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EFFECTS OF ANABOLIC STEROID AND ANAEROBIC TRAINING ON ORGAN WEIGHT, BODY COMPOSITION, FOOD INTAKE AND SKELETAL MUSCLE FIBER SIZE OF THE MALE RAT

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ABSTRACT

The effects of an anabolic steroid (Deca-Durabolin) and an anaerobic sprint training program on 1) organ weight, 2) body composition, 3) food intake and 4) skeletal muscle fiber size of male, Sprague-Dawley albino rats were investigated in two experimental periods. In period one, organ weights were employed as measures of the androgenic side effects of the drug, body composition was used to assess lean body mass and food intake was used to assist in interpreting the effects of the training program. In period two, gastrocnemius weight and the histochemical assessment of skeletal muscle fiber size were employed as measures of muscle hypertrophy. In each period, the rats were assigned to one of four groups: control, drug, training and drug plus training. The training program consisted of 10 second sprints run on the level, and interspersed with 30 second rest periods. They were performed five days per week for eight and nine weeks, respectively, during periods one and two. Both the number and speed were increased until the animals ran 18 sprints at 91 and 78 meters per minute, respectively, in periods one and two. The drug was administered intramuscularly at three week intervals at a dosage of 1 mg/kg body weight. The results were analyzed using a two-way ANOVA and the $P<0.05$ was used to reject the null hypothesis. At the end of period one, analysis of organ weights predicted by the method of least squares regression revealed that training decreased liver and kidneys weights, increased gastrocnemii and heart weights and increased testes weight in the placebo animals. Adrenals weight was unchanged. The drug decreased kidneys weight in

both the trained and sedentary animals, heart weight in sedentary animals and testes weight in trained animals. It also increased the weight of the gastrocnemii, and the testes weight in sedentary animals. Liver and adrenals weights were unchanged. Analysis of the body composition data revealed that training decreased the percentage of the carcass composed of fat with no change in lean body mass. The body composition changes were due entirely to the training program for food intake was unchanged. The drug had no effect on either variable. At the end of period two, analysis of both adjusted gastrocnemii weight and skeletal muscle fiber size showed no effect of either drug or training. In conclusion, the drug appeared to produce no anabolic effects in these animals as muscle weight, fiber size and lean body mass were not significantly changed. There were androgenic side effects produced, as kidneys and testes weights were decreased in the trained animals.

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CHAPTER I

INTRODUCTION

The use of ergogenic aids to enhance athletic performance is a controversial subject which has received much attention in recent years. A most discussed aid is the group of pharmacological agents known as the anabolic steroids.

Anabolic steroids are the synthetic analogs of the male sex hormone testosterone. They are designed to possess a high anabolic effect, the ability to enhance protein synthesis; and a low androgenic capacity, the ability to produce secondary sex characteristics. These drugs were developed primarily for use in clinical medicine and have been used in the treatment of such maladies as osteoporosis and muscular dystrophy. Due to their purported anabolic capacity, they have been used by individuals engaged in athletics, particularly by those for whom strength is a major prerequisite to success.

The theoretical basis of this application by athletes begins with the enhancement of protein synthesis. If this does occur, then skeletal muscle mass could increase. If skeletal muscle mass can increase, a subsequent increase in strength is possible for greater training loads are permitted. With an increase in strength, performance itself should improve. The question arises as to the validity of this rationale. Is protein synthesis enhanced? Is muscle mass increased or hypertrophied? Is performance affected? Are there any androgenic side effects which would outweigh any anabolic benefits incurred?

The purpose of this study is to investigate some of the factors involved in the rationale behind the use of anabolic steroids by athletes. Protein content and lean body mass will be determined by an analysis of whole body composition. Muscle mass and hypertrophy will be measured by muscle weight and histochemical analysis of fiber size, respectively. Finally, androgenic side effects will be determined by weight measurements of selected organs.

CHAPTER II

RELATED LITERATURE

This chapter has been divided into six sections. They are: 1) orientation to anabolic steroids, 2) organ weights, 3) skeletal muscle hypertrophy, 4) body composition and food intake, 5) strength and performance and 6) summary.

I. ORIENTATION TO ANABOLIC STEROIDS

In 1935, Kochakian and Murlin (118) were the first to show that injections of male urinary androgenic extracts, the "male hormone", produced a decrease in urinary nitrogen level. Concomitant with this nitrogen retention in their castrate dogs, was an increase in body weight. This study showed that androgens have a pronounced effect on protein anabolism.

A subsequent study on man substantiated this finding. Kenyon and coworkers (107) gave four eunuchs daily injections of testosterone propionate for three months. This administration produced an increase in the size of the prostate gland, a deepening of the voice and an increase in body weight.

In 1938, Papanicolau and Falk (158) studied the effects of testosterone propionate on the skeletal musculature of the guinea pig. A definite hypertrophy occurred, particularly for the temporal muscle, after prolonged administration of the androgenic hormone.

With these findings and the subsequent elucidation of the chemistry of testosterone, the search began for a synthetic steroid

which would have a high anabolic capacity and a low androgenic effect (136). In 1958, CIBA Research Laboratories developed the first major anabolic steroid, methandrostenolone, and gave it the trade name Dianabol. Since that time, numerous synthetics have been developed, each attempting to reduce the androgenic component of the naturally occurring steroid. These synthetic analogs can be divided into two groups based on the route of administration. One group is taken orally and includes methandrostenolone (Dianabol), ethyloestronol (Maxibolon), norethandralone (Nilevar), oxandralone (Anavar) and stanazolol (Winstrol). The second group is administered intramuscularly and includes nandralone phenpropionate (Durabolin) and nandralone decanoate (Deca-Durabolin) (57, 216).

These drugs were initially developed for use in clinical medicine and have found wide application (1, 122, 124). The reported indications for their therapeutic use include malnutrition, protein deficiency, tumor growth after extensive radiation therapy, skeletal disease, muscle disease, kidney disease, diabetic retinopathy, hyperthyroidism, heart disease, liver disease, blood disease and pediatric medicine. This application is based on the protein synthetic properties of these drugs. Though the clinical indications are numerous, their usefulness is considered restricted (222), and there have been few controlled studies which support their effectiveness and value (1). In fact, their effectiveness has only been substantiated in the treatment of male hypogonadism and mammary cancer (1).

With the use of anabolic steroids there are unwanted androgenic side effects. Their occurrence appears to be less with the injectable

forms as opposed to those which are administered orally (222). These effects are normally reversible with discontinued application of the drug (100). Some of the unwanted side effects include:

1. Impairment of liver function as noted by an increase in serum-glutamic-pyruvic transaminase (SGPT) and serum-glutamic-oxaloacetic transaminase (SGOT) levels (3, 52, 55, 124, 201, 223, 224).

2. Changes in blood levels of cholesterol, glucose and triglycerides (124, 189, 190, 222), which may be associated with atherosclerosis (188).

3. Androgenicity (99, 129, 215).

4. Decreases in testosterone and gonadotropin levels (78, 85, 194).

5. Increases in blood pressure (53, 85, 189).

6. Premature epiphyseal closure (53, 166, 215).

7. Voice changes which may be permanent (14, 53, 129, 215).

8. Various changes in enzyme levels such as lactate dehydrogenase (LDH) (103, 154, 179, 223).

9. Decreases in spermatogenesis (78).

10. Macrogenitosemia praecox (166, 215).

11. Various other symptoms such as headache, dizziness and changes in libido (52, 85, 191).

12. Prolonged administration can lead to serious and potentially fatal associations such as hepatoma, peliosis hepatitis and acute myelogenous leukemia (100).

The developments in androgenic steroid chemistry and their widespread use in clinical medicine produced the inevitable. Athletes

who could see the potential for increases in musculature and strength began to consider and employ these drugs as ergogenic aids. The Russians have been credited with the first application of these drugs to sports (203), although many believe this distinction belongs to the Americans (161).

Since that initial application in the mid 1950's their use has become widespread, particularly among weightlifters and weightmen in track and field athletics (3, 31, 50, 53, 187), and has received much publicity in the popular press and athletic publications (17, 30, 57, 58, 59, 83). This application is illegal for anabolic steroids have been included on the doping list of the I. A. A. F. (International Amateur Athletic Federation) since 1970. They are considered an artificial training aid and a violation of the fair play ethic (168), although the research findings are inconclusive as to their ergogenic capabilities. This situation has developed to such proportions that a concerted effort to produce efficient detection methods has received much support to insure the adherence to the fair play ethic (15, 210).

II. ORGAN WEIGHTS

The use of organ weights has been considered an important source of information on the physiologic effects of both drug and exercise (119, 193). There have been a number of studies that have measured various organ weights and are summarized in Tables 1 and 2. An examination of the information shows that definitive conclusions are difficult to draw due to differences in species, sex of the animals, means of expression of weights (absolute vs. relative), the absence of

Table 1. Effect of forced and spontaneous exercise on organ weights.[a]

	Heart		Liver		Kidneys		Adrenals		Testes	
Reference	F	S	F	S	F	S	F	S	F	S
Young male rats										
Borovansky (12)[b]	+		-		+		+		+	
Donaldson (37)		+		+		+		+		-
Donaldson (36)		+		+		+		+		+
Donaldson (37)		+		-		+		+		+
Donaldson (38)		+		-		+		+		+
Hatai (80)		+		+		o	(+)	o	(o)	+
Kimeldorf (109)[r]	(+)				(o)					
McClimtock (134)		(o)					(+)			
Gollnick (65)[r]	(+)		(o)		(+)		(+)			
Gollnick (67)[r]	(+)		(-)				(+)			
Gollnick (68)[p]	(o)						(+)			
Montoye (140)[r]	(+)						(+)			
Ring (170)[r]		(o)		(o)		(o)		(+)		
Buuck & Tharp (19)[r]	(+)									
Oscai (151)[r]	(o)									
Oscai (150)[r]	(+)									
Crews (28)[r]	(+)									
Arcos (4)[r]	(+)									
Adult male rats										
Hearn & Wainio (81)	(+)						(+)			
Donaldson (37)		+		+		+		+		
Montoye (139)[r]		(o)		(o)		(+)		(o)		
Gollnick (66)[r]	(+)				(-)		(+)			
Young female rats										
Borovansky (12)[b]	+				+		+			
Donaldson (37)		+	-	+		+		o		
Donaldson (36)		+		+		+		+		
Donaldson (37)		+		+		+		+		

Table 1 (continued)

	Heart		Liver		Kidneys		Adrenals		Testes	
Reference	F	S	F	S	F	S	F	S	F	S
Donaldson (38)		+		+		+		+		
McClimtock (134)		+								
Oscai (151)[r]	(+)									
Adult female rats										
Donaldson (37)		+		+		+		+		
Rats, no age given										
Van Liere (198)[r] male	(+)									
Van Liere (198)[r] female	(+)									
Dogs										
Bruns (18)[c]		+		+		+				
Grober (73)[c]		+		+		+				
Junkersdorf (106)[c]		+		+		+				
Steinhaus (192)[r] run	+		-		+		-		-	
Steinhaus (192)[r] swim	+		+		+		+		-	
Mice										
Colacino (29)[r]							(o)			
Guinea Pig										
Petren (165)		+								

[a]In the table + indicates increase, - indicates decrease and o no change in weight. Symbols in parenthesis indicates a statistical analysis. r denotes relative weight, p denotes predicted weight. F indicates forced and S indicates spontaneous.

[b]From Montoye, H. J., et al. Effects of Exercise on Swimming Endurance and Organ Weight in Mature Rats. Res. Quart. 31:474-484, 1960.

[c]From Donaldson, H. H. and R. E. Meeser. Summary of Data for Effects of Exercise on Organ Weight of Albino Rat. Comparison Data from Dog. Am. J. Anat. 56:56-70, 1935.

Table 2. Effects of training and drug on organ weights.[a]

	Heart			Liver			Kidneys			Adrenals			Testes		
Reference	D	T	DT	D	T	DT	D	T	DT	D	T	DT	D	T	DT
Young male rats															
Murphy & Eagan (145)	o	o	o	o	o	-							-	+	-
Cheek (25)[r]	o	o	o	o	o	o	o	o	o	o	+ R	o	- Rb	o	o
Brown & Pilch (16)[r]	o	+ R	o	o	o	o	o	o	o	o	+ R	o	- b	o	o
Taylor (196)	o	o	o	o	-	o				o	+	o	-	o	o
Exner (45)[r]	o	o	o												
Young female rats															
Exner (44)[r]	o	o	o												

[a]In the table + indicates increase, - indicates decrease and o no change in weight. All studies used statistical analysis. r indicates relative weight, b indicates absolute weight and R indicates running program. D indicates drug, T indicates training and DT indicates drug plus training.

statistical analysis, the nature of the exercise (forced vs. spontaneous) and the various types of the drug administered.

