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ANTHROPOMETRIC, STRENGTH AND HORMONAL EFFECTS OF HIGH-RESISTANCE WEIGHT-TRAINING IN WOMEN

BY MARC REGIMBAL

A thesis submitted to the School of Graduate Studies and Research in partial fulfillment of the requirements for the degree of Master of Science

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ABSTRACT

This study investigated the anthropometric and the hormonal changes following short and long-term programs of heavy-resistance weight-training.

The experimental group (age 18-25 years) consisted of previously untrained university students (N=10) that trained for 2 months (4 times/week, 1 hour/session). Endocrine data from two menstrual cycles obtained prior to training was used to establish baseline values. The effect of short-term weight-training was analyzed by comparing baseline values with those obtained during the second cycle of training. Body weight and the relative body fat were unchanged following training. Girth measurements were unchanged except for a significant increase in thigh and arm girths ($p = 0.0128$ and $p = .0016$ respectively). Both increases reached statistical significance despite the fact that they were rather modest, averaging 1 to 1.5 cm in both cases. Despite these small changes in body composition, strength increases (as measured by the total of 4 lifts) were rather rapid with an average 36.6% increase (from 135.4 to 185.0 kg). The leg press score increased by 55.7% in comparison to the 17.3% - 25.4% increases seen for measures of upper body strength. Such findings agree with previous studies reporting small changes of body composition in females following training and a greater strength potential in lower body versus upper body. Furthermore, strength increases occurred despite very little hypertrophy, suggesting that an increased neuromuscular recruitment was the primary mechanism for strength increase. Hormonal values

collected during the second cycle of training were compared to baseline values. There were no significant differences in hormone levels at any point of the menstrual cycle. Thus, it was concluded that short-term heavy-resistance weight-training had no effects on the basal levels of estradiol, progesterone, free-testosterone and androstenedione. Furthermore, no subject from the experimental group reported menstrual problems before, and as a result of training.

The long-term effects ef heavy-resistance weight-training were determined by comparing bodybuilders (N=9) and the reference group (N=15) consisting of the pre-exercise values of the experimental group and an additional 5 control subjects. Prior statistical analysis revealed that experimental and control subjects were not statistically different and could be therefore pooled together to form the reference group. Bodybuilders were, on average, 6 kg lighter and 35.4% leaner (both significant at $p < .05$) than the reference group. However, the reference group had significantly increased waist, thigh and arm girths over bodybuilders. When the combined total was used as strength index, bodybuilders were, on average, two times stronger than the reference group (significant at $p < .0001$). Individual strength scores showed the same results with the leg strength score being 2.5 times higher in the latter group. However, upper body strength scores displayed less difference between both groups. The incidence of amenorrhea defined as the cessation of menses for at least 3 months, was very high in bodybuilders, affecting 7 out of 9 (78%) of the athletes. This is much higher than the

incidence of amenorrhea reported in competitive runners (30-50%). Empirical observations on the group tend to show that they possess most of the main predisposing factors to amenorrhea (exercise, altered diet and low body fat). This data should be viewed with caution since the sample size is rather small and it is conceivable that the experiment design (i.e. having volunteer subjects) may have biased the results toward a higher incidence. Endocrine data were averaged over 4 samples (i.e. 28 days) for comparisons between both groups as done in other studies. Data of amenorrheic bodybuilders only were utilized for comparisons since they were more numerous than normally-cycling athletes. The 17 β-estradiol concentration was not decreased in amenorrheic bodybuilders despite amenorrhea. This is rather surprising since a decrease in estrogen status is often seen in highly trained athletes. Progesterone levels were drastically reduced in bodybuilders when compared to the reference group, strongly suggesting anovulation in these athletes. In fact, the data indicated that most athletes have progesterone values characteristic of the follicular phase (i.e. around 1 ng/ml) for all the periods of sampling (4-8 weeks). Such decreased progesterone values are of concern for endometrial hyperplasia especially in view of unchanged estradiol levels. Thus, it is assumed that these athletes are at high risk for endometrial hyperplasia due to the action of "unopposed estrogens". The data obtained in this study would suggest a need for progesterone supplementation in these athletes as suggested by recent clinical reviews. The mean free-testosterone values of bodybuilders were

increased by 27.2% over the reference group values, without reaching, however, statistical significance. Nevertheless, bodybuilder values congregate around the upper limits of normal females. It is tempting to speculate that this difference may be of physiological significance especially since only the biologically active fraction was measured. Finally, androstenedione values were increased by 17.6% in bodybuilders without however reaching statistical significance. It is doubtful that this difference is of any physiological significance, especially in the view of the low biological potency of androstenedione. The results of this study strongly suggest that only the long-term heavy-resistance weight-training can trigger menstrual and hormonal changes.

Chapter One

THE PROBLEM

1.1) INTRODUCTION:

Weight training is now widely utilized by various athletic groups, including women, in order to increase athletic performance. However, the physiological effects of this type of training, particularly on the reproductive system of women are relatively unknown.

Weight-training exerts several positive effects on the body, i.e., strengthening of most functions of the body such as the muscular system. It is only recently that the effects of aerobic exercises on the reproductive system of women have been studied rather extensively. Two major findings have come out from these studies: athletes experience a later menarche than inactive women and the incidence of oligo/amenorrhea is higher in athletes that inactive controls. A late onset of menarche has been demonstrated repeatedly in various groups of athletes (Warren 1980, Frisch et al. 1981). Also associated with this late development of puberty in dancers was a depressed breast development with periods of rapid development occurring during periods of relative inactivity (Warren 1980). Surprisingly however, the development of pubic hair was not affected by training. In runners, the effects of prepubertal training in delaying menarche was demonstrated by Frisch et al. 1981. Every year of prepubertal training delayed menarche by 5 months. Secondary to a late menarche is an increased incidence of secondary amenorrhea

among athletes. For instance, the incidence of exercise-induced secondary amenorrhea is already high among dancers and Abraham (1982) has shown a constant deterioration of the menstrual function i.e., an increased incidence of amenorrhea throughout 12 months of intense ballet training. Among joggers, the incidence of amenorrhea is higher than the inactive population and intense training also triggers an increased incidence of menstrual abnormalities (Baker et al. 1981, a). It appears that the incidence of amenorrhea is proportional to the amount of energy expended as demonstrated by a significant correlation between the incidence of amenorrhea and the number of miles run per week. When menses are normal despite training, one can still observe a significant ($p < .05$) decrease in the number of menses/year in well trained joggers versus controls, with recreational joggers showing somewhat intermediate values (Dale et al. 1979). Competitive runners (more than 50 miles/week) can have an incidence of amenorrhea somewhere between 30-50% (see: Baker 1981b, Hale 1983, Jacobs 1982, Wall 1983).

Amenorrhea is considered to be the end point of a series of events occurring in the reproductive cycle, which includes a short luteal phase. Exercise-induced changes in basal hormonal concentrations are probably responsible for such abnormalities.

The effects of regular exercise on the hypothalamo-pituitarian axis have been proposed as possibly being the first step leading to secondary amenorrhea. When exercise levels are intense enough to trigger oligomenorrhea, LH levels are reduced to low-normal or to low levels (Dale et al. 1979, Russell et al.

1984a, Russell et al. 1984b, Weicker et al. 1984) with a concomittant decrease in FSH (Dale et al. 1979, Russell 1984b, Weicker 1984, Bonen 1981). It appears that the concentration of both gonadotropins is decreased proportionally to the training volume (Weicker et al. 1984). The low levels of both gonadotropins in addition to the impaired cyclic pattern strongly suggest an impaired follicular growth (Bonen et al. 1981). This impaired follicular growth would suggest that estradiol and progesterone concentrations may be altered. In fact, a very significantly reduced estradiol concentration (Boyden et al. 1983, Dale et al. 1979, Russell et al. 1984a, Ronkainen et al. 1985, Bonen et al. 1981) is universal in athletes involved in intense and prolonged training. When the menstrual cycle is still present, despite low estradiol levels, blood loss during menses can be decreased quite significantly (Boyden et al. 1983) and the frequency of menstrual cycles/year is also reduced (Dale et al. 1979). As a result of a low estradiol concentration, folliculogenesis is impaired reducing in turn the progesterone concentration (Ronkainen et al. 1985). The popular belief of an important role for androgen for successful sports participation have lead to several unwarranted conclusions about the role of androgens. Furthermore, the striking paucity of information concerning the long-term effects of exercise on androgen concentration in females suggest the need for research in that particular area. Studies show opposing results with either an increased (Dale et al. 1979), decreased (Ronkainen et al. 1985) or unchanged (Boyden et al. 1983) basal testosterone concentra-

tion in female athletes. Furthermore, very little information is available concerning the effects of weight-training on the basal concentration of androgens in females.

From this review, one can appreciate that a number of studies have evaluated the endocrine effects of aerobic exercises. On the other hand, there is a striking paucity of information concerning the endocrine effects of high-resistance weight-training in women. Also, no studies have attempted to qualify the exercise-related endocrine changes and their effects on the ovarian function. As such, the effects of high-resistance weight-training programs on the endocrine and ovarian functions of females are basically unknown.

1.2) STATEMENT OF THE PROBLEM:

This study was undertaken to evaluate the anthropometric, strength, and hormonal profiles of previously untrained university students (18-25 years) following a two month high-resistance weight-training program. In addition, a group of bodybuilders (18-30 years) was compared to the pre-training values of the university students in an attempt to generate data about the possible long-term effect of such type of training.

1.3) NEED OF THE STUDY:

Our current knowledge of exercise-related endocrine changes and menstrual disorders is for practical reasons, confined to studies involving aerobically-trained subjects. Since high-resistance weight-training is a relatively new sport for women, no extensive research has been performed on the endocrine changes related to this sport.

Dale (1981) found elevated baseline values for testosterone

in runners (0.41 ng/ml) when compared to controls (0.33 ng/ml). The physiological repercussions of this effect are unknown but one may suggest that the same phenomenon could occur in well-trained females involved in weight-training since androgens are thought to be the major hormones responsible for muscular hypertrophy.

The research that has been performed in males has been directed toward the acute hormonal effects of high-resistance weight-training. No research has analyzed the long-term effects of this activity on the ovarian cycle. Also, the multihormonal analysis of these athletes may give us more information about exercise-induced amenorrhea.

Finally, exercise-associated amenorrhea is probably due to an inter-relationships between predisposing factors such as: low body fat, stress of training, intensity of exercise... Since weight-training is typically anaerobic, the impact of these weight-training exercises may be quite different from those caused by aerobic exercises. No studies have looked at the effect of regular weight-training on exercise-associated amenorrhea.

1.4) HYPOTHESES:

There are no significant differences in all hormonal values (testosterone, androstenedione, estradiol, progesterone) and in ovarian cycle parameters before and after an 8 week weight-training program.

There are no significant differences in all hormonal values between a group of well-trained bodybuilders and a group of non-training controls.

1.5) SCOPE OF THE STUDY:

This study was undertaken to evaluate the effects of a weight-training program on the estrogen, progesterone, testosterone and androstenedione concentrations in females and to evaluate at the same time any exercise-related effects on the menstrual cycle. In total, 24 women (18-25 years) volunteered for the study. All of them were in good health and a prior history of menstrual pattern was obtained at the beginning of the study. Subjects were assigned to one of the three groups:

I) Experimental (N = 10):

This group trained for a period of time equal in length to two of their menstrual cycles. Training was 4 times/week, 1 hour/session with high-resistance exercises (80% of one's 1-RM, 3-4 sets/exercise, 6-8 repetitions/exercise). Each workout stressed all the major muscle groups of the body. The subjects were university students and most of them had no or very little experience with weight-training prior to the study.

II) Bodybuilders (N = 9):

These were bodybuilders from the Ottawa region with some of them competing in regional bodybuilding contests. They had trained regularly 8-12 months before their entry in the study. Two menstrual cycles were studied and a diary of their training was also obtained.

III) Controls (N = 5):

These were non-training students of the same age group as the experimental group. Two menstrual cycles were also studied.

All subjects provided blood samples once every week, using

the first day of menstruation as the reference day throughout the experiment. Each subject took her basal body temperature every morning, before getting out of bed. All endocrine assays were performed in the laboratories of the Physiology Department, University of Ottawa.

1.6) LIMITATIONS:

I) Basal body temperature was measured orally instead of rectally which is a more accurate method. We had no control over the temperature measurements and they were left to the subject's voluntary compliance.

II) The group of bodybuilders recorded all the data related to their training in a diary. Again, we were dependent on the subject's cooperation for reliable data recording of all training.

III) When one compares heavy resistance exercises with aerobic exercises, it is difficult to quantify precisely the workload lifted during training other than multiplying the sets and the repetitions. The relative intensity was established by calculating the percentage of one's 1-RM.

IV) The personal history of menstrual pattern is related to the subject's memory, perception and level of understanding of their own menstrual cycle.

V) Due to ethical and financial restrictions, blood sampling was restricted to one sample weekly. While this procedure provides an adequate overview of the subject's endocrine pattern, it is appreciated that it was not as complete as would have been desired to give a thorough analysis of the temporal variations of

the menstrual cycle during training.

VI) The androstenedione assay required an extraction of the blood samples prior to standard analysis. No calculations were made to measure the recovery from such extraction. The manufacturer obtained an efficiency of 97% for that manipulation, suggesting that only minimal amounts of the hormone could be lost during extraction. It was realized, however, that this figure may be different from what we could have obtained.

VII) The possible repercussions of long-term weight-training were evaluated by comparing bodybuilders and the group of reference subjects. This cross-sectional comparison makes conclusions about the possible effects of long-term training difficult due to confounding variables that are inherent to such design. Bodybuilders were a self-selected group of subjects and prior predisposition to amenorrhea may have affected the incidence of menstrual disorders.

CHAPTER II REVIEW OF LITERATURE

SECTION I: PHYSIOLOGICAL COMPONENTS OF STRENGTH TRAINING

2.1.1) TRAINING PROGRAMS, THE VARIABLES:

Heavy resistance weight-training programs increased in popularity at the end of World War II. This was the result of a requirement for an expedient and optimal rehabilitation system to assist soldiers injured during the war. Heavy resistance weight lifting programs involve an infinite combination of sets and repetitions of specific exercises. It is therefore important to analyze these parameters in order to determine the importance of each one in developing an optimal training program. The numbers of series and repetitions, the workloads and the frequency of training will be described. An analysis of these contributing factors to the development of training programs follows.

Berger (1962,a) assigned 199 male subjects to 6 groups performing one set of either 2, 4, 6, 8, 10 or 12 RM. The notation (1RM) represents the maximal weight that can be handled for one repetition. All subjects trained 3 times/week on the bench press. Subjects were tested using the 1-RM lift on the bench press as the strength index. The best gains were registered in programs utilizing 4, 6 or 8 repetitions. However, there were no statistical differences among the three programs that showed the best results. Berger (1962,b) then utilized 177 male subjects in a study which compared nine groups of either 1, 2, 3 sets of 2, 6 or 10 repetitions. Strength testing consisted of a 1RM lift on the bench press. All groups trained for nine

consecutive weeks, 3 times/week. The combination involving 3 sets of 6 repetitions was found to be statistically the most efficient. O'Shea (1966) randomly assigned 30 subjects to three groups:

I) 3 x 9-10 RM

II) 3 x 5-6 RM

III) 3 x 2-3 RM

Subjects were tested with dynamometers measuring static leg and back strength. Dynamic strength was assessed using the 1-RM technique for squat. Each group performed only one exercise (full squat), 3 times a week. All groups increased significantly their dynamic and static strength levels but there were no statistical differences between the groups. However, the greatest percentage of increase in dynamic strength was seen in group II (26.7% average increase) when compared to group III 21.8% and to group I (20.4%). One might speculate that a longer program would have produced significant results. (However, this remains to be demonstrated). Withers (1970) divided 55 subjects into 3 groups:

I) 3 x 7 RM

II) 4 x 5 RM

III) 5 x 3 RM

The training program consisted of 3 exercises (squat, curl, bench press) repeated 2 times/week for 9 weeks. Subjects were tested using the 1-RM technique for the 3 lifts. No statistical differences were seen among the groups but group II had the greatest gains averaging a 22.9% increase compared to 19.3%

increases observed in the two other groups. Withers concluded that: "It would appear that performing 3-4 sets with 5-6 RM is the best strength development program for beginners". Recently, Anderson (1982) in his study, confirmed Berger's experiment. A total of 43 subjects were assigned to 3 groups:

I) 3 x 6-8 RM

II) 2 x 30-40 RM

III) 1 x 100-150 RM

In terms of strength gains, group I had statistically better results when compared to the other groups. However, the programs utilized were too different in terms of the number of repetitions performed and it is difficult to generate some conclusions. Two programs (II and III) had more than 30 repetitions per series, a number well above what is considered for optimal strength development (8-12 repetitions).

Nevertheless, it would appear that training programs involving 3-4 sets of 6 to 8 repetitions are the most efficient mode for strength development according to the literature reviewed (Berger 1962a, Berger 1962b, Anderson 1982).

Variations in workloads is another important variable in a strength training program. Experiments using light and heavy loads have been tested in order to see which one will produce the best strength gains. Barney (1961) had 80 subjects randomly allocated to 3 groups:

I) DeLorme - Watkins program (N = 47):
1 x 10 (50% of a weight that could be handled for no more than 10 repetitions) (10 RM)

1 x 10 (75% of 10 RM)

1 x 10 (100% of 10 RM)

II) 3 x 10 RM (N = 15)

III) 1 x 10 RM (N = 18)

1 x max. number of repetitions (previous weight + 5-10 pounds)

1 x max. number of repetitions (previous weight + another 5-10 pounds)

Training involved only one exercise (leg extension) and was repeated 3 days/week using the Friday as a testing day. Strength was measured using the 1-RM technique for the leg extension. Group I had significantly greater results in terms of strength gains and hypertrophy. Therefore, Barney concluded:

> The DeLorme-Watkins is superior to the traditional program when both increased strength and hypertrophy are desired. (Barney 1961, p. 146).

In order to analyze more thoroughly the optimal percentages of workloads needed to gain strength, Berger (1965) randomly assigned 79 subjects to one of the 7 following groups:

I) (N = 11) 1 x 66% of 1-RM twice/week
determine new RM once/week

II) (N = 12) 1 x 80% of 1-RM twice/week
determine new RM once/week

III) (N = 12) 1 x 90% of 1-RM twice/week

determine new 1-RM once/week

IV) (N = 10) 1 x 1-RM

V) (N = 13) 1 x 66% of 1-RM 3 times/week
determine new 1-RM once every 3 weeks

VI) (N = 12) 1 x 1-RM once/week

VII) (N = 9) control group

Subjects were tested using the 1-RM for the squat. Significant strength improvements were found in groups I, II, IV, and VI. However, there were no statistical differences between the four groups. It would appear that the best programs are the ones involving at least one maximal effort (1-RM) in combination with various workloads. Berger (1967) also compared two different training programs utilizing two different percentages of the maximal load:

I) (N = 24) 1 x 10 RM

II) (N = 26) 10 x 1 RM

The subjects were randomly assigned to the training groups and the program lasted 8 weeks, 3 times/week. Subjects were tested using the 1-RM procedure on the bench press. Both groups increased in strength but a higher increase ($p < .05$) was obtained in group II. From the studies reviewed, it would appear that the use of maximal workloads (100% of 1-RM) along with the use of increasing loads (i.e. a conventional strength training program) is the optimal way to develop strength. The program must therefore involve few attempts at a maximal lift.

Each training session imposes a stress on the organism and recuperation from a work-out is most effective when the organism

is resting. This induced supercompensation involves the replenishment of high-energy phosphate stores, and protein synthesis for contractile purposes. Workouts should therefore be spaced with an optimal interval of time between training sessions in order to give time for that important physiological mechanism to occur. These will be discussed in greater detail in the following sections. Capen (1956) noted that his subjects using the 3 x 5 RM program had better results when it was 3 times/week instead of 5. Recently Darden (1977) claimed that the best gains in strength were achieved when training sessions were spaced 48 hours apart. This principle was then applied to his Nautilus program which utilizes only 3-4 workouts per week. Greater recuperation was thought to be the major reason for better results (Capen 1956, Darden 1977). However, Gillam-MacKenzie (1981) had different results. He compared 5 groups training either 1, 2, 3, 4 or 5 times/week. A sample of 68 males was randomly assigned to one of the following:

I)	18 x 1-RM	once/week
II)	18 x 1-RM	twice/week
III)	18 x 1-RM	three times/week
IV)	18 x 1-RM	four times/week
V)	18 x 1-RM	five times/week

All groups trained for 9 weeks. Only the bench press was used during training and subjects were tested using the 1-RM technique. Group V had significantly greater results ($p < .001$) with a pre-and post-training difference of 42 pounds compared to 31 pounds or less for the other groups. However, the use of only

one exercise performed 18 times produces a rather low workload during a workout. In turn, this might lead to a decreased need for recuperation. A frequency of 5 times/week may be optimal in those conditions.

Nevertheless, it seems that a training frequency of 3 to 4 times/week interspersed by a day of rest between is recommended by most of the authors reviewed.

In summary, one should perform 3-4 sets of 6-8 repetitions for optimal improvements in strength. Weights used should be near-maximal to maximal and at least one attempt of 1-RM should be made each training week. It is advisable to use this training program only 3-4 times/week in order to give the body a better chance to recuperate.

2.1.2) STRENGTH GAINS DUE TO DIFFERENT PROGRAMS:

The constant increase in the participation of women in athletic activities has now spread to the weight training room. It becomes important to quantify the average strength gains that can be made by females along with the increases in hypertrophy which could also occur as a result of training. This way, one has an idea of what changes can be expected from females training regularly with weights. In reviewing the literature, one will find great variations in the gains achieved due to: the type of subjects involved in the study (trained vs untrained), the training program and/or the duration of the training.

Wilmore (1974) compared the training response of 47 women and 26 men. All subjects were volunteers with a mean age of 20.3 years old. The two groups trained for 10 weeks with an average

of two 40 minute sessions/week. Subjects performed two sets of 7-9 repetitions/exercise. The weight was increased when the subjects could perform 14-16 repetitions. Leg and grip strength were measured with a dynamometer. Bench press and the curl were measured with the 1-RM technique. Body composition was determined by hydrostatic weighing. Women demonstrated better strength gains than men, gains averaging 29.5% and 28.6% of improvement for leg and bench press respectively. For men, values were 26% and 16.5% respectively. The women's post-test on leg strength was equal to the men's pre-test. When the women's scores on leg press were expressed by unit of body weight, they were almost equal to the men's scores. When expressed by unit of lean body mass, the women's scores were better. In terms of upper body strength however, the men's scores for bench press, handgrip and arm curl were superior no matter how they were expressed. The table below gives the values for the body composition changes:

	men	women
increase in lean body mass	1.9%	2.4%
decrease in absolute body fat	-10%	7.6%

A surprising finding was the statistically significant increase in girth measurements. However, in practical terms, these changes were very minimal with the greatest being only 0.6 centimeter. From these results, Wilmore suggested that the "quality" of muscle is the same for men and women since both sexes have similar scores when expressed per unit of lean body mass. Therefore, both sexes have the same leg training potential but women are much weaker in upper body strength. Finally, the

results show that an increase in strength is possible without a concomittant gain in hypertrophy.

In their experiment, Brown and Wilmore (1974) studied 7 women (16-23 years old) of national caliber specializing in throwing events. During the first two months, the athletes used a program designed to prepare them to handle heavy weights:

1 x 10	50% of 1-RM
1 x 8	60% of 1-RM
1 x 7	65% of 1-RM
1 x 6	70% of 1-RM
1 x 5	75% of 1-RM
1 x 4	75% of 1-RM

This very progressive program decreased the risk of injuries due to heavy-squatting or bench pressing. The subjects were trained and tested on the bench press and half-squat (1-RM). Body composition was determined by the skinfold and densitometry techniques. The strength increases ranged from 15 to 44% and from 16 to 53% for the bench press and leg press respectively. This resulted in a combined strength increase ranging from 15 to 44% after 6 months of training. The program was supplemented with 3-4 sessions/week of physical conditioning. Each session lasted approximately 90 minutes. Because some subjects had superior body weight (75 to 111 kg) at the beginning of the program and because all the subjects participated in the fitness classes, it is rather difficult to determine how much of the changes in body composition are due to the weight training program. Increases in girth (1.6% for thigh, 3.8% for upper arm,

5.4% for deltoid) are rather small after a 6 month program. The increase in lean body mass accompanying these changes is rather insignificant (1 kg in average). In men, this magnitude of increase is seen after only a few weeks of training. These findings would tend to support the role of androgens in muscle hypertrophy since males secrete greater amounts of androgens. Finally, the use of elite subjects along with their greater-than-normal body weights made the findings of this research rather inapplicable to the general population.

