, 10.0 mg epinephrine free base, and 111.1 mg dopamine HCL in 100.0 ml of 0.1 M $HClO_4$ using a 100 ml graduated cylinder accurate to 0.08%.
10. Catecholamine Standard Solutions: Dilute 1.0 ml of the stock solution to 50.0 ml with 0.1 M $HClO_4$. The resulting concentrations (μg free base/ml) of catecholamines are: Norepinephrine. 6.0μg/ml; Epinephrine, 2.0 μg/ml; and Dopamine, 18.0 μg/ml. (If Norepinephrine bitrate, MW=337.3, is used instead of the HCL, MW=205.7, then 36.5 x (337.3/205.7) mg would be required.
11. Internal Standard Solution: Dissolve 15.8 milligrams dihydoxybenzylamin hydrobromide (DHBA) in 100 ml of 0.1 M $HClO_4$. Prepare the Working Internal

Solution by diluting 1.0 ml of this stock solution to 10.0 ml using 0.1 M $HClO_4$. The resulting DHBA concentration will be 10 μg/ml.

Reagents Used During Metabolite Extraction

1. 0.5 M Sodium Hydroxide. Dissolve 2g in 80 ml distilled H2O. Bring up to 100 ml with same grade waterusing a 100 ml graduated cylinder accurate to 0.08%. Mix well. Stable at room temperature.
2. 2M HCL. Under a fume hood, slowly add 50 ml concentrated HCL to 250 ml distilled water, with continuous mixing, using a 250 ml graduated cylinder accurate to 0.10%. Continue stirring for 5 minutes or until the solution cools to room temperature. Stable at room temperature.
3. 0.05 M HCL. Under a fume hood, dilute 1.0 ml concentrated HCL to 250 ml with distilled waterusing a 250 ml graduated cylinder accurate to 0.10% . Mix. Stable at room temperature.
4. Ammonium pentaborate buffer. Dissolve 40 g ammonium pentaborate and 1.0 g disodium EDTA in 900 ml distilled water. Bring up to 1000 ml using a 1000 ml graduated cylinder accurate to 0.30%. Mix well and transfer to a 1000 ml dispenser, set to deliver 4.0 ml. Stable ar room temperature up to 3 months.
5. 2M ammonium hydroxide. Under a fume hood, add 135 ml concentrated ammonium hydroxide to 865 ml distilled water using a 1000 ml graduated cylinder accurate to 0.30%. Mix well and transfer to a 1000 ml dispenser bottle, set to deliver 8.0ml. Stable at room temperature up to 3 months.
6. 1M acetic acid. Mix 5.7 ml of glacial acetic acid with 94.3 ml distilled water using a 100 ml graduated cylinder accurate to 0.08%. Stable at room temperature.
7. Elution buffer. Dissolve 15.4 g ammonium acetate in 950 ml distilled water. Adjust pH to 6.00 ± 0.05 using 1M acetic acid. Bring up to 1000 ml, using a 1000 ml graduated cylinder accurate to 0.30%, and transfer to a 1000 ml dispenser set to deliver 5.0 ml. Stable at 2-8°C up to 3 months.
8. 1M KH2PO4.Dissolve 68.05 g potassium dihydrogen phosphate in 400 ml distilled water. Bring up to 500 ml and mix well using a 500 ml graduated cylinder accurate to 0.20%. Filter through a 0.45 micron filter. Stable up to 1 year at 2-8°C.
9. HPLC mobile phase. Combine 60 ml 1 M KH2PO4 and 890 ml HPLC grade or glass distilled water using a 100 ml graduated cylinder accurate to 0.08% and a1000 ml graduated cylinder accurate to 0.30%. Adjust pH to 5.20 ± 0.02 pH units with approximately 2.3 ml 0.5M sodium hydroxide. Add 50 ml HPLC grade acetonitrile and mix at least 5 minutes. Filter through a 0.45 or 0.2 μ filter. Mobile phase is stable at

least 1 week at room temperature. Check for evidence of bacterial growth before each usage.

10. HPLC wash reagent. Add 25 µl of concentrated phosphoric acid to 1000 ml HPLC grade water. Check pH is between 2.9 and 3.1. Adjust pH if necessary by changing volume of acid. 200 µl of 2M phosphoric acid may also be used.

11. Urine Standard. Reconstitute with 25 ml of 0.05M HCL. Let stand 10 minutes the agitate gently to dissolve. Store at 2-8°C. Stable for 30 days at 2-8°C.

12. Internal standard. Reconstitute with 25 ml of 0.05M HCL. Agitate gently to dissolve. Store at 2-8°C. Stable 3 months.

13. Urine controls. 25 ml controls may be reconstituted with 25 ml of 0.05M HCL. Stable 30 days at 2-8°C.

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