A general impression after perusal of the tables is that exercise causes an increase in heart weight, kidneys weight, adrenals weight and testes weight. The liver weight change varies with the particular study.

In the studies involving training and anabolic steroids there are two major findings. The testes weight is decreased in response to the drug, while the adrenals weight is increased in response to the training. There are very few changes in the weight of the heart, liver and kidneys.

III. SKELETAL MUSCLE HYPERTROPHY

The response to training can include an increase in strength and muscle size. The increase in muscle size is usually associated with isotonic strength training as initially quantified by DeLorme (32, 33). DeLorme's system required the execution of three sets of ten repetitions of weight lifting with a progression in resistance over the three sets to the maximum that could be lifted in the final set. This method is commonly referred to as the progressive resistance exercises (PRE). This regimen of near maximal weight training, designed to increase power, produced a rise in strength and girth of the working muscles. Substantiation of the simultaneous girth and strength increases have been reported in a number of studies on the effects of anabolic steroids upon the strength of weightlifters (13, 102, 103). However, in two other studies this was not so. One study found an increase in strength

without a concomitant girth increase (191), while another found a girth increase without an increase in strength (194).

Isometric strength training as initially reported by Hettinger and Muller (84), also produced an increase in strength and muscle size. They claimed a 5% strength increase per week above the original strength value when the isometric tension was maintained for six seconds at 2/3 maximum tension. This finding was not confirmed. Later studies showed that the strength changes were not as large as first suspected (142, 143), while the size increase was not substantiated at all (90, 128, 207).

The factors that have been suggested in explanation for the girth increase attendant with isotonic strength training are an increase in number (hyperplasia) and/or size or volume (hypertrophy) of the muscle fibers. The initial inquiry was made by Morporgu in 1897 (141). He removed the sartorius muscle from two dogs and various muscles from adult rats and followed this with an arduous wheel training program. These treatments produced a 55% and 13% increase, respectively, in the average fiber diameters of the dogs and rats and no increase in the number of muscle fibers of the contralateral muscles. This concept was later supported by the data of MacCallum (127), Seibert (182, 183), Thorner (198) and Hoffman (91).

Other studies have also shown evidence of muscular hypertrophy in laboratory animals. Rowe (174) showed a 140% increase in cross-sectional area in muscle fibers of the mouse soleus after tenotomy of the gastrocnemius. Goldberg (61) showed a 30-50% and 20% increase in the weight of the soleus and plantaris, respectively, after tenotomy of

the gastrocnemius. Mean fiber diameters were also increased.

The above studies used surgical means and produced compensatory hypertrophy. Other investigators have used training programs to produce work induced hypertrophy. Walker (205) found a 49% increase in the average fiber area of the mouse soleus after a treadmill running program. Fitts (49) found an increase in the area of the fast-twitch fibers of the miniature pig after a seven month program of treadmill running. Carrow and coworkers (20) found an increase in both red and white fibers of young rats forced to swim after a voluntary running program.

There are a number of studies that investigated the effects of anabolic steroids on skeletal muscle in laboratory animals. Wydra (221) studied the effects of a treadmill running program and/or Dianabol on the fiber area of various muscles of the mouse. Muscle weight rose slightly but not significantly. The fiber sizes were increased, with training and drug producing similar effects. The combination of the drug and training did not produce a greater effect than either stimulus alone. Pongratz and Mittelbach (167) studied the effects of training and two anabolic steroids (methenolone-enanthate and nandralone decanoate) on normal and denervated skeletal muscle fibers of the the mouse. They stated that the training produced the same degree of hypertrophy as the drugs and that atrophy of denervated muscle does not appear for eight weeks when anabolic steroids were administered. In other studies using anabolic steroids, Taylor and coworkers (196) found an increase in gastrocnemius weight with endurance treadmill running but not with drug administration. Both Brown and Pilch (16) and Exner and coworkers (44,

45) found no weight change in the gastrocnemius with either training or anabolic steroid administration.

Morporgu (141) suggested that the hypertrophy associated with training was due to an increase in the sarcoplasmic fraction of the muscle. As corroboration for that suggestion Holmes and Rasch (97) found no increase in the number of myofibrils per muscle at seven points along the longitudinal length of the enlarged sartorius of rats trained to run for seven weeks. In contrast to this finding, Helander (82), who produced the first biochemical study of hypertrophy, found a 15% increase in the myofibrillar nitrogen fraction of the enlarged gastrocnemius of guinea pigs who were trained on a treadmill for four months.

In support of the finding of an increase in the myofibrillar protein fraction, Goldspink (64) observed a three-to-fourfold increase in the number of myofibrils per muscle fiber of the enlarged biceps brachii of young female mice who were conditioned to pull a weight to retrieve their food. Denny-Brown (34) also reported such an increase. He found a two-fold rise in the myofibrillar portion of the enlarged soleus muscles of cats placed on a regimen of forceful exercise. Gordon and coworkers (70) found that rats trained to climb a vertical ladder while carrying weights attached to their backs had an increase in the myofibrillar protein of the quadriceps. Rats trained to run on a treadmill had an increase in the sarcoplasmic fraction of the same muscles. Both effects occurred without an increase in whole muscle weight and were attributed to an increase in white fiber area, while the red fiber area decreased. They suggested that the red fibers were more

sensitive than white to possible undernutrition brought about by the training programs.

Protein content of muscle has also been studied in animals given an anabolic steroid. Exner and coworkers (44, 45) studied the effects of Deca-Durabolin and/or isometric training on the biochemical and contractile properties of fast and slow muscles of male and female rats. In the females, the slow soleus muscle weight was unchanged, while the fast rectus femoris weight decreased with steroid treatment and increased with training. In the males, neither training nor steroid produced a weight change in either muscle. There was no change in the protein content of the rectus femoris, while the soluble protein fraction of the soleus was increased due to the drug. In another study, Parker (157) placed young rats on a six week period of swimming in conjunction with the administration of Dianabol. He found an increase in both the total and structural protein of the gastrocnemius muscle in animals receiving both the drug and training. In a human study, Penman (162, 163) employed electron microscopy and observed an increase in myosin filament diameter and concentration with no change in fiber diameter after a strength training program.

It appears that the stimulus for inducing hypertrophy is an increase in the contractile activity (62). This stimulus is somehow transferred to the genetic apparatus. Hamosh and coworkers (77) found an increase in myofibrillar nitrogen fraction concomitant with rises in DNA and RNA concentrations from the compensatory hypertrophied soleus of the rat. Rogozkin (171) found an intensification of RNA-synthesis due to the administration of Nerobol in rats trained to support a heavy

weight while suspended on a rod. This led to an increase in the synthesis of the sarcoplasmic enzyme proteins which was greater than that of the increase in myofibrillar proteins.

Contrary to the classical concept of hypertrophy with training is the work of Faulkner and coworkers (47). They found that the red and white fibers of treadmill trained young guinea pigs were smaller in area than those of controls, although the opposite was true for the mature animals used in their pilot study. They proposed that this decrease in area was a functional adaptation to training which would facilitate the diffusion of gases and metabolites and the transport of nutrients.

Another possibility which could explain the increase in muscle size associated with training is the formation of new muscle fibers. This is called hyperplasia, although what may be assumed to be new fibers may be no more than an evidence of fiber splitting. Van Linge (200) engaged female rats in one of a number of strenuous running programs after surgically implanting the plantaris muscle into the calcaneus after denervation of the triceps surae. The muscle weight increased by 98% with what appeared to be new fiber sprouts having an unusually high RNA content, a large volume and no visible myofibrils. A large increase in the sarcoplasm was also noted. Rowe and Goldspink (175) found that after tenotomy of the gastrocnemius in the female mouse, there was a 32% increase in the mean fiber size of the soleus muscle and a slight increase in the number of muscle fibers. Reitsma (169), by means of surgical intervention, made the rectus femoris the only knee extensor, the plantaris the only plantar flexor or

the soleus the only plantar flexor in three different groups of rats. They were placed on an arduous running program. At the end of the study there was marked hypertrophy ranging from 28 to 151%, as well as evidence of pathology such as longitudinal fiber splitting, particularly for the soleus muscle. Hall-Craggs (76) found that after tenotomy of the gastrocnemius and plantaris, a pathologic condition of longitudinal fiber splitting occurred in the soleus of young rats.

The above studies on hyperplasia used surgical methods to induce results and could thus be pathologic in nature. But a number of exercise studies have also reported similar findings. Edgerton (41) found fiber splitting in male rats only in the soleus muscle, whether the animals were sedentary or engaged in either a moderate or heavy swimming training program. This splitting did not appear to be a manifestation of myopathy and was consistent in all groups. However, the number of fibers (subfibers) resulting from the split fibers was proportional to the level of activity. Carrow and coworkers (21) undertook the first study in which total and differential counts were made in an attempt to investigate the volumetric versus numeric basis of whole muscle hypertrophy. They placed male rats into one of seven training groups of varying types, intensities and durations. They then examined the soleus, plantaris and gastrocnemius muscles and found a decrease in fiber size for the running groups which was due to extensive fiber splitting. It would thus appear that the above findings of fiber splitting were just that, and not the formation of new fibers. It would also appear that this phenomenon is not pathologic in nature for there were no invasive techniques applied.

The data in this section shows that endurance training causes an increase in the fiber size and/or weight of skeletal muscle (20, 49, 91, 141, 167, 182, 198, 205, 221). This has been shown to be due to an increase in sarcoplasmic protein (70) and not to a change in myofibrillar protein (97), although an increase in the myofibrillar protein fraction has been reported (82). These results are curious for a number of reasons. One, endurance training is not normally associated with weight gains in exercising animals (94, 95, 160). Two, work with forceful-type exercise has been shown to increase fiber size and myofibrillar protein in animals (34, 64, 70). Three, fiber sizes have been shown to decrease with endurance training (47, 70), although these findings may be due to an unrecognized fiber splitting (21, 41). And four, it has been reported that strength training does not increase fiber size while increasing the myosin filament diameter and concentration in humans (162, 163). It would appear that the model to consistently induce hypertrophy is yet to be devised, or that the association of strength work and hypertrophy is not as obvious as once thought and needs refining.

IV. BODY COMPOSITION AND FOOD INTAKE

This section has been divided into three divisions. They are the effects of anabolic steroids and/or training on body composition and food intake in 1) the aged and underweight, 2) animals and 3) human training studies.

Aged and Underweight

The usual response to anabolic steroid administration in the aged and underweight is an increase in body weight. Watson and cowrokers (211) gave 25 mg and 50 mg doses of Nilevar daily to two groups of underweight patients and found weight gains of 11.0 and 7.1 pounds, respectively, after 24 weeks of administration. It is difficult to know if these increases are significant for no control group comparisons were made. In a study in which a group of 25 female schizophrenics were compared to a similar control group, Wilson (218) found a weight increase of 6.5 pounds for the drug group as compared to 2.2 pounds for the controls. No statistical analysis was performed so this gain may have not been significant. Jungek and Greenblatt (105) found that 79 underweight female patients averaged a 0.5-0.7 pound increase in body weight per week when given an anabolic drug. They also reported an increase in appetite. Lambert and Site (123) reported a similar increase in weight for the underweight when given 10 mg/day Dianabol. The weight increase was retained for 10 weeks after administration of the drug was discontinued. Kenyon and coworkers (108) reported an increase in weight for two, 76 year old men, given daily injections of testosterone propionate for seven days. Settel (184) found an increase in body weight of 6.3% in 32 elderly patients, average age 77 years, and an increase in appetite.

Contrary to the above findings, Gherondache and coworkers (56) found no increase in weight in 24 male and female patients, 71 to 90 years old, who were administered 7.5 mg/day oxandralone for one year. Also, Nathan and associates (146) gave four elderly men two injections

of 400 mg testosterone per week for four weeks. They found that the percent fat decreased in all cases. They theorized that the anabolic effect may be due to a decrease in protein catabolism while the anabolism remains constant, and that this protein phenomenon may be secondary to a catabolic effect of the drug on fat. In another study, Gilder and others (60) gave one normal man, two normal females and five female patients 25 to 50 mg Nilevar. The drug increased the lean body mass, while also appearing to have a catabolic effect on fat. They suggested that the drug enhanced lean body mass at the expense of fat.