O'Shea and Wegner (1981) compared the training responses of 13 women and 13 men. All subjects had followed a previous beginner's class in weight training and they undertook another 2 weeks of familiarization with the experimental procedure. After this familiarization, 7 weeks of training were given (3 times/ week) using 4 sets of 3 to 5 repetitions with the intensity set at 70% of 1-RM. Wednesday served for active recuperation using 3 sets of 6-8 repetitions (50% of 1-RM). Training consisted of two exercises (squat, bench press) and testing was performed using the 1-RM technique for these two lifts. Increases of 5 and 10 pounds were added weekly to the bench press and leg press respectively. This procedure was stopped at the fourth week for the bench press due to incapacity of the subjects to lift the increasing weights. Both sexes had significant strength increases on the two lifts ($p < .01$) and, as shown previously, women had better scores on the squat when it was expressed by units of body weight. Women also had greater relative increases

($p < .05$) in both lifts:

	bench press	squat
women	13.25%	24.31%
men	7.54%	15.66%

There was a significant increase in the body weight of the females ($p < .05$) but it was mostly due to increased body fat. Again, this study showed that significant increases in women's strength cannot be correlated to increases in lean body mass.

Gettman (1982) assigned 36 women and 41 men to a circuit weight-training program or to a combined running and circuit weight-training program. Training was three times/week for 12 weeks. Subjects performed 12 to 15 repetitions on 10 excercise stations using weights set at 40% of 1-RM. Strength was measured using the 1-RM technique for leg press and bench press. For women, strength increases from both groups averaged 22% and 19% for bench press and leg press respectively compared to 21% and 15% for men.

Jette et al. (CJASS, in press) compared the training response of a group of female university students (N = 122). From these, a group of 80 completed the experiment with a compliance of 80% in the training sessions and 10 others served as controls. After an accomodation period of one week (3 sessions, 60% of 1RM), the subjects were randomly assigned to one of three protocols:

I) 3 sets x 8-12 reps (70-80% of 1-RM) for 6 weeks

II) 3 sets x 8-12 reps (70-80% of 1-RM) for 4 weeks
3 sets x 4-8 reps (80-90% of 1-RM) for 2 weeks

III) as for group II but with a change in the grip used to lift the weight.

The training was conducted three days/week, thirty minutes/session. Four exercises were performed: bench press, upright row, shoulder press arm curls and strength was measured using the 1-RM technique for each of these. Statistical analyses showed a significant improvement in strength and there was an overall 18% strength increase for the four exercises combined. However, there were no statistical differences between the three training protocols. Changes in body weight, body composition as measured with fat calipers and girth measurements did not change significantly following training except for a 0.5 cm increase in forearm girth. In general, these results also indicate that women possess 60% of the upper body strength of males.

In summary, one can conclude that women possess the same leg training potential for strength, especially when the results are expressed relative to their lean body mass. However, upper body strength is always greater in men than in women irrespective of how the results are expressed. On the average, upper body strength of females is approximately 60% of that of males. No or only slight changes in lean body mass or percentage of body fat are seen after weight training of short duration unless it is supplemented with dietary changes or aerobic activities. Significant anthropometric changes are seen following long-term training (1-2 years or more). They will be discussed in further details in the following section.

2.1.3) INTERSEXUAL DIFFERENCES:

Up to a certain point, women seem to be able to increase

their strength levels in the same proportions than men especially in lower body strength. Sex differences in strength are reduced when results are expressed relative to lean body mass. Changes in lean body mass following a short term training program are, on the average, very modest in women. This conclusion has been substantiated by several authors (Brown & Wilmore 1974, Kowal et al. 1977, Mayhew & Gross 1974).

Brown and Wilmore (1974) found a statistically significant increase in lean body mass but it was, in practical terms, very limited since the mean increase was less than 1 kg. In his experiment, Mayhew & Gross (1974) used body potassium to evaluate the possible changes in body composition. A significant increase in lean body mass was found and it was accompanied by slight increases in upper body girths as reflected by enlarged biceps, forearms and shoulder circumferences. However, the magnitude of these changes was rather minimal. Kowal et al. (1977) also reported a slight increase in lean body mass following a strength training program of 11 exercises on the Nautilus and Universal equipment. One might conclude that body composition changes following a short-term (8 weeks or so) program are rather limited. However, the use of longer or more intense training programs may give different results.

In that respect, Freedson et al. (1983) compared 10 female bodybuilders with the reference woman described by Behnke and Wilmore (1974). All bodybuilders were competitive athletes placing in the top eight positions in various regional, national and international competitions. In general, they had been

training three to four hours/day, 5 to 6 days/week, from 4 to 30 months. Body composition was determined by the underwater weighing technique and skinfold measurements were taken with a fat caliper. Thirteen girths and nine diameters using the Behnke and Wilmore procedures were also measured. Bodybuilders had an average of 13.2% body fat compared to 26% for the reference woman. They were also 4 cm shorter and 4.8 kg lighter. However the female bodybuilder's mean lean-to-fat ratio was 6.9 which is 2.5 times larger than the reference woman (2.8) and at least 15% higher than other competitive female athletes. The bodybuilder's upper trunk (shoulders, chest, biceps and forearm) was larger than the reference woman suggesting muscular hypertrophy. Using Behnke's procedure, the excess muscle for the female bodybuilders is 8.3 kg. When this excess of muscles is divided by body weight in order to normalize for sex differences, the calculated excess of muscle is 0.19 kg for the male bodybuilders compared to 0.15 kg for the females. This way, sex differences are reduced to 21%. This 7% higher lean body mass occurred without the use of anabolic steroids. In summary, women appear to be limited in terms of lean body mass following a short-term weight-training program. However, the use of longer programs show that women may exhibit hypertrophy to a certain extent. Physiological differences such as: fiber type population, enzyme concentrations and hormone levels could explain partly this different adaptation response to training.

The analysis of muscle samples in sedentary men and women reveal no differences in fiber type percentages (Ready et al.

1981, Wells & Plowman 1983). Also, the ratio strength/cross-sectional area is also the same for both sexes (Brown & Wilmore 1974, Wilmore 1974, Komi & Karlsson 1978, Ready 1981, Wells & Plowman 1983). Therefore, both sexes possess the same "muscle quality" since the tension developed per unit of surface is the same. The difference in absolute strength could then be explained by the greater cross-sectional area of the male muscles (Ready et al. 1981, Wells & Plowman 1983). Men and women therefore possess the same muscle quality due to equal distribution of fibers and to equal tension/cross-sectional area. Greater absolute strength in men is probably only a function of the male's greater muscle mass.

More in-depth studies were attempted to quantify the possible biochemical differences between male and female muscle. These studies were made mostly with biopsies, a method somewhat contested as is the result emanating from them. Thorstensson et al. (1976) found no sex-related differences in concentrations of Mg^{++} stimulated ATPase, CPK and PFK. Later, Komi & Karlsson (1978) also found no significant differences in HK, LDH (forward reaction) and MK concentrations. Interestingly however, concentrations of Mg^{++} stimulated ATPase, Ca^{++} stimulated ATPase, CPK and phosphorylase were 15 to 67% higher in men. In her review, Ready et al. (1981) could only report sex-related differences in phosphorylase, PFK and LDH (backward reaction) while no differences were found in MK and HK concentrations. Nevertheless, she concluded that men seem to possess higher glycolytic capacities. One may suppose that these higher

glycolytic capacities would give men an advantage in anaerobic sports such as strength training. However, more studies are needed before we can draw significant conclusions.

In summary, one can conclude that even with great increases in strength following training, women do not respond to the same extent than men do in terms of increase in lean body mass. Fiber type population and muscle quality appear to be the same in both sexes. However, the greater muscle mass of males, their higher glycolytic potential and the hormonal concentrations of androgens may contribute to greater body composition changes. The latter factor will be objects of a section of its own.

2.1.4) MECHANISMS OF MUSCLE HYPERTROPHY & ULTRASTRUCTURAL CHANGES RELATED TO TRAINING:

Muscular hypertrophy is the phenomenon by which lean body mass will increase following strength training. It is one phenomenon causing strength improvements although not the only one. Few studies were made in order to elucidate the underlying mechanisms causing hypertrophy. Unfortunately, most of them deal with experimentally-induced hypertrophy which may not be quite comparable to exercise-induced hypertrophy.

At the cellular level, hypertrophy results in an increased fiber area (Hettinger 1961). It has been found to occur mostly in FT fibers as a result of weight-training (Thorstensson et al. 1976, Gonyea & Sale 1982, MacDougall et al. 1982). The increased total muscle proteins (Hettinger,1961, Edgerton 1976, Booth 1982, MacDougall et al. 1982) along with the increased myosin synthesis (Clarke 1973, MacDougall 1982) are probably the two main factors

contributing to this increased fiber area. Booth (1982) suggested also that greater protein reutilization following some types of exercise may also occur. However, this increased protein synthesis is not necessarily followed by changes in mitochondrial volume within the muscle fiber (MacDougall et al. 1982). Theoretically, this means that the decreased ratio of mitochondria/myofibrils would suggest lower aerobic capabilities in strength-trained athletes.

A limited number of studies dealt with the histological changes occurring during the hypertrophy process. Penman (1970) looked at ultrastructural changes of human muscle following strength training in 3 college males. The subjects trained 10 weeks, 5 times/week on the following program:

leg extensions: 5 x 66% of 1-RM
5 isometric contractions
20 round trips on stairs

There was a mean 38% strength increase at the end of the program but no changes occurred in leg girth. Interestingly, there were 3 statistically significant changes occurring at the ultrastructural level: changes in myosin filaments concentration, in the distance between myosin and actin filaments and an increase in the number of actin filaments around the myosin. This is the only known study to report such changes. Therefore, they should be interpreted with caution especially since the physiological meaning of such changes are unknown. However, the hypothesis of such ultrastructural changes without hypertrophy is interesting since it may explain strength gains of females without the usual

increase in muscle girth. More studies are required before any definite conclusions can be made.

An attempt was also made to study and quantify the biochemical changes occurring with weight training (MacDougall et al. 1977). A group of 9 healthy male subjects were trained for 5 months using 4 triceps exercises (3-4 sets/exercise x 8-10 repetitions). There was a 28% strength increase following training. Significant increases ($p < .05$) in creatine, CP and ATP concentrations were found. Glycogen concentration was significantly increased (66%). High-energy phosphate sources and the glycogen reserves would therefore be the two energy sources used during weight training.

In another study, MacDougall et al. (1979) looked at the mitochondrial changes occurring in weight training in a group of 6 healthy males. Their training was 3 times/week for a duration of 6 months. Following training, there was a significant decrease (26%, $p < .05$) in the mitochondrial volume/myofibrillar volume ratio. It would therefore appear that there is a loss in the muscle's capacity for aerobic metabolism. This may have important applications for the strength training programs designed for aerobically trained athletes since that interference could have a detrimental effect on performance.

MacDougall et al. (1982) conducted another study to compare chronic histological changes following weight training. Comparisons were made between the experimental group (5 elite bodybuilders and 2 elite powerlifters) and the control group (5 "normal" subjects trained regularly for 6 months). The

experimental group had trained for an average of 7.1 years compared to 0.5 year for the controls. A rather surprising finding was that there were no significant differences between the two groups in fiber area of both fiber types. There was also a high incidence of pathological findings in the experimental group such as: centrally located nuclei, fatty pigments proliferation within the muscle fiber, enlarged cytoplasm spaces. However, since 6 out of 7 subjects had used or were still using anabolic steroids, so that conclusions about these pathological changes were difficult to make.

Recently, Friden et al. (1983) analyzed the ultrastructural changes occurring following intense eccentric exercise. Twelve male physical education students (25 to 27 years of age) pedalled for 20 minutes on a modified ergometer designed to allow eccentric muscle contractions only. The exercise ranged from 80 - 100% of max VO2. Biopsies from the vastus lateralis were obtained 1 hour after exercise as well as 3 and 6 days after. Histologically, frequent focal disturbances of cross-striated muscle were observed in 32% of specimens withdrawn 1 hour after exercise, in 52% of specimen withdrawn 3 days after the exercise and in 12% of samples obtained 6 after days. Electron microscopic evaluation revealed a marked streaming and broading of the Z band and, at some places, there was a total disruption of some fibers. Accumulation of polyribosome complexes adjacent to disruption sites was also seen in samples obtained 3 days after the exercise bout. It appears that Z disks are subjected to repeated stretching during eccentric work. Friden et al.

(1983a) concluded that this stretching may have induced excessive levels of intracellular calcium which in turn, have weakened the Z band. It is also possible that lysosomal enzymes liberated in damaged fibers may have initiated the degradation of myofibrillar material. Following these findings, Friden et al. (1983b) trained eccentrically 15 male students (24 ± 4 years of age) in order to see if muscular discomfort caused by eccentric exercises could be reduced by training. Training was performed 2-3 times/week for 4 and 8 weeks on a modified eccentric ergocycle. Biopsies were made within one hour after exercise and also 3 days later. This was repeated after 4 and 8 weeks of training. All subjects suffered from pronounced soreness in the first 2 weeks of training. The training program was sufficient to cause an increase of 375% in the eccentric work performed during training. Again, Z-band streaming was occasionally found in tissues sampled after training. However, the frequency of Z-band damage was clearly reduced after 4 and 8 weeks of training. Therefore, it appears that the Z-band adapts to repeated tensions although the Z-band width was not affected by training. The authors hypothesized that synthesis of a stronger protein chain may have occurred but this remains to be demonstrated.

Studies dealing with hypertrophy often use an animal model. However, these were not reviewed for the following reasons:

1) tenotomy is a drastic stress constantly applied on the muscle and this does not mimic the intermittent stress of weight-training routines (Gonyea & Sale 1982).

2) tenotomy causes a type of hypertrophy that does not result from voluntary exercises. We do not know to which extent the two kinds of hypertrophies are the same (Gonyea & Sale 1982).

3) biochemical and histological changes resulting from tenotomy-induced manipulations are precipitated and they might not be exactly the same as the ones resulting from intermittent workouts repeated over a long period of time.

In conclusion, it would appear that hypertrophy is one of the mechanisms responsible for strength increases. It is the result of an increase in fiber area, mostly in the FT fibers resulting from an increase in myosin and total protein content. Concomittant with protein increase, there is also an increase in the content of high energy phosphates and glycogen. Few ultrastructural changes are thought to occur. However, this will require further investigation.

2.1.5) SUMMARY:

In summary, this review of literature would indicate that:

1) For best strength gains, the use of 3-4 sets of 6-8 repetitions is recommended for beginners. Loads used should be near-maximal although an attempt to lift maximal loads (1-RM) should also be made on a regular basis, i.e. monthly. The best training frequency was reported to be 3-4 times/week, allowing normally a day of rest between workouts.

2) Women possess the same potential as men for strength

development of the lower body, especially when results are corrected for the lean body mass in females. However, the potential for upper body strength development in the female is rather limited.

3) Even with great strength increases, women do not normally show significant changes in lean body mass, at least in programs of short duration. However, female bodybuilders experience significant changes in lean body mass and this may be due to heavy training carried for expended periods of time (at least a year). Alternatively, physiological differences between the sexes may partly explain these results.

4) The phenomenon of hypertrophy is one of the mechanisms for strength increases. It occurs mostly in FT fibers, and is generally accompanied by increases in high-energy phosphates and glycogen stores. It has also been shown that adaptation of the neuromuscular component also occurs with strength training, making the individual more efficient when lifting.

SECTION II: BASIC PHYSIOLOGY

2.2.1) PHYSIOLOGY OF ANDROGENS

I) Synthesis/Production:

Cholesterol esters serve as the major reserve for cholesterol conversion into androgens (Tepperman 1980, Ganong 1983). In turn, cholesterol is also synthesized from glucose and fatty acids in steroidogenic cells (Bardin & Paulsen 1981). The conversion of cholesterol molecules to steroid hormones occurs in the mitochondria and it requires a desmolase enzyme complex and cytochrome P450 (White et al. 1978). The enzyme machinery necessary for that conversion is found in all tissues producing steroids (White et al. 1978). In females, most of the androgen synthesis occurs in theca cells of the ovaries (Ross et al. 1981, Berne & Levy 1983). The conversion of cholesterol to androgens involve several steps each catalyzed by an enzyme. Gonadotropins have a stimulatory action on steroid synthesis via activation of certain enzymatic steps (Berne & Levy 1983). Luteinizing hormone (LH) stimulates androgen synthesis by:

1) binding to the plasma membrane receptor
2) the complex formed increases adenylate cyclase activity which will in turn increase the cyclic AMP concentration
3) this leads to activation of the protein kinase and the subsequent steps for steroid synthesis (Berne & Levy 1983).

Recently, prostaglandins have been implicated as intermediates in LH actions (Berne & Levy 1983). The major action is

on the mitochondrial conversion of cholesterol to pregnenolone where it stimulates the removal of isocaproic aldehyde from the cholesterol molecule (Orten & Newhauss 1975, Berne & Levy 1983). Luteinizing hormone might also facilitate the movement of cholesterol from its esterified storage into the mitochondrial matrix and it may activate the 20, 22 desmolase reaction (Berne & Levy 1983). Follicule-stimulating hormone (FSH) acts in granulosa cells via membrane receptors to activate steroidogenesis involving aromatase (i.e. conversion of androgen to estrogen) and 3β-hydroxysteroid dehydrogenase-isomerase systems (Berne & Levy 1983, Hsueh et al. 1984).

In the female, it is estimated that 40-50% of the testosterone production is synthesized by the ovaries and adrenals and the remaining 50-60% is derived from conversion of adrenal precursors (Killinger 1970, Tagartz & Gurpido 1973, Vermeulen 1979, Tepperman 1980). Androstenedione is the major precursor for extraglandular production of testosterone (Tagartz & Gurpido 1973, Bardin & Paulsen 1981). The normal concentrations and production rates for females are listed below (Berne & Levy 1983):

	concentration (ng/dl)	production rate (μg/day)
androstenedione	150	3000
testosterone	40	250

II) Transport:

Similar to other steroids, androgens are transported in the plasma mainly attached to different proteins. Normally, in males, 2-3% of testosterone in circulation is unbound or free (Vermeulen 1979, Tepperman 1980, Ganong 1983). In females only 1-2% is unbound in the plasma (Vermeulen 1979). Of the remaining

97%, 40% is bound to a special carrier: the sex-hormone binding globulin (SHBG), another 40% is bound to albumins, and the remaining 17% is bound to globulins (Ganong 1983). The latter category include the corticosteroid binding globulin which also exhibit a low affinity for testosterone (Vermeulen 1973). The SHBG concentration is higher in females and this explains the lower free-fraction of testosterone (Vermeulen et al. 1969, Vermeulen 1979). The mechanisms affecting the SHBG concentration might therefore be important in the expression of the hormone's androgenic activity. It has been shown that estrogen secretion will increase that concentration whereas the androgen secretion will decrease it (Bardin & Paulsen 1981, Berne & Levy 1983). Therefore, the ratio of androgen/estrogen might be the most important factor determining the SHBG level (Vermeulen et al. 1969). This protein binds testosterone and estrogens but it does not bind androstenedione and DHEA (Bardin & Paulsen 1981, Ross et al. 1981). The hormone bound to the protein (SHBG) is not available for catabolism (Vermeulen 1969, Bardin & Paulsen 1981).

III) Metabolism/degradation:

There are 3 pathways for androgen metabolism:

1) some androgens are converted to a more potent androgen, mostly DHT (Killinger 1970, Wilson 1972, Minguell & Sierralta 1975, White et al. 1978, Bardin & Paulsen 1983). This reaction is catalyzed by an enzyme, the 5 α reductase (Minguell & Sierralta 1975, White et al. 1978, Bardin & Paulsen 1981, Ganong 1983). This reaction takes place in certain tissues but not in the

skeletal muscle or in the bone (Tepperman 1980, Ganong 1983). Also, conversion of androstenedione to testosterone accounts for 50-60% of the female testosterone concentration (Killinger 1970, Vermeulen 1979). This occurs by the removal of the 2 carbon-side chain of circulating adrenal steroids (White et al. 1978).

2) some androgens are conjugated to form a less active one that will be excreted in the urine (Vande Wiele et al. 1963, Killinger 1970, Orten & Newhauss 1975, White et al. 1978, Vermeulen 1979). These compounds are conjugated as glucoronides or sulfates in order to be excreted (Orten & Newhauss 1975). The major metabolites of testosterone are androsterone and aetiocholanolone after they undergo these transformations (Orten & Newhauss 1975, White et al. 1978).

3) some androgens are converted into steroids that possess a different biological activity than its precursor (Bardin & Paulsen 1981). The peripheral conversion of androstenedione to estrogen occurs by aromatization of the A Ring by the actions of the aromatase-enzyme complexes and the cytochrome P450 (Berne & Levy 1983).

The liver is the major site for androgen metabolism (Vermeulen 1973, White et al. 1978). Therefore, the factors influencing the hepatic metabolic clearance rate will have a great effect on androgen concentration. Among these factors, the hepatic blood flow is important (Vermeulen 1973), especially

during exercise where blood flow can be drastically reduced. The hepatic extraction of the hormone is another factor influencing the MCR (Vermeulen 1973). For example, 82-100% of the androstenedione in the plasma is metabolized in one passage through the liver compared to lower values for testosterone (Vermeulen 1973, Vermeulen 1979). The latter has more time to exert its biological activity. Finally, the binding of hormones to their proteins will also affect the hepatic MCR (Vermeulen 1979).

IV) Mechanisms of action/physiological effects:

Like all steroids, androgens enter passively into the cell by diffusion (Orten & Newhauss 1975, Vermeulen 1979, Tepperman 1980, Berne & Levy 1983, Ganong 1983). Inside the cell, it interacts with cytosol receptor and the complex formed moves into the nucleus (Vermeulen 1979, Tepperman 1980, Berne & Levy 1983, Ganong 1983). The complex will act on the nucleus to stimulate the transcription and the effective translation of the stored genetic information (Wilson 1972, White et al. 1978). This process takes place via an interaction at the DNA and RNA polymerase levels (Minguell & Sierralta 1975). The resulting stimulation of RNA synthesis will produce the increased production of specific ribosomal proteins (Wilson 1972, White et al. 1978, Tepperman 1980, Berne & Levy 1983, Ganong 1983).

Androgens have androgenic and anabolic properties and different steroids exert these properties to a different degree. Interestingly, the same biochemical mechanisms are responsible for the two properties (Bardin & Paulsen 1981, Berne & Levy

1983). The most noticeable anabolic property is an increase in protein synthesis in accessory sex tissues (Minguell & Sierralta 1975, Orten & Newhauss 1975, Ganong 1983) with a concomittant decrease in protein breakdown (Ganong 1983). Testosterone is also known for its moderate mineralocorticoid activities on several electrolytes: Na^+, K^+, Ca^{++} (Ganong 1983). The retention in proteo-nitrogen caused by androgens will produce the increase in muscle mass (White et al. 1978, Berne & Levy 1983).

2.2.2) PHYSIOLOGY OF ESTROGENS AND PROGESTERONE

I) Synthesis/Production:

Estrogenic steroids are synthesized from cholesterols or acetyl coA (Turner 1966, Guyton 1976). Pregnenolone is the common precursor to estrogen and progesterone synthesis (Turner 1966, Guyton 1976). The biosynthetic pathways are similar to the ones for androgen production (Orten & Newhauss 1975). Estrogens are classes of steroids formed with an 18-carbon atom skeleton compared to 19 for androgens (White et al. 1978). Estrogens are secreted by the ovaries (theca cells) and minute amounts are produced by the adrenals (Turner 1966, Guyton 1976, White et al. 1978). Of the relatively few estrogen molecules biosynthesized, 17-β estradiol is considered to be the one of major biological importance (Tagartz & Gurpido 1973, Orten & Newhauss 1975, Guyton 1976). The bulk of progesterone in the non-pregnant female is secreted by the corpus luteum during the latter half of the ovarian cycle (Guyton 1976, Meyer 1977, White et al. 1978).

The normal concentrations and production rates for females are listed below (Berne & Levy 1983):

	concentration (ng/dl)	production rate (μg/day)
estradiol:		
early follicular	6	80
late follicular	50	700
middle luteal	20	300
estrone:		
early follicular	5	100
late follicular	20	500
middle luteal	10	250
progesterone:		
follicular	100	2000
luteal	1000	25000

II) Transport:

Plasma estrogens are largely bound to carrier proteins, namely SHBG and albumins (Turner 1966). Progesterone is bound to several proteins: albumin, orosomucoid proteins and transcortin (Meyer 1977, White et al. 1978). The latter binds more strongly to progesterone than cortisol (Meyer 1977).

