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The Relationship of Free and Total Serum Thyroxine Concentrations to the Reproductive Condition of the White-Footed Mouse (Peromyscus leucopus noveboracensis)

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THE RELATIONSHIP OF FREE AND TOTAL SERUM THYROXINE CONCENTRATIONS TO THE REPRODUCTIVE CONDITION OF THE WHITE-FOOTED MOUSE (*PEROMYSCUS LEUCOPUS NOVEBORACENSIS*)

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Master of Arts

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by

Gerald William Peden

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APPROVAL SHEET

This thesis is submitted in partial fulfillment of the requirements for the degree of

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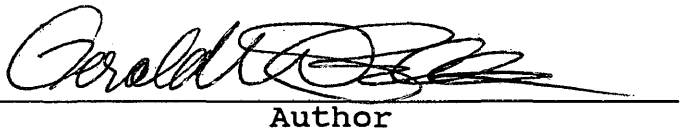

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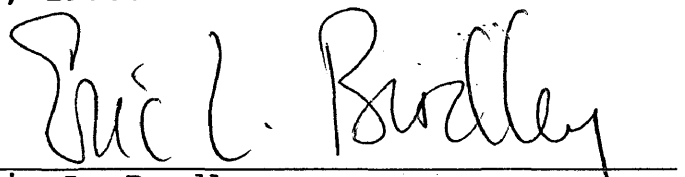
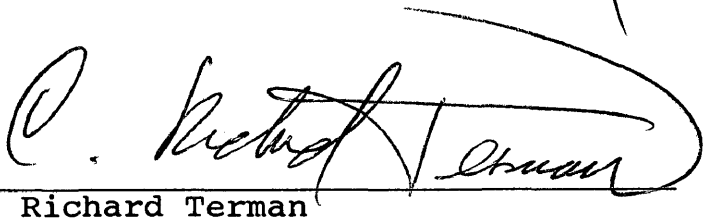


Eric L. Bradley



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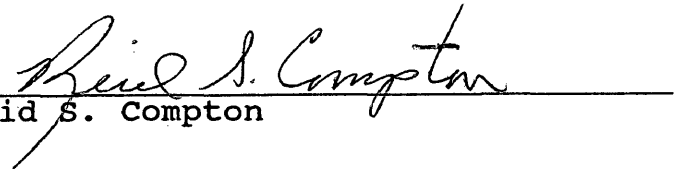

Reid S. Compton

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ABSTRACT

Several parameters of thyroid function were compared between reproductively inhibited white-footed mice of both sexes taken from laboratory populations and reproductively capable controls. Measurements of body weight, paired reproductive organ weights, and pelt coloration were evaluated. Determinations of both total and free serum thyroxine concentrations were made using radioimmunoassay. These values represent the first known reported thyroid hormone parameters for this species.

The data indicated the following: 1) total serum thyroxine concentrations were significantly lower in reproductively inhibited population males, while females showed a similar trend compared with their respective controls; 2) reproductively inhibited males and females displayed free serum thyroxine concentrations significantly below those of reproductively capable controls; 3) weights of selected organs from male and female reproductively inhibited white-footed mice were significantly less than those of controls; 4) analyses of pelage coloration showed that population males and females differed significantly from reproductively proven animals. Taken together, these evaluations suggest that a hypothyroid state exists in reproductively inhibited males and females maintained in laboratory populations. It is concluded that the thyroid may play a role in the inhibition of reproduction in this species of Peromyscus, but as yet, no conclusive data are available that indicate that the thyroid is wholly responsible.

THE RELATIONSHIP OF FREE AND TOTAL SERUM THYROXINE CONCENTRATIONS TO THE REPRODUCTIVE CONDITION OF THE WHITE-FOOTED MOUSE (*PEROMYSCUS LEUCOPUS NOVEBORACENSIS*