It should be noted that few of the above studies provided any statistical analysis to assist in the interpretation of the data. This fact makes it difficult to assess the significance of the findings, although any aid to the infirmed is noteworthy.

Animals

The changes in body composition and food intake parameters in animals are divided into two categories. The first concerns non-exercised animals, the second, exercised animals. It is difficult to draw conclusions concerning these studies for there are differences in species, age of the animals, the steroid used, the dosage of the drugm the route of injection and the training regimens employed.

Non-exercised. The response to an anabolic steroid appears to fall into two categories with non-exercised animals. There is a decrease in body weight in young animals, and an increase in weight in adult and castrate animals. There are exceptions in both cases.

Kochakian (113) found a decrease in weight in young male mice given injections of testosterone propionate. There was also a loss of

body hair. Rubinstein and others (176) gave young rats daily one mg injections of testosterone propionate for 26 to 80 days. They too found a decrease in body weight which they thought may have been due to a depressed growth hormone synthesis.

Contrary to the above findings in young animals, Shay and associates (185) found that in rats given either one mg or five mg of testosterone propionate for 30 to 60 days after birth, had no change in body weight as compared to controls. McEuen and coworkers (135) also found no effect on body weight of young male rats given two mg testosterone daily for five to eight weeks.

The normal response of castrate animals is to gain weight with the administration of steroids. Kochakian and Murlin (118) found a weight increase in castrate dogs given injections of the "male hormone" taken from the urinary extract of medical students. Kochakian and Stettner (115) found that testosterone propionate caused an increase in body weight in castrate mice. This change in weight was due to an increase in percent water and protein of the whole animal, with a reduction in percent fat. Kochakian and coworkers (114) found that injections of testosterone propionate in castrate rats caused an increase in body weight with a decrease in percent fat. The weight increase was due to an increase in the rate of protein synthesis in the carcass, seminal vesicles, prostate and kidneys, in that order. Nimni and Bavetta (147) in a similar study found that the sites of protein synthesis were only in the sex organs and skin, and not in the muscles or kidneys.

In adult animals the normal response to anabolic drugs is an increase in body weight. Coffman and Koch (26) found in a study of creatinuria that 0.9 mg testosterone propionate per day caused an increase in body weight in three month old rats. Korner and Young (121) found that the effect of methyl androstenediol was to increase body weight in 3½ month old rats. This increase in weight was due to an increase in percent water and protein and a decrease in percent fat. Drobeck (40) found that stanazolol produced an increase in body weight when administered in therapeutic doses to rats, mice, dogs and monkeys for 28 weeks. Kochakian and his colleagues (117) have shown that testosterone propionate causes an increase in body weight in rats, but that a "wearing off" effect occurs wherein the weight declines toward normal despite continued injections. This phenomenon appears to be due to a feedback mechanism which inhibits further increases in nuclear and microsomal RNA and the incorporation of amino acids into protein after the tissues attain their maximal growth (110). This effect can be suspended by an increase in the dose of the androgen (114).
Contrary to the normal response of an increase in body weight in adult animals is the work of Korenchevsky and others (120). They found that testosterone propionate produced a decrease in body weight which was predominantly a decrease in the percent fat. Likewise, Hervey and Hutchinson (86) also found a lower body weight in rats which was characterized by a decrease in percent fat as a result of testosterone administration. There was also a decrease in lean body mass.

Exercised. The response of body composition and food intake parameters to training in animals can be divided into two categories.

The first concerns the effects of training alone, the second deals with the effects of training in conjunction with anabolic steroids.

The response of animals placed on a training regimen is a reduction in body weight characterized by a decrease in the percent fat. Thomas and Miller (197) studied the adaptation of young rats to forced treadmill running. They found that the initial response to the work was a decrease in food intake and body weight. As the distance run per day was increased, food intake returned to normal while the body weight remained reduced. Jones and coworkers (104) placed male rats on a strenuous nine week swimming program. They found that the reduction in final body weight was due primarily to a decrease in percent fat. Stevenson and associates (195) placed male rats on various programs of regular and irregular swimming and running exercise. They found that running and swimming reduced both the food intake and body weight. Crews and associates (27) placed young (49 days old) male rats on a program of endurance treadmill running. These animals gained less weight than sedentary free-eating controls as a result of both an increase in caloric expenditure and a decrease in caloric intake. The weight loss was due to a reduction in percent fat, although there was a slight reduction in lean body mass. They also noted that the animals deficient in dietary protein had a coarse coat of hair. Oscai and coworkers (149) found that very young (eight days old) male rats placed on a 14-16 week swimming program gained weight more slowly and had lower body weights than controls. The slower rate of weight gain was due primarily to a decrease in caloric intake and an increase in caloric expenditure. The reduction in body weight was due primarily to a

decrease in percent fat, although there was a reduction in lean body mass. Ring and coworkers (170) reported that spontaneous activity in young male rats caused an increase in body weight with no changes in the percent water or fat.

In studies pertaining to the effects of a training program and an anabolic steroid, varying effects are noted. Endurance treadmill training produces a decrease in body weight, forceful training regimens plus the drug produce an increase in body weight and swimming usually produces no change in body weight.

Taylor and others (196) found that treadmill running decreases body weight in male rats while the drug had no effect. Murphy and Eagan (145) reported similar findings. These appear surprising due to the relatively slow speed of the training program. They explained the weight loss to a lipolytic effect of exercise.

In studies on the effects of isometric training and steroids, Exner and coworkers (44, 45) found an increase in body weight with the training in both male and female rats. The drug produced an increase in body weight only in the males. Rogozkin (171) found that Nerobol increased the body weight of rats trained to carry loads while suspended on a vertical rod during an 84 day training period. Brown and Pilch (16) used a high jumping technique as a training stimulus and found that body weight was increased with both the training and low levels of the drug. These findings may not be significant though, for the level of significance used was high ($P=0.10$) and should lead one to doubt the significance of their findings. In support of this possibility, Cheek (25), who used an identical high jumping training regimen reported

no change in body weight of the male rats with either the training or the drug.

Several studies that used a swimming regimen as the training stimulus reported no changes in body weight. Chapuzio (24) found that a six week endurance swimming program and Dianabol produced no weight change in male rats. Feldscher (48) used an intermittent swimming schedule and increased the number of repetitions over a six week period. There was no change in either body weight or specific gravity of the male rats. These findings are not surprising due to the buoyant effect of the water. This would reduce the body weight of the animals during training and thus reduce the load they had to support.

With these training studies it should be noted that both the swimming and endurance treadmill programs are inappropriate exercise stimuli relative to strength training. Also, the high jumping technique produced no significant changes in the parameters measured and would cause one to question its applicability. Finally, both the isometric training and the pole hanging training stimuli appear questionable in light of the passive manner of the work and the minimal strength gains associated with isometric strength training.

Human Training Studies

The effects of anabolic steroids on body composition parameters, particularly lean body mass, have been studied using skinfold measurements and densitometry, and using both experienced and inexperienced weightlifters. These facts make it difficult to draw conclusions concerning the results noted below. Also, the steroid used

differs in these studies, although Dianabol at the recommended dose of 10 mg/day is used most often.

Skinfold studies. When the skinfold value decreases or remains the same and is accompanied by an increase in body weight, it is assumed that lean body mass has increased. There have been four studies that have used experienced subjects and five studies which have employed inexperienced subjects to assess lean body mass using this technique. In five of these studies lean body mass is purported to have increased, three with inexperienced subjects and two with experienced weightlifters.

The first study to investigate the effects of anabolic steroids on both strength and performance was made by Fowler and others (51). They placed 47 untrained men on an unspecified 16 week training program. Half the subjects were given 20 mg/day Nibal on a double blind basis. There was no change in body weight or skinfold measurements, thus no change in lean body mass. This finding may have been due to the nature of the training which apparently was not one designed to increase strength.

Contrary to the above finding, other studies have found an increase in body weight associated with no change in skinfold values. Johnson and O'Shea (103) matched 12 pairs of volunteers on a six week weight training program. One group received 10 mg/day Dianabol on a single blind basis and received a protein supplement. The body weight increased and there was no change in skinfold thickness. Munson (144) placed 32 volunteers on a four week training program. One group received 20 mg/day Anavar on a double blind basis. The skinfold values

decreased with a concomitant increase in body weight. In another study, Johnson and coworkers (102) placed 31 volunteers on a seven week weight training program. One of the groups was given 10 mg/day Dianabol on a double blind basis and received a protein supplement. At the end of the study there was an increase in body weight and no change in skinfold thickness. Finally, Win-May and Mya-tu (220) studied 31 volunteers for a three month period. One half of the subjects were given five mg/day Dianabol on a double blind basis and none of the subjects engaged in a training program. At the conclusion of the study, body weight had increased while skinfold measurements had decreased. There was also a significant increase in the creatinine coefficient which is indicative of an increase in muscle mass.

The above studies used inexperienced weightlifters as subjects and suggest that anabolic steroids increase lean body mass. There have been four studies which have employed experienced weightlifters as subjects. Two of the studies report an increase in lean body mass while the other two do not.

O'Shea (152) reported an increase in body weight with no change in skinfold thickness for weightlifters given 10 mg/day Dianabol and a protein supplement in a four week double blind study. Freed and Banks (52) divided 13 experienced weightlifters into two groups and studied them for twelve weeks. The subjects were given either 10 mg or 25 mg/day Dianabol on a double blind basis. At the end of the experimental period body weight had increased with no change in skinfold thickness. The difference between the high and normal dosage groups was negligible.

In opposition to these studies, Maul (133) found in a single blind study that Dianabol given to weightlifters for 12 weeks produced no changes in body weight or skinfold measurements. Golding and others (63) also reported such a finding. They placed weightlifters on a 12 week training program. The subjects were given 10 mg/day Dianabol on a three week on-one week off pattern and either did or did not receive a protein supplement. There was no change in body weight or percent fat as measured by both skinfolds and densitometry.

In support of the finding that a protein dietary supplement does not effect weight gains is the work of Kochakian (112). He found that raising the protein content of the diet from 18.4% to 27.5% to 42.5% for different groups of animals did not result in an additional nitrogen retention above the amount obtained with 18.4% content in male rats given injections of testosterone propionate. Another point should be mentioned relative to the ingestion of protein by weightlifters as used by investigators in this area. The recommended daily protein intake is 0.8-1.0 g/kg body weight. The average daily intake is approximately 110-120 g/day and is even higher for athletes whose food consumption is quite high. This means, that at the least, the average intake is twice as great as that recommended, and thus the ingestion of an extra 30 g/day by weightlifters would appear superfluous.

Densitometry studies. All of the above studies used skinfold measurements to assess the nature of a weight gain brought about by the use of anabolic steroids. However, skinfold changes have been found to be unreliable indicators of changes in body composition (217).

Therefore, the above findings would need to be verified with a more accurate and reliable technique such as underwater weighing. There have been five studies that have used either experienced and inexperienced subjects to assess body composition changes with hydrostatic weighing. In four of the studies there was a weight increase due to the steroids, but the data from the studies concerning inexperienced subjects provides additional information in evaluating this change.

There are two studies that used experienced weightlifters to assess lean body mass with densitometry. Ward (209) studied 16 subjects for five weeks during which eight of the men received 10 mg/day Dianabol on a double blind basis. Body weight increases occurred which were due to an increase in lean body mass. There was also a decrease in the percent fat. As mentioned previously, Golding and coworkers (63) used densitometry and found no changes in body weight or in percent fat.

When the subjects used are inexperienced, weight gains occur, but other important findings are noted. Casner and associates (22) placed 27 young men on an eight week double blind study of weight training and/or 2 mg Winstrol given three times per week. They measured total body water using the tritium dilution technique as well as specific gravity with densitometry. They found that the percent fat remained unchanged while the body weight increased. They felt that this increase may have been due to fluid retention and not to an increase in muscle protein. Hervey (85) studied 13 men divided into two groups for a 12 week period during which some of the subjects received 100 mg/day Dianabol on a double blind basis. Both total body water and body

composition were measured. At the conclusion of the program the body weight had increased while the percent fat had decreased. They too surmised that the increased weight may have been due to water retention brought about by an increased intracellular electrolytes concentration. Fahey and Brown (46) placed 20 students on a nine week weight training program and gave one group of subjects the recommended dose (1 mg/kg body weight) of Deca-Durabolin once every three weeks. They found no changes in either body weight or lean body mass.