III) Metabolism/degradation:

The metabolites of 17-β estradiol are estrone and estriol (White et al. 1978). From the two, estriol is the predominant urinary end-product (Turner 1966). As for androgens, the liver is the major site of metabolic transformation (White et al. 1978). There is an hepatic conjugation of the hormone to form glucoronides and sulfate compounds (Orten & Newhauss 1975, Guyton 1976, Meyer 1977). Other metabolic transformations occur in other tissues (White et al. 1978). Part of the metabolites are excreted into the bile and the remainder is eliminated through the urine (Guyton 1976). It is estimated that 33-50% of estrogens are eliminated in the bile (Meyer 1977). Progesterone is degradated to other steroids with no progesterone effects,

mainly pregnanediol which is eliminated by way of the urine (Guyton 1976, Meyer 1977).

IV) Mechanisms of action/physiological effects:

The cellular mechanisms of action of estradiol is similar to that of androgen in promoting the anabolic effects (Guyton 1976). However, the effects of estrogens are almost exclusively on the reproductive target organs (uterus, breast) whereas testosterone has a more generalized effect (Guyton 1976). In general, estrogens are responsible for:

1) the growth of the genital tract (Tagartz & Gurpido 1973, Meyer 1977, White et al. 1978) and the proliferation of glandular tissue of the mucosal lining of the fallopian tubes (Guyton 1976).
2) the deposition of fatty tissue (Lloyd 1968, Guyton 1976, Meyer 1977).
3) an increased osteoblastic activity of bones via an increased calcium fixation and the early uniting of the epiphyses (Lloyd 1968, Guyton 1976, Meyer 1977).
4) an increased retention of calcium and phosphates but to a lesser extent than human testosterone (Guyton 1976).
5) an increased water retention (Meyer 1977, White et al. 1978).
6) a slight increase in body proteins as evidenced by a positive nitrogen balance (Lloyd 1968, Guyton 1976, Meyer 1977).

Specific receptors for estrogens have been identified in the

uterus, the vagina, the mammary glands, the adenohypophysis and the hypothalamus (White et al. 1978).

Progesterone acts synergistically with estrogens on certain tissues (Turner 1966, Meyer 1977). By far, the most important actions of progesterone is to develop secretory changes in the endometrium (Lloyd 1968, Guyton 1976, White et al. 1978). Progesterone also exerts a mild catabolic effect on the body's proteins (Lloyd 1968, Guyton 1976, Meyer 1977).

2.2.3) THE OVARIAN CYCLE

The ovarian cycle is a complex mechanism regulated by changing hormonal concentration. The length of a normal cycle varies depending upon the writers i.e. 25-35 days (Shangold 1984a) or 21-35 days depending mostly on the length of the follicular phase (Berne & Levy 1983). However, an average of 28 days is the generally accepted value. The menstrual blood flow normally lasts 5 days (Ganong 1983).

The complete ovarian cycle can be described in terms of 8 major features:

1) There is an increase in the FSH concentration during the first part of the follicular phase (Tepperman 1980, Berne & Levy 1983). During the beginning of the follicular phase, the LH/FSH ratio is approximately equal to 1 (Berne & Levy 1983).
2) This increasing FSH concentration in turn stimulates several follicles to develop but only one is normally destined for complete maturity (Tepperman 1980). The

"chosen" follicle produces its own estrogen thereby increasing its sensitivity to gonadotropins stimulation through the generation of FSH receptors (Tepperman 1980). During the second half of the follicular phase, FSH decreases modestly but LH gradually rises giving a LH/FSH ratio of approximately 2 (Berne & Levy 1983). The maturing follicle concurrently produces increasing amounts of estrogens.

3) Ovulation is preceeded by a very sharp and transient rise in gonadotropins with LH increasing much more than FSH so that the LH/FSH becomes approximately 5 (Berne & Levy, 1983). The peak in LH is elicited by estrogen stimulation and it induces rupture of the follicle i.e. ovulation (Tepperman 1980). This increase in LH is also responsible for the increased androgen synthesis that will be converted to estrogen (Shangold 1984a).

4) During the immediate post ovulatory period (i.e. the luteal phase), the ruptured follicle is transformed into the corpus luteum with cells producing large and increasing amounts of progesterone and estrogens (Tepperman 1980).

5) The high concentration of these two hormones inhibit the release of gonadotropins therefore both decrease progressively (Tepperman 1980). The most distinctive feature of the luteal phase is a 9-fold rise in progesterone emanating from the corpus luteum (Berne & Levy 1983).

6) When the corpus luteum degenerates, there is a sharp decrease in estrogen and progesterone causing a selective increase in serum FSH to initiate a new wave of follicle development and maturation (Berne & Levy 1983).

The cyclic pattern of hormones depends on cyclic changes in gonadotropins which are in turn regulated by positive and negative feedback from gonadal steroids (Berne & Levy 1983). It appears that gonadotropins secretions are regulated by a tonic center responsible for continuous secretion of these hormones and a cyclic center for periodic ovulatory surge of hormones (Tepperman 1980).

SECTION III: EFFECTS OF EXERCISE ON THE MENSTRUAL CHARACTERISTICS AND ON THE ENDOCRINE PHYSIOLOGY OF THE FEMALE REPRODUCTIVE SYSTEM.

2.3.1) Menstrual Abnormalities Associated with Rigourous Physical Training:

Two types of menstrual abnormalities are often associated with regular and rigorous training:

i) delayed age of menarche

ii) increased incidence of secondary amenorrhea

Investigations of these abnormalities have centered upon ballet dancers, runners and athletes participating in various sports.

Until recently, ballet dancing was not recognized as an intense athletic activity. Today, the rigourous training and the dedication of dancers is well-recognized. Warren (1980) studied the pubertal development of 15 dancers (12-15 years) over a period of 4 years. The dancers were compared to an age-matched control group (N=20). In addition, 20 music students with similar goal-oriented lifestyles, and patients (N=20) with a history of secondary amenorrhea were employed to compare ages of menarche. All groups were assessed for height and weight, breast development, and pubic hair growth. There was a striking delay in the onset of menarche in dancers (15.4 ± 1.9 years), compared to controls (12.5 ± 1.2 years), or to music students (12.9 ± 1.9 years, $p < .001$). Interestingly, the music students as a group had a high psychological stress profile comparable to dancers without the energy drain associated with dancing. Pubertal

progression measured by breast development using the Tanner scale was also markedly influenced by exercise. Most of the dancers showed delayed breast development interspersed with periods of rapid development associated with periods of relative inactivity. By age 13, all of the dancers showed little or no breast development (stage 1 or 2) while 75% of them were still at stage 3 at the time of menarche. Control girls took an average of 1.96 ± 0.93 years to progress from a stage 2 to stage 4 in breast development; dancers took only 8.6 ± 2.8 months. This accelerated development occurred during periods of relative inactivity without any significant changes in body weight or percentage of body fat. The development of pubic hair was normal despite the delayed breast development. Pubarche arrived at a normal age in dancers since 50% of dancers were at a stage 4 by age 13 and 70% were at this stage when menarche occurred (Tanner scale). Values were similar in the control group. Therefore, delayed breast development appeared to be associated with a significant delay in menarche. In another study of dancers, Abraham et al. (1982) analyzed the menstrual characteristics of 29 dancers (mean age 16.8 ± 0.8 years) before and after their first year in a professional ballet school. These dancers practiced 25-40 hours per week during the school years as opposed to 7-12 hours/week during their vacations (approximately 3 months). A relatively late age of menarche (14.8 ± 1.2 years) was observed for 25 dancers (86%) while the remainder suffered from primary amenorrhea at ages of 15.8 to 18.0 years.

In a questionnaire study of 89 professional ballet dancers

(Frish et al. 1983), 97% of the postmenarcheal dancers had a significantly later age of menarche when compared to the average age for the American population (13.7 ± 0.1 years vs 12.8 ± .05 years, $p < .001$). The authors concluded that hard training and the low caloric intake typical of these dancers were contributing factors to the delay of puberty.

In essence, the results of these studies show a consistently older age of menarche for dancers compared to the normal sedentary population.

In recent years, studies into the effects of long-distance running on the onset of puberty, have been undertaken. Frisch et al. (1981) compared a group of intercollegiate athletes (21 swimmers and 17 runners) to a group of 10 non-active women. The average age of menarche was 13.9 ± 0.3 years versus 12:7 yrs for the control group ($p < .001$). A comparison was then made between athletes who started training before the onset of menarche (N=18) and those who started after (N=20). Premenarcheally trained athletes had a mean age of menarche significantly higher than that of other athletes (15.1 ± 0.5 years vs 12.8, $p < .001$). It was estimated that every year of training before menarche retarded it by 5 months. This finding might explain the significant delay in menarche found in ballet dancers, since most dancers train from an early age. Indeed, there is now considerable evidence to support the proposal that premenarcheal training delays menarche (see Erdelyi 1965, see Baker 1981b, see Editorial 1982, see Jacobs 1982, see Shade 1983). Wackat et al. (1982) surveyed long-distance runners for their menstrual pattern.

Runners were divided into two groups according to their menstrual pattern: normal-cycling runners (N=19) and oligo/amenorrheic athletes (N=19). The onset of menarche was significantly later in the latter groups (12.9 vs 14.3 years, $p < .05$), and this could be related to the fact that the oligo/amenorrheic athletes started training around the time of menarche as opposed to 1.8 years later for normal-cycling runners ($p < .10$). In contrast, Schwartz et al. (1981) did not see any significant differences in the age of menarche for middle (N=25, 5-30 miles/week) and long-distance runners (N=41, more than 30 miles/week) compared to controls (N=10). From these studies, it appears that the age of menarche in runners is significantly later than sedentary controls. In the case of ballet dancers, the onset of training prior to menarche, appears to be of prime importance in the delay of puberty.

Erdelyi (1965) studied athletes from various sports and detected no differences in the mean menarcheal age of Hungarian athletes (13.6 years) compared to the Hungarian population. Malina et al. (1978) interviewed non-athletes (N=110) participating in physical instruction classes, highschool athletes (N=59), collegiate athletes (N=53), members of their respective intercollegiate teams and candidates of the U.S. Olympic volleyball team (N=18). Highschool and college athletes had a significantly later age of menarche when compared to the control population (12.5 to 13.7 vs 12.3 years respectively, $p < .001$). The authors proposed that exercise is responsible in part for delayed menarche and/or that early maturers may be

socialized away from sports. Malina et al. (1979) also interviewed 145 women, (mostly from Canada, the United States and Great Britain), who participated at the Montreal Olympic Games. The mean age of menarche (13.7 years) was significantly later than the population of their respective countries. The study also derived some interesting comparisons between sports:

Sport	age at menarche (±SE)
swimmers	13.1 ± .23
jumbers/hurdlers	13.4 ± .64
rowers	13.7 ± .15
runners	14.3 ± .39
gymnasts	14.5 ± .25
others	13.1 ± .20
Total	13.7 ± .12

Gymnasts, runners and rowers attained menarche significantly later than swimmers. No explanations were given for these differences. However, one can speculate that these differences may be due in part to a particular physique or to a particular training program associated with certain sports. Recent studies carried out with different groups of athletes (Malina et al. 1978, Malina et al. 1979) again confirmed the effects of exercise in delaying menarche. Furthermore, specific sports appear to cause a higher incidence of late menarche than others.

Therefore, one can conclude that the later age of menarche is characteristic of most groups of athletes. In most studies reviewed, the test subjects appeared to train regularly and intensely as judged by their level of performance or training schedule. It is possible that a certain training threshold must be obtained before there is any delay on menarche. Of particular interest is the impact of strenuous premenarcheal training on the

onset of puberty. It is interesting to note that breast development as well as menarche are most affected by severe training, while pubarche remains generally unaffected. This would suggest that different mechanisms are involved in the development of different sex characteristics (Warren 1980).

Vigorous physical training after menarche is associated with other menstrual disorders.

The incidence of secondary amenorrhea, characterized by menstrual absence for 3 consecutive months, is a common problem associated with strenuous training in women. The incidence of secondary amenorrhea in ballet dancing was described in a few studies. Abraham et al. (1982) studied the incidence of menstrual disorders in 29 dancers, before and after their first year in a professional school. The table below shows the changes in menstrual status over time:

status	6 months before school	first 6 months	12 months
Regular (25-34 days)	6	3	5
Irregular but frequent (14-24 or 35-45 days)	2	0	1
Oligoamenorrhea (7-11 weeks)	6	5	0
Secondary amenorrhea (no menses for 3 months)	11	17	20
Primary amenorrhea	4	4	3

The incidence of secondary amenorrhea was initially high (38%) but a clear trend toward a greater incidence of amenorrhea (69%) after 12 months of professional ballet dancing is evident. From the group, 23 dancers could have shown an improvement in the regularity of their cycle but only 3 did so. The menstrual pattern of 14 students could have deteriorated (i.e. a reduced

frequency of menses) during the 12 months and 10 subjects did so. In this study, the high incidence of secondary amenorrhea (38%) was further augmented by an even more rigorous dancing program than the one followed previously. The data also shows a constant worsening of the menstrual status over time. The data of Frisch et al. (1983) was not so clear-cut. Incidence of secondary amenorrhea was 15% while 30% and 33% of the dancers had irregular and regular cycles respectively. Calabresse et al. (1983) studied a professional ballet company (N=29) and advanced ballet dancers (N=5). The professional dancers trained 40 hours/week as compared to 30 hours/week for the students. The incidence of secondary amenorrhea (defined, in this study, as absence of menses for 90 days or more and irregular cycles were defined as one menses every 35-90 days in duration) is given in the table below:

	present	absent
secondary amenorrhea	15	19
menstrual irregularities	17	16

Amenorrhea was strikingly high among dancers: When amenorrhea does not occur, the menstrual status seems to worsen (more infrequent and irregular menses) in most cases as demonstrated in the study described by Abraham et al. (1982) described earlier.

Scientific interest in the incidence of amenorrhea among runners is fairly intense. Baker et al. (1981b) analyzed the incidence of secondary amenorrhea (18-42 years old) with normal menses prior to the beginning of heavy training. Subjects were between 10 to 70 miles per week. Six runners became amenorrheic

following the initiation of heavy training and 3 others became amenorrheic during the study for a total incidence of amenorrhea of 39% amongst runners from that study. In a study of 83 runners attending various running clinics and competing in local races, Schwartz et al. (1980) observed an incidence of amenorrhea of only 15%. However, in this instance, the experimental group consisted mostly of recreational joggers which do not meet the criteria of being intensive trainers. In order to establish sports-related differences in the incidence of amenorrhea, Feicht-Sanborn et al. (1982) studied swimmers (N=197) and runners (N=237). In addition, cyclists (N=33) competing in a world-class event were also surveyed. The incidence of amenorrhea was; 12.1% for cyclists, 12.3% for swimmers and 25.7% for runners. Aged matched controls displayed a 2% incidence. In runners, there was a positive correlation ($p < .001$) between the frequency of amenorrhea and the number of miles run per week. No explanation is available regarding these differences between groups of athletes. In a study of marathon runners, Dale et al. (1979) obtained the following results:

	controls	runners (>30 miles/week)	joggers (5-30 miles/week)
Average # of menses/year	11.8 ± .92	9.16 ± 4.04	10.32 ± 3.23
Current oligo/ amenorrhea	2/54 (4%)	30/89 (34%)	5/22 (23%)

As shown, physical exertion appears to result in amenorrhea as demonstrated by a higher incidence ($p < .05$) of oligo/ amenorrhea in runners. They also had significantly less number of periods/year ($p < .05$) when compared to controls. Joggers

showed an intermediate pattern between both groups. The authors concluded that the severity of physical exertion is proportional to the degree of physical effort as illustrated commonly by the number of miles run per week (see Baker 1981b, see Editorial 1982, See Erdelyi 1965, see Hale 1983). Therefore, one would assume that incidence of amenorrhea is even higher amongst actual competitive runners. Indeed the incidence in competitive runners (more than 50 miles/week) is increased to 30-50% (see Baker 1981b, Hale 1983, Jacobs 1982, Wall et al. 1983). Nevertheless, there are reports of a failure to observe changes in the incidence of amenorrhea following strenuous training programs. For instance, Boyden et al. (1982) studied 14 women (mean age 29 years) who were enrolled in a 14-15 month training program to complete a marathon. In an attempt to minimize drop-outs, subjects were initially running 15 miles/week. Subjects were tested when the weekly mileage was increased by 30 and 50 miles (Δ30 and Δ50). Surprisingly, no subject developed secondary amenorrhea during the course of this training program. However, 93% subjectively reported minor menstrual changes with an average decreased blood loss of 80%. The authors suggested that this is a reflection of a decreased estrogen status.

In summary, it would appear that most categories of female runners are at an increased risk of suffering exercise-induced amenorrhea. Furthermore, the incidence is higher in competitive runners compared to joggers, and it increased with the degree of effort such as the number of miles completed per week.

Other groups of athletes have been studied in relation to

the incidence of secondary amenorrhea. Zaharieva (1965) was among the first to look at the incidence among athletes (N=66) competing at the Tokyo Olympics. Subjects included those from track and field, swimming and gymnastic competition, with the majority of subjects being close to 25 years of age. Of those tested, 93% had regular cycles, and 6% had irregular cycles with most of the subjects being under 16 years of age. The menstrual profile as determined by the length of menses and time between cycles was normal in most athletes. Interestingly, Malina et al. (1978) (see preceding text) found no differences between control, highschool, collegiate and olympic athletes regarding the incidence of amenorrhea. More recent studies did show, on the average, a higher incidence of amenorrhea amongst female athletes. Carlberg & Riedesel (1979) surveyed varsity athletes (N=81), dance students (N=72) and biology students (210) who served as controls. Athletes showed a higher ($p < .002$) incidence of amenorrhea compared to dancers (3%) or biology students (2%). Interestingly, amenorrhea was more frequent in the best athletes of this group (5 out of 8 amenorrheic athletes were among the top 25% performers, $p < .01$). The study of top German authors also reported a higher incidence of amenorrhea in athletes (Weicker et al. 1984). Athletes (N=97) randomly selected from 300 german top athletes were studied in relation to various menstrual disorders. Primary amenorrhea affected 8% of the group while secondary amenorrhea and anovulatory cycles accounted for 23% and 21% respectively of the athletic population. The incidence of secondary amenorrhea was higher in

athletes with high training volumes. A very similar group of athletes was studied in Norway. Øian et al. (1984) found that the incidence of amenorrhea was 10% with another 21% of the athletes on various Norwegian teams suffering from irregular cycles.. From the studies reviewed, it appears that varsity or nationally-ranked athletes are at a slightly higher risk for amenorrhea than sedentary controls. The incidence of amenorrhea amongst players from various sports is intermediate between sedentary controls and ballet dancers/competitive runners.

From the literature, two problems appear to be particularly associated with rigourous participation in sports:

i) a delayed onset of menarche

ii) a higher incidence of secondary amenorrhea

An increased incidence of these two disorders is a relatively consistent feature of various groups of very active women (eg. ballet dancers, runners, varsity athletes). However, even amongst these groups, dancers and runners show normally a later age of menarche and a higher incidence of amenorrhea than other athletes. Irrespective of the physical activity, premenarcheal training appears to be particularly important in the delay of menarche as well as in increasing the likelihood of amenorrhea (see Baker 1981a, see Erdelyi 1965, Baker 1981b).

One should realize that exercise-induced amenorrhea represents only the end of the continuum of menstrual disorders. However, more subtle physiological changes may occur before amenorrhea sets in. It is therefore possible for an athlete to experience various abnormalities before the cessation of menses.

Shangold (1984b) identifies 3 steps leading to exercise-induced amenorrhea:

Condition	Clinical Status
-resting conditions	-normal follicular & luteal phases
-as exercise begins	-prolonged follicular phase & short luteal phase
-with increasing exercise intensity	-estrogenic anovulatory oligomenorrhea
-with prolonged intense training	-hypoestrogenic amenorrhea

The short luteal phase is a common phenomenon that accompanies sport participation. An example of alterations in the luteal phase is presented in the table below from the study by Bonen et al. (1981):

	teenage swimmers (15-19 yrs)(N=4)	teenage controls (16-18) (N=4)	adult women
Menstrual cycle	20.0 ± 1.8 days	28.3 ± 6.4	28.5 ± 3.4
Follicular phase	unspecified but no difference between groups		
Luteal phase	4.5 ± .6	7.8 ± 3.0	13.4 ± 1.7

Swimmers showed a significantly shorter ($p < .05$) menstrual cycle when compared to both control groups. As shown, the follicular phase was unchanged by exercise while swimmers showed a very short luteal phase ($p < .05$) when compared to adult women. In turn, teenage controls had a shorter luteal phase ($p < .05$) than adult women. Physiologically, it remains unclear as to what causes a shortening of the luteal phase. Hormonal data from this study will be discussed later in an attempt to explain such findings. In a case study, Shangold et al. (1979) reported basically the same finding with regard to the luteal phase. One

woman (30 years old) was studied during a control cycle, i.e. she ran 26 miles/week during the follicular phase of her cycle only. A total of 18 "training cycles" (20 miles/week in both phases) were then compared to the control cycle. During training, the length of the luteal phase was inversely related to the weekly mileage ($r= -0.70$, $p < .005$). The luteal phase was 13-14 days in cycles in which running averaged less than 5 miles/week while it lasted 9 days or less in cycles of 35 miles/week or more. Furthermore, an inverse relationship between the length of the luteal phase and the distance ran during the first week of the follicular phase was observed ($r= -0.81$, $p < .001$). It is however difficult to extrapolate any definite conclusions from a case study. However, a shortened luteal phase was also reported in other studies (see Cumming & Rebar 1983).

Therefore, a shortened luteal phase occurs in a certain portion of the female athlete population. Although no known physiological mechanisms can presently explain such shortened luteal phase in athletes, one may assume that such imbalance in phase length could eventually lead to euestrogenic anovulatory oligomenorrhea and, finally, to hypoestrogenic amenorrhea.

It appears that in athletes, several steps may lead eventually to amenorrhea. Furthermore, clinical evaluations of patients suffering from exercise-induced amenorrhea has yielded two types of amenorrhea (Shangold 1980). However, this classification should be considered as preliminary since no studies can presently confirm such hypotheses.

1. hypoestrogenic amenorrhea: Apparently, this would be

the most common type of amenorrhea associated with exercise. It occurs in women of very low body weight and/or low body fat. The low estrogen found probably results from inadequate gonadotropin stimulation or from inadequate ovary responsiveness.

2. euestrogenic anovulation: This type of amenorrhea would originate from excessive androgen production by either the ovaries or the adrenals. Elevated androgen levels would in turn lead to anovulation. In this situation, LH levels are normally slightly elevated and the normal estrogen concentration could probably result from aromatization of androgens to estrogens in the adipose tissue.

2.3.2) ACUTE ENDOCRINE CHANGES IN RESPONSE TO EXERCISE:

Exercise is a "stress" which leads to hormonal changes. Endocrine responses to exercise are controversial because they are difficult to control. Furthermore, inherent interindividual variations in endocrine response to exercise further complicates the picture from a statistical standpoint. A review of the gonadotropins, estrogen and progesterone, prolactin and androgens will be presented in response to acute exercise.

A) Gonadotrophic response to short-term exercise:

The gonadotrophin response to exercise is of importance since LH and FSH have of course, marked effects on the steroid secretion at the level of the ovaries and the corpus luteum. Baker et al. (1982) studied the hormonal response of women (N=6) with regular menstrual cycle immediately after (within 20

minutes) their participation in a 10-mile race. These samples were compared with samples obtained 12-24 hours after the race. The acute exercise induced a significant ($p < .05$) increase in LH concentration (pre: 10.2 ± 0.7 mIu/ml vs 18.9 ± 3.2 mIu/ml after exercise). However, FSH was not changed by acute exercise therefore leading to a decreased FSH/LH ratio (0.44 vs 0.91 post-exercise, $p < .05$). The authors suggested that this shift in the FSH/LH ratio along with the increased prolactin concentration may predispose athletes partly to amenorrhea. A comparison between 5 untrained subjects, 5 runners (regular menses) and 6 amenorrheic runners reveal also significant increases in gonadotrophin concentration (Cumming et al. 1981). The exercise bout consisted of 12 to 18 minutes of incremental exercise on a bicycle ergometer. Serial samples were obtained every 5 to 15 minute intervals from 30 minutes before to 90 minutes after the exercise. There was a significant increase in LH concentration during the anticipatory phase and exercise further augmented that rise. FSH also increased following the exercise bout ($p < .01$). Bonen et al. (1979) utilized an exercise protocol of slightly longer duration and found different results. Ten young women exercised on an ergometer for 30 minutes at a mean exercise intensity of 74% VO2 max. Blood samples were obtained 15 minutes before, at mid, and following exercise. Significant increases in estradiol and progesterone occured but no significant changes in gonadotrophins were observed. If this is the case, one would wonder about the mechanisms causing an increased steroid concentration without

concomittant stimulation of the gonadotrophins. Keizer & Bonen (1984) submitted 7 healthy and moderately trained women (mean age: 22 years) to a prolonged exercise on a bicycle ergometer until exhaustion (15 minutes of exercise at 60%, 70%, 80% of VO2 max and 90% of VO2 max until exhaustion). All subjects had normal menstrual cycles and they were tested between the 7th and 10th day of their cycle. Values were corrected for hemoconcentration. Individual variations were too great to permit definite statistical comparisons. During and shortly after exercise, the pulse amplitude and increments of LH were increased, but not in FSH. No clear picture therefore emerged from that study. One can also appreciate the interindividual variations in endocrine status that exist between individuals. Finally, Jurkowski et al. (1978) also studied the gonadotrophin response following an exhaustive exercise (20 minutes at 30-35% VO2 max, 60-66% VO2 max and 85-90% VO2 max until exhaustion). All subjects were in good health and fairly active (N=9). Each of them were tested during the follicular (6-9 days after the onset of menses) and during the luteal phase (6-9 days after ovulation). Blood samples were obtained before, during and 5 to 10 minutes following exercise. No significant changes were seen in LH concentration in either phase of the cycle. There was a significant increase in FSH only when the resting state and the exhaustive state were compared.