INTRODUCTION

Wide fluctuations in the natural population size of some small mammals can occur due to disease, predation, social behaviors, seasonal reproductive processes, and/or lack of resources so that massive die-offs occur. For example, such population fluctuation occurs in populations of Lemmus (Andrews 1968), Microtus (Krebs et al 1973 and Louch 1958), and Norway rats (Andrews et al. 1972). These density-dependent mechanisms that control population numbers may involve an adrenal response to stress described by Christian (1950, 1959, 1963). His hypothesis is that hyperplasia and hypersecretion of the adrenal glands result in a reciprocal relationship between the adrenals and gonads such that reproduction in a population is diminished. Specifically, Christian (1975, 1980) has shown that limits of population growth may occur through inhibition of reproductive maturation. He suggests that aggressive encounters in dense populations result in increased pituitary-adrenal activity that cause diminished pituitary-gonadal activity. Mechanisms of this reciprocal relationship are explained by peripheral feedbacks in the

form of adrenal androgens and possibly progesterone, or by a short loop feedback in the form of elevated glucocorticoid and/or adrenocorticotropic hormone (ACTH) inhibition on gonadotropin secretion (Christian 1975).

In sharp contrast to Lemmus, Mus, and Norway rats, the natural population densities for other mammals vary within a much narrower range below the carrying-capacity for the population. Narrow variations in population size have been seen in Peromyscus (Terman 1966). In P. maniculatus, laboratory population numbers appear to be controlled more by a curtailment of reproduction, than a pathological adrenal stress response (Terman 1965, 1969). The manner in which the logistical growth pattern of laboratory populations of the prairie deermouse ceases can be due to the failure of young to survive, but more often it is due to a supression of reproductive maturation in the few young born into the population (Terman 1969, 1973a,b). Indeed, in P. maniculatus, 90% of females born into laboratory populations remain non-parous throughout their lifetime if maintained within the population context (Terman 1965, 1969, 1973b). In addition, it has been demonstrated that normal reproductive function in 50% of previously inhibited males and females will occur only 50 days after removal from the population context and subsequent mating with a proven animal (Terman 1973a).

Studies on populations of P. maniculatus have shown that although reproductive inhibition is evident, adrenal hyperplasia does not occur with a concomitant rise in the corticosterone levels of population animals (Bradley and Terman 1981a; and Sung et al. 1977). Indeed, ACTH secretion was found not to be significantly different in population animals when compared with controls (Coppes and Bradley 1984). Still, these animals are clearly reproductively inhibited. In fact, it has been suggested that reproductively inhibited animals from a population are suspended in a pre- or peri-pubertal reproductive condition. This is based on histological analyses of the gonads of both sexes, as well as the lack of an LH surge and high levels of FSH in population females, and low LH associated with low levels of testosterone in population males (Bradley and Terman 1981b, c).

Two previous studies on P. maniculatus bairdi have indicated the possibility of a thyroidal influence on reproductive inhibition. Peebles et al. (1984), reported that the mean serum thyroxine concentration was significantly reduced in population males and tended to be reduced in population females as compared to controls. A correlation between decreased serum hormone concentration versus decreased body weight, and also versus reduced reproductive organ weights, suggested that hypothyroidism may play a role in the reproductive inhibition of deermice.

Later, Pitman and Bradley (1984) described a circadiel variation of thyroxine in P. maniculatus bairdi. Additionally, it was postulated (based on histological evidence) that in population males, the decreased hormonal concentrations were due to secondary hypothyroidism, while in females a primary hypothyroid state was suggested. Both previous studies suggested that there is probably some population-based, behavioral/endocrine regulatory mechanism involving the thyroid that results in a marked inhibition of reproductive function.

The evidence for the requirement of thyroid hormones for the normal maturation and differentiation of tissues is extensive. Specifically, thyroid dysfunction has been shown to disrupt normal reproduction in a variety of species, including man. It is the purpose of this study to test the hypothesis that reduced thyroid function also exists in a previously uncharacterized Peromyscus species, and to compare the extent and nature of reproductive inhibition that occurs in laboratory populations of the white-footed mouse. As part ofthis study, measurements of both free and total serum thryoxine (T4) by radioimmunoassay, selected reproductive organ weights, body weights, and pelt color evaluations were made.

MATERIALS AND METHODS

FOUNDING OF THE LABORATORY BREEDING STOCK

Animals used in this study were Peromyscus leucopus noveboracensis derived from wild populations. A laboratory breeding stock of P. leucopus was initiated by mating trapped animals from indigenous wild populations with laboratory stocks. One male was caged with two sibling females (when possible) to enhance the probability of pregnancy and reduce aggression between females. In each triad, at least one individual was wild in origin, and males and females were not related. The progeny from this stock (the F1 generation) were weaned after 21 days and housed in same-sex cages with their siblings until needed for future matings as outlined below. All of these subsequent matings were assembled using F1 animals paired with non-siblings of 60 days of age. These pairs were maintained as producers for the laboratory colony. F2 animals served as control or population manipulated animals for this study.