It appears from the above information that the weight changes in lean body mass produced by anabolic steroids may be due to fluid retention. This may not be altogether undesired for the increased weight may assist in an increased work output of that weight does not result in a loss of speed during the performance of an activity.

V. STRENGTH AND PERFORMANCE

This section has been divided into three divisions. They are the effects of anabolic steroids on strength and performance in 1) the aged, 2) animals and 3) human training studies.

Aged

Simonson and coworkers (188) administered 30-40 mg/day methyltestosterone to six men, age 48 to 67 years. Dynamic work output was measured by having the subjects lift a dumbbell 20 times per minute until exhaustion. It increased in three of the four men. Freeman and associates (54) gave 14 men, age 71 to 91 years, a mixture of four steroids once per day for five months. Using a similar measure of

dynamic work output as Simonson and others, they found an increase in 10 of the subjects. Hettinger (87, 88) placed a group of males, age 65 to 75 years, on an eight week training program and gave some a 100 mg injection of testosterone at two week intervals. Strength was increased at a rate three times as fast as without the injections. He also measured the performance of the circulatory system by determining an index based upon blood pressure and heart rate. When the injections began this performance index increased 40% relative to the beginning value and was thought to be due to an increase in strength of the heart muscle itself.

Animals

Palacek (157) studied the effects of an anabolic steroid (dimethylandrostanalone) on the weight and tension development of denervated rat gastrocnemius. He found no change in muscle weight and tension when compared to controls. Exner and coworkers (44, 45) studied the effects of Deca-Durabolin and isometric training upon *in situ* contraction properties of the rectus femoris and soleus muscles of both male and female rats. There was no change in isometric twitch contraction time for either muscle in the males. In the females, only training had an effect; a decrease in contraction time for the rectus femoris an increase in contraction time for the soleus. Maximum tetanic tension increased with training for the rectus femoris of both sexes and decreased with the drug in the soleus of the females.

Brown and Pilch (16) placed 18 male rats in one of two training programs, high jumping and slow treadmill running. A six week

administration of Dianabol did not improve the performance of the animals in any training program. Heart rate and blood pressure were also monitored and were not affected by either the training or the drug. Feldscher (48) swam male rats for one minute with a 30 second rest period, five days per week, so that by the sixth week they were swimming 24 bouts with a weight equivalent to 5% body weight attached to their tails. They were given 10 mg/day Anavar. The rats were swum to exhaustion at the end of the sixth week and it was found that the drug did not improve swim to exhaustion times. Finally, Maglio and others (130) noted that 25 mg/kg body weight Steranabol given to trained guinea pigs caused an increased resistance to fatigue while running on a treadmill.

Human Training Studies

The studies on the effects of anabolic steroids on strength in young subjects present a general tendency. Strength gains are usually reported when the subjects are experienced weightlifters and are not usually reported when the subjects are inexperienced and naive to weight training.

In assessing these strength gains it is necessary to be aware of the psychological effect that the ingestion of a substance purported to increase strength may have that may be additional to any chemical action it may produce. That this effect does exist is shown by two studies. Ariel and Saville (5) administered a placebo during a five week training period to experienced athletes who believed they were ingesting Dianabol. The six subjects had a significant increase in dynamic strength in three

of the four weightlifting exercises tested. Stamford and Moffatt (191) also reported a probable "positive placebo" effect. They found that a group of experienced weightlifters who were given a placebo and a protein supplement outgained groups in dynamic strength who were given only a protein supplement or no treatment at all during an eight week study. The design of this study, which compared groups of prison inmates with persons outside the institution, makes it difficult to draw any conclusions due to the nature of the group assignment. The non-random assignment dictated by the separateness ofthe subjects used violates the rule of randomness necessary for valid statistical analysis. Also, the lack of any treatment for one of the groups would appear to negate any placebo effect for they did not receive one.

In order to avoid the confounding factor of the psychological component, two major precautions are taken. First, the subjects who do not receive the drug are given an indistinguishable placebo. Second, the drug and the placebo are dispensed on a double blind basis so that the investigator cannot influence the subjects.

Inexperienced subjects. There are 12 studies which have used inexperienced subjects to investigate the effects of anabolic steroids on strength. Only four have found an increase in strength.

Steinbach (192) placed 125 males, age 17 to 19, into one of five groups and studied the effects of training and three mg/day Dianabol for three months. At the end of the training period, the drug had produced an increase in isometric strength for both the arms and legs. This finding is surprising because of the low level of the drug and may have been due to growth factors present in this age group. Johnson and

O'Shea (103) studied normal young men for six weeks during which time they were given a protein supplement and 10 mg/day Dianabol. They found an increase in both static and dynamic strength. These findings are somewhat suspect because of the single blind nature of the study, which would have given the investigators an opportuinity to influence the subjects. Johnson and coworkers (102) in a training study measured the effects of a three week double blind administration of 10 mg/day Dianabol and a protein supplement on static strength and dynamic strength. They found an increase in strength and no change in the maximal aerobic power. Finally, Win-May and Mya-tu (220) found in a double blind study that five mg/day Dianabol given for three months to men, age 18 to 23 years, increased grip strength, as well as the number of situps and pullups performed and the distance of a standing broad jump test. These findings are curious in light of the low level of the drug administered. They may be explained by the age of some of the subjects, but are most likely due to a training effect for the data was collected every week for three months.

The remainder of the studies have found no improvement in strength. Samuels and coworkers (179) produced the first study on the effects of an anabolic steroid on performance in young men. They investigated weekly the effects of methyltestosterone on grip dynamometer strength and on blood concentrations of pyruvate, lactate, hemoglobin and creatine of four men after a treadmill test. They reported no changes in strength or general blood concentrations. This lack of strength improvement is not peculiar since the subjects did not train. In 1965, Fowler and others (51) measured the effects of Nibal

given on a double blind basis to 47 men over a 16 week period. They found no differences between experimental and control groups in tests of static strength, motor performance (pullups, pushups, vertical jump and broad jump), vital capacity and aerobic capacity. These results are not totally surprising for the training was of an unidentified nature and did not appear to be a strength program. Munson (144) studied the effects of Anavar on static strength and predicted oxygen uptake in an eight week double blind study. He found no change in either variable. Casner and coworkers (22) investigated the effects of Winstrol on static strength in an eight week double blind study and found no changes in strength. Fahey and Brown (46) measured both static and dynamic strength and maximal oxygen uptake under the influence of Deca-Durabolin administered on a double blind basis for nine weeks. They found no change in either variable. Stromme and coworkers (194) studied the effects of Mestoranum on static strength and predicted oxygen uptake in an eight week double blind study. They too found no effect of the drug on either variable. Hervey (85) studied the effects of a large dose of Dianabol (100 mg/day) on maximal oxygen uptake and dynamic strength in a 12 week double blind study. Again, no significant findings were noted. Weiss and Muller (213) compared two groups of subjects on grip dynamometer strength after 10 mg/day Dianabol was administered for three weeks. They found no changes in static strength.

Experienced subjects. There have been seven studies which have used experienced subjects to investigate the effects of anabolic steroids on strength. Six of these studies found a significant strength enhancement, five of which were of good design.

O'Shea and Winkler (154) studied the effects of a six week administration of Anavar given on a double blind basis on the dynamic strength of weightlifters and on the swimming time of competitive swimmers. They found an increase in strength for the lifters and no improvement in performance time for the swimmers. They thought that the latter finding may have been different due to an earlier finding of an increase in aerobic capacity (103). O'Shea (153) administered 10 mg/day Dianabol for three weeks of a six week period to 15 varsity swimmers. He found no effects of the drug on predicted aerobic capacity, static strength and performance times.

O'Shea (152) again measured the effect of Dianabol and a protein supplement on weightlifters in a four week double blind study. He found that dynamic strength increased. In 1971, Maul (133) found that isometric strength increased in three subjects given a steroid on a single blind basis. The small sample size and the single blind design cast a doubt as to the validity of these findings. He also reported that reaction time was unchanged.

Contrary to the latter finding of Maul is the study of Ariel and Saville (6). They found that 10 mg/day Dianabol administered for six weeks on a double blind basis produced faster motor times and slower latencies of the patellar knee jerk reflex.

Bowers and Reardon (13) studied the effects of Dianabol and a protein supplement for six weeks on the dynamic strength and aerobic capacity of weightlifters. They found an increase in strength but no change in the aerobic capacity. Ward (209) subjected his subjects to a five week period of strength training during which 10 mg/day Dianabol

was administered on a double blind basis. He found that dynamic strength increased. Finally, Freed and Banks (52) conducted a six week study on the effects of Dianabol and found that both static and dynamic strength increased.

A factor which partially confounds the findings of strength gains obtained with anabolic steroids is the ingestion of a protein dietary supplement. Both Kruskemper (122) and Saarne and coworkers (178) have stated that an adequate supply of protein is necessary for anabolic steroid effectiveness. And Celejowa and Homa (23) and Serbin (183) have shown that intensive weightlifting often places individuals in negative nitrogen balance. But this ingestion may interfere with the interpretation of results on the effectiveness of an anabolic steroid alone. In response to this problem Golding and coworkers (63) showed that a protein supplement given during a 12 week study had no effect on dynamic strength, as well as on body composition mentioned previously.

Aerobic capacity. A number of studies have included an investigation of the effects of an anabolic steroid on aerobic capacity (13, 40, 85, 102, 153, 154, 194, 220). It would not be expected to find a significant relationship and this has been verified. But all of the above studies have not trained their subjects with an aerobic program. Johnson and coworkers (101) have conducted the only study of this type. They placed 21 male volunteers on a three day per week, six week endurance training program, supplemented their diet with protein and gave one group 6 mg/day Winstrol on a double blind basis. They found no changes in maximum aerobic power, mile run times and static strength due to the drug. Conversely, in a study of the effects

of altitude hypoxia, Albrecht and Albrecht (2) found that metenolone acetate had a stimulating effect on the hemopoietic system. They subjected 42, 21 year olds to a physical work capacity test at various altitudes during a 35 day ascent of a mountain. In each subject the predicted aerobic capacity decreased as the altitude increased, but the steroid group had an 8-10% smaller drop when compared to controls. Apparently anabolic steroids do not enhance maximal aerobic power but can reduce its decline during hypoxia.

VI. SUMMARY

The initial work with the male sex hormone and its synthetic analogs showed that these drugs had an ability to enhance protein synthesis (107, 118, 158). These findings led to the search for a drug that would enhance this anabolic effect so that it could be safely applied in clinical medicine (122). Eventually athletes for whom strength is a major prerequisite to success began to employ these drugs as ergogenic aids (203) and research has attempted to assess what effect they might have in this regard.

Strength has been shown to increase when the subjects are experienced weightlifters (13, 52, 152, 153, 154, 209), though not always (64). When the subjects are naive to weightlifting strength is not normally enhanced (22, 46, 51, 85, 144, 179, 194, 213), though there are exceptions (102, 103, 192, 220). Animal work reports variable results. Some studies show performance improvement (44, 45, 130), while one does not (157).

An increase in strength is thought to occur by an increase in muscle mass. This hypertrophy is studied in humans by the assessment of lean body mass and has been investigated sparingly with animals with studies of fiber size, protein content and nucleic acid levels.

An increase in lean body mass has not been found in a number of studies (46, 63, 133). Those that have indicated such an increase (52, 102, 103, 144, 152, 209, 220) may not indicate an increase in lean mass but a fluid retention (22, 85). One study showed that the strength increase was not due to an increase in muscle fiber size, but to an increase in myosin filament diameter and concentration (163).

Animal studies have shown anatomical and biochemical changes brought about by these drugs in skeletal muscle. Fiber size enlargement has been shown in the mouse (167, 221). There is also an increase in total and structural protein (159) and nucleic acid levels (171).

Finally, these drugs are not without hazard. Testicular atrophy has been shown in rats (16, 25, 145, 196) and numerous side effects have been shown in humans such as liver function impairment (3, 52, 55, 124, 202, 223, 224).

CHAPTER III

METHODS

Two separate experimental periods were employed to investigate the desired parameters. The first period investigated selected organ and muscle weights, body composition and food intake. The second period investigated skeletal muscle hypertrophy.

I. ANIMALS

Period One

Forty-eight male albino rats (Sprague-Dawley Farms, Madison, Wisconsin), 103 days old and ranging in weight from 312 to 410 grams were used. This age was desired to ensure that the rats were adults. Gordon and coworkers (71) have shown that DNA levels rise to a fixed level in 90 days and sarcoplasmic and myofibrillar proteins in 120 days. This age removes growth as a confounding variable in assessing any anabolic effects associated with training and/or anabolic steroid administration.