In summary, gonadotrophin response to acute exercise remain unclear. Half of the studies reviewed showing a significant increase in either LH or FSH with the remainder showing no increase. It is possible however that gonadotrophin changes are

related to the estrogenic status of the subjects as suggested by Keizer & Bonen (1984). Therefore, more attention should be given to gonadotrophin changes.

B) Estradiol and progesterone responses to short-term exercise:

Estradiol and progesterone are of prime importance to normal menstrual cycle. Change in gonadotrophin following exercise undoubtedly affects the concentration of both steroids. Cumming et al. (1981) reported a significant ($p < .01$) rise in estradiol concentration following 12 to 18 minutes of progressive exercise on an ergometer. Significant increases ($p < .05$) in both steroids were also reported by Bonen et al. (1979) following 30 minutes of exercise on the bicycle ergometer. In this study, most of the subjects were tested during the luteal phase (2-6 days before onset of menses) while others were also tested during menses. On average, there was an increase of 38% for progesterone and 14% for estradiol. Increases in estradiol occur when the exercise intensity approached 60% of VO2 max or higher. For progesterone, increases were significant at intensities of 70% VO2 max or higher. Thus, there appears to be a threshold above which significant increases in steroid concentration occur. Wurster et al. (1984) reported significant progesterone increases in German track and field athletes (N=52) and marathon runners (n=5) exercising on a treadmill. Pre-ovulatory progesterone increases ranged from 32 to 77% while post-ovulatory increases ranged from 14 to 79%. The authors claimed similar increases in estradiol. The table below gives the magnitude of increases

for progesterone according to the exercise mode:

	n	Basic value	increase	% increase
Follicular:				
short-distance	12	0.31	.24	77
middle-distance	9	.48	.37	77
long-distance	8	.84	.28	33
untrained	15	1.04	.33	32
Luteal:				
short-distance	4	14.5	2.0	14
middle-distance	2	13.0	3.4	26
untrained	6	10.2	8.1	79

It is however difficult to explain such pre-ovulatory progesterone increase. One may speculate that a reduced hepatic clearance of progesterone is a possible mechanism causing the increase.

In contrast to Wurster's findings, Jurkowski et al. (1978) found that the ovarian steroids changes during exercise are relatively dependent on the phase of the cycle. Most of the subjects (N=9) were physical education students and were quite active. Each subject was tested during the follicular phase (6-9 days after onset of menses) and during the luteal phase (6-9 days after ovulation). Subjects were tested on the ergometer with a progressive exercise to exhaustion (20 minutes at 30-35% VO2 max, 20 minutes at 60-66% VO2 max and to exhaustion at 85-90% VO2 max). As opposed to previous findings, progesterone showed no recordable changes during the follicular phase while the increase during the luteal phase is significant at all exercise intensities ($p < .05$ at 30-35%, $p < .02$ at 60-66%, $p < .01$ at exhaustion). Furthermore, the increase of progesterone during the exhaustive bout is significantly higher ($p < .05$) than the one observed during the mild exercise (30-35% VO2 max), a finding

that corroborates the importance of a reduced hepatic MCR in the increased steroid concentration. Furthermore, estradiol values were also slightly influenced by the menstrual phase. During the follicular phase, a significant estradiol increase was only significant at exhaustion while significant increases during the luteal phase were seen at 60-66% VO2 max ($p < .02$) and at exhaustion ($p < .01$).

Keizer et al. (1980) tried to determine what was the course for the estradiol increase during acute exercise. A group of 6 women (mean age 21 years) with regular menstrual cycles were tested on a bicycle ergometer (70% of VO2 max for 10 minutes followed by 30 minutes at 25%). Half of the subjects were fairly active physical education students while the other half were highly trained runners. Injection of 8 uCi of tritiated estradiol was followed by baseline infusion measurements in an attempt to determine the changes in metabolic clearance rate (MCR) during exercise. As expected, there was a sharp and consistent decrease in the MCR of estradiol in all subjects following 10 minutes of exercise at 70% VO2 max. The average decline was 37% (range 18-67%). The authors concluded that the increased estradiol concentration during exercise was mostly due to a decreased metabolic clearance rate. Furthermore, the MCR remains depressed for at least 30 minutes upon cessation of exercise (see Bonen 1984). Therefore, a reduced MCR appears to be the main contributing factor for the increased concentration of estradiol and probably of progesterone especially following acute exercise. Acute rises in estradiol were also reported in

other reviews (see Bonen 1984, see Shangold 1984a). These findings are however, not universal. Baker et al. (1982) in an experimental design described previously did not report significant increase in estradiol in the samples of 6 runners obtained within 20 minutes after exercise. Furthermore, no acute and significant increase in estradiol was reported following a long and strenuous exercise (Loucks & Horvath 1984). In their study, amenorrheic (N=7) and eumenorrheic (N=8) runners running more than 35 miles/week and with a mean percentage of body fat lower than 27% were studied. The exercise consisted of 40 minutes of running (80% VO2 max) on a treadmill during the 3rd to the 8th day of the follicular phase. The lack of increase in estradiol concentration is rather surprising especially when one considers that the intensity and duration of this exercise should decrease the estradiol's metabolic clearance rate quite significantly, thereby increasing its concentration.

In conclusion, most (Bonen et al. 1979, Cumming et al. 1981, Keizer et al. 1980, Jurkowski et al. 1978, Wurster et al. 1984, see Bonen 1979, see Shangold 1984) but not all the studies (Baker et al. 1982, Loucks and Horvath 1984) has shown estradiol increases following acute exercise. Progesterone increased in all studies reviewed (Jurkowski et al. 1978, Wurster et al. 1984). It may be reasonable to assume that the magnitude of the increase is dependent on the phase of the menstrual cycle as demonstrated by Jurkowski et al. 1978. Finally, it appears that most of the steroids increase following acute and intense exercise would be secondary to a reduction in MCR (Keizer et al. 1980).

C) ANDROGENIC CHANGES DURING EXERCISE:

Androgens might be of importance in the etiology of exercise-induced amenorrhea (see previous section). Their importance may be linked to the capacity of adipose and muscular tissue to aromatize androgens to estrogens (Longcope et al. 1969, Longcope et al. 1978).

Shangold & Levine (1982) reported a 37% increase in testosterone following a 30 minute run. However, all post-exercise values remained well within the normal range for adult females. Baker et al. (1982) similarly found a significant increase in 6 runners when post-exercise samples (within 20 minutes) are compared to samples obtained 12 to 24 hours after the race. Testosterone, androstenedione and dehydroandrosterone were all significantly increased. Cumming et al. (1981) studied the androgenic response of "regular-cyclic" subjects (N=5) to an incremental workload on the ergometer (12-18 minutes). Surprisingly, testosterone was increased before the onset of exercise and was further augmented by it ($p < .01$). Furthermore, androgens of less biological potency (i.e. androstenedione and dehydroepiandrosterone) were also significantly elevated ($p < .01$) following exercise. However, such findings are not universal. For instance, Loucks & Horvath (1984) reported no significant increase in testosterone in amenorrheic and eumenorrheic runners after 40 minutes of exercise on a treadmill. The androgen of adrenal origin, dehydroepiandrosterone, was however increased in both groups of runners while androstenedione only increased in eumenorrheic runners. The authors suggested

that the increased production of androgens were due to adrenal rather than ovarian hyperfunction. Sutton et al. (1973) found the intensity of exercise to be very important in the magnitude of androgen increase. Female swimmers (N=4, mean age 14.7 years) were submitted to exercise bouts of various intensities. Only the maximal intensity workout produced a significant increase ($p < .05$) in testosterone (82 ± 5 ng/100 (SEM) ml pre vs 98 ± 5 ng/100 ml post).

Very few studies have been pursued to determine the hormonal response to weight training. Even fewer studies utilized women as subjects. Furthermore, the effect of an anaerobic and intermittent activity such as weight training may trigger a slightly different hormonal response than aerobic training previously reviewed. The pre- and post-exercise testosterone concentration was determined in 3 groups of subjects (Fahey et al. 1976) who underwent weight training:

I) (N=10) university male students (mean age: 20 years); 5 were experienced weightlifters and 5 were physical education students

II) (N=13) male teenagers (mean age: 16 years)

III) (N=5) university female students (mean age: 22 years)

An acute and significant increase in testosterone was seen only in group I. However, the use of different training routines for group I vs group II and III includes another variable and therefore warrants any definite conclusions about the lack of hormonal response in females.

Hetrick and Wilmore (1979) analyzed the hormonal response of a male group (N=19) and a female group (N=35). Both groups were

following an 8 week program not specified in terms of exercises, intensity, etc. Again, there were no differences in pre-, intermediate- and post-training androgen levels in either groups.

Weiss et al. (1983) measured the concentration of testosterone and androstenedione in both groups of males (N=20) and females (N=20). All tests were performed during the early follicular phase since it is a period of minimal variability in blood androgen levels. The results are shown below:

testosterone ($ng.ml^{-1}$)

	pre	post-exercise increase	% increase	P value
men	3.51 ± 0.24	0.76	22%	$p < .01$
women	0.36 ± 0.04	0.06	17%	NS

androstenedione ($ng.ml^{-1}$)

	pre	post
men	0.88	increase of 8% (NS)
women	1.26	increase of 11% (NS)

There was only a significant increase in testosterone levels in the males. The magnitude of the absolute response was 12.7 times greater in males compared to females. However, expressed in terms of percentage increase above resting level, the results are quite similar with 21.6% and 16.7% for males and females respectively. He concluded:

> "Whether or not the greater absolute testosterone response by men, as found in the present investigation, contributes to a difference in the potential of men and women for work-induced skeletal muscle hypertrophy is unclear." (Weiss et al. 1983, p.417).

Therefore, most studies (Baker et al. 1982, Cumming et al. 1981, Shangold et al. 1981, see Shangold 1984) reported significant increases in androgens following acute aerobic exercise. The physiological basis for such increases is unclear. Sympathetic activation of the adrenal cortex and a reduced hepatic metabolic clearance rate appear to be important. However, in spite of a significant increase following exercise, most values remain within the normal range for females (Shangold et al. 1981). Androgens do not appear to be increased by weight-training exercises (Fahey et al. 1976, Hetrick & Wilmore 1979, Weiss et al. 1983) in females.

SUMMARY:

A number of conclusions can be drawn from the literature reviewed herein. These are summarized below. Acute exercise could be considered a powerful stimulus for specific hormones.

The gonadotrophin response to exercise remains controversial. Some studies showing increased either LH or FSH whereas others did not report changes. One possibility remains that gonadotrophin changes are related to the estrogenic status of the individual (Keizer & Bonen 1984). Since there are great interindividual variations in estrogen status (especially in athletes), one could theoretically expect wide variations in gonadotrophin response to exercise. More studies monitoring the cyclic nature of gonadotrophins over longer periods of time are needed to further elucidate LH and FSH behaviours.

Ovarian steroids (i.e. estradiol and progesterone) show normally increasing values with exercise. A number of studies

have shown a significant estradiol increase during an acute bout of exercise. It appears that this increase is mostly due to a substantially reduced metabolic clearance rate rather than an increased secretion (Keizer et al. 1980). Progesterone showed significant increased in all the studies reviewed. Jurkowski et al. (1978) found that both steroids are affected by the phase of the menstrual cycle.

Androgens are, in most instances, augmented by acute aerobic exercise. However, the statistically significant post-exercise increases reported in the studies reviewed are well within the normal female range (Shangold 1981). Furthermore, androgens of lower biological potency (i.e. androstenedione and dehydroepiandrosterone) are also increased following exercise. It is possible that the increased androgen production is due to adrenal rather than ovarian activation (Loucks & Horvath 1980).

2.3.3) BASAL ENDOCRINE ADAPTATIONS TO EXERCISE:

In general, exercise induces acute changes in hormonal levels. However, it is difficult to make any significant conclusions regarding long-term endocrine changes related to acute exercise regimens, i.e. that acute hormonal response to exercise does not necessarily mimick the long-term effects of exercise. Furthermore, it is important to establish the basal hormonal values in long-term trained athletes in order to assess the possible repercussions on the reproductive system. The effects of chronic and intense exercise on the basal hormonal levels will be reviewed in relation to the clinical repercussions resulting for such changes.

A) Basal gonadotrophin levels in long-term trained subjects:

There is a growing interest in the impact of high-intensity exercises on the hypothalamus-pituitarian axis. Some authors propose that a part of exercise-induced amenorrhea may be due to changes in this particular axis.

Since the level of competition and the demand of training far exceeded those of several years ago, Dale et al. (1979) undertook a study to define the characteristics of long-term trained runners as well as to define their endocrine profile. In their study, women competing in a marathon (N=168, age range 18-48 years) were divided into 3 groups:

1) runners (those running more than 30 miles/week at a good pace and doing also speed training)
2) joggers (those running 5 to 30 miles/week at a slow and easy pace)
3) controls from hospital personnel

Endocrine data comprising 1 sample every 7th day for 4 weeks were obtained from 18 controls, 14 runners and 6 joggers, and questionnaires together with other measurements were performed on the remainder of the subjects. Their results indicated that the 3 groups were quite similar with respect to age, height, education and occupation.

Runners were defined as anovulatory when progesterone levels remained below 2.0 ng/ml in the 4 consecutive samples. Ovulatory cycles were characteristic of 85%, 67% and 50% of controls, joggers, and runners respectively. In both groups of athletes anovulatory runners showed consistently low to low-normal

gonadotrophin levels for both FSH and LH. In addition, both gonadotrophins did not show a cyclic pattern, characteristic of a normal menstrual cycle. The authors concluded that the gonadotrophic pattern was indicative of primary or secondary hypothalamic-pituitarian dysfunction. When relatively young athletes are studied, the effects of exercise become even more apparent. Weicker et al. (1984) looked at 97 athletes (17 ± 7 years) randomly selected from a group of 300 German top athletes. In this group, 8% of the athletes sufferred from primary amenorrhea, 23% from secondary amenorrhea, 21% were anovulatory while the remainder of the group had normal cycle. When training exceeded 10 hours per week, hormone levels were significantly lower. The authors concluded:

> "The results of the hormonal investigation indicated clearly that the concentrations of gonadotrophins and ovarian hormones depend on intensity and duration of the training as well as on the onset of competitive sports." (p.202)

Swimmers represented a good study group due to their rigorous training schedules, especially at a young age. Russell et al. (1984a) studied 6 young swimmers (mean age 14.8 years), adult runners (30.9 years, N=7) and controls (25 years, N=7) selected to match the other groups with regard to height, weight and percentage of body fat. Swimmers became oligomenorrheic (no menses for the last 2 months) when training was very intense (5 days/week, up to 5 hours/day). Runners had normal cycles and they ran 6 days/week for 25-30 miles. The LH surge, a prerequisite for successful ovulation, was present in 1 swimmer,

and in all runners and controls. Furthermore, basal LH levels were significantly lower in swimmers when compared to controls. However, no changes were seen in FSH values between the 3 groups. The table below summarizes the gonadotropin values for all groups:

	swimmers	runners	controls
FSH	6.8 ± 7.0	6.11 ± 1.8	7.6 ± 2.0
LH	32.3 ± 8.8	39.0 ± 29.9	79.0 ± 88.0

The authors suggested that the low LH levels in oligomenorrheic swimmers could be related to increased levels of β-endorphins and catecholestrogens. This suggestion will be discussed in more detail further on. In a second study, Russell et al. (1984b) studied 13 swimmers during peak training (100,000 yards of swimming per week) and during "moderate" training (30,000 yards/week). Heavy training induced oligomenorrhea in 5 athletes and normal menses resumed following a reduction in training. Endocrine data of swimmers (mean age 14.4 years) were compared to that of a control group (19.0 years, $p < .01$). Despite the lack of significant changes in body fat between both training regimens, there were significant reductions in gonadotrophin values during periods of heavy-training. The table below summarizes the median gonadotrophin changes:

changes	swimmers		controls
	intense training	moderate training	
LH(mIU/ml)	*10.9 ± 2.8	22.9 ± 5.7	23.1 ± 10.5
FSH(mIU/ml)	6.54 ± 2.1	**20.2 ± 5.1	***10.9 ± 3.5

*different from moderate swimming and from control ($p = .02$)
**different from intense swimming ($p = .001$)
***different from intense swimming ($p = .04$)

Thus, despite the fact that young age per se could affect gonadotrophin secretion it appears in this study that variation in exercise intensity can have a substantial effect on gonadotrophin release. Bonen et al. (1981) obtained different findings. In this study, 4 teenage swimmers (15 to 19 years) were compared to a teenage control group (N=4, 16 to 18 years of age) and to an adult control group (number of subjects and age is undefined). The first striking finding was that training and age markedly altered the menstrual cycle.

	swimmers	adults	teenage
cycle length(days)	***20.0 ± 1.8	28.5 ± 3.4	28.3 ± 6.4
follicular phase (days)	----------no difference----------		
luteal phase(days)	4.5 ± .6*	13.4 ± 1.7	7.8 ± 3.0*

*significantly different from teenage control ($p < .05$)
**significantly different from adult controls ($p < .05$)
***significantly different from both control groups

Before the LH peak (i.e. during follicular phase), LH patterns were relatively similar with LH levels being higher in the swimmers when compared to both control groups ($p < .05$). During the luteal phase, differences between all groups were not significant. The characteristic FSH peak was not observed in any of the swimmers and it showed little changes throughout the cycle. Levels of FSH in swimmers were therefore significantly depressed in both phases when compared to both control groups. Changes in both gonadotrophins lead to a significantly reduced ($p < .05$) FSH/LH ratio throughout the cycle when compared to both control groups. The authors suggested that decreased FSH and imbalances in LH may account for the improper follicular growth

and maturation in swimmers.

In summary, it would appear that when exercise is intense enough to cause minor menstrual abnormalities (in this case, mostly oligomenorrhea), low to low-normal levels of LH are almost always seen (Dale et al. 1979, Russell et al. 1984a, Russell et al. 1984b, Weicker et al. 1984, Bonen et al. 1981). Furthermore, FSH is most often decreased as a result of heavy training (Dale et al. 1979, Russell 1984b, Bonen 1981, Weicker 1984, Russell 1984a). Indeed, both gonadotrophins are decreased proportionally to the volume of training (Weicker et al. 1984). However, the use of teenaged athletes in most studies is of concern since gonadotrophin changes could be partly due to young age alone. In this regard Bonen et al. (1981) demonstrated that teenage and adult controls are relatively similar from a gonadotrophin standpoint and exercise caused a decrease in hormone values greater than what could be due to the young age of the subjects alone. These low basal values for both gonadotrophins suggest a mild hypothalamic-pituitarian dysfunction (Dale et al. 1979) and this impairment could be due to increased levels of β-endorphins or catecholestrogens (Russell et al. 1984b). This hypothesis will be discussed in greater details later on.

B) Basal estradiol and progesterone levels in long-term trained subjects:

That regular and high-intensity training decrease gonadotrophin levels raises the possibility that there could be some repercussions at the level of the ovaries.

In their study of estrogen concentrations in women training

for a marathon, Boyden et al. (1983) studied a group of runners (initially running 15 miles/week) who trained 14 to 15 months in order to complete a marathon. Blood samples were obtained when their weekly mileage was increased by 30 and by 50 miles/week. Estrone and estradiol are shown below:

	Baseline	30	50
E_2(pg/ml)	70.6 ± 13.9	53.6 ± 8.7	33.6 ± 4.8*
E_1(pg/ml)	52.6 ± 3.2	48.8 ± 2.9	44.7 ± 3.4

*significantly different from baseline ($p = 0.03$)

Estradiol, the main estrogen showed therefore a gradual decrease as training load increased. Clinically, 18 out of 19 runners reported ~~a subjective de~~crease in menstrual blood loss as a result of the decline in estrogen status. Surprisingly however, no one became amenorrheic during training despite a rather heavy training program. The same kind of results were reported by Dale et al. (1979). Their analysis of runners, joggers and controls showed significant differences in the menstrual pattern of the 3 groups:

	Controls	Runners	Joggers
# menses/year	11.8 ± .92	9.16 ± 4.04	10.33 ± 3.23
oligo/amenorrhea	(2/54) 4%	(30/89) 34%	(5/22) 23%

Runners had less ($p < .05$) menstrual period per year and they reported a lighter blood flow during menses ($p < .009$). In addition, the estrogen concentration was in the low-normal range for runners. The study of young swimmers and runners yielded basically comparable results to those reported previously (Russell et al. 1984a). Six swimmers (training 5 days/week,

up to 5 hours/day) were compared to 7 runners (6 days/week, 25-30 miles/week) and to controls (N=7). As shown in the table, basal values are reduced ($p < .1$) in both groups of athletes:

	Swimmers	Runners	Controls
Estradiol (pg/ml)	74 ± 56	108 ± 40	286 ± 232

On average, swimmers trained harder than the group of runners and they showed the lowest estradiol values, suggesting that the increased intensity and duration of training is of importance in the reduction of estradiol. In another study, 13 swimmers were compared during two phases of their training program (Russell et al. 1984b). Median estradiol levels during strenuous exercise (52 pg/ml) were not different from those obtained during moderate exercise (65 pg/ml). However, both levels were significantly lower than controls. As suggested by the authors, the low levels of estradiol during moderate exercise may have prevented a further decrease during heavy training. Therefore, estradiol concentration may not decrease further once a relatively low concentration is already attained.

Of interest are studies investigating the changes in estradiol and progesterone concentrations. Ronkainen et al. (1985) compared 18 endurance runners (amongst the top 10 in their respective category in Finland) and 13 non-competitive joggers (trained for 3-10 years, 2-5 times/week, 15-70 km) with their respective control groups (12 and 11 subjects respectively). Both groups of athletes were evaluated during periods of light (fall) and heavy (spring) training. Blood samples were obtained

twice during the follicular and luteal phase in addition to one sample withdrawn at ovulation time. Ultrasonographic examinations of the ovaries were performed to assess folliculogenesis. Surprisingly. seriously disturbed folliculogenesis was more frequent during the light training phase with runners showing consistently higher incidences of disturbed folliculogenesis:

	Light Training	Heavy Training
Runners/controls	61% vs 17% ($p < .02$)	36% vs 0% ($p < .05$)
Joggers/controls	8% vs 18% (NS)	8% vs 11% (NS)

At various points during their cycles, runners showed significantly lowered estradiol and progesterone concentrations. The authors concluded that lowered E_2 and P concentrations along with disturbed folliculogenesis are good indicators of a decreased ovarian activity. Furthermore, the data suggests that the disturbed follicular development begins in the follicular phase. Therefore, the decreased progesterone concentration seen in the luteal phase would be a direct consequence of impaired follicular development during the follicular phase rather than being a direct consequence of exercise. In a study reported previously, Bonen et al. (1981) analyzed the chronic estradiol and progesterone adaptation to a heavy swimming program. These teenage swimmers (N=4) were compared to teenage (N=4) and adult controls. Estradiol was similar between swimmers and both control groups during the mid-follicular phase but it was significantly ($p < .05$) lower in swimmers during the luteal phase. The progesterone secretion pattern was also altered as a

result of training. Progesterone concentration was increased during the follicular phase in 3 out of 4 swimmers. In fact, values were almost double the adult values. During the luteal phase, significantly lowered progesterone values were found in swimmers; an indication that the corpus luteum failed to function. This is the first study showing an "inverse" progesterone pattern following long-term exercise. As shown previously mid-luteal progesterone levels are also reduced in menstrual cycles where training was intense (Shangold et al. 1979, see Shangold 1985).