ANIMAL MAINTENANCE

All cages used for pairings and housing of weaned pups and control groups measured 12.5 x 27 x 14.5 cm and were constructed of opaque plastic with wire tops. Bedding was clean, dry wooden shavings, and food (Prolab Rat, Mouse, Hamster 3000, Agway Syracuse, NY) and water were provided ad libitum. Animal rooms (13.5m x 13.5m) were maintained at between 18-24 C on a 14 hour light (0700-2100 hours EST), 10 hour dark cycle for the period of the study. Air was changed in each room 5 to 10 times per hour depending upon the temperature. Litter was changed in colony producers every two weeks, and in other groups according to the appropriate protocol below.

Control Animals

When young (F2 generation) were born to a producing pair (F1 generation) in the colony, cages were not disturbed until the young reached seven days of age. At seven days of age, the cage of the "family" unit was cleaned and soiled bedding replaced. At twenty-one days of age, weaning was accomplished by removing individuals from their parents and by separating young by sex into non-sibling bisexual pairs. Each individual of a pair was kept in a separate compartment and was never allowed physical contact with the other member of the same pair. Bedding of these manipulated assemblies

was not changed. Every two weeks the control mice were switched from one side of the cage to the other (allowing contact with soiled bedding, but not physical contact with the opposite sex) until sacrificed at seventy days of age.

Population Animals

Populations were assembled with three reproductively "proven" founding pairs placed into enclosures constructed of an 80cm high aluminum wall bolted inside a stainless steel bottom (1.5m in diameter) which was covered with wood shavings to a depth of 4cm. Populations were provided with food and water ad libitum. Added to each enclosure were eight 0.75L plastic nest boxes placed in a circle. Populations were inspected every two weeks, at which time pregnancies and the reproductive condition of all animals (perforation of vagina, prominant nipples suggesting lactation, or descended testes) were recorded. Animals born into a population were toe clipped to aid in their future identification. At the time of tissue collection, appropriately selected animals (those with both a past and current reproductive history of outward signs of inhibited reproductive function) were sacrificed at 70 $\pm$ 2 days of age. The criterion for the selection of males was the absence of descended testes, and for females criteria were the absence of prominant nipples, an imperforate vagina, and

obviously a past and current, non-pregnant history. All animals were selected for sacrifice from three separate populations. Sampling of more than one animal of each sex from the same litter was not permitted. Twenty-four hours previous to sampling, a UV-fluorescent marker dye (Blak-Ray Ink A-946 Blue, Ultraviolet Products, Inc., San Gabriel, CA) was painted on the tails of population animals. This insured identification and capture of experimental animals in less than two minutes, and with a minimum amount of disturbance time.

TISSUE COLLECTION:

All individuals were administered diethyl ether anesthesia between 1530 and 1730 hours EST (after Pitman, 1984). Immediately thereafter, the dorsal aorta was cut at the level of the renal artery and a blood sample was drawn into a 1ml tuberculin syringe. Blood samples were collected within two minutes of initial disturbance, and allowed to clot. Clotted blood was centrifuged at 9000g in a microcentrifuge (Beckman Instruments) for two minutes to obtain serum. Serum samples were frozen at -70 C until assayed. After blood collection individuals were immediately weighed to the nearest 0.1 gram on a Dial-o-gram balance (Ohaus, Floram Park, NJ).

Gonads and accessory organs were removed through mid-saggital dissection, and fixed in vials containing a phosphate buffered 10% formalin solution. At time of weighing, fine dissection of gonadal tissues was accomplished by the previously described method of Terman (1969). Paired testes and paired seminal vesicles or paired ovaries and uteri were weighed to the nearest 0.01mg on a Sartorius electrobalance interfaced with a Commodore 64 computer.