The rats were housed in individual, wire-mesh-bottom cages, 38 x 23 x 23 cm. The day was artificially divided into alternating 12 hour periods of light and darkness. The room temperature was maintained at 22 $\pm$ 1° C. No control for humidity was possible. Purina Lab Chow and water were provided continuously.

The animals were randomly assigned to one of four groups and the groups were randonmly assigned to one of four treatments: control, drug, training and drug plus training.

Period Two

Fifty-two male Sprague-Dawley albino rats (Charles River Laboratories, Boston), with initial weights ranging from 395 to 465 grams and 106 days old were used. Two animals were housed in a sedentary cage, 45 x 25 x 15 cm. The same environmental, dietary and group assignments were made as in period one.

II. ANAEROBIC TRAINING PROGRAM

Period One

The rats were trained on a homemade motor driven treadmill with a variable speed control. The program consisted of 10 second sprints run on the level and interspersed with 30 second rest periods. They were performed five days per week for eight weeks. The animals began with four sprints run at 18 meters per minute and both the number and speed were increased in equal weekly increments until most animals were running 18 sprints at 91 meters per minute during the final week of training. This program is based on the work of Margaria and coworkers (131, 132). They showed that only an alactic acid debt is incurred in supramaximal work of 10 seconds duration on a treadmill. Only phosphocreatine and adenosine-triphosphate are employed. This would appear to mimic the energy utilization pattern involved in weight training. The nontrained rats were removed from their cages daily and placed on the treadmill to account for the effects of handling on body weight and endocrine organs (214). Body weight was recorded weekly.

Period Two

The rats were trained on the same treadmill. The program consisted of the same 10 second sprint, 30 second rest period ratio, performed five days per week for eight weeks. They began with four sprints at 18 meters per minute and were required to run 18 sprints at 78 meters per minute during the final week. The final speed is slower than that used in period one for that final speed of 91 meters per minute appeared too stressful and caused much agony and suffering for some of the rats. This was evidenced by two factors. The animals made attempts to escape from the front of the treadmill and not the back. Also, some of the rats could not move in response to the increased speed. Both observations were different from those found in animals that protest to exercise, while these animals were willing but unable. Due to an unforseen scheduling problem the rats were placed on a maintenance program of 15 sprints at 72 meters per minute for an additional week.

III. ANABOLIC STEROID ADMINISTRATION

The same anabolic steroid and schedule of administration were used for both experimental periods. Deca-Durabolin (Organon, East Orange, New Jersey) a brand of nandralone decanoate was used. It is a slow hydrolyzing ester (35, 155), chemically known as 19 nor-Δ^9-androstene-17-beta-ol-3-one-decanoate (Figure 1). It was diluted 1:100 in sesame oil and injected intramuscularly in the right thigh or leg at the recommended dosage of 1 mg/kg body weight at the beginning of weeks one, four and seven. The non-drug groups received an appropriate placebo injection of sesame oil.

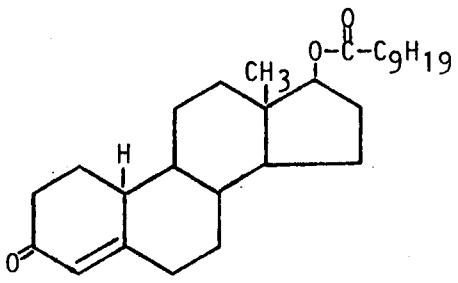

Figure 1. Chemical structure of nandralone decanoate.

IV. FOOD AND WATER INTAKE

Dietary habits were measured weekly during period one only. Water intake was determined by weighing the water bottle and its contents at the beginning and end of each week. The difference in weight was converted to a volume using a water density factor of 0.998 grams per milliliter (212).

The food intake was determined by recording the difference in the weight of the uneaten food at the beginning and end of each week. The uneaten food trapped in the waste tray of the cage was recovered by separating it from the excrement with a hand sifter.

V. ORGAN AND MUSCLE WEIGHTS

Twenty-four to seventy-two hours after the last bout of exercise and following an overnight fast, the rats in period one only were weighed and then killed by inhalation of 30% CO_2. The body hair was

removed with electric clippers. The autopsy was then performed (72). The gastrocnemii, testes, adrenals, kidneys, liver and heart were removed in that order and weighed on an analytical balance. The fecal remains were also removed and weighed so that a corrected body weight necessary for the body composition analyses could be obtained. The animal and its organs were then wrapped in aluminum foil, placed in a plastic bag and stored in a freezer until the body composition analyses were performed.

VI. BODY COMPOSITION

The body composition analyses were performed on the animals from period one following the method of Mickelsen and Anderson (137) with the following modifications. After homogenation of the autoclaved carcass, the colloid mill was not used according to the revision of Hartsook and Hershberger (79). In place of petroleum ether, 2:1 chloroform-methanol was used for the Soxhlet fat extraction. Finally, macro-Kjeldahl was used in place of the micro-Kjeldahl technique for protein determination.

VII. HISTOCHEMICAL PROCEDURES

On the day following the last bout of exercise in period two, the animals were anesthetized with Nembutal (Abbott Laboratories, North Chicago), a brand of sodium pentobarbital. It was injected intraperitoneally at the recommended dosage of 50 mg/kg body weight (11). When the rat was sedated the gastrocnemii were removed, trimmed of excess connective tissue and fascia, blotted on a paper towel and

weighed on a torsion balance. The two heads of each muscle were then separated. Approximately 1 cm^2 pieces were ablated from the belly of each head with a razor blade and rolled in talcum powder to prevent freezing damage (138). They were then frozen in liquid nitrogen to a temperature of -160° C, wrapped in a labeled aluminum foil packet and stored in a liquid nitrogen container until the histochemical assays were performed.

When the histochemical determinations were to be made, the sample was removed from storage in the liquid nitrogen, mounted on a specimen holder with cork and mounting medium (Lipshaw, Detroit) and allowed to warm to -20° C in the cryostat. The muscle sample was then trimmed when necessary and transverse serial sections 12 thick were cut in a microtome-cryostat (Lipshaw, Detroit) at -20° C. The sections were mounted on cover slips and placed in staining jars to dry. The sections were then assayed for NADH-D using the procedure of Engel and Brooke (43) and myofibrillar ATPase according to the method of Padykula and Herman (156) as modified by Guth and Samaha (74, 75). The optimum pH for the preincubation and incubation mediums of the ATPase assay were 10.6 and 9.6, respectively. The stained sections were mounted on glass slides with glycerol gel.

After all available muscle samples were assayed, 35 mm black and white photomicrographs were taken of the "red" gastrocnemius, the inside portion of the lateral head; and the "white" gastrocnemius, the outer portion of the medial head, with a Wild Photomicroscope (Heerbrug, Switzerland) at the magnification of x60. This differentiation of the gastrocnemius into red and white portions was necessary because of the

differential distribution of fiber types found in most mammals. The periphery normally contains more glycolytic (white) fibers while the central regions are predominantly oxidative (red) fibers (148, 172). The photomicrographs were then enlarged to an 8 x 10 positve print on lightweight paper (Polycontrast, Type A, Eastman Kodak) and used for the measurement of muscle fiber area (size) and the determination of fiber types. Photomicrographs of the scale used were also made so that proper dimensions could be obtained.

Muscle fibers in each serial section were classified as described by Peter and coworkers (164) and identified as fast-twitch-oxidative-glycolytic (FOG), fast-twitch-glycolytic (FG) and slow-twitch-oxidative (SO). The cross-sectional area of 20 fibers of each type, when available, were determined with a compensating polar planimeter (Dietzgen D-1838-D, Tucker, Georgia) from the enlargement of the NADH-D stain and converted to square microns. The muscle composition was determined by both percent number and percent area of each fiber type present. The percent number is the ratio of the number of each fiber type to the total number of fibers present in each photomicrograph enlargement. The percent area is determined by multiplying the mean area of each fiber type by its percent number, and then dividing this value by the sum of the values for each type present in the portion of the gastrocnemius under consideration.

VIII. STATISTICS

A two-way ANOVA was used to test for significant differences (212) and is depicted in Figure 2. This design has three tests of significance. The first is for the training effect which tests the difference between

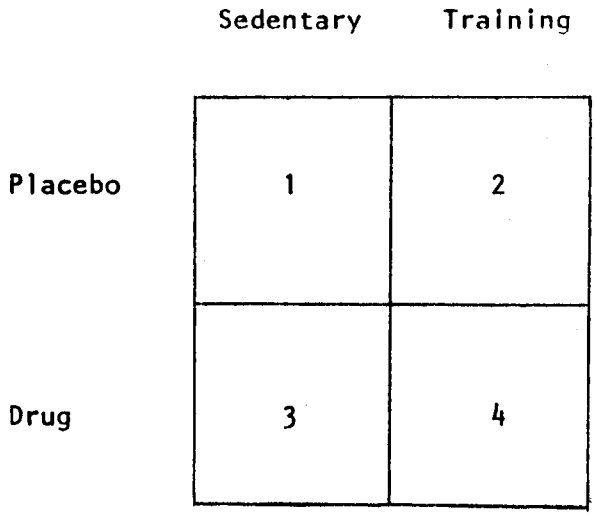

Figure 2. Block diagram of two-way ANOVA.

sedentary groups (cells 1 and 3) and training groups (cells 2 and 4). The second test is for the drug effect which tests the difference between placebo groups (cells 1 and 2) and drug groups (cells 3 and 4). The third test is for the interaction of drug and training (all the cells). A probability less than 0.05 was used to reject the null hypothesis of no significant difference. The organs and muscles weights were treated as absolute, relative to body weight (organ or muscle weight/body weight x 100) and predicted from a corrected final body weight by the method of least squares regression for each homogeneous group (84).

CHAPTER IV

RESULTS

I. ORGAN WEIGHTS

Absolute Weights

The findings are summarized in Table 3 (group means in Table 13, Appendix). Training produced a decrease in liver and kidney weights, an increase in heart weight and no change in adrenal and testis weights. The drug had no effect on any organ weight measured.

Relative Weights

The findings are summarized in Table 4 (group means in Table 14, Appendix). The results are the same as those found for the absolute weights with one additional effect. The drug produced a decrease in kidney weight.

Predicted Weights

When organ weights are predicted by the method of least squares regression and compared to the relative weight findings, further effects are noted (Table 5, group means in Table 15, Appendix). Training also produced an increase in testis weight but only in the rats that received the placebo injection. The drug also produced a decrease in testis and heart weights but only in the sedentary animals.

Table 3. Effects of training and drug on absolute organ and muscle weights in period one.

	Training Effect			Drug Effect			Drug x Training Interaction
	Sedentary	Training	P	Placebo	Drug	P	P
Liver	23.1 ± 0.5	17.7 ± 0.5	0.01	20.4 ± 0.8	20.6 ± 0.7	0.86	0.62
Adrenals	52.0 ± 0.2	52.6 ± 0.2	0.87	52.4 ± 0.2	52.2 ± 0.2	0.95	0.76
Kidneys	4.2 ± 0.1	3.6 ± 0.1	0.01	4.0 ± 0.1	3.8 ± 0.1	0.09	0.22
Testes	3.6 ± 0.1	3.8 ± 0.1	0.61	3.6 ± 0.1	3.8 ± 0.1	0.97	0.41
Gastrocnemii	3.2 ± 0.2	3.8 ± 0.2	0.02	3.2 ± 0.2	3.8 ± 0.2	0.03	0.88
Heart	1.4 ± 0.1	1.6 ± 0.1	0.01	1.6 ± 0.1	1.5 ± 0.1	0.28	0.63
N	22	21		20	23		

Values are absolute weight in grams, adrenals are in milligrams, expressed as means ± SE

Table 4. Effects of training and drug on relative organ and muscle weights in period one.