A universal finding is that basal estradiol concentration are significantly lowered in different groups of athletes undertaking heavy training programs (Boyden et al. 1983, Dale et al. 1979, Russell et al. 1984a, Ronkainen et al. 1985, Bonen et al. 1981). However, when low estradiol levels are reached (50-60 pg/ml), it appears that an increase in training intensity would not decrease further the estradiol concentration (Russell et al. 1984b). This lowered estradiol concentration results in reduced blood loss during menses (Boyden et al. 1983) or in less menstrual cycles per year (Dale et al. 1979). The impaired folliculogenesis as a result of low estradiol concentration could in turn reduce progesterone concentration (Ronkainen et al. 1985). Progesterone has been shown to decrease following training (Bonen et al. 1981). It has been suggested that this would be a consequence of a reduced ovarian activity.

C) Basal androgen levels in long-term trained subjects:

Popular beliefs have always given a lot of credit to

androgens for their role in successful athletic performance (i.e. muscular hypertrophy of the female's body, agressive behaviour necessary for successful participation in sports, etc.) . However, there is a striking paucity of information dealing with the long-term effects of exercise on androgen concentrations, especially in females. Furthermore, controversial results have been obtained which make any conclusions very speculative, at least at this point in time. Dale et al. (1979) compared the basal testosterone values of controls (N=18), joggers (N=6) and runners (N=14). A highly significant difference ($p < .001$) was observed between the runners and the controls (.41 ng/ml vs .33 ng/ml respectively) with joggers exhibiting somewhat intermediate values (0.38 ng/ml). One may however question the physiological significance of such small difference (0.08 ng/ml) especially when one considers that interassay variations are subject to an average of 10% in variation. In their experience reported previously, Boyden et al. (1983) trained 19 runners for a marathon. Basal values are presented when weekly mileage is increased by 30 and by 50 miles/week.

	Baseline	30	50
T (pg/ml)	242.0 ± 29.2	206.3 ± 20.8	222.5 ± 32.6
Free % (%)	1.1 ± 0.1	1.2 ± 0.1	1.2 ± 0.1

No significant variations were seen for either values during the training program. In a study, basal testosterone values have even been shown to decrease when training of high and low intensity were compared (Ronkainen et al. 1985). When highly trained endurance runners (N=18) were compared to a control

group, a significant decrease only in the basal testosterone was observed during the high-intensity training. However, non-competitive joggers (N=13) showed no difference with their respective control group in basal testosterone values, a result which would support the necessity of a high intensity threshold in triggering endocrine changes.

In summary, no definite conclusions can be made at this point with regard to basal androgen values. It is unfortunate that androstenedione was not analyzed in conjunction with testosterone in any of the studies reviewed here. Despite its low biological potency, androstenedione is secreted to a greater extent in the female body and on this basis could have an important biological effect. The unchanged testosterone free-fraction reported by Boyden et al. (1983) is of interest since free-testosterone is the only fraction exerting a biological action at the tissular level. Therefore, studies looking at the androgenic changes following exercise should measure the free form due to its biological importance.

SECTION IV: POSSIBLE MECHANISMS TO EXPLAIN THE ETIOLOGY OF EXERCISE-INDUCED AMENORRHEA:

The exact mechanisms by which exercise induced changes in basal hormonal levels and consequently amenorrhea is unknown. Several mechanisms have been proposed. The evidence presented at this point is however inconclusive. Thus, the preliminary facts presented should be viewed as tentative until they have been subjected to well-controlled studies.

2.4.1) ENDORPHINS:

Endorphins are neuropeptides secreted in the brain in response to various stimuli. Their involvement in many physiological processes has been proposed, notably in gonadotropin release.

In response to exercise, ß-endorphins are secreted in substantial amounts (Carr et al. 1981, Colt et al. 1981, Gambert et al. 1981, Farrell et al. 1982, Fraioli et al. 1980, Ziporyn 1984). However, wide variations in endorphin response to exercise have been reported (Farrell et al. 1982), making statistical analysis difficult. In a review of the effects of exercise on endorphins, McArthur (1985) reported significant increases of endorphin concentration over basal values in all studies utilizing women as subjects. All studies reported increases of at least 100% over basal values with most of them ranging from 200% to 300%. There was also a tendency for the more intense exercise to cause a greater increase in endorphins although this was not universal. Furthermore, training per se

seems to facilitate endorphin release (Carr et al. 1981), suggesting higher absolute levels following exercise in well-trained athletes.

Interest in endorphins in the etiology of exercise-induced amenorrhea stems from recent research in neuroendocrinology depicting the inhibitory effect of exercise on the hypothalamo-pituitary axis. In rats, the injection of endorphin inhibit LH release (Akil et al. 1976) and the same phenomenon has been reported in males (see McArthur 1985, Reid et al. 1981). Naloxone, an inhibitor of endorphin action, has been shown to increase basal LH and FSH levels in rats (Akil et al. 1976, Bruni et al. 1977, Blank et al. 1979, Cicero 1980, Meites 1980). In women, naloxone affects LH levels only in certain phases of the menstrual cycle: Naloxone had no effects during the early follicular phase whereas LH levels of the late follicular and mid-luteal phase were increased suggesting that the role of endorphin is relatively dependent on high levels of estradiol and progesterone (see McArthur 1985, Quigley & Yen 1980, Yen et al. 1985). It is generally accepted that the inhibitory action of endorphin on LH occurs at the hypothalamic level, probably by decreasing LH-RH release (Akil et al. 1976, Blank et al. 1979, Bruni et al. 1977, Cicero 1980, Cox & Baizman 1982, Morley et al. 1980, Quigley et al. 1980, Quigley & Yen 1980).

Several researchers have postulated a role for the exercise-induced increase in endorphin concentration in exercise-induced amenorrhea (see: Cumming & Rebar 1983, Drinkwater et al. 1981, Speroff 1981, Wall et al. 1983, Ziporyn 1984). The assumption

was based on the fact that an increase in endogenous endorphins would inhibit gonadotropin release, in turn affecting the steroid biosynthesis and the follicular development. However, no controlled studies can presently substantiate this hypothesis. In fact, preliminary results tend to disprove this hypothesis. Cumming & Rebar (1983) claim the effects of Naloxone on LH secretion. None of the 4 amenorrheic runners tested showed an increased LH secretion following Naloxone infusion. Furthermore, amenorrheic athletes do not show an increased basal production of endorphin (see Wall et al. 1983). Finally, it appears that the inhibitory action of endorphin is dependent on high levels of estradiol and progesterone (see McArthur 1985, Quigley & Yen 1980, Yen et al. 1985) whereas athletes normally show decreased basal values of both hormones as reported previously. Thus, there is presently little evidence to support the role of endorphins in the etiology of exercise-induced amenorrhea.

2.4.2) CATECHOLESTROGENS

Most studies clearly show decreased levels of estrogen in athletes when compared to the sedentary population. Recent evidence suggests that in addition to low estrogen levels, athletes have increased levels of catecholestrogens.

Catecholestrogens are by-produces of estrogen metabolism and have been suggested to play a role in exercise-induced amenorrhea. Martucci & Fishman (1976) suggested that they act as antiestrogens since they have a high affinity for uterine cytosolic receptors despite their lack of uterotrophic activity.

The antiestrogenic properties of catecholestrogens were also suggested by Parvizi & Ellendorf (1980). Furthermore, Davies et al. (1975) showed their appreciable affinity for receptors of the hypothalamus and the pituitary, making them possible competitors for estradiol. Thus, it is thought that high levels of catecholestrogens may inhibit the action of estrogens at the level of the uterus and at the hypothalamo-pituitary level.

Studies were undertaken to evaluate the effects of exercise on the endogenous production of catecholestrogens. Russell et al. (1984a) compared swimmers (N=6, very strenuous training program) to runners (N=7, moderate by intense training) and to controls (N=7). Swimmers trained 5 days per week, up to 5 hours/day, averaging 60,000 to 100,000 yards/week while runners ran 6 days/week for a total of 25-30 miles. All swimmers had regular cycles before oligomenorrhea was induced by training while runners and controls had regular cycles. Basal levels of estradiol and 2-hydroxyestrone (a catecholestrogen) were measured for each group:

	Swimmers(N=6)	Runners(N=7)	Controls(N=7)
E2 (pg/ml)	74 ± 56	108 ± 40	276 ± 232
2-hydroxyestrone (pg/ml)	90 ± 13	83 ± 13	44 ± 6
LH (IV/ml)	32.3 ± 8.8	39.0 ± 29.9	79.0 ± 88.0

Basal values of 2-hydroestrone were significantly elevated ($p < .01$) in both groups of athletes while estradiol was significantly reduced ($p < .05$) in both groups of athletes. Although not reported, the acute post-exercise values of catecholestrogen were also significantly elevated when compared

to pre-exercise values in both athletic groups. The authors concluded that exercise did indeed shift the estrogen metabolism from the 16-hydroxylation to 2-hydroxylation, producing increased amount of catecholestrogens. Furthermore, they suggested that the decreased LH levels seen in the oligomenorrheic groups (swimmers) can be related to the increased endorphin and catecholestrogen levels. Another study was undertaken to compare two exercise intensities in relation to the catecholestrogen production (Russell et al. 1984b). Heavy training consisting of 100,000 yards/week of swimming induced oligomenorrhea in all 5 swimmers while a reduction of training to 60,000 yards/week restored normal menses. In addition, 6 sedentary women with normal cycles served as controls. Variations in training intensities did not change the relative adiposity of athletes. The endocrine values are summarized below:

Hormones	Controls	Swimmers	
		Moderate (60,000 yards)	Strenuous (100,000 yards)
LH (MIU/ml)	23.1 ± 10.5	22.9 ± 5.7	10.9 ± 2.8
FSH (MIU/ml)	10.9 ± 3.5	20.2 ± 5.1	6.5 ± 2.0
PRL (ng/ml)	10.8 ± 15.0	10.6 ± 3.6	1.36 ± 0.9
E2 (pg/ml)	264 ± 253	61.8 ± 16.8	76.8 ± 61.9
Catecholestrogens (pg/ml)	35.3 ± 7.5	28.0 ± 1.2	92.4 ± 12.8

Heavy training induced very significant changes in hormonal pattern. Catecholestrogens were significantly ($p < .001$) increased during the strenuous exercise program while moderate intensity had no significant effect.

On the contrary, estradiol levels during both exercise

intensities were significantly reduced when compared to controls. Thus, increased levels of catecholestrogens were seen during intense exercise, a period during which all swimmers were oligomenorrheic.

In summary, exercise appears to exert a rather significant effect on the endogenous catecholestrogen concentration. Since menstrual irregularities developed during periods of heavy-training, i.e. when catecholestrogen are increased (Russell et al. 1984a, 1984b) it is tempting to suggest a role for these metabolites in the etiology of exercise-induced amenorrhea. Their possible interaction with cytosolic receptors in the uterus or in the hypothalamic-pituitarian axis are the proposed pathways by which they could reduce the biological activity of estrogens and consequently affect the menstrual cycle.

2.4.3) BODY FAT:

The possible influence of body weight and/or body composition in the etiology of exercise-induced amenorrhea has received a lot of attention in recent years. It became a popular risk factor for athletic amenorrhea since athletes and anorexic subjects both demonstrate a high incidence of amenorrhea that is thought to result from a decreased peripheral conversion of androgens to estrogens due to low body fat.

The early work of Frisch & McArthur (1974) supported this theory. Two major conclusions stem from their 3 longitudinal studies performed with 181 adolescent girls:

1) a minimum of 17% body fat was necessary for onset of

menarche

2) a minimum of 22% body fat was necessary for maintenance or restoration of normal menses.

From this study, a nomogram was calculated and critical weight for height values constituted a threshold for a normal menstrual pattern. Thus athletes or other subjects falling below the calculated threshold were expected to have abnormal menstrual cycles. It is presently difficult to estimate the exact role of body composition in the etiology of athletic amenorrhea. If an association exists, it is probably much more complex than first thought.

Most of the recent endocrine studies of amenorrheic athletes included body composition measurements. In numerous studies, a subgroup of oligo/amenorrheic athletes were compared to their regularly cycling counterparts. Oligo/amenorrheic athletes were shown repeatedly to have significantly lower scores in several anthropometric measurements such as relative adiposity, percentage of ideal weight, and fat weight (Carlberg & Riedesel 1979, Carlberg et al. 1983, Feicht-Sanborn et al. 1982, Frisch et al. 1983, Galle et al. 1983, Schwartz et al. 1980) whereas other studies failed to report significant differences (Baker et al. 1981a, Abraham et al. 1982, Øian et al. 1984). Despite such findings, recent reviews concluded that body fat was not important in the etiology of this disorder (see: Bonen 1984, Drinkwater et al. 1981). In fact, the recent trend in the literature favors the exercise intensity and the energy drain as being more important factors than body composition (Abraham et

al. 1982, Øian et al. 1984, Russell et al. 1984b).

The relative importance of body fat in the etiology of exercise-amenorrhea is thought to be linked to the ability of fat tissue to convert androgens to estrogens. Thus, it was hypothesized that athletes with low body fat have a decreased ability to obtain estrogen from peripheral conversion. It has been suggested that this metabolic conversion is of importance during adolescence (see Editorial 1982) but, during adult life, peripheral conversion is a negligible source of estrogen in comparison to the ovarian production of estradiol (Shangold 1985, see Bonen & Keizer 1984, Longcope et al. 1969). Furthermore, it has been shown at least in males, that the muscular tissue can convert androgens to estrogens (Longcope et al. 1978). Thus, it may be hypothesized that in athletes, an increased muscle mass may compensate for the decreased body fat, keeping the rate of peripheral conversion constant.

In summary, the importance of body fat and/or body weight in the etiology of exercise-induced amenorrhea is rather puzzling. Although some studies (Øian et al. 1984, Baker et al. 1981a, Abraham 1982, see Bonen 1984, see Roundtable 1981) could not demonstrate a significant relation between the two variables, the majority of studies (Frisch & McArthur 1974, Feicht-Sanborn et al. 1982, Carlberg et al. 1979, Carlberg et al. 1983, Schwartz et al. 1980, Galle et al. 1983, Frisch 1983) still demonstrate an association between the two variables. The amount of adipose tissue is, according to this theory, too low in athletes to provide an adequate extragonadal source of estradiol. However,

the results from Longcope et al. (1969) (see also Bonen & Keizer 1984) suggest that the aromatization of testosterone to estradiol is insignificant in comparison to estradiol synthesis by the normal ovaries. In addition, the ability of the muscle tissue to aromatize androgens to estrogens (Longcope et al. 1978, see Bonen & Keizer 1984) would probably balance the low adiposity of athletes. If the relationship between body fat and amenorrhea exists, a possible explanation may be that the increased catecholestrogen production in lean individuals (Fishman et al. 1975) may impair the biological effects of estradiol.

2.4.4) DIET:

With increasing standards in all competitive disciplines, athletes have to maintain an optimal percentage of body fat almost all year long. For this reason, medical authorities are now concerned with food aversion and excessive weight loss, that are increasing in popularity among the athletic population (see Jacobs 1982, see Smith 1980). The same behavior is found in anorexic patients, a group with a particularly high risk for amenorrhea. Furthermore, some have speculated that nutritional deficiencies may at least have a secondary role in amenorrhea. In addition, vegetarian diet is relatively popular among athletes and it has been linked to an increased incidence of amenorrhea.

Of all athletic activities, ballet dancing is definitely one of the activities with the most stringent requirements for a low body fat. An analysis of the dietary habits of 25 dancers (dancing 40 hours/week) was undertaken (Calabresse et al. 1983).

The average caloric intake was 71.6% of the recommended daily allowance (RDA) for the reference woman of similar height and weight with some dancers with some dancers eating even less:

76% of dancers ate less than 85% RDA

40% of dancers ate less than 60% RDA

20% of dancers ate less than 50% RDA

Protein intake was low especially in the face of caloric deficit and the vitamin intake was also reduced:

	Percent of dancers eating less than 85% RDA	Percent of dancers with deficit EVEN AFTER supplementation
B_{12}	84%	52%
A	52%	40%
D	92%	80%
Iron	96%	76%
Calcium	68%	60%
Phosphorus	36%	36%
Folic Acid	96%	80%

From this study, it appears that ballet dancers are at an increased risk of developing dietary deficiencies.

Most endurance athletes who require increased energy intake normally favor high intakes of complex carbohydrates at the expense of meat consumption. Recent studies have shown a relation between vegetarian diets and an increased incidence of amenorrhea. In their study, Brooks et al. (1984) found that 82% of their amenorrheic athletes were vegetarians in comparison to only 13% for the regularly menstruating athletes. They suggested that vegetarian diet may be deficient in hormonal precursors and in minerals due to the absence of meat consumption. Furthermore, the evaluation of 172 active women yielded a similar association (Slavin et al. 1984). All subjects participated in vigorous

physical activity at least twice/week and were classified according to their dietary habits:

1) vegetarians
2) high intake of carbohydrates, low intake of fats
3) balanced diet (four groups of food)

The incidence of amenorrhea were 31%, 14% and 4% respectively. The effects of diet may be linked to changes in hormonal concentrations. Goldin et al. (1982) compared 10 vegetarians (milk & eggs) to 10 omnivorous women. The fecal excretion of estrogens (estrone, estradiol, estriol) were 2-3 fold higher in vegetarian women due to increased fecal excretion. Plasma concentration of estrone and estradiol were reduced unsignificantly however by 15% and 19% respectively.

In summary, it is tempting to associate diet as a contributing factor in the etiology of exercise-induced amenorrhea especially when one considers that some groups of athletes are prime candidates for severe nutritional deficiencies (Calabresse et al. 1983). Furthermore, some athletes experience food aversion (see: Jacobs 1982, Smith 1980), a behavior known to result in anorexia, a disorder associated with an increased risk for amenorrhea. In addition, an increased incidence of athletic amenorrhea was shown in vegetarian athletes (Brooks et al. 1984, Slavin et al. 1982). Increased fecal excretion of hormones and the slightly reduced plasmatic levels of estrogens in vegetarians (Goldin et al. 1982) may contribute to the etiology of exercise-induced amenorrhea. However, the lack of conclusive evidence warrants any definite conclusions at this point.

2.4.5) EXERCISE-INDUCED CHANGES IN THE BASAL LEVELS OF VARIOUS HORMONES:

Exercise-induced changes in the basal levels of various hormones (in particular estradiol and progesterone) could also be related to changes in the metabolism of such compounds. For instance, acute exercise induces a decrease in the estradiol metabolic clearance rate (Keizer et al. 1980). It has been hypothesized that changes in the basal metabolic clearance rate of certain hormones may be related to amenorrhea.

To investigate the effects of a basal increase in renal and hepatic blood flow on steroid levels, Casper et al. (1984) injected a beta adrenergic agonist (isoproterenol) to 6 healthy women. Following injection, estradiol and progesterone were substantially reduced by 70% and 50% of basal values respectively ($p < .001$ for both) whereas LH was unchanged. The authors postulated that a chronic increase in the metabolic clearance rate of both steroids could lead to reduced basal hormonal levels which would in turn alter the positive and negative feedback of these hormones on gonadotropin secretion, resulting in a possible altered follicular development. They reported results from Keizer et al. (1980) in which the basal MCR of estradiol was doubled in trained subjects when compared to untrained controls (1439 vs 845 litres/day respectively, $p < .05$). Frenkl et al. (1980) also reported markedly faster metabolic clearance rates for various drugs (aldactone, antipyrine) in athletes when compared to untrained subjects. Furthermore, the antipyrine was proportional to the fitness level of 3 groups of subjects (Frenkl

et al. 1980). In addition, the role of an increased metabolic clearance rate in the etiology of exercise-induced amenorrhea has also been suggested in a recent review (Bonen 1984).

In summary, a greater inactivation of various drugs in trained athletes suggest some biochemical changes in the enzymatic activity of the liver (Frankl et al. 1980). Athletes have been shown to have increased basal MCR (Keizer et al. 1980) that would be the result of increased renal and hepatic blood flow (Casper et al. 1984). Increased MCR would result in reduced steroid concentrations (estradiol and progesterone), predisposing to amenorrhea. Of interest is the possible impairment of the steroid feedback, a factor explaining increased gonadotropin levels found in some athletes (Casper et al. 1984). However, the paucity of information warrants against any definite conclusions at this point.

SECTION V: THE POSSIBLE SIDE-EFFECTS OF EXERCISE-INDUCED AMENORRHEA:

Until recently, studies related to exercise-induced amenorrhea focused on the possible endocrine causes of such disorder. Since this area is relatively new, almost no studies have been designed to follow longitudinally amenorrheic athletes. Since amenorrhea constitutes a disruption of the normal endocrine functions, one may wonder if there could be, in the long run, side-effects on the health of amenorrheic athletes. Thus, the paucity of longitudinal studies make conclusions about the possible side-effects rather difficult. Nevertheless, the effects of amenorrhea on bone density have been recently investigated.

2.5.1) DECREASED BONE DENSITY:

Besides the development and maintenance of normal reproductive functions, estrogens are involved in metabolic processes, notably in the fixation of calcium on bones. One of the most significant effects of chronic and intense training is a significant reduction in the estrogenic status of the athletes. Therefore, one may assume that decreased estrogen levels could result in an impairment of calcium fixation. However, exercise has been shown to increase bone density via increased stimuli at the bone level. Thus, it is rather difficult to predict which effects may override the other.

Several studies were therefore undertaken to study the effects of exercise and amenorrhea of the calcium content of

bones. In their experiment, Drinkwater et al. (1984) compared bone mass of 14 severely amenorrheic athletes (not more than 1 menses in the last year) with 14 eumenorrheic athletes selected to match in height, weight, sport, participation, age, etc. Subjects reported to the laboratory on 4 occasions at 7-day intervals for endocrine determination by RIA and for determination of bone mass by photon absorptiometry using 2 sites on the forearm and on the spinal cord. No differences were seen between amenorrheic and eumenorrheic athletes in all physical characteristics except for the weekly mileage (42 for amenorrheic runners vs 25 for eumenorrheic). The endocrine analysis of both groups suggests anovulation (values < .65 ng/ml for progesterone) in 13 of 14 amenorrheic athletes whereas 11 of 14 of eumenorrheic athletes had ovulatory cycles. Furthermore, estradiol values were significantly reduced in amenorrheic athletes (39 pg/ml vs 107 pg/ml, $p < .01$) as shown in the table:

	AM	E	P
Estradiol (pg/ml)			
Mean	38.58 ± 7.03	106.99 ± 9.80	.01
Peak	67.75 ± 13.77	205.39 ± 70.6	.01
Progesterone (ng/ml)			
Peak	1.2 ± 1.00	12.75 ± 2.4	.01
Testosterone (ng/ml)	0.47 ± 0.04	0.42 ± .04	NS
Prolactin (ng/ml)			
Peak value	23.73 ± 3.74	44.74 ± 7.34	.02
Mean	17.04 ± 2.28	33.96 ± 6.80	.02

Bone measurements	AM	E	P
Radius (S1)			
mineral content(g/cm)	.89 ± .03	.85 ± .03	NS
mineral density(g/cm^2)	.54 ± .02	.54 ± .01	NS
Radius (S2)			
mineral content(g/cm)	.91 ± .02	.88 ± .03	NS
mineral density(g/cm^2)	.67 ± .02	.67 ± .02	NS
Vertebrae (g/cm^2)	1.12 ± .04	1.30 ± .03	.01

Thus, ~~both~~ sites on the radius showed no significant differences in terms of bone mineral content or bone density but the mineral density at the lumbar vertebrae was significantly reduced in amenorrheic athletes. When the values for vertebral mineral density were compared to those reported in another study (N=120), the values from the eumenorrheic athletes were similar to what could be predicted by an age-based regression. In contrast, the average bone mineral density of amenorrheic athletes was equivalent to that of women 51 years of age. Difference in vertebral bone mineral density occurred despite similar diets in both groups notably in terms of intake of calcium. The authors concluded that exercise did not protect amenorrheic athletes from an apparent loss of vertebral bone despite unchanged values for the radius. The effects of a more strenuous training program on bone composition were investigated in 11 marathon runners (Marcus et al. 1985). These subjects were severely amenorrheic, i.e., no menses for the last 1 to 7 years. They were compared to 6 regular women runners and to sedentary controls (N=20). Both groups of runners ran an average of 93 km/week (range: 56-160) in addition to several hours of bicycle riding, swimming and weight training. Mineral density of the first and second lumbar vertabrae (trabecular bone) and of the radius (cortical bone) were measured by computed tomography and photon absorptiometry respectively. Blood samples were obtained for endocrine analysis. Amenorrheic runners were younger ($p < .01$), lighter ($p < .01$) but height, mean VO_2, percentage of body fat and age of menarche were similar among both groups. The table below

summarizes the results for mineral density:

	Runners		
	Amenorrheic	Regular	Controls
spine density mg/cm³	151 ± 8*	182 ± 5	166 ± 4
forearm density g/cm²	.694 ± 0.1	.720 ± 0.1	.71 ± 0.1 NS

* significant from controls at $p < .05$ and from regular runners ($p < .02$)

Thus, forearm density (cortical bone) was similar in all three groups whereas spine density (trabecular bone) is significantly reduced in amenorrheic athletes when compared to controls ($p < .05$) or to regular runners ($p < .02$). Interestingly, one out of 6 regular runners experienced a running-related fracture while 6/11 amenorrheic runners reported it ($p < .05$). Endocrine analysis revealed lowered ($p < .01$) estradiol values in amenorrheic runners with the sedentary subjects having the highest values (36.3 ± 3.5 pg/ml vs 92.5 ± 27.4 respectively). The analysis of the diet revealed unexpectedly low calorie intakes in athletes (1300 - 1700 kcal) despite running 96 km/week with 40% and 50% of the regular and amenorrheic group eating respectively 66% or less of the RDA of calcium. As shown by Drinkwater et al. (1984), spinal bone density in this study was also significantly reduced in amenorrheic runners whereas cortical bone mass was unaffected. The incidence of cortical bone stress fracture in amenorrheic athletes is striking but it is rather difficult to link it with the bone density status since running mechanics and other characteristics may also influence it. Of particular interest is the drastically lowered caloric and calcium intake, two factors that may act synergically with

the lowered estradiol value to reduce vertebral bone density in amenorrheic athletes. However, vertebral density values previously reported for amenorrheic subjects (amenorrhea was not induced by exercise) is significantly lowered than for amenorrheic athletes (121 ± 6.9 vs 151 ± 8 mg/cm^3 respectively, $p < .05$), a finding suggesting that weight-bearing exercise may partially overcome a low estrogen status. Finally, the authors suggested that amenorrheic athletes showing low estrogen values should increase their intake of calcium to 1500 mg, a value recommended for postmenopausal women. The strikingly high incidence of running-related injuries (stress fractures) among amenorrheic runners was also reported by other investigators (Lindberg et al. 1984). Five groups of women were compared for peripheral bone content (radius) by single photon absorptiometry:

1) 11 amenorrheic runners (no menses for the last 6 months)
2) 5 oligomenorrheic runners (menses every 6 weeks to 6 months)
3) 15 eumenorrheic runners
4) 14 eumenorrheic controls
5) 10 postmenopausal women

Spinal bone measurements were also performed in 9 amenorrheic runners using a dual photon absorptiometer. In the year preceding the study, 49% of amenorrheic runners experienced stress fractures compared to none for regular runners. However, amenorrheic runners ran greater distances than regular runners, a factor that could be of importance in the decreased bone

density. In addition to vertebral bone density, peripheral bone density (radius) was also reduced in amenorrheic runners in comparison to runners with regular cycle or to sedentary controls. The authors concluded that the demonstration of reduced bone mineral content at two sites using two different methods may be representative of a substantial bone loss.