Pelts were removed through a series of incisions (anterior to the ear pinnae dorsally, at the base of the tail dorsally, and around each paw), tagged, then salted and refrigerated until tanned. Pelts were tanned by soaking in a solution of 1.02M NaCl to which 72mM sulfuric acid was added, for a period of one to five days (or until all visible fat was dissolved and fascia turned white). After tanning, pelts were pinned to a styrofoam board covered in absorbant paper to dry, then hair was brushed in an anterior to posterior direction with a toothbrush to allow further drying.

Tanned and brushed skins were evaluated using a subjective ranking protocol for scoring their coloration. Pelts were evaluated by 10 separate, unbiased individuals by a two-step design. First, evaluators were asked to separate pelts into piles according to color, creating as many piles

as deemed necessary. Once completed, individuals were asked their criteria for their scheme of separation into piles. Piles were given scores based on each evaluator's subjective color patterns. Scores ranged from 1 to 4, with 1 representing the pile with the lightest color, and 4 denoting the pile with the darkest color.

After re-shuffling, pelts were compared against a color-card composed of four standard color paint chips (Sherwin Williams [Cleveland, OH] numbers: 1221-B, 1220-E, 1519-D, and Benjamin Moore Paints [Montvale, NJ] number: 1-874-22:EF). Each evaluator determined a score for each pelt by a subjective judgement of which color chip the pelt color was closest to. Scores of 1 through 4 were utilized in the same manner as before: 1=lightest color standard, and 4=darkest color standard. Each pelt was given a score determined by the evaluator that best represented the coloration of the majority of the pelt.

RADIOIMMUNOASSAY PROCEDURE

Radioimmunoassay was performed using Clinical Assays GAMMACOAT 125-I Free/Total Thyroxine (T4) Radioimmunoassay Kit purchased from Dade Baxter Travenol Diagnostics, Inc. Cambridge, MA.

The GAMMACOAT kit procedure for total T4 is a competitive binding assay which is performed entirely in the

coated tubes provided. T4, which is displaced from its serum binding proteins by 8-anilino-1-naphthalenesulfonic acid (ANS) and salicylate, competes with a T4 tracer for a limited number of binding sites of antibody immobilized on the lower inner wall of the GAMMACOAT tube. The amount of tracer that binds to the tube is inversely proportional to the T4 concentration in the sample. After an incubation period of 45 minutes at room temperature (20-25 degrees C), the tube contents are decanted and the tubes counted in a Biogamma II gamma counter (Beckman) set for 125-I. For the total T4 assay the standard curve was established through a serial dilution of the highest standard provided with the kit (20ug/dl) and using the serum blank provided (0ug/dl) as the diluent. Duplicate standards of 0, 0.5, 1, 2, 4, and 8ug/dl were made in order that the standard curve would be within the effective range of the samples to be analyzed.

Free T4 determinations were also performed entirely in the coated tubes provided according to the method described with the kit. During the first incubation, the free T4 fraction in each sample is bound to the T4 specific antibody immobilized on the lower inner wall of the GAMMACOAT tube. The T4 fraction which remains in solution bound to serum binding proteins is removed from the coated tube by decantation. The tubes are rinsed once with incubation buffer, and then incubated with T4 tracer. The tubes are

decanted again and counted on the Beckman Biogamma II gamma counter set for 125-I. Standard curves were prepared from the five serum standards provided with the kit at concentrations of 0, 0.15, 0.65, 1.4, 2.3, and 4.8ng/dl.

RADIOIMMUNOASSAY VALIDATION

P. leucopus serum samples were collected and pooled into one standard serum, then serially diluted and run in each assay to be compared with the standard curve. Cross-reactivity of other protein hormones is negligable in this system according to information provided with the assay kit. Indeed, slopes of the standard curve and serially diluted serum were parallel in all assays, indicating that thyroxine was, in fact, measured. The large sample number necessitated that the free thyroxine determinations be made in three separate assays. In order to be certain that each assay was comparable to the next, slopes and y-intercepts of the standard curves were compared statistically. It was found that none of the standard curves differed significantly from one another, allowing valid comparisons between the data derived from the three curves.

Standards were run in triplicate and all samples were run in duplicate and counted to less than 1% error (40,000 counts). The standard curve for the total procedure is shown in FIGURE 1, and the mean standard curve for the free procedure is shown in FIGURE 2.

FIGURE 1: The standard curve for the total thyroxine radioimmunoassay.

TOTAL STANDARD CURVE