	Training Effect			Drug Effect			Drug x Training Interaction
	Sedentary	Training	P	Placebo	Drug	P	P
Liver	4.9 ± 0.08	4.0 ± 0.07	0.01	4.5 ± 0.16	4.5 ± 0.01	0.80	0.25
Adrenals	11.7 ± 0.05	11.9 ± 0.05	0.27	11.6 ± 0.02	11.4 ± 0.04	0.79	0.50
Kidneys	0.9 ± 0.02	0.8 ± 0.01	0.01	0.9 ± 0.02	0.8 ± 0.01	0.02	0.06
Testes	0.8 ± 0.02	0.8 ± 0.01	0.06	0.8 ± 0.02	0.8 ± 0.02	0.78	0.81
Gastrocnemii	0.7 ± 0.03	0.8 ± 0.04	0.01	0.7 ± 0.03	0.8 ± 0.04	0.04	0.65
Heart	0.3 ± 0.01	0.4 ± 0.01	0.01	0.4 ± 0.02	0.3 ± 0.03	0.21	0.44
N	22	21		20	23		

Values are relative weight (organ or muscle weight/body weight x 100) expressed as means ± SE

Table 5. Effects of training and drug on predicted organ and muscle weights in period one.

	Training Effect			Drug Effect			Drug x Training Interaction
	Sedentary	Training	P	Placebo	Drug	P	P
Liver	23.1 ± 0.35	17.7 ± 0.15	0.01	20.4 ± 0.77	20.6 ± 0.08	0.77	0.41
Adrenals	52.0 ± 0.09	52.6 ± 0.06	0.66	52.4 ± 0.08	52.2 ± 0.07	0.86	0.43
Kidneys	4.2 ± 0.06	3.6 ± 0.03	0.01	4.0 ± 0.15	3.8 ± 0.07	0.01	0.03
Testes	3.6 ± 0.02	3.8 ± 0.02	0.01	3.6 ± 0.02	3.6 ± 0.01	0.81	0.01
Gastrocnemii	3.2 ± 0.08	3.8 ± 0.08	0.01	3.2 ± 0.07	3.8 ± 0.08	0.01	0.33
Heart	1.4 ± 0.01	1.6 ± 0.08	0.01	1.6 ± 0.02	1.5 ± 0.02	0.01	0.03
N	22	21		20	23		

Values are predicted weight in grams, adrenals in milligrams, expressed as means ± SE

II. BODY COMPOSITION AND FOOD INTAKE

Body Weight and Food Intake

The body weight of the trained rats was lower than that of the sedentary animals in both period one (Table 6, group means in Table 16, Appendix) and period two (Table 7, group means in Table 17). The drug had no effect on body weight during either period. The weight loss was due to the training alone and not to an appetite suppression, as there was no change in food or water intake in period one (Table 6, group means in Table 16, Appendix).

Body Composition

In period one the training regimen resulted in a decrease in the percentage of the carcass composed of fat and ash and an increase in the percentage composed of water (Table 8, group means in Table 18, Appendix). Most of the difference between the body weights of the trained and sedentary animals can be accounted for on the basis of the lower fat content for the lean body mass was unchanged (Table 9, group means in Table 19, Appendix). The drug had no effect on any composition variable. The decrease in the protein and ash content may be due to the strenuous nature of the training program, as all trained rats were characterized by a coarse and thin coat of hair as compared to the placebo and drug animals. Otherwise they appeared healthy and alert.

Table 6. Body weight and weekly food and water intake in period one.

	Training Effect			Drug Effect			Drug x Training Interaction
	Sedentary	Training	P	Placebo	Drug	P	P
Body Weight	468 ± 5	443 ± 5	0.01	452 ± 5	459 ± 6	0.36	0.24
Food Intake	199 ± 3	194 ± 3	0.91	198 ± 3	195 ± 3	0.51	0.97
Water Intake	326 ± 17	323 ± 7	0.12	330 ± 11	330 ± 7	0.75	0.98
N	22	21		20	23		

Values are weight in grams for body weight and food intake and volume in milliliters for water intake expressed as means ± SE

Table 7. Body weight and absolute (A), relative (R) and predicted (P) weight of the gastrocnemius muscles in period two.

	Training Effect			Drug Effect			Drug x Training Interaction
	Sedentary	Training		Placebo	Drug	P	P
Body Weight	598 ± 11	561 ± 8	0.01	584 ± 11	576 ± 10	0.65	0.57
Gastrocnemii (A)	5.80 ± 0.04	5.65 ± 0.06	0.30	5.76 ± 0.05	5.70 ± 0.06	0.68	0.68
Gastrocnemii (R)	0.97 ± 0.01	1.01 ± 0.01	0.10	0.98 ± 0.01	0.99 ± 0.01	0.80	0.30
Gastrocnemii (P)	5.80 ± 0.04	5.65 ± 0.06	0.08	5.76 ± 0.05	5.70 ± 0.06	0.36	0.37
N	24	21		22	23		

Values are weight in grams expressed as means ± SE

Table 8. Effects of training and drug on body composition in period one.

	Training Effect			Drug Effect			Drug x Training Interaction
	Sedentary	Training	P	Placebo	Drug	P	P
Protein	19.9 ± 0.4	19.5 ± 0.5	0.48	19.7 ± 0.5	19.7 ± 0.4	0.98	0.65
Water	65.8 ± 0.7	70.2 ± 0.4	0.01	67.8 ± 0.8	68.3 ± 0.7	0.31	0.36
Fat	14.2 ± 0.6	9.7 ± 0.2	0.01	12.1 ± 0.8	11.7 ± 0.6	0.37	0.52
Ash	2.7 ± 0.3	2.0 ± 0.2	0.04	2.6 ± 0.3	2.2 ± 0.2	0.19	0.52
N	20	21		18	23		

Values are the percent of each component expressed as means ± SE

Table 9. Effects of training and drug on total body content of protein, water, fat, ash and lean body mass in period one.

	Training Effect			Drug Effect			Drug x Training Interaction
	Sedentary	Training	P	Placebo	Drug	P	P
Protein	93.6 ± 1.9	86.4 ± 3.1	0.02	89.0 ± 2.3	90.6 ± 3.1	0.73	0.97
Water	309.3 ± 5.0	311.1 ± 4.0	0.62	306.7 ± 4.4	313.0 ± 4.4	0.30	0.23
Fat	66.5 ± 2.6	43.0 ± 1.1	0.01	55.1 ± 3.7	54.0 ± 3.3	0.48	0.65
Ash	12.7 ± 1.3	8.8 ± 0.9	0.02	11.7 ± 1.3	9.9 ± 1.1	0.41	0.58
Lean Body Mass	415.6 ± 5.0	406.3 ± 4.6	0.25	407.4 ± 4.9	413.6 ± 4.6	0.41	0.33
N	20	21		18	23		

Values are the weight of each component in grams expressed as means ± SE

III. SKELETAL MUSCLE HYPERTROPHY

Muscle Weight

In period one the gastrocnemius weight increased in response to both the training program and the drug (Table 5, page 50; group means in Table 15, Appendix). These findings are a gross indication of hypertrophy. The weight increase is practically identical for both treatments.

In period two the gastrocnemius weight was not increased in response to either drug or training despite the fact that the trained animals did undergo a training effect as indicated by the decrease in body weight (Table 7, group means in Table 17, Appendix).

Fiber Size

The muscle weights of the rats increased in period one. A cellular examination of this phenomenon was undertaken in period two. This was done by the use of histochemical techniques and is exemplified in Figure 3. A total of 2077 fibers were measured and the mean fiber areas are shown in Table 10 (group means in Table 20, Appendix). Results from both the red (inside) and white (outside) portions of the gastrocnemius show no change in fiber sizes as a result of either the training program or the drug. This finding verifies the gross indication of a lack of muscle hypertrophy in period two.

Fiber Distribution

A total of 4350 fibers were examined in order to determine the percentage distribution of each fiber type and the effects of training and drug on this distribution. Neither the drug nor the training

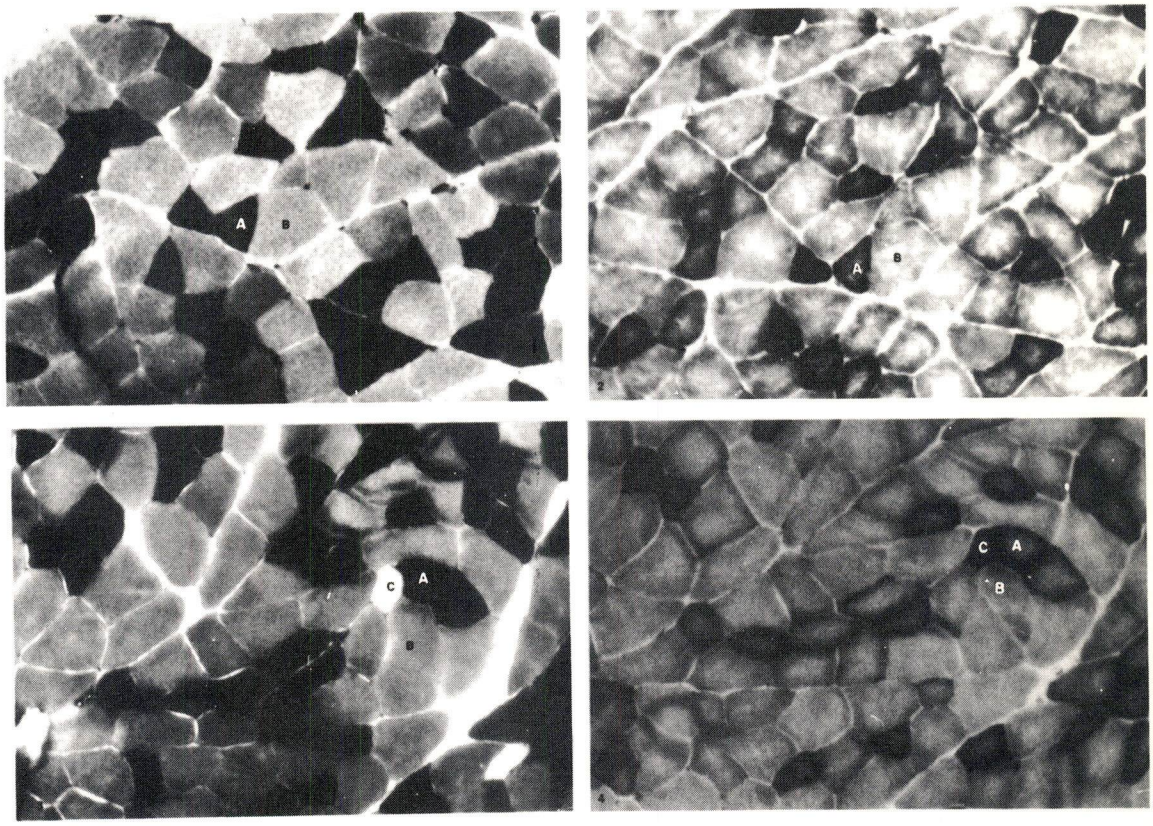

Figure 3. Sample serial sections of the red (inside) and white (outside) portions of the gastrocnemius (RG and WG) muscles in period two.

Sections 1 and 2 - WG
Sections 3 and 4 - RG
Sections 1 and 3 - ATPase
Sections 2 and 4 - NADH-D
Fiber types are (A) FOG, (B) FG and (C) SO x 60.

Table 10. Cross sectional area (μ^2) of fast-twitch-oxidative-glycolytic (FOG), fast-twitch-glycolytic (FG) and slow-twitch-oxidative (SO) fibers in samples of the red (inside) and white (outside) portions of the gastrocnemius (RG and WG) muscles in period two.

Muscle Source	Fiber Type	Training Effect			Drug Effect			Drug x Training Interaction
		Sedentary	Training	P	Placebo	Drug	P	P
RG	FOG	3497 ± 259	3683 ± 166	0.49	3577 ± 160	3697 ± 292	0.65	0.87
	FG	4383 ± 365	4358 ± 238	0.89	4214 ± 210	4699 ± 419	0.29	0.99
	SO	2863 ± 414	3488 ± 269	0.12	3062 ± 245	3682 ± 501	0.15	0.74
	N	7	12		13	6		
WG	FOG	3177 ± 191	3177 ± 184	0.83	3328 ± 198	2991 ± 157	0.25	0.57
	FG	5452 ± 286	5459 ± 200	0.98	5501 ± 290	5399 ± 192	0.79	0.98
	SO	0	0		0	0		
	N	16	13		16	13		

Values are the area of each fiber type expressed as means ± SE

affected the percent composition by number (Table 11, group means in Table 21, Appendix) or area (Table 12, group means in Table 22, Appendix). It can be seen that the fiber percentage by number does not represent the composition of the red and white gastrocnemius. This is because the fast-twitch-glycolytic (FG) fibers account for a greater percent area than their percent number would suggest, while the slow-twitch-oxidative (SO) fibers account for a lesser percent area than their percent number indicates.