Comparisons of various groups of subjects yielded more conservative results at least in two studies. Parker-Jones et al. (1985) selected 39 women (18-43 years) with a diagnosis of secondary amenorrhea (no menses in the last year) to participate in the study. The groups were distributed as follows:

1) 8 runners (running more than 30 miles/week) with onset of amenorrhea corresponding to the beginning of intense training
2) 20 women suffering from hypogonadotrophic hypogonadism associated with simple weight loss
3) 11 women with premature ovarian failure
4) 25 nonathletic women with regular menses served as controls

In the first three groups, the diagnosis regarding amenorrhea was confirmed by hormonal analysis. Bone density was determined by direct photon absorptiometry. The results suggested that exercise-induced amenorrhea did not influence bone density when compared to controls whereas both other types of amenorrhea decrease bone density. The authors concluded that exercise may therefore protect from bone loss even when the estrogenic status is decreased. However, the linear regression analysis showed a

significant but modest correlation ($r = 0.56$, $p < .001$) between the duration of amenorrhea and the decrease in bone density suggesting that, in the long run, athletes may be at risk. Finally, the study of Linnell et al. (1984) did not demonstrate significant differences between amenorrheic runners and their regularly cycling counterpart. Women were divided into amenorrheic runners (0 to 3 menses per year, N=10), regular runners (N=12) and 15 non-athletic controls. Body composition was determined by hydrostatic weighing and bone mineral density was measured by direct photon absorptiometry at 2 sites along the radius (wrist, forearm). A dietary history was also obtained over a 4-day period to evaluate intakes of calcium and phosphorus. The table below illustrates the results obtained:

	wrist(g/cm^2)	forearm(g/cm^2)
Controls	.544 ± .044	.707 ± .046
Am. Runners	.508 ± .082	.707 ± .069
Regular Runners	.529 ± .040	.700 ± .061

	Calcium	Phosphours	Ca/P
Controls	1038 ± 877	1488 ± 8.18	.67 ± .18
Am. Runners	870 ± 428	1260 ± 459	.69 ± .19
Regular Runners	884 ± 417	1428 ± 675	.62 ± .10

No differences were seen in bone mineral content (BMC) expressed relative to body weight (BMC/BW) in all three groups, despite similar diet and similar intake of calcium and phosphorus. Thus, the authors concluded that the bone mineral content was independent of the menstrual cycle. However, in amenorrheic runners, a positive correlation between relative fatness and BMC/BW and between body weight and BMC/BW is of interest. The authors concluded that amenorrhea does not predispose to a lower

BMC/BW but the combination of amenorrhea and low body fat/body weight (common in runners, see section on body composition) may result in a decreased bone density. The interaction of the two appeared to be of importance at least in this study.

Most studies (Drinkwater et al. 1984, Lindberg et al. 1984, Marcus et al. 1985) have shown a significant decrease in vertebral bone density in exercise-induced amenorrhea whereas, other studies could not demonstrate significant decrease in bone mineral density (Linnell et al. 1984, Parker-Jones et al. 1985). Nevertheless, regression analyses in the latter studies showed that length of amenorrhea is related to a decreased bone density (Parker-Jones et al. 1985) and that amenorrheic athletes of low body weight may also be at an increased risk (Linnell et al. 1984). Thus, the relatively thin and small athlete that had suffered from amenorrhea is at a particular risk. In addition, Lindberg et al. (1984) and Marcus et al. (1985) have shown that stress fractures are strikingly more common in amenorrheic athletes (50% incidence approximately vs 0 to 15% in regular runners). This data is however difficult to interpret since amenorrheic athletes have been shown to run greater distances at least in two studies (Lindberg et al. 1984, Drinkwater et al. 1984). Interestingly however, cortical bone density (measured at the forearm) appeared to be unchanged in amenorrheic athletes (Drinkwater et al. 1984, Marcus et al. 1985) whereas Lindberg et al. (1984) found a significant reduction. It is tempting to involve the estrogen levels found in most studies (Drinkwater et al. 1984, Marcus et al. 1985, Lindberg et al. 1984) in the

decreased bone density values but the low caloric and calcium content of the diet of athletes (Marcus et al. 1985) is another confounding variable. More studies are needed to further elucidate this possible side-effect of amenorrhea. Nevertheless, the recent literature reviewed suggest that the possibility of a decreased bone mineral density should not be overlooked. Vertebral density of amenorrheic athletes is however higher than for other amenorrheic subjects (151 mg/cm^3 vs 121 mg/cm^3, $p < .05$), a finding suggesting that weight-bearing exercises may partially overcome low-estrogen status.

2.5.2) REVERSIBILITY OF EXERCISE-INDUCED AMENORRHEA

Exercise-induced amenorrhea raises important questions concerning the possible deleterious effects of exercise on the menstrual function, especially if such disorder extends for long periods of time. Since this is a relatively new area, no longitudinal studies have examined the long-term effects of amenorrhea on fertility.

Fortunately for the athlete, preliminary data consistently indicate that exercise-induced amenorrhea is reversible, decreasing the probability of deleterious effects on the menstrual function. In questionnaires given to women (N=168, 18-48 years of age), Dale et al. (1979) noted the reversibility of amenorrhea in runners following a reduction in training. Furthermore, the longitudinal study of ballet dancers (N=15) showed that episodes of very rapid progression in puberty, onset of menarche or reversion of secondary amenorrhea were all related to periods of relative inactivity despite no changes in body

composition (Warren 1980). Thus, reduced physical activity also favor the development of the reproductive system. The reversibility of exercise-induced amenorrhea has been demonstrated by Stager et al. (1984). Questionnaires were sent to collegiate runners (N=45), former collegiate runners (N=26) and sedentary controls (N=78). As expected, current athletes had fewer menses/year than controls (7.1 vs 10.0 respectively, $p < .05$) whereas ex-athletes were not different from controls (9.5 vs 10.0). Most of the ex-athletes (83%) indicated that their menses were affected by training and that they resumed an average of 1.7 month after discontinuation of training. Interestingly, no relation was observed between the length of amenorrhea and its persistence following training. In her review, Baker (1981b) gives 4 reasons supporting the reversibility of amenorrhea:

1) when training resume, runners and ballet dancers recover normal menses despite changes in weight
2) when training decreases below a certain threshold, amenorrhea frequently resolves
3) resolution of amenorrhea in rowers occurs after the rowing season
4) normal reproductive functions are found in young swimmers 10 years after discontinuing strenuous training

Thus, in the majority of athletes, normal menses resume following a significant reduction or complete cessation of training.

As expected when normal menses resume, hormonal levels tend to revert back to "normal" values (Russell et al. 1984b). In

their experiment, 5 swimmers became oligomenorrheic following intense training (100,000 yards/week). A reduction in training to 30,000 yards/week increased significantly both gonadotropins values ($p < .01$). Interestingly however, estradiol values remain depressed (65 pg/ml) despite a reduction in training. It is however difficult to explain the latter finding.

In summary, studies have shown consistently that menses resume following a significant decrease or complete cessation of training (Dale et al. 1979, Warren 1980, Stager et al. 1984, Baker 1981b, Russell et al. 1984b). Surprisingly, it appears that the duration of amenorrhea is of little importance in the persistence of amenorrhea following training (Stager et al. 1984).

CHAPTER III: METHODOLOGY

3.1) INTRODUCTION:

This study was undertaken to evaluate the effects of a heavy resistance weight lifting programme on the reproductive hormone and their influence on the ovarian cycle of healthy young women. This chapter describes the methodology and the statistical analysis employed in this study.

3.2) SUBJECTS:

A total of 24 healthy volunteers participated in the study. Groups 1 and 3 were students (18 to 25 years old) registered at the University of Ottawa. Group 2 consisted of subjects from the Ottawa region, between the ages of 18 to 30 years. The subjects were assigned to one of the following three groups:

Group 1: (N = 10) These subjects participated in a training programme for a duration of two complete ovarian cycles.

The training sessions were approximately one hour long and were held four times weekly. The training programme is described in detail in a further section. Prior to the training programme, two cycles were monitored to obtain basal values. Two cycles were again monitored during the training programme.

Group 2: (N = 9) This group consisted of 9 experienced bodybuilders who had been training on their own for at least one year. They were also monitored during two full cycles. The nature and intensity of their training were analyzed as well.

Group 3: (N = 5) These subjects were age-matched controls who were not engaging in any regular form of exercise during the period of the study.

3.3) MEASUREMENTS:

The following measurements were recorded for all subjects:

1) Basal temperature: This was recorded (in degrees Celsius) daily throughout the experiment in a booklet provided for this purpose. Each subject was given a thermometer and instructed on how to measure her temperature. This was taken orally, every morning before getting out of bed.

2) Anthropometric characteristics: Height, weight and skinfolds were measured according to the Standardized Test of Fitness (STF).

a) Girths: Girth measurements were made in order to assess any hypertrophic changes. Chest, waist, gluteals and thigh were all made according to the STF procedures. Other measures added were:

1°) arm: This was taken at mid-bicep with

the arm fully contracted.

2°) forearm: with the hand in a flexed position, this was taken at the largest portion of the forearm.

b) Blood samples: Approximately 10 cc. of blood was taken antecubitally every 7th day starting with the first day of menstruations recorded as day 0. In order to decrease diurnal variations, all samples were taken between 8h00 and 11h00 AM. A total of 160 to 200 cc. of blood was withdrawn for each experimental subject. For the 2 other groups, a total of 80-100 cc. of blood was withdrawn. Serum was separated by centrifugation at 4°C during 15 minutes at 2000 RPM. All samples were centrifugated within 3 hours after collection. It was frozen (-20°C) for further radioimmunoassay analysis.

Blood samples were classified retrospectively from the last day before the onset of menstruations with this last day counted as day 28. Thus, the cycle was counted backward (i.e. from the end to the beginning) and each day was given a number. According to this method, 4 categories were obtained:

early follicular : all values until day 7

late follicular : days 8 to 12

early follicular : days 15 to 21

late luteal : days 22 until the end of the cycle

This method of classification is a common procedure in clinical endocrinology. It allows comparisons of hormonal values between blood samples despite the inter-individual variability in the length of the menstrual cycle. Thus according to this method, ovulation occurs 14 days before the onset of menses whereas the follicular phase varies from one subject to another (Barber et al. 1979, Chamberlain et al. 1977, Judd & Meldrum 1981, Proust et al. 1982). Thus, the cycle is classified according to the onset of the following menstruations:

"It should be remembered that the cycle being biopsied is a new cycle, unrelated to the last menstrual flow, and whereas the luteal phase is constant, the length of the proliferative phase may vary. Therefore, the duration of the menstrual cycle must ultimately be determined from the day of onset of the next cycle. For example, if a biopsy is taken on day 17 and the next menstrual period occurs on day 35, ovulation would have taken place on day 20 or 21, and the day 17 endometrium would then be expected to have the appearance of a late proliferative phase rather than that of a day 17 endometrium from a normal 28 day cycle." (Judd & Meldrum 1981, p. 886).

c) Questionnaires: Two questionnaires were administered to the subjects. The first one evaluated their menstrual patterns before and after the study and any problems related to amenorrhea, dysmenorrhea, or oligomenorrhea. Age of menarche was collected. The second questionnaire dealt with general lifestyle, past participation in sports and nutritional habits. A personal interview with each participant supplemented the questionnaires related to menstrual pattern. This was to ensure a good comprehension of the menstrual disorder that may have been encountered by each participant.

3.4) TRAINING PROGRAMME:

The following programme was administered to the experimental subjects (group 1).

1°) Adaptation period (2 weeks): Weights corresponded to 60% of one's 1-RM and subjects tried to perform 3 sets of 8-10 repetitions. A rest of 1 minute was given between every set.

2°) Training period I (6 weeks): The maximal weight that can be lifted for 3 sets of 8-10 repetitions was used. Again, a 1 minute rest spaced each set.

The sequence of exercise performance was as follows:

1°) Leg press: The exercise was performed on the new Universal machine with the stack of weight at 45 degrees from the subject. Each repetition was carried almost to full range-of-motion except that the legs were kept slightly bent at the end of each repetition.

2°) Squats: This was performed with an Olympic barbell and subjects stopped at a parallel position before going up again.

3°) Leg curl: This exercise was performed on a "Universal" leg curl with dynamic variable resistance. Each repetition was carried to full range-of-motion and the weights were not allowed to touch the weight stack until completion of exercise.

4°) Latissimus pull-down: Pull-downs were made using a "Universal" lat pulley. Subjects had to pull down the bar to their neck and a complete extension was performed before the next repetition.

5°) Bench press: Bench press was not performed with an olympic barbell. The bar was not allowed to bounce on the chest.

6°) Seated dumbbell press: This exercise was performed on an "Erilom" seated press. The back pad enables the subjects to have their back secured against it.

7°) Seated dumbbell curls: Subjects curled both weights at the same time and they were not allowed to "cheat" using their back.

8°) Curl ups: Subjects performed a modified sit up to

strengthen the abdominal, a muscle important in stabilizing the spine during various lifting movements. Every subject was instructed on how to perform each of these exercises. All training sessions were supervised in order to reduce any risk of injury.

Strength measurements: In total, 4 dynamic strength measurements were made prior to, and at 3-week intervals, for the duration of the training program. All tests were performed after a warm-up consisting of 4-5 repetitions. The maximal weight lifted was attained normally within 4 to 5 ~~tr~~trials.

Subjects were tested for:

- leg strength with a "Universal" leg press sliding at 45° angle
- upper body strength with a bench press lift
- back strength with a "Universal" lat pulley apparatus
- shoulder strength with a dumbbell press lift

Subjects were told to avoid any jerking movements during the lifts and the maximal weight was recorded to the nearest 5 pounds.

3.5) SPECIAL CONSIDERATIONS:

An information session was held to instruct the subjects on how to lift weights properly. The physiological basis of this sport were explained in order to give the subjects a basic knowledge of this kind of training. At the same time, all subjects were informed to eat a well-balanced diet with vitamin and iron supplements. The importance of an

appropriate fluid intake especially during training was also emphasized.

3.6) HORMONAL ANALYSES:

All hormonal analyses were performed using commercially available radioimmunoassay procedures (Coat-a-count products from Diagnostic products, California).

1° Estradiol:

Standards provided in the kit gave a logit-log calibration curve with the percent bound plotted against the concentration. Non-specific-binding (NSB) of estradiol and the total counts (T) were obtained using polypropylene tubes. Seven calibrators (in duplicate) were utilized to establish the standard curve:

	Concentration(pg/ml)
A (maximum binding) 100%	0
B (binding expressed relative to A)	20
C (binding expressed relative to A)	100
D (binding expressed relative to A)	300
E (binding expressed relative to A)	900
F (binding expressed relative to A)	1800
G (binding expressed relative to A)	3600

Thus, the average counts/minute (CPM) of all calibrators were expressed relative to A and each value (in percentage) was in turn plotted against their respective concentration. All subject results were intrapolated from this curve.

Each subject's result was computed according to these formulae:

1°) the net counts were obtained; substracting the non-specific binding from the average counts/ minute binding

$$\text{Net counts} = \text{Subject's sample CPM} - \text{NSB(CPM)}$$

2°)

$$\text{Percent bound} = \frac{\text{Net count in CPM (Subject's sample}}{\text{Net count in CPM (Calibrator A)}} \times 100$$

In turn the percent bound was plotted against concentration for standards to yield the calibration curve from which the unknown concentration was obtained for every sample. The average was taken since all samples were done in duplicate. All chemicals were brought to room temperature prior to use. Coated tubes containing the estradiol antibody were labelled and then filled with 100 µl of the subject's plasma. One ml of the buffered solution (containing I^{125} estradiol) was added to each tube. All tubes were mixed gently (Vortex) and were then incubated for 3 hours at room temperature. Tubes were then decanted thoroughly and bound steroid counted in the gamma counter (LKB Wallac. model 1282), for 10 minutes.

Specificity: The antiserum is highly specific for estradiol with a low crossreactivity to other naturally occurring steroids or therapeutic drugs. The 17 ß-estradiol-3 -D glucuronide had the highest crossreactivity (6.1%) with the serum. This assay had a detection limit (sensitivity) of approximately 20 pg/ml. Intrassay and interassay values were both lower

than 15% over a broad range of estradiol levels making the immunoassay relatively precise and reliable.

2°) Progesterone:

Standards provided gave a logit-log calibration curve with the percent bound plotted against the concentration.

Standards	Concentration(ng/dl)
A(maximum binding)	0
B(binding expressed relative to A)	0.1
C(binding expressed relative to A)	0.5
D(binding expressed relative to A)	2
E(binding expressed relative to A)	10
F(binding expressed relative to A)	20
G(binding expressed relative to A)	40

All calculations were identical to the ones used for estradiol.

Specificity: The coat-a-count progesterone method is highly specific with a very low cross-reactivity (less than 3%) to other steroids present in subject samples. Intra and Interassay variations were both below 10%. The detection limit (sensitivity) was approximately 0.5 ng/ml.

3°) Free-Testosterone

The calibration curve to measure the free testosterone concentration was plotted utilizing 6 standards:

	Concentration(pg/ml)
A(maximum binding)	0
B(binding expressed relative to A)	1.5
C(binding expressed relative to A)	5.0
D(binding expressed relative to A)	15.0
E(binding expressed relative to A)	32.5
F(binding expressed relative to A)	50.0

All calculations were identical to the ones used for previous methods.

The free testosterone method involved the same steps as for previous methods. However, only 50 µl of patient sample was pipetted into the tube. In addition, the incubation period was extended to 4 hours at 37°C using a low-speed shaking.

Specificity:

The free testosterone was highly specific with an extremely low cross-reactivity (0.16% at the most) to other naturally occurring steroids or therapeutic drugs. Intra and interassay variations were both below 10%. The low-end sensitivity was approximately 1.50 pg/ml.

4°) Androstenedione

The calibration curve obtained to measure androstenedione consisted of 7 standards:

	Concentration ng/ml
A(maximum binding)	0
B(binding expressed relative to A)	0.1
C(binding expressed relative to A)	0.2
D(binding expressed relative to A)	0.5
E(binding expressed relative to A)	1.0
F(binding expressed relative to A)	3.0
G(binding expressed relative to A)	6.0

An extraction step was necessary before the standard steps reported for all other methods. The recovery following extraction was not measured independently to see which fraction of androstenedione was lost in this procedure. However, this was measured by the manufacturer (Diagnostic Products) and recovery averaged 97%.

1°) 0.5 ml of the subject sample was pipeted into high quality borosilicate glass tubes

2°) for the extraction, 5.0 ml of ethylacetate was added to the tubes. The tubes were capped securely using teflon-lined caps.

3°) the tubes were then shaken vigorously by hand for 1 minute.

4°) they were then centrifuged for 5 minutes at approximately 1500 x g (4°C).

5°) finally, 3.0 ml of the upper phase (ethylacetate) was evaporated under a gentle stream of nitrogen at 37°C.

6°) the extract was resuspended with 0.6 ml of androstenedione buffer (calibrator A). This extract was then ready for assay using the standard procedures reported previously. For each sample, 200 µl were pipetted and incubation was for 3 hours at room temperature. The low-end sensitivity was approximately 0.1 ng/ml.

3.7) THE EXPERIMENTAL DESIGN:

Prior to training, experimental subjects were studied during two menstrual cycles in order to establish endocrine and anthropometric baseline values. Anthropometric measurements were repeated at the end of the training program. In terms of hormonal values, only the second menstrual cycle was analyzed statistically in comparison to baseline values.

This was to ensure a minimal period of time for the possible exercise-induced hormonal changes to occur. Pre- and during training comparisons were made using the experimental subjects as their own controls.

Hormonal values for the control group could only be measured over 1 menstrual cycle due to major problems, mostly subjects desisting after the first cycle. However, the anthropometric measurements were repeated twice and the data is compared to the pre- and post-training values obtained in the experimental group. Since the endocrine data are available over only one cycle for this group, they were pooled with the pre-training data of the experimental group. Thus, a larger group of untrained university students were available enabling us to establish hormonal reference values for comparisons with bodybuilders. Before pooling with groups together, detailed statistical analysis were performed to analyze their degree of similarity. Bodybuilders were studied longitudinally. Anthropometric, strength, and endocrine data were available only at one point in time. From our original group of bodybuilders (N=9), seven were amenorrheic (no menses in the last 3 months) at the time of the study. The fact that amenorrhea was induced by exercise was supported by a gynecological questionnaire where other causes of amenorrhea (primary amenorrhea, post-pill amenorrhea, anorexia, etc.) were ruled out. Since there were no menstruations for 7 bodybuilders, there was no reference point to classify the

blood samples obtained as being part of the follicular or the luteal phase. In order to compare with our reference group, hormonal values of 4 consecutive blood samples were averaged. This represented a length of time (ie. 28 days) typical of a normal menstrual cycle and, in our opinion, took into account the possible hormonal fluctuations of the amenorrheic athletes. Such method has been utilized in the past (Dale et al. 1979) to compare amenorrheic athletes with regularly cycling controls. Thus, hormonal data of the two cycling bodybuilders were omitted for that analysis. The number of cycling athletes was too small to compare with the other groups. However, the anthropometric data of all bodybuilders except one were studied due to the loss of one subject.

Statistical analysis:

The similarity between the experimental group (pre-exercise values) and the control group was analyzed using repeated t tests. Normally, repetition of t test is not recommended since it increases the chance of finding significant differences just by chance alone. In this case however, it represents a more conservative approach since the chance of finding significant differences is increased artificially. Thus, if no major differences occur despite this repetitive approach, it strongly suggests that both groups were similar enough to be pooled together as a unique reference group. On the other hand, endocrine values were compared using an analysis of variance with repeated

measures, using a separate analysis for each hormone. Before doing the analysis of variance, the equality of variance between groups was calculated since equality of variance is the major requirement for a valid analysis. Possible clinical differences in hormonal values were discussed even though they did not reach statistical significance.

The effectiveness of the strength training program was partly analyzed using repeated t tests. Hotelling t^2 was also computed in an attempt to protect the alpha level. There were too many variables to analyze in comparison to the number of subjects. Thus, a correlation matrix was first computed and when a group of variables were highly correlated, only one was chosen for further statistical analysis using the repetition of t tests. Few variables were included in this first analysis to protect the alpha level. When significant differences were established, the other variables that were highly correlated to the one analyzed were studied in a descriptive fashion. Repeated t tests were also utilized. Comparisons between bodybuilders and the reference group (control and experimental before exercise) were made using the same method.

Chapter Four

THE RESULTS

The purpose of this study was to evaluate the anthropometric and strength changes in addition to the short and long-term effects of a weight-training program on the menstrual function of the subjects. Specifically, statistical analyses were undertaken to answer the following questions:

1) Did the heavy-resistance weight-training program of short duration (2 months) induce endocrine changes in a group of previously untrained women?
2) Did the long-term trained (at least a year) body-builders differ in endocrine parameters from a reference group?

Three steps were followed to better answer these questions:

1) Comparisons between the experimental (pre-training) and the control group were performed in an attempt to establish the degree of similarity between groups. Assuming that both groups were not statistically different, they could then be utilized together as a unique reference group for comparisons with the bodybuilders.
2) The efficiency of the strength training in inducing hypertrophy and in increasing strength was analyzed by comparing the pre- and post-training scores. The possible repercussions of the training program on the endocrine parameters were also analyzed.
3) Comparisons between established bodybuilders and the

reference group were undertaken to evaluate the effects of long-term training on the endocrine function.

4.1) SIMILARITIES BETWEEN THE EXPERIMENTAL AND CONTROL GROUP:

Both groups were compared on the basis of their anthropometric, strength and endocrine profiles. Repeated t-tests were performed on the anthropometric and on the strength characteristics. As mentioned previously, this procedure represents a conservative approach since the chance of finding significant differences is increased artificially. Significant differences were observed only for the gluteal girth ($p = 0.0315$) and for the suprailiac skinfold ($p = 0.0170$). It should be noted that all girth measurements were greater in the control group whereas all their strength measurements were lower. The higher skinfold values in the control group possibly explains their 16.3% difference in percent adiposity (not significant). The initial anthropometric and strength characteristics of both groups are summarized in Table 1.

TABLE 1

Anthropometric and strength characteristics of the experimental (N=10) and the control group (N=5)

	Experimental (±SD)	Control (±SD)	P value
age(yrs)	21.2(2.20)	20.8(1.64)	.7268
height(cm)	166.0(3.94)	167.7(4.68)	.4733
weight(kg)	61.5(6.41)	66.2(3.54)	.1542
Girths(cm):			
chest	75.2(3.74)	77.9(3.13)	.1975
waist	66.4(3.35)	70.7(4.87)	.0639
gluteal	92.1(3.60)	96.9(3.64)	.0315*
thigh	59.5(3.10)	59.5(3.19)	.1068
arm	27.0(1.69)	28.1(1.30)	.2380
forearm	24.6(1.42)	25.3(1.45)	.3937
Skinfolds(mm):			
biceps	7.0(2.21)	7.7(2.26)	.5815
triceps	17.0(5.50)	19.2(4.94)	.4708
subscapular	11.6(3.28)	12.6(3.56)	.5575
suprailiac	12.2(4.23)	20.0(6.92)	.0170
Percent adiposity(%)	25.1(4.28)	29.2(3.52)	.0863
Strength(lbs):			
leg press	132.6(33.16)	113.0(9.75)	.1108+
bench press	63.0(7.53)	61.0(6.52)	.6221
lat pull	82.5(11.88)	72.6(6.03)	.1069
dumbbell press	20.5(2.84)	20.0(0.0)	.7053
combined score	298.6(46.21)	266.6(15.01)	.1613

* significant at $\alpha = 0.05$

\+ when the variance of each sample is significantly different, the t-test using the separate variances was utilized.

The endocrine profile of both groups was compared using an analysis of variance with repeated measures for each hormone studied (Table 2). All the results were within the normal female range as will be discussed later. Free-testosterone and androstenedione values were quite similar in both groups and no significant difference was observed at any point of the menstrual cycle. Estradiol and progesterone values were not statistically different despite some relatively great differences in certain phases of the menstrual cycle. Thus, early follicular and late luteal values for estradiol were relatively similar for both groups whereas late follicular and early luteal phase values were 77.1% and 20.3% respectively higher in the reference group. In addition, luteal phase progesterone values were 56.1% and 129.8% lower in the reference group. However, such differences did not reach significance suggesting that they may be due to sampling variations.

4.2) THE EFFECTIVENESS OF THE STRENGTH TRAINING PROGRAM:

The strength training program was analyzed to establish its effectiveness in increasing strength as well as in inducing anthropometric changes. The first concern was to reduce the number of variables to analyze since the number of subjects is rather small. Thus, a correlation matrix was computed and only one of a group of highly correlated variables was kept for further statistical analysis. The correlation matrix is listed in Appendix A. As such, the gluteal girth was ommitted due to its high correlation ($r = 0.88$) with the thigh girth especially.

TABLE 2

Hormonal data of the experimental group (prior to training) and of the control group

	Experimental(±SD) n=10	Control(±SD) n=15	
Estradiol(pg/ml)			
early follicular	147.4(135.1)	156.9(57.9)	
late follicular	153.5(142.5)	271.9(119.2)	
early luteal	189.4(164.3)	227.8(152.0)	
late luteal	158.5(155.2)	139.0(80.0)	NS
Progesterone(ng/ml)			
early follicular	0.99(.66)	0.32(.15)	
late follicular	0.87(.75)	0.54(.28)	
early luteal	9.01(5.09)	5.77(8.03)	
late luteal	12.02(8.53)	5.23(6.38)	NS
Free-testosterone(pg/ml)			
early follicular	2.42(.92)	3.14(1.96)	
late follicular	3.12(1.92)	3.72(2.51)	
early luteal	3.00(1.53)	3.04(2.21)	
late luteal	2.82(1.67)	2.72(1.33)	NS
Androstenedione(ng/ml)			
early follicular	3.09(.86)	2.98(2.00)	
late follicular	3.77(1.13)	3.79(2.08)	
early luteal	3.29(1.65)	3.18(1.90)	
late luteal	4.13(1.42)	3.01(1.86)	NS

All strength parameters were highly correlated (0.74 or above) to the combined total representing the sum of the 4 lifts. Thus, only the combined score was utilized. Repeated t-tests using the Hotelling T^2 to protect the alpha level were computed on a restricted number of variables. The results are listed in Table 3.

TABLE 3

Anthropometric and strength changes in experimental subjects (n=10) following the 8-week training program

	Pre(±SD)	Post(±SD)	Change of	% Change	P value
weight(kg)	61.5(6.41)	62.1(6.40)	.61	0.1%	.0842
percent adiposity(%)	25.1(4.28)	25.8(3.8)	.78	3.1%	.1077
Girths(cm)					
chest	75.2(3.74)	74.9(2.80)	.29	0.4%	.6673
waist	66.4(3.35)	65.8(3.61)	.65	1.0%	.0893
thigh	56.5(3.10)	57.7(3.15)	1.14	2.0%	.0128*
arm	27.0(1.69)	28.2(1.88)	1.18	4.4%	.0016*
Strength(kg)					
combined total	135.4(21.0)	185.0(29.0)	49.6	36.6%	.0000*

Mahalanobis Δ square 128.5376
Hotelling T square 1385.3811
F values 61.2089 P value 0.0031
Degrees of freedom 7, 3.0

* significant at $\alpha = 0.05$

When additional analyses are applied to the strength measurements the following results are obtained.

Body weight and the relative adiposity were unchanged following the 8 week program. Chest and waist girths were unchanged but arm and thigh were significantly increased ($p = 0.0016$ and .0128 respectively) suggesting a modest degree of hypertrophy. The combined total score for strength was increased very significantly ($p = 0.0000$) with a 36.6% increase over the pre-training value.

Notwithstanding, a second statistical analysis was performed on the individual lifts in an attempt to establish the relative increase in strength for various muscle groups. These results should be considered as being mostly descriptive since the relatively small sample size do not enable the analysis of so many variables.

TABLE 4

Strength changes in experimental subjects following an 8-week training program

Exercise(kg)	Pre(±SD)	Post(±SD)	Change of	% Change	P value
leg press	60.1(15.04)	93.7(15.68)	33.5	55.7%	.0000
bench press	28.6(3.42)	35.8(5.74)	7.3	25.4%	.0009
lat pull	37.4(5.39)	43.9(8.08)	6.5	17.3%	.0063
dumbbell press	9.3(1.29)	11.6(1.67)	2.3	24.4%	.0011

The high correlation of each lift with the combined score and the high significance of each suggest that the possibility of a type I error is rather minimal despite the repetitive analysis of the data. Furthermore, when the alpha level is protected (i.e. α/number of observations), the results are still significant.

Therefore, it seems that training had no significant effect

on weight, relative fatness, and on chest and waist girths. Significant increases in thigh and arm girth suggest a modest degree of hypertrophy. Strength scores were all increased significantly suggesting that the program was intense enough to elicit the desirable effects.

Short-term training may have induced hormonal changes in the experimental group. To further investigate this hypothesis, an analysis of variance with repeated measure was performed for each hormone. All endocrine data are listed in Table 5. No significant differences were seen for estradiol, progesterone, androstenedione and free-testosterone. It is conceivable that the program may have not been long enough to elicit endocrine changes.

4.3) COMPARISONS BETWEEN THE BODYBUILDING AND THE REFERENCE GROUP

Aerobic exercises have been shown repeatedly to induce changes in the basal concentrations of several hormones. However, nothing is known of the effect of intense and chronic weight-training on the endocrine function. Thus, the effects of intense and long-term (at least a year) weight-training were determined by comparing bodybuilders and a group of untrained university students (reference group). The same statistical analysis than for the experimental group were applied in an attempt to protect the alpha level. Comparisons were therefore undertaken between the bodybuilders (N=9) and the reference group (N=15). The results obtained are summarized in Table 6.

TABLE 5

Endocrine variations in the experimental group following an 8 week training program

Estradiol (pg/ml)	Pre (±SD)	Post (±SD)	
early follicular	147.4 (135.0)	187.0 (136.6)	
late follicular	153.5 (142.5)	189.9 (213.9)	
early luteal	189.4 (164.3)	185.6 (114.2)	
late luteal	158.5 (155.2)	172.3 (141.0)	NS
Progesterone (ng/ml)			
early follicular	.99 (.66)	1.06 (1.65)	
late follicular	.87 (.75)	.58 (.40)	
early luteal	9.01 (5.09)	11.40 (7.08)	
late luteal	12.02 (8.53)	10.31 (8.31)	NS
Free-Testosterone (pg/ml)			
early follicular	2.42 (.92)	2.70 (1.29)	
late follicular	3.12 (1.92)	2.87 (1.56)	
early luteal	3.00 (1.67)	3.05 (1.68)	
late luteal	2.82 (1.67)	3.55 (2.21)	NS
Androstenedione (ng/ml)			
early follicular	3.09 (.86)	3.26 (.79)	
late follicular	3.77 (1.13)	3.80 (1.31)	
early luteal	3.29 (1.65)	3.15 (1.32)	
late luteal	4.13 (1.42)	3.55 (1.12)	NS

*An analysis of variance for repeated measures was utilized for each hormone.

TABLE 6

Strength and anthropometric profile of bodybuilders (N=9) and of reference subjects (N=15)

	Bodybuilders(±SD)	Reference Group(±SD)	P value
age (yrs)	22.9 (4.45)	21.1 (1.98)	.1884
height (cm)	163.5 (4.43)	166.6 (4.11)	.1124
weight (kg)	57.0 (5.09)	63.0 (5.94)	.0237
percent adiposity (%)	19.5 (3.16)	26.4 (4.40)	.0008
Girths (cm)			
chest	78.0 (4.90)	76.1 (.95)	.2962
waist	63.5 (3.82)	67.9 (4.28)	.0244
thigh	53.1 (3.83)	57.5 (1.61)	.0094
arm	29.6 (3.16)	26.4 (4.40)	.0039
Strength(kg)			
combined total	252.9 (42.4)	130.9 (18.6)	.0000

hotelling T^2: 201.6846 p = 0.0000

The bodybuilders were slightly older and smaller than the reference group although both values were not statistically significant. They were significantly lighter (10.5% less than the reference group) and their relative adiposity was also decreased by 35.4% in comparison to the reference group. Waist and thigh girth were significantly enlarged in the reference group probably as a reflect of the increased body fat. Bodybuilders were much stronger with a combined strength score 93.2% higher than the reference group. Individual strength scores are summarized in Table 7.

TABLE 7

Comparisons between individual strength scores in bodybuilders and reference subjects

Exercise(kg)	Bodybuilders(±SD)	Reference Group(±SD)	P value
leg press	149.5 (37.90)	57.3 (13.10)	.0002
bench press	47.2 (3.38)	28.3 (3.2)	.0000
lat pull	44.3 (5.83)	36.0 (5.07)	.0018
dumbbell press	12.0 (1.05)	9.2 (1.31)	.0000

As mentioned previously, the high correlation between the individual lifts and the combined score and the very significant alpha level strongly suggests that the possibility of a type I error is practically non-existant. Furthermore, the differences between both groups are still highly significant when the alpha level is protected (α/number of observations).

The endocrine variations induced by long-term training were studied using an analysis of variance with repeated measures (Table 8). It should be noted, however, that only the amenorrheic body builders (N=7) were utilized in this analysis since they were far more numerous than their regularly cycling counterparts. As utilized by Dale et al. (1979), the mean of 4 consecutive blood samples (i.e. 28 days) was obtained for each group in an attempt to obtain values that would be more representative of a menstrual cycle.

TABLE 8

Mean endocrine profile of amenorrheic bodybuilders (N=7) and of reference subjects (N=15)

	Amenorrheic bodybuilders (±SD)	Reference group (±SD)	P value
Mean estradiol (pg/ml)	161.6 (64.8)	174.4 (107.0)	0.77
Mean progesterone (ng/ml)	0.42 (0.06)	4.81 (0.77)	.001
Mean free-testosterone (pg/ml)	3.74 (0.64)	2.94 (0.39)	.28
Mean androstenedione (ng/ml)	4.07 (0.35)	3.46 (0.33)	.28

The mean concentrations of estradiol, testosterone and androstenedione were not statistically different in both groups, suggesting that exercise may not have an effect on these hormones. However, the mean progesterone level was 91.3% lower in bodybuilders strongly suggest anovulatory cycles in amenorrheic bodybuilders.

CHAPTER V

DISCUSSION

Part A: Similarities between the experimental and control groups:

Baseline values of the experimental and control groups were examined for possible differences before the pooling of both groups in a single reference one. They were found to be similar in age, an important feature since the variability in menstrual status could be related to age alone (Patterson et al. 1973). Similarly, differences in hormonal levels could also have been affected by age. Furthermore, weight, height and the relative adiposity were not statistically different although the latter approached significance ($p = 0.0863$) with a 16.3% difference between both groups (25.1% and 29.2% of body fat for experimental and reference group respectively). Girth measurements were not statistically different in both groups except for the gluteal which was significantly larger (52%, $p = 0.0315$) in the reference group. All other girth measurements were consistently higher in the reference group without reaching, however, statistical significance. Comparisons of skinfolds yielded basically the same pattern. Biceps, triceps, and subscapular values were not statistically different but they were consistently higher in the controls. However, the suprailiac was markedly different with a higher value (64%, $p = 0.0170$) in the controls. Increased girth and skinfold measurements in the reference group suggest a higher fat content in controls as shown by their higher relative adiposity.

Statistical analysis of the strength score did not reveal any significant differences. However, strength scores were consistently lower in the controls, especially on the leg press and lat pull scores where mean differences of 17.3% and 13.8% respectively were seen. On the opposite, the bench press and the dumbbell press scores were quite comparable. Therefore, differences in the former two exercises explain almost entirely the 13.6 kg difference observed on the combined score that serve as an index of overall body strength.

In summary, most of the anthropometric data were not statistically different between both groups. In fact, only two parameters reached significance. In terms of strength, no values reached significance despite differences of 13.8% and 17.3% on two lifts. On the basis of these results it appears that both the experimental and control groups were sufficiently similar to be pooled as a reference group.

The endocrine patterns of both groups were compared together and also to the normal values published in the literature to establish their similarity with the values of the normal population. Before analyzing the data, it is important at this point to rationalize the choice of our reference standards since they vary from author to author. Therefore, several sets of endocrine values were compared and are listed in Appendix B. In this study, the standard values given with the radioimmunoassay procedures currently utilized (Diagnostic Products, California) were chosen as reference for the following reasons:

- A significant source of variation when dealing with hormonal analyses is the assay methods utilized

especially from the percent cross-reactivity and the sensitivity standpoint. The variability related to the assay method per se is therefore eliminated by using the same assay procedures.

- The standard values reported by Diagnostic Products also included a range of acceptable values as opposed to means only as reported in certain textbooks. It is more appropriate to utilize ranges of normal values especially when great variability is expected.
- Finally, the standard values reported by Diagnostic Products are comparable to the well established and widely accepted standards reported by Yen & Jaffe (1986).

Estradiol:

Estradiol values obtained for both groups fall well-within the normal range reported for healthy females (Diagnostic Products). This is especially apparent for all measurements except for those of the early follicular phase where values measured (145-155 pg/ml) may seem high in view of the 10-50 pg/ml reported as being normal. However, such variation may be explained by our method of classification of the samples. We have classified as being representative of the early follicular phase all samples taken between the onset of menses and the subsequent 7 days. These values are found to be higher than the values reported (Diagnostic Products) since they were measured only 2 days after the onset of menses. Thus, such values would be representative of a very early proliferative phase, a time

when estradiol levels are low.

Variability between groups:

Comparisons between groups indicate that both groups are relatively similar since the analysis of variance did not reveal any significant differences ($p = .3096$). Of concern, however, is the 43.5% difference between late follicular values despite the fact that it did not reach significance. It is difficult to explain such differences especially when considering that other values are relatively similar. However, since both values are well within normal range (120-375 pg/ml), one may assume that such difference is at least partly due to a sampling error especially when dealing with small samples. This also suggests an appreciable variability between subjects.

Progesterone:

Progesterone values obtained during the follicular phase fall below 1 ng/ml (range 0.1 - 1.5 ng/ml, Diagnostic Products), a characteristic of a normal progesterone pattern (Greenspan & Forsham 1983, Hall et al. 1980, Israel et al. 1972, Reeves & DicFaluszy 1971, Yoshimi & Lipsett 1968). However, values obtained during the luteal phase for the control group are more subject to controversies. Since progesterone reflects the ovulation process, one may wonder to which extent reduced concentrations (approximately 5 ng/ml) in the luteal phase still reflects normal ovulatory cycles. The critical threshold above which ovulation is thought to occur is still a poorly defined

area. From the literature, it appears that progesterone levels of 5 ng/ml or above are considered an acceptable indicator of ovulation (Cargill et al. 1969, Israel et al. 1972, Greenspan & Forsham 1983). In fact, it has been demonstrated that the majority of women with progesterone levels of 5 ng/ml also show a thermogenic shift characteristic of ovulation. Furthermore, results from the same study show that levels of 3-5 ng/ml were always accompanied by a secretory endometrium (Cargill et al. 1969). In his study, Israel et al. (1972) also concluded:

> "In this study, a single serum sample obtained in the mid-luteal phase between 11 and 4 days prior to subsequent menses, with a progesterone concentration greater than 3 ng/ml was always accompanied by a secretory endometrium. Therefore, the finding of progesterone levels greater than 3 ng/ml in this time period provides the clinician with presumptive evidence that ovulation has occurred in that cycle."

In addition, other studies have also used a luteal phase concentration of at least 5 ng/ml as an indicator of a normal ovulation process (Abraham et al. 1972, Abraham et al. 1974a). However, others have suggested values of at least 10 ng/ml as being representative of the normal ovulation process (Hall et al. 1980, Reeves 1971). There is no doubt that the latter represents a much more conservative approach. Nevertheless, we can still conclude with a certain degree of certainty that our controls had normal ovulation despite the relatively low progesterone levels.

Variability between groups:

All samples were consistently lower in the control group without however reaching statistical significance ($p = .2973$). As mentioned previously, there is more concern with the 36.0 and 56.5% lowered values of the luteal phase than for those of the follicular phase. It may seem appropriate to use our combined control group as well as progesterone levels reported by the literature for further comparisons with the bodybuilders. This way, the latter group could be compared to a group of women of the same age in whom progesterone assays were made using the same technique, thus eliminating age and the radioimmunoassay technique as sources of variability. In addition, comparisons with the published values will determine to which extent both groups are either deviant or representative of the population as a whole.

Free-testosterone:

We have measured free testosterone concentration, i.e. the form that is biologically active, to determine the effects of exercise on circulating androgen levels. However, most studies reported in the literature deal with total testosterone concentration. For this reason, values are compared with those given by Diagnostic Products. Values around ovulation time (i.e. late follicular and early luteal) are slightly elevated when compared with both ends of the cycle. This pattern is particularly apparent in group 1. Such findings agree with Abraham et al. (1974a) and Judd & Yen (1972) who reported

increased androgen concentration in the middle third of the cycle. The LH peak seen at ovulation is thought to be responsible for such increase (Judd & Yen 1972). Adrenal contributions to the testosterone pool is rather constant throughout the cycle whereas the ovarian contribution fluctuates, giving rise to the variations in plasmatic concentrations (Abraham et al. 1974b). In this study, the free testosterone values obtained range from 2.5 to 3.75 pg/ml as compared to the 0.7-3.6 pg/ml reported (Diagnostic Products). The results suggest that our subjects, despite normal values, tend to congregate in the high-normal range. Values were not different ($p = .4437$) in both groups of subjects.

Androstenedione:

The androstenedione concentration also exhibit minor fluctuations throughout the cycle with an increased concentration around ovulation (Abraham et al. 1974b, Judd & Yen 1972). This typical pattern is noticeable in the controls but values from group 1 do not show such variations. Increased levels at ovulation are also related to the LH peak (Judd & Yen 1973) that affects mostly the ovarian secretion, with the adrenal secretion remaining rather constant throughout the cycle (Abraham et al. 1974b). In women, 50-60% of the circulating testosterone arises from the peripheral conversion of androstenedione, explaining the inter-relationship between the two (Judd & Yen 1973).

No significant differences ($p = .3120$) were observed between both groups. Most values are essentially identical with only a 37.2% difference in the late luteal phase.

Part B: The effectiveness of the strength training program

Except for occasional muscular discomforts, there were no injuries due to the weight-training programme indicating that the women adapted well to the nature and intensity of the routine. The motivation of the subjects was exceptionally high and there were no dropouts. This may be due to the fact that the subjects were personally supervised and that their progressions were closely monitored, particularly with respect to technique.

We analyzed the effects of the training program in an attempt to determine to which extent it was effective. All data relating to anthropometry and strength are summarized in Table 3.

No significant changes in body weight and in percent body fat were found following the program. The former finding agree with most other studies utilizing young females as subjects for weight training of similar duration (Gettman et al. 1982, Jette et al. In press, Mayhew & Gross 1974, Wilmore 1974). In general, the percentage of body fat is not significantly altered following weight training (Brown & Wilmore 1974, Jette et al. In press, O'Shea 1981) although some authors reported statistically significant but rather minimal decrease in relative fatness following training (Gettman 1982, Wilmore 1974, Mayhew & Gross 1974).

For purpose of comparisons, we have reported studies of Wilmore (1974) and Jette et al. (In press) to further explore the anthropometric changes following training:

	Wilmore et al. (1974) (N=47)			Jette et al. (In press)(N=80)			Present Study (N=10)		
age	20.3			21.2			21.2		
height (cm)	164.8			164.22			166.0		
weight (kg)	59.95	59.90	NS	57.7	58.0	NS	61.5		
body fat (%)				25.8	26.0	NS	25.1		
chest(cm)	73.8	74.3	NS	74.2	74.8	NS	75.2	74.9	NS
waist	67.5	67.3	NS	67.2	67.8	NS	66.4	65.8	NS
gluteals	94.9	94.5	NS	91.4	91.0	NS	92.1	92.4	NS
thigh	54.0	53.8	NS	53.4	53.7	NS	56.5	57.7	SIGN
biceps	27.3	27.9	SIGN	-	-	-	27.0	28.2	SIGN
forearm	23.5	23.6	SIGN	23.1	23.6	SIGN	24.6	24.8	NS
bench press(kg)				62.4	73.8	SIGN	63.0	79.0	SIGN

Thus, our results agree with previous studies in demonstrating very few significant anthropometric changes following weight-training of approximately 2 months duration. In this study, we found significant changes in thigh and arm girths of 1.2 cm as opposed to a 0.6 cm increase in arm girth in Wilmore's study and a 0.5 cm increase in forearm girth in Jette's study. Despite statistical significance, they all represent minor changes from a practical standpoint (0.5 to 1.2 cm). Nevertheless, such increases in the present study probably reflect a certain degree of hypertrophy. The relative importance accorded to leg training in this study probably explains such increase in thigh girth. Although we did not particularly emphasize arm training to the same extent, the workload imposed was high enough to induce hypertrophy especially when considering the low intensity of arm work in everyday activity of previously untrained subjects. In summary, the present study confirms that short-term weight training is generally ineffective in altering

body composition of females as well as most anthropometric parameters as reported previously by Mayhew & Gross (1974).