Table 11. Muscle composition by number of fast-twitch-oxidative-glycolytic (FOG), fast-twitch-glycolytic (FG) and slow-twitch-oxidative (SO) fibers in samples of the red (inside) and white (outside) portions of the gastrocnemius (RG and WG) muscles in period two.

Muscle Source	Fiber Type	Training Effect			Drug Effect			Drug x Training Interaction
		Sedentary	Training	P	Placebo	Drug	P	P
RG	FOG	47.2 ± 3.5	43.4 ± 1.9	0.66	44.5 ± 1.9	45.5 ± 4.2	0.87	0.87
	FG	29.7 ± 4.2	31.1 ± 3.0	0.97	30.2 ± 3.0	31.7 ± 4.3	0.65	0.39
	SO	22.9 ± 5.3	25.4 ± 3.6	0.91	25.3 ± 3.6	22.7 ± 6.2	0.56	0.61
	N	7	12		13	6		
WG	FOG	32.8 ± 2.4	29.6 ± 3.9	0.54	32.7 ± 3.1	29.5 ± 2.9	0.50	0.43
	FG	67.2 ± 2.4	70.7 ± 3.8	0.50	67.3 ± 3.1	70.5 ± 2.9	0.54	0.44
	SO	0	0		0	0		
	N	16	13		16	13		

Values are the percent number of each fiber type expressed as means ± SE

Table 12. Muscle composition by area of fast-twitch-oxidative-glycolytic (FOG), fast-twitch-glycolytic (FG) and slow-twitch-oxidative (SO) fibers in samples of the red (inside) and white (outside) portions of the gastrocnemius (RG and WG) muscles in period two.

Muscle Source	Fiber Type	Training Effect			Drug Effect			Drug x Training Interaction
		Sedentary	Training	P	Placebo	Drug	P	P
RG	FOG	44.6 ± 3.1	41.1 ± 2.4	0.65	42.9 ± 2.4	41.2 ± 2.9	0.41	0.11
	FG	37.9 ± 7.1	35.0 ± 4.1	0.62	34.9 ± 4.2	38.5 ± 7.2	0.64	0.44
	SO	17.7 ± 7.1	23.9 ± 4.1	0.49	22.2 ± 3.9	20.3 ± 8.4	0.94	0.99
	N	7	12		13	6		
WG	FOG	24.3 ± 2.5	19.8 ± 3.3	0.33	23.2 ± 3.0	21.2 ± 2.7	0.71	0.55
	FG	75.7 ± 2.6	80.2 ± 3.3	0.52	76.9 ± 3.0	78.8 ± 2.8	0.49	0.36
	SO	0	0		0	0		
	N	16	13		16	13		

Values are the percent area of each fiber type expressed as means ± SE

CHAPTER V

DISCUSSION

I. ORGAN WEIGHTS

The analysis of absolute organ weights revealed that the training reduced the liver and kidney weights and increased the heart and gastrocnemius weights, while the drug increased the gastrocnemius weight. However there was also a difference in the final body weight as a result of the training program. Therefore a comparison of absolute weights is tenuous as organ weight is relative to body weight.

Historically relative weights have been used to account for the differences in final body weights. Using this technique, analysis revealed an additional effect of the drug. It reduced the weight of the kidney. But there are problems associated with this mode of organ weight expression also. First, it implies that organs from a 500 gram animal are twice as large as organs from a 250 gram animal. This has been shown to be an incorrect assumption as it violates the basic principle of biological growth (84). The second difficulty associated with the use of relative weights concerns body composition. If the body composition differs, particularly with respect to the percentages of fat and water, then comparisons between groups where such a difference exists is fallacious (216). For example, the heart has little fat while the body contains large amounts. A difference in heart weight/body weight ratios may then be due to differences in the metabolic character of these components. The body composition data showed that the percent fat was

decreased and that the percent water was increased as a result of the training program. This would obviate the use of relative weights as an analytical tool.

An adjustment was then made for the differences in body weight and body composition by using the organ weight as predicted by least squares regression for each homogeneous group (84). Analysis of the predicted weights revealed additional effects of drug and training when compared to relative weights. These differences in results produced by the various techniques illustrate the importance of selecting the correct method to account for differences in final body weight and body composition.

Despite the differences in the analytical methods used in assessing changes in organ weights, comparisons can be made. The heart weight increased in response to the training. This is in accord with the previously cited findings for exercise studies (Table 1, page 7). In the investigations of the effects of anabolic steroids given in conjunction with a training program there was no increase in heart weight in three of the four studies that used a running program (25, 145, 196). This is not surprising considering the relatively slow pace used in two of the studies (25, 145). The fourth study (16) would probably have been nonsignificant had a more convential confidence limit been applied.

The increase in heart weight of the rats in this study was surprising. Previous studies using training regimens designed to mimic weight training did not report hypertrophy (16, 25, 44, 45) and the anaerobic program used in this study was designed with the same intent.

Apparently prolonged anaerobic training produces cardiac hypertrophy.

The effect of the drug was to decrease the weight of the heart in sedentary animals. This catabolic effect was not expected for it had not been previously reported. It should be regarded as detrimental even though the animals appeared healthy and alert.

The adrenal weight was not significantly effected by the training or the drug. This is in contrast to almost every previously reported finding, with the exception of a report in the mouse (29). A study by Buuck and Tharp (19) reported that adrenal hypertrophy in chronically exercised rats was due to an increased width of the region which secretes corticosterone, the zona fasciculata. Their training program was prolonged endurance activity, as were all the studies that reported hypertrophy, whereas the rats in this study ran an intermittent schedule as did some of the mice in the Colacino study (29). This might suggest that the duration of an activity program produces adrenal hypertrophy while intensity does not, or that there is a species/strain difference in response to work. Biochemical assays would be needed to verify this finding.

The weight of the testis increased in response to the training in the placebo animals. This is in agreement with previously reported findings (Table 1, page 7), and would appear necessary to meet the protein synthetic demands of the stressed organism. The effect of the drug is not so clear.

The anabolic steroid was anabolic in the sedentary animals and catabolic in the trained animals. The latter finding is not surprising because of an expected negative feedback effect along the hypothalamic-

pituitary-gonadal axis. It is also in agreement with other studies (Table 2, page 9). The former effect of testicular hypertrophy, though small, was not expected. This may have been due to a direct action of the drug on this tissue. Ludwig (126) reported a biphasic effect of testosterone on the testes when injected in male rats. A low dose produced atrophy while a high dose produced hypertrophy. The dosage given the animals in this study, which was the recommended human dose, may have been high for the sedentary animals. It might be considered a high dose for the turnover rate may have been slower than that found in the exercising rats and would have had time to produce a direct hypertrophic effect on the testis.

Both the liver and kidney weights decreased in response to the training program. A similar but not as dramatic a decrease in liver weight has been previously reported (145). The drug decreased only the kidney weight and only in the sedentary animals. This finding is curious in light of the nephrotropic effect normally attributed to the androgens (111, 122). In reference to the former effect of training, a series of studies has shown that both liver and kidney protein is the most labile source in the rat (204). Also, it has been shown that an acute exercise bout can reduce liver protein in untrained rats (98). it would appear that the training program caused the reduced weights by producing a mobilization of this protein source for utilization by the heart and gastrocnemius, both of which hypertrophied in response to the training.

II. BODY COMPOSITION AND FOOD INTAKE

Previous studies regarding the effects of anabolic steroids on the body weight of animals have shown that endurance training reduces body weight (145, 196). The training program used in this study showed the same effect though not intentionally designed to do so. This response would indicate a larger than expected aerobic component in this regimen. This possibility is surprising for anaerobic work in the rat has shown no effect on a major oxidative enzyme, succinic dehydrogenase, while increasing the glycolytic capacity (phosphorylase and pyruvate kinase) of the soleus muscle (180).

Studies relative to the effects of forced exercise alone have shown that the decrease in body weight is a result of a decrease in the percentage of the carcass composed of fat (27, 104, 149). The results of this study confirm this finding.

It has also been demonstrated that the decreased fat percentage is not only due to the increased energy expenditure associated with the training but also to a decreased caloric intake (27, 195). This study, like that of Thomas and Miller (197), does not support this finding because the appetite was not suppressed. Crews and coworkers (27) state that appetite suppression may be linked to the increase in levels of catecholamines associated with vigorous exercise (177, 201). Possibly an intermittent training program does not produce these high levels and therefore appetite would not be reduced. An alternative hypothesis is found in the work of Baile and others (8). They found that food intake decreased in the monkey as a result of intravenous

injections of lactate. The intermittent regimen used in this study was designed to produce only an alactic acid debt (131, 132) and the absence of lactate would account for the lack of appetite suppression. Conversely, the lack of appetite suppression may be evidence that the intermittent program was indeed alactic in nature.

In the study by Crews and coworkers (27) the decrease in body weight was due in part to a reduction in lean body mass. This study and others did not report a similar finding (94, 109). This finding may be relative to a combination of the training intensity and duration since their program was quite intense and of long duration relative to the other studies. It may indicate that such a combination may provoke a decrease in lean body mass while duration and intensity alone do not.

The drug had no effect on any component of body composition. This is contrary to the studies on sedentary animals that have reported an increase in body weight (26, 40, 116, 121) characterized by an increase in lean body mass and a decrease in percent fat (115), and those that have found a decrease in body weight characterized by a decrease in percent fat (86, 120).

Comparing the findings of this study relative to body composition changes with the data on humans is difficult, if not impossible. This is due to the apparent aerobic component of the training regimen. The attempt to mimic weightlifting fell short of expectations and produced results different from those in human studies using weight training. Most of the human studies report an increase in lean body mass with no change in percent fat (22, 52, 85, 102, 103, 144, 152, 209). Those studies that report no change in body weight also report no change in the percent fat (46, 51, 63, 133).

III. SKELETAL MUSCLE HYPERTROPHY

The finding of an increase in gastrocnemius weight due to both the drug and the training in period one signifies an anabolic effect of both treatments and would appear to verify the premise that this type of training produces muscular hypertrophy. In other studies on the effects of an anabolic steroid and training on muscle weight only Taylor and coworkers (196) reported a similar finding. That they found a muscle weight increase with endurance training is surprising for the endurance program they used is normally considered to have no hypertrophic effect on skeletal muscle (94, 95, 160). This discrepancy may be due to strain differences for they used Wistar rats whereas the other endurance studies used the Sprague-Dawley strain.

An increase in muscle weight can be taken as a gross measure of hypertrophy, although a weight increase could be due to some other factor such as water retention. A possible validation of this gross measure would be the assessment of muscle fiber area using histochemical techniques. The results of such an investigation in period two have been noted. The drug and the training did not produce any detectable instances of muscular hypertrophy. This is surprising for two reasons. One, the conditions of period two were almost identical to those of period one and it would be expected to find similar results. It could be said that the approximately 15% reduction in final running speed to 78 meters per minute from 91 meters per minute in period one could be responsible for this lack of hypertrophy. This is a possibility but it is doubtful. The final speed of 78 meters per minute is still much

greater than the 53.6 meters per minute that elicits a maximal oxygen uptake in rats (186) and would further substantiate the anaerobic nature of the training program. A possible problem in this regard may be in the differences in the breeding of the rats. Although both were Sprague-Dawley albino rats they were purchased from different farms. A difference in genetic makeup may have occurred and might explain the differing responses to the training treatment. An example of a difference in the two groups of animals is the approximately 90 gram difference in initial body weights even though there was only a three day difference in age.

The second reason for surprise at the lack of hypertrophy in period two is that previous research has demonstrated that fiber area increases with forced exercise (20, 49, 70, 174, 205), with drug and training (167, 220); and that muscle girth increases with increases in strength in humans (13, 102, 103) and remains unchanged when strength is not enhanced (46, 51, 63, 144).

There are two studies whose findings may offer some insight into the findings of this study. Both involve human subjects. One found a strength increase without a commensurate increase in muscle girth (191). The second found no change in muscle fiber diameter or muscle girth in subjects placed on a strength training program but did discover an increase in myosin filament diameter and concentration using electron microscopy (162, 163). Based on these findings an enhanced ability of the rat to perform may have been due to an increase in myofilament diameter and concentration which could not be detected with histochemical techniques.

The lack of change in the fiber type distribution is not surprising. The original work by Edgerton and others (42) used histochemical techniques and showed that the hindlimb muscles of endurance guinea pigs had a higher percentage of red fibers with a decrease in the percentage of white fibers. They surmised that this was a conversion of white fibers to red fibers and was the mechanism for the adaptation to aerobic work. Subsequent work reported similar findings (10, 47). Baldwin and associates (9) used biochemical techniques to show that this was not so. They found that the respiratory capacity of all three muscle fiber types of the leg muscles of the rat had a twofold increase in response to aerobic training. The original findings were incorrect due to the insensitivity of the qualitative changes uncovered by the biochemical methods. Several other investigations have also reported that fiber types do not interconvert with training on the basis of actomyosin ATPase Staining (7, 69), and that to the contrary, the differences between white and red muscle fibers are accentuated (96).

CHAPTER VI

SUMMARY AND CONCLUSIONS

The purpose of this study was to assess the efficacy of anabolic steroids in athletics by measuring body composition, organ weight and skeletal muscle hypertrophy of the male albino rat. Two experimental periods were used. Body composition and organ weight were measured in period one and muscle hypertrophy was measured in period two.

The rats were divided into four groups: control, drug, training and drug plus training. The training program consisted of 10 second sprints interspersed with 30 second rest periods with both the number and speed increasing with time. Deca-Durabolin, the anabolic steroid of choice, was administered intramuscularly every third week at 1 mg/kg body weight. Period one lasted for eight weeks while period two lasted nine weeks.

In period one it was discovered that lean body mass was not changed by the drug. This would indicate that an anabolic effect did not occur. Only the training program had an effect on body composition and it reduced the percentage of the carcass composed of fat.

Also in period one the drug produced a decrease in kidney and testis weights in the trained animals. This would indicate unwanted androgenic side effects.

In period one the drug increased the gastrocnemius weight. This could be considered a gross measure of hypertrophy. But this effect was not greater than that produced by the training alone, nor did the drug

enhance the training effect when used in combination with the training. In period two there was no evidence of skeletal muscle hypertrophy. This was evidenced by no change in both the weight and fiber area of the gastrocnemius muscle.

Based on the conditions of this study the findings suggest that the use of anabolic steroids is not beneficial. There appear to be no anabolic effects but a number of androgenic side effects. The major limitation of this study, the anaerobic sprint training program, could be cited as a confounding factor in the drawing of conclusions and recommendations. But this does not nullify the findings that organ weight changes occurred, that lean body mass was unchanged and that fiber size did not increase in the steroid treated animals.

It should be noted that even though there was no clear anabolic effect uncovered by this study, it does not mean that muscle performance was not improved. A recommended study would be to investigate this parameter with an *in situ* measurement of the contractile properties of an appropriate muscle. Also the lack of hypertrophy noted using the techniques of this study does not mean that some changes did not occur for there was a training effect as noted by the decrease in body weight and the increase in heart weight. The excellent possibility of investigating biochemical and molecular levels of change are still available. Finally, it would seem that these investigations should not be undertaken until the elucidation of a model that will consistently induce muscular hypertrophy in laboratory animals is found.

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APPENDIX

Table 13. Group means for absolute organ and muscle weights in period one.

	Control	Training	Drug	Drug + Training
Liver	23.2 ± 0.90	17.5 ± 0.57	23.0 ± 0.49	17.9 ± 0.70
Adrenals (mg)	52.6 ± 3.32	52.2 ± 2.56	51.5 ± 2.04	52.9 ± 3.66
Kidneys	4.3 ± 0.17	3.6 ± 0.11	4.0 ± 0.07	3.6 ± 0.09
Testes	3.5 ± 0.20	3.7 ± 0.07	3.6 ± 0.10	3.6 ± 0.05
Gastrocnemii	2.9 ± 0.12	3.4 ± 0.25	3.4 ± 0.21	4.0 ± 0.24
Heart	1.5 ± 0.09	1.7 ± 0.10	1.4 ± 0.03	1.6 ± 0.05
N	10	10	12	11

Values are weight in grams expressed as means ± SE

Table 14. Group means for relative organ and muscle weights in period one.

	Control	Training	Drug	Drug + Training
Liver	5.0 ± 0.14	3.9 ± 0.12	4.9 ± 0.09	4.1 ± 0.15
Adrenals	11.5 ± 0.78	11.8 ± 0.59	10.8 ± 0.39	12.1 ± 0.87
Kidneys	0.9 ± 0.02	0.8 ± 0.02	0.8 ± 0.02	0.8 ± 0.02
Testes	0.8 ± 0.04	0.8 ± 0.02	0.8 ± 0.03	0.8 ± 0.02
Gastrocnemii	0.6 ± 0.02	0.8 ± 0.06	0.7 ± 0.05	0.9 ± 0.06
Heart	0.3 ± 0.02	0.4 ± 0.02	0.3 ± 0.01	0.4 ± 0.01
N	10	10	12	11

Values are relative weight (organ or muscle/body weight x 100) expressed as means ± SE

Table 15. Group means for predicted organ and muscle weights in period one.

	Control	Training	Drug	Drug + Training
Liver	23.2 ± 0.75	17.5 ± 0.12	23.0 ± 0.24	17.9 ± 0.24
Adrenals (mg)	52.6 ± 1.67	52.2 ± 0.43	51.5 ± 1.05	52.9 ± 1.12
Kidneys	4.3 ± 0.11	3.6 ± 0.04	4.0 ± 0.01	3.6 ± 0.04
Testes	3.5 ± 0.01	3.7 ± 0.03	3.6 ± 0.02	3.6 ± 0.02
Gastrocnemii	2.9 ± 0.10	3.4 ± 0.06	3.4 ± 0.04	4.0 ± 0.09
Heart	1.5 ± 0.02	1.7 ± 0.02	1.4 ± 0.01	1.6 ± 0.02
N	10	10	12	11

Values are weight in grams expressed as means ± SE

Table 16. Group means for body weight and weekly food and water intake in period one.

	Control	Training	Drug	Drug + Training
Body Weight	460 ± 7	444 ± 6	475 ± 6	442 ± 8
Food Intake	200 ± 4	200 ± 3	198 ± 3	198 ± 4
Water Intake	343 ± 17	323 ± 12	339 ± 10	319 ± 10
N	10	10	12	11

Values are weight in grams for body weight and food intake and volume in milliliters for water intake expressed as means ± SE

Table 17. Group means for body weight and absolute (A), relative (R) and predicted (P) weight of the gastrocnemius in period two.

	Control	Training	Drug	Drug + Training
Body Weight	640 ± 16	561 ± 11	591 ± 13	562 ± 11
Gastrocnemii (A)	5.80 ± 0.13	5.71 ± 0.15	5.80 ± 0.13	5.59 ± 0.16
Gastrocnemii (R)	0.95 ± 0.02	1.02 ± 0.03	0.98 ± 0.03	1.00 ± 0.02
Gastrocnemii (P)	5.80 ± 0.06	5.71 ± 0.05	5.80 ± 0.09	5.59 ± 0.09
N	10	10	12	11

Values are weight in grams for body weight, gastrocnemii (A) and gastrocnemii (P); and muscle/body weight x 100 for gastrocnemii (R).

Table 18. Group means for body composition in period one.

	Control	Training	Drug	Drug + Training
Protein	20.9 ± 0.8	19.4 ± 0.7	19.8 ± 0.5	19.7 ± 0.6
Water	64.8 ± 0.6	70.2 ± 0.6	66.4 ± 1.1	70.3 ± 0.6
Fat	15.0 ± 1.0	9.8 ± 0.3	14.4 ± 0.7	9.6 ± 0.3
Ash	3.1 ± 0.5	2.1 ± 0.3	2.5 ± 0.4	2.1 ± 0.2
N	8	10	12	11

Values are the percent of each component expressed as means ± SE

Table 19. Group means for total body content of protein, water, fat, ash and lean body mass in period one.

	Control	Training	Drug	Drug + Training
Protein	93.1 ± 3.4	85.8 ± 3.0	94.0 ± 2.4	86.9 ± 2.9
Water	300.5 ± 6.2	311.6 ± 6.1	315.2 ± 6.9	310.6 ± 6.0
Fat	69.5 ± 4.7	43.5 ± 1.1	68.5 ± 3.1	42.4 ± 1.8
Ash	14.5 ± 2.0	9.4 ± 1.3	11.9 ± 1.8	9.1 ± 1.1
Lean Body Mass	408.1 ± 8.3	406.8 ± 5.9	421.1 ± 6.6	406.6 ± 7.1

Values are the weight of each component in grams expressed as means ± SE

Table 20. Group means for cross-sectional area (μ^2) of fast-twitch-oxidative-glycolytic (FOG), fast-twitch-glycolytic (FG) and slow-twitch-oxidative (SO) fibers in samples of the red (inside) and white (outside) portions of the gastrocnemius (RG and WG) muscles in period two.

Muscle Source	Fiber Type	Control	Training	Drug	Drug + Training
RG	FOG	3454 ± 397	3631 ± 167	3553 ± 388	3840 ± 506
	FG	4173 ± 454	4233 ± 247	4664 ± 672	4733 ± 653
	SO	2615 ± 361	3260 ± 304	3193 ± 917	4171 ± 419
	N	4	9	3	3
WG	FOG	3386 ± 297	3253 ± 268	2908 ± 193	3088 ± 266
	FG	5502 ± 505	5500 ± 204	5389 ± 173	5410 ± 387
	SO	0	0	0	0
	N	9	7	7	6

Values are the area of each fiber type expressed as means ± SE

Table 21. Group means for muscle composition by number of fast-twitch-oxidative-glycolytic (FOG), fast-twitch-glycolytic (FG) and slow-twitch-oxidative (SO) fibers in samples of the red (inside) and white (outside) portions of the gastrocnemius (RG and WG) muscles in period two.

Muscle Source	Fiber Type	Control	Training	Drug	Drug + Training
RG	FOG	50.4 ± 2.4	41.8 ± 2.0	42.9 ± 7.7	48.0 ± 4.6
	FG	26.4 ± 6.1	31.7 ± 3.5	34.0 ± 6.0	29.2 ± 7.0
	SO	23.1 ± 5.3	26.3 ± 4.4	22.6 ± 11.9	22.7 ± 7.1
	N	4	9	3	3
WG	FOG	35.5 ± 3.8	29.0 ± 5.2	29.3 ± 2.1	29.8 ± 6.2
	FG	64.5 ± 3.8	71.0 ± 5.2	70.7 ± 2.1	70.3 ± 6.2
	SO	0	0	0	0
	N	9	7	7	6

Values are the percent number of each fiber type expressed as means ± SE

Table 22. Group means for muscle composition by area of fast-twitch-oxidative-glycolytic (FOG), fast-twitch-glycolytic (FG) and slow-twitch-oxidative (SO) fibers in samples of the red (inside) and white (outside) portions of the gastrocnemius (RG and WG) muscles in period two.

Muscle Source	Fiber Type	Control	Training	Drug	Drug + Training
RG	FOG	48.9 ± 3.1	40.2 ± 2.9	38.7 ± 4.3	43.7 ± 4.0
	FG	33.3 ± 8.8	35.7 ± 5.0	44.0 ± 12.8	33.0 ± 8.3
	SO	17.9 ± 5.9	24.1 ± 5.0	17.3 ± 16.8	23.3 ± 8.2
	N	4	9	3	3
WG	FOG	26.1 ± 3.6	19.4 ± 5.0	22.0 ± 3.6	20.4 ± 4.5
	FG	73.9 ± 3.6	80.6 ± 5.0	80.9 ± 3.7	79.6 ± 4.5
	SO	0	0	0	0
	N	9	7	7	6

Values are the percent area of each fiber type expressed as means ± SE

VITA

Howard James Wood was born in Elmira, New York on May 26, 1946. He attended the public schools of Spring Valley, New York and was graduated from Spring Valley Senior High School in 1964.

The following year he entered the Arnold College Division of Physical Education at the University of Bridgeport, Bridgeport, Connecticut. He received the Bachelor of Science degree in 1968.

He attended the same institution and received the Master of Science degree in Education in 1969. He served as the institution's track and field coach for that and the following year.

He was employed by Queens College, CUNY as an instructor in the Department of Health and Physical Education from 1970 to 1972. He also served as the cross country and assistant track and field coach.

He entered the Graduate School at the University of Tennessee, Knoxville in 1972. He was a graduate assistant in the School of Health, Physical Education and Recreation, Division of Physical Education. He received the Doctor of Education degree with a major in Physical Education, specializing in Exercise Physiology in 1976.

He is married to the former Judith Carole Peterson of Trumbull, Connecticut and they have one daughter, Fabrienne Lee.