In terms of strength increases, we have used mostly the 1-RM technique to assess the magnitude of the increment. The leg press, bench press, lat pull, dumbbell press were used in an attempt to obtain a good idea of overall strength. When considered individually, all exercises were significantly improved. When the four exercises are considered together as an index of overall strength, we found a 36.5% increase. One can appreciate the importance of the leg strength increase (55.7%) as compared to other measures of upper body strength (25.4% for bench press, 17.3% for lat pull, 24.4% for dumbbell press). The increase in leg press is relatively similar to the 48% increase reported by Mayhew & Gross (1974). However, lower improvements were reported in other studies. Gettman et al. (1982) reported an increase of only 19% in leg press following 12 weeks of training. However, this can be due to the relatively low training load utilized in that study (40% of 1-RM). Furthermore, a 29.5% increase was reported by Wilmore (1974) but the average training frequency of 2 sessions/week may not have been enough to elicit maximal changes. Finally, Brown & Wilmore (1974) reported only a 16.5% increase on the squat but they utilized high caliber athletes who probably had achieved a good part of their strength potential prior to onset of training, making further gains more difficult. It is not possible to compare absolute scores between studies since different testing modes were used (squat, leg press, tensiometer). In addition, the range of motion was rather

limited in some studies (ex. half squat in O'Shea & Wegner 1981), making it easier for the subjects to lift more weight due to a more efficient leverage. In this study, subjects were asked to perform the exercises using the greatest range of motion possible thus, making the exercise more difficult. It is easier to compare scores obtained on the bench press with results from other studies since the testing procedure is more standardized. In this study, the 25.4% increase in bench press is somewhat intermediary to the 18-29% increases reported utilizing programs of similar duration (Gettman et al. 1982, Jette et al. In press, Mayhew & Gross 1974, Wilmore 1974). In fact, our mean increase is 38.8% higher than the one reported for another university population:

	Pre(kg)	Post(kg)	% Increase
Jette et al.(In press)	28.3	33.5	18.3%
This study	28.6	35.9	25.4%

The use of longer training sessions (60 instead of 30 minutes) and a more frequent training program (4 vs 3 times/week) could probably explain such differences. However, results from this study despite being 38.8% higher only represents a mean difference of 2.4 kg. Finally, when all 3 exercises of upper body strength are pooled together we obtain a 21.3% increase in upper body strength which is relatively similar to the 18% increase reported by Jette et al. (in press).

In summary, it appears from this study that the program was quite effective in enhancing strength in women as judged by the relative increases obtained. In addition, two major conclusions

stem from this study:

- the significant increases in strength occurred despite very little increases in girth. This finding corroborates that increases in strength in women occur mostly via an increased neuromuscular coordination instead of hypertrophy (Moritani & DeVries 1979).
- the leg potential for strength training in females is much higher than the potential for upper body strength as suggested by Wilmore 1974.

Part C Endocrine changes following the 8 week program

This study probably represents one of the first attempts to analyze the effects of a short-term weight training on the female's endocrine function. Two baseline cycles were compared with the hormonal values of the second training cycle. An analysis of variance with repeated measures was performed on each of the four hormones to evaluate the potential changes.

Estradiol:

No significant differences were observed between the pre- and post-training values ($p = .2725$). Interestingly, all post-training values were consistently higher throughout the menstrual cycle. This is especially apparent when one considers the follicular phase values. In fact, early and late follicular values were increased by 26.9 and 21.8% respectively. However, the variability as measured by the standard error is too high to permit any conclusions at least from a statistical standpoint.

It is difficult to establish clearly the biphasic pattern of estradiol with only four samples but it appears that the values obtained during training show even less variations throughout the cycle. This remains purely speculative but it is tempting to suggest a decreased biphasic pattern following training. This will have to be shown more conclusively in further studies.

Progesterone:

The significant statistical ($p = .0002$) time interaction reflects clearly the characteristic increase in progesterone during the latter part of the cycle in the pre- and post-training data. In addition, all values of the luteal phase are close to or above 10 ng/ml, a conservative threshold for normal ovulatory cycle. Furthermore, the exercise did not alter significantly the progesterone concentration ($p = .9081$).

Free-testosterone:

It appears that short-term weight-training did not have a significant effect on the free-testosterone concentration ($p = .4304$). These results agree with the findings of Hetrick & Wilmore (1979) who did not observe a significant increase in androgen value following an 8-week weight training in females ($N = 35$).

Androstenedione:

In this study, we have included measurements of androstenedione since this androgen is known to be secreted in

greater amount than testosterone in females. However, its biological potency is only 20% of testosterone (McKerns 1969). No significant changes in androstenedione were observed at any points of the menstrual cycle ($p = .5726$). As far as we know, this is the first study measuring basal androstenedione concentration following weight training. However, Weiss et al. (1983) studied the pre and post-exercise androstenedione behaviour of 20 females following 30 minutes of weight training. The androstenedione levels did not increase and even dropped significantly ($p < .01$) below pre-exercise values 2 hours following training. This pattern of response differs from the one reported by Kuoppasalmi et al. (1976) for well-trained male runners. In their study, androstenedione levels increased significantly following sprint training and it did not decrease to pre-exercise levels until 6 hours post-exercise. However, differences in conditioning status of the subjects as well as different modes and intensity of exercise make comparisons rather difficult.

It is quite conceivable that our small sample size and the great interindividual variations in basal levels prevented some of the data to reach statistical significance. Therefore, comparison of the data on an individual basis, i.e. using each subject as her own control, could yield interesting trends. Thus, subjects were classified according to the magnitude and to the difference between pre- and post-exercise values. In this study, values were considered clinically different when they differed by at least 20%, i.e. approximately two times the

interassay variability for most hormones. The following classifications were established:

PRE-EXERCISE: when pre-exercise values are higher than the exercise values by at least 20%

NO CHANGES: when pre- and exercise values did not differ by at least 20%

EXERCISE: when exercise values are higher than the pre-exercise values by 20%.

Using this classification, we obtained the following results:

TABLE 6
Endocrine changes following the 8-week training program

Estradiol	Phases of the cycle			
Categories of changes	early foll. (N=10)	late foll. (N=9)	early lut. (N=10)	late lut. (N=9)
PRE-EXERCISE	2	1	3	3
NO CHANGES	2	2	4	1
EXERCISE	6 (mean increase of 55%)	6 (mean increase of 44%	3	5
Progesterone	(N=9)	(N=9)	(N=10)	(N=9)
PRE-EXERCISE	7 (mean increase of 49%)	3	4	3
NO CHANGES	2	4	1	3
EXERCISE	1	2	5	3
Testosterone	(N=9)	(N=10)	(N=10)	(N=10)
PRE-EXERCISE	3	7 (mean increase of 36%)	3	1
NO CHANGES	2	1	4	5
EXERCISE	4	2	3	4
Androstenedione	(N=10)	(N=10)	(N=10)	(N=10
PRE-EXERCISE	2	2	2	2
NO CHANGES	4	5	6	7
EXERCISE	4	3	2	1

It is clear to us that such results, because of their nature,

remain purely descriptive and they remain observations that could be verified in further studies. Nevertheless, a few observations are worth mentioning:

- The training program seems to have induced an increase in the estradiol concentrations by 65% and 44% for the early follicular and late follicular phases respectively in the majority of subjects. It is unclear however as to why exercise seem to exert an effect only in this phase.
- Exercise seems to decrease progesterone levels (mean decrease of 49% in 7 out of 9 subjects). Such change also occurs during the early follicular phase.
- While it is clear that androstenedione was unchanged on an individual basis, it appears that free testosterone was also altered during the late follicular phase. In fact, a mean 36% decrease was observed during the late follicular phase of the exercise cycle.

While any conclusions at this point would be premature, it is interesting to note that all changes that could be of importance occurred in the follicular phase of the cycle. From a purely statistical standpoint however, no significant changes were observed following an 8-week weight-training program.

Part D Comparisons of bodybuilders with reference subjects

In this study, weight-training exercises induced only significant increases in strength but no appreciable changes in

anthropometry or in the endocrine pattern of the subjects were seen. One may wonder, however, to which extent a more serious and rigorous training programme could induce significant changes. As far as we know, this study represents the first attempt to analyzing the endocrine response of long-term weight-training. A group of 9 bodybuilders was studied.

Results of the present study are listed with those of Freedson et al. (1983) who studied 10 high-caliber bodybuilders.

	Freedson et al. (1983)	Bodybuilders	Controls	P value
age	27	22.9	21.1	.1884
height(cm)	160.8	163.5	166.6	.1124
weight(kg)	53.8	57.0	63.0	.0237
percent adiposity(%)	13.2	19.5	26.4	.0008
circumferences(cm)				
chest	90.6	78.0	76.1	.2962
waist		64.5	67.9	.0244
hips/gluteals	87.0	88.6	93.7	.0103
thigh	53.0	53.1	57.5	.0094
arm/biceps	28.9	29.6	27.3	.0039
forearm	24.0	25.4	24.8	.3393

In this study, bodybuilders were on average 6 kg lighter and 3 cm shorter with a mean percentage of body fat 35.4% lower than controls. In addition, most anthropometric characteristics were significantly different. Areas of increased fat deposition in women (i.e. waist, thigh and buttocks) are significantly reduced in bodybuilders explaining the reduced percentage of body fat. Conversely, athletes showed an increased ($p = .0039$) arm girth suggesting hypertrophy in this group. Results from Freedson et al. (1983) give the same pattern. Height and weight were also significantly reduced in comparison to the "reference woman"

described by Benkhe & Wilmore (1974). This suggests a smaller stature in this group of athletes when compared to the normal population. In addition, body fat obtained in this study was markedly reduced by 47.7% when compared to what we obtained with our group of athletes. Two reasons may explain such differences:

- Bodybuilders from this study had not started their "cutting" phase at the time of measurements. This particular phase is characterized by a significant weight loss in the last weeks preceeding competition. Although not specified, one can assume that the low values in Freedson's study were characteristic of this particular pre-competition phase.
- The presence of national and international caliber athletes in Freedson's study would suggest better trained athletes.

In comparison with the reference woman, Freedson et al. (1983) also found an increased biceps girth as a result of hypertrophy. Comparisons of thigh and arm measurements show comparable results in both groups of athletes. These results suggest that hypertrophy tend to plateau in females despite different levels of training and of competition. Thus, it is tempting to conclude that females have a rather limited potential for hypertrophy and once it is attained no more gains seem to occur.

In this study, comparisons of strength scores between the reference group and bodybuilders gave interesting results (Table 6). There is a striking mean difference of approximately

91 kg (161%) on the leg press (149.4 vs 57.3 for bodybuilders and controls respectively). Differences of 66.7%, 23.1% and 24.6% are observed for the bench press, lat pull and dumbbell press respectively. However, comparisons between bodybuilders and post-exercise strength score show quite clearly that strength differences are reduced significantly following even a short training program.

Exercises (kg)	Group 1 (pre-exercise)	Group 1 (post-exercise)	Bodybuilders
leg press	60.1	93.7	149.4
bench press	28.6	35.8	47.2
lat pull	37.4	43.9	44.3
dumbbell press	9.3	11.6	11.9
combined	135.9	185.5	252.9

These results suggest that rapid strength increases occur within the first 8 weeks of training probably as a result of increased neuromuscular recruitment (Moritani & DeVries 1979). Thus, if the combined exercises are utilized, bodybuilders are on average 86.1% stronger than untrained females but this difference is reduced to 36.3% following 2 months of training. However, one should keep in mind that our university females are, on average, 6 kg heavier than bodybuilders making absolute scores less reliable for comparisons. Thus, when results of both groups are expressed relative to their body weight the following results are obtained:

	Group 1(pre)	Group 2(post)	Bodybuilders
leg press	0.98	1.52	2.62
bench press	0.46	0.58	0.83
lat pull	0.61	0.71	0.78
dumbbell press	0.15	0.20	0.21
combined	2.21	3.01	4.43

Results obtained on the leg and bench press are quite different

in both groups while the lat pull and the dumbbell press are relatively comparable.

Hormonal values:

The high proportion of amenorrheic bodybuilders presents a real problem for endocrine analysis. Since many female athletes involved in rigorous training lack menses, it is difficult to classify the blood samples with respect to the phase of the menstrual cycle. Therefore, the hormonal levels obtained during four consecutive blood samples (i.e. 28 days, a length of time theoretically equal to a normal menstrual cycle) were averaged. Such technique had also been utilized with runners (Dale et al. 1979). This procedure may depict more realistically the endocrine pattern of amenorrheic athletes.

As seen on Table 7, estradiol concentration was not different between the bodybuilders and the reference group despite the high incidence of amenorrhea in the former group. One would expect reduced estradiol levels in bodybuilders since the absence of menses is a clinical sign of a depressed estrogenic status (Boyden et al. 1983). This rather normal estradiol concentration is particularly unexpected especially when considering that reduced estradiol levels in athletes is the most universal finding associated with exercise-induced amenorrhea (Boyden et al. 1983, Bonen et al. 1981, Dale et al. 1979, Russell et al. 1984a, Ronkainen et al. 1985). Comparisons

with the results from Dale et al. (1979) are made below:

	Progesterone (ng/ml)	Estradiol (pg/ml)
Dale et al.(1979):		
controls (N=17)	9.4	187
joggers (N=6)	9.0	180
runners (N=14)	5.1	129
Present study:		
controls (N=15)	4.81	174.4
amenorrheic bodybuilders	0.42	161.6

Thus in the present study, estradiol levels were not depressed in bodybuilders when compared to controls whereas runners from Dale's study had approximately a 60 pg/ml decrease when compared to controls. Furthermore, progesterone levels in amenorrheic bodybuilders were drastically reduced in amenorrheic bodybuilders with values 91% lower than our reference group. In fact, progesterone levels in all 7 amenorrheic bodybuilders were below 1 ng/ml for the 4 consecutive samples, strongly suggesting anovulation. This finding agrees with Ronkainen et al. (1985) who also reported lowered progesterone concentrations during periods of intensive training. As reported previously, the ultrasonographic examinations performed in that study reveal that exercise could impair folliculogenesis. Therefore, the authors concluded that the lowered progesterone concentration seen during the luteal phase was a result of the impaired follicular development during the follicular phase of the cycle. Other studies also reported suppressed progesterone levels during the luteal phase of athletes (Shangold et al. 1979, Bonen et al. 1981, Shangold et al. 1983). In fact, it has been shown that

training during the luteal phase had a direct effect on that portion of the cycle by reducing the length of this phase as well as the progesterone concentration (Shangold et al. 1979). However, the reduced progesterone level during training (from 30.2 ng/ml as peak during control cycle to 9 ng/ml during training, $p < .01$) in this jogger were by no means comparable to ours (0.42 ng/ml). It is tempting to speculate that weight-training has, for some reasons, a rather potent effect in reducing progesterone concentration. Furthermore, this decrease in progesterone is of concern especially in view of a rather unaltered estradiol concentration. Some authors have suggested that this particular condition could eventually lead to endometrial hyperplasia due to "unopposed estrogens" (Shade 1983, Shangold 1980, Shangold 1984b, Shangold 1985).

To our knowledge, this study represents one of the first attempts at studying the basal testosterone in bodybuilders. There was no significant difference between all bodybuilders (N=9) and the reference group in their free-testosterone concentration (3.74 pg/ml vs 2.94 pg/ml respectively, $p = 0.28$). This agrees with the results of Boyden et al. (1983) who did not see significant changes in the basal free-testosterone levels of relatively untrained runners following 15 months of serious training. However, Dale et al. (1979) reported a highly significant ($p < .001$) increase in total testosterone levels in runners when compared to controls. Nevertheless, one may wonder to which extent a difference of 27.2% (0.8 pg/ml) may be of physiological significance especially when dealing with the

biological active form, i.e. the free-testosterone. Furthermore, the mean value of 3.74 pg/ml reported for bodybuilders represents the upper end of the continuum (0.7 - 3.7 pg/ml, Diagnostic Products) of normal female values.

As for free-testosterone, the basal androstenedione concentration was not significantly increased in bodybuilders when compared to the reference group ($p = .28$) despite a 17.6% increase. Studies have shown acute increases in androstenedione concentration following exercise (Chaikovski et al. 1985) but very few of them if any, have studied the effects of exercise on its basal concentration. As mentioned previously, androstenedione has only 20% of the biological potency of testosterone (McKerns 1969) and it is doubtful that the 17.6% difference between both groups could be of any physiological significance. Weiss et al. (1983) demonstrated that the androstenedione response to a single bout of exercise was similar in men and women. Surprisingly however, the concentration decreased for two hours following exercise. In other studies, androstenedione levels were similar in runners and controls (Baker et al. 1981b) and no differences were seen between regularly cycling and amenorrheic athletes.

Incidence of amenorrhea:

In this study, the incidence of secondary amenorrhea as defined by absence of menses over the last 3 months was strikingly high among bodybuilders (77.8%). This is markedly higher than what was found with most other groups of athletes. The highest incidence of amenorrhea reported so far was the 30-50% incidence reported among real competitive long-distance runners (see Baker 1981b, Hale 1983, Jacobs 1982, Wall 1983). While numerous studies have reported the incidence of secondary amenorrhea in aerobic athletes, there has been so far only one study reporting the incidence of amenorrhea in bodybuilding. Elliot & Goldberg (1983) surveyed the menstrual history of the participants at the Pacific Northwest Body Building Competition. They reported a 33% incidence among participants, a figure much lower than our results. Unlike runners (Dale et al. 1979), Elliot & Goldberg (1983) found that prior pregnancies did not protect bodybuilders from exercise-induced amenorrhea. In fact, the only parous athlete from the present study, a 31 year old female with 2 children, also suffered the longest episode of secondary amenorrhea, i.e. 12 consecutive months.

In contrast, the reference and the experimental groups did not report any significant episodes of amenorrhea. In one study of college students (N=900) attending the university clinic for gynecologic disorders, the incidence of oligomenorrhea and secondary amenorrhea were 5.6% and 5% respectively (Singh 1981). Together, both problems accounted for 72.5% of the minor disorders reported at the gynecologic clinic. In a subgroup of

amenorrheic patients, the mean duration of the disorder was 6.3 months (range 3 to 16 months). When examined epidemiologically, the frequency of secondary amenorrhea appeared to be quantitatively related to the separation from home and friends and to the severity of stress associated with such separation. Thus, the incidence of amenorrhea among the student population (5% in Singh 1981) is slightly higher than the 3.3% reported for a sample of the overall population (Petterson et al. 1973). According to Braunstein (1980) the emotional stress caused by exams is one of the factors that may lead to temporary or prolonged amenorrhea. In addition, irregularities and anovulatory cycles are more common during adolescent and young adult years than in mid-years menstruating women (Eskin 1970).

It should be pointed out that the design of this study may have exaggerated the results obtained especially with respect to the incidence of secondary amenorrhea. Since all groups consisted of volunteers, it is quite conceivable that bodybuilders who had menstrual problems were more interested in the study. On the other hand, the control and the experimental subjects may represent a self-selected group of regularly cycling women. From the subject standpoint, a regular menstrual cycle may have been seen as a pre-requisite before entering the study.

CONCLUSION

The results from the study indicate that short-term heavy resistance weight-training had no effects on the basal levels of estradiol, progesterone, free-testosterone and androstenedione. Furthermore, training did not induce any menstrual disorders since all of the experimental subjects continued to menstruate regularly during the program. There were no changes in body weight and in body fat following training. However, a relatively modest but statistically significant degree of hypertrophy was observed for arm and thigh. Thus, anthropometric changes seen in this study agree with those of previous studies indicating that only small changes in body composition are to be expected from programs of 8 to weeks duration. A 36.6% overall strength increase occurred as a result of intensive training. The magnitude of the increase in strength despite the rather modest degree of hypertrophy achieved, suggest that in females, increased neuromuscular recruitment may be the primary mechanism responsible for increases in strength. Leg strength potential appears to be much higher than upper body strength potential as determined by the relative increases on the 4 different exercises.

In this study, long-term heavy-resistance weight-training in the form of bodybuilding produced significant changes in the endocrine and menstrual pattern of athletes. A very high incidence of amenorrhea was observed. This was higher than that reported in the literature. It should noted, however, that the observed incidence of this study, may be biased by the small

sample size and by the non-randomized experimental design. Endocrine data of amenorrheic bodybuilders was averaged over a 28-day period. In contrast to other studies using aerobically-trained athletes, estradiol levels were not significantly reduced in athletes. However, progesterone levels were drastically reduced when compared to reference values. For amenorrheic atheltes, values were always characteristics of the early follicular phase, strongly suggesting anovulation. Therefore, it was concluded that bodybuilders seem to be at high risk for endometrial hyperplasia due to the action of "unopposed estrogen", especially since progesterone values were drastically reduced whereas estradiol was practically unchanged. Furthermore, free-testosterone and androstenedione levels were increased in bodybuilders, not reaching however, statistical significance. It was hypothesized that the increase in free-testosterone in bodybuilders may be physiolgically important, especially since only the biologically active form was measured. Bodybuilders had levels of free-testosterone near the upper limit of the normal female range reported by Diagnostic Products Corporation (Los Angeles). From the data of this study, it is not possible to determine whether this slightly increased concentration is a result of training, or if it is an inherent characteristic of female athletes. Finally, the small difference in androstenedione concentration between bodybuilders and reference subjects is most probably not significant especially in view of its very low biologic potency.

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APPENDIX A

CORRELATION MATRIX FOR STRENGTH AND ANTHROPOMETRIC PARAMETERS

A) Anthropometry:

Girths	Chest	Waist	Gluteal	Thigh	Arm	Forearm	Biceps	Triceps	Subdcapular	Suprailiac
Chest	----	.5177	.2658	.1856	.7021	.4029	.2488	.3953	.3727	.2705
Waist	.5177	----	.7812	.7341	.1866	.3424	.6620	.8387	.6265	.8381
Gluteal	.2658	.7812	----	.8785	.0247	.2229	.6471	.6986	.4589	.7207
Thigh	.1856	.7341	.8785	----	.0189	.1117	.6146	.6798	.4951	.6257
Arm	.7021	.1866	.0247	.0189	----	.5007	.0273	.1192	.0838	.0031
Skinfolds										
Biceps	.2488	.6620	.6471	.6146	.0273	.0935	----	.8468	.5844	.7610
Triceps	.3953	.8387	.6986	.6798	.1192	.1754	.8468	----	.3237	.8228
subscapular	.3727	.6265	.4588	.4951	.0838	.3237	.6317	.5844	----	.6277
suprailiac	.2705	.8381	.7207	.6257	.0031	.3762	.8228	.7610	.6277	----

B) Strength:

	Leg Press	Bench Press	Lat Pull	Dumbbell Press	Combined Total
leg press	----	.8957	.7052	.6885	.9929
bench press	.8957	----	.7091	.7748	.9303
lat pull	.7052	.7091	----	.6847	.7671
dumbbell press	.6885	.7748	.6847	----	.7402
combined total	.9929	.9303	.7671	.7402	----

APPENDIX B

TABLE OF HORMONAL VALUES (DIAGNOSTIC PRODUCTS, CALIFORNIA)

ESTRADIOL: Values in pg/ml for ovulating females by day in cycle relative to LH peak (day 0)

Follicular phase:	-12	10- 50 pg/ml
	- 4	60-200 pg/ml
Mid-cycle	- 1	120-375 pg/ml
Luteal phase	+ 2	50-155 pg/ml
	+ 6	60-260 pg/ml
	+12	15-115 pg/ml

PROGESTERONE: Values in ng/ml for ovulating females

	median	absolute range
Follicular phase	0.4	0.1- 1.5 ng/ml
Luteal phase	8.5	2.5-28.1 ng/ml
Mid luteal phase	23.2	5.7-28.1 ng/ml

FREE-TESTOSTERONE: Values in pg/ml

	Absolute range
Serum	0.7-3.6 pg/ml
Heparin	0.9-3.8 pg/ml

ANDROSTENEDINE: Values in ng/ml

	Percentiles		
age group	5	50	95
20-29	1.50	2.80	5.80

*Values were not different from those reported by Yen & Jaffe 1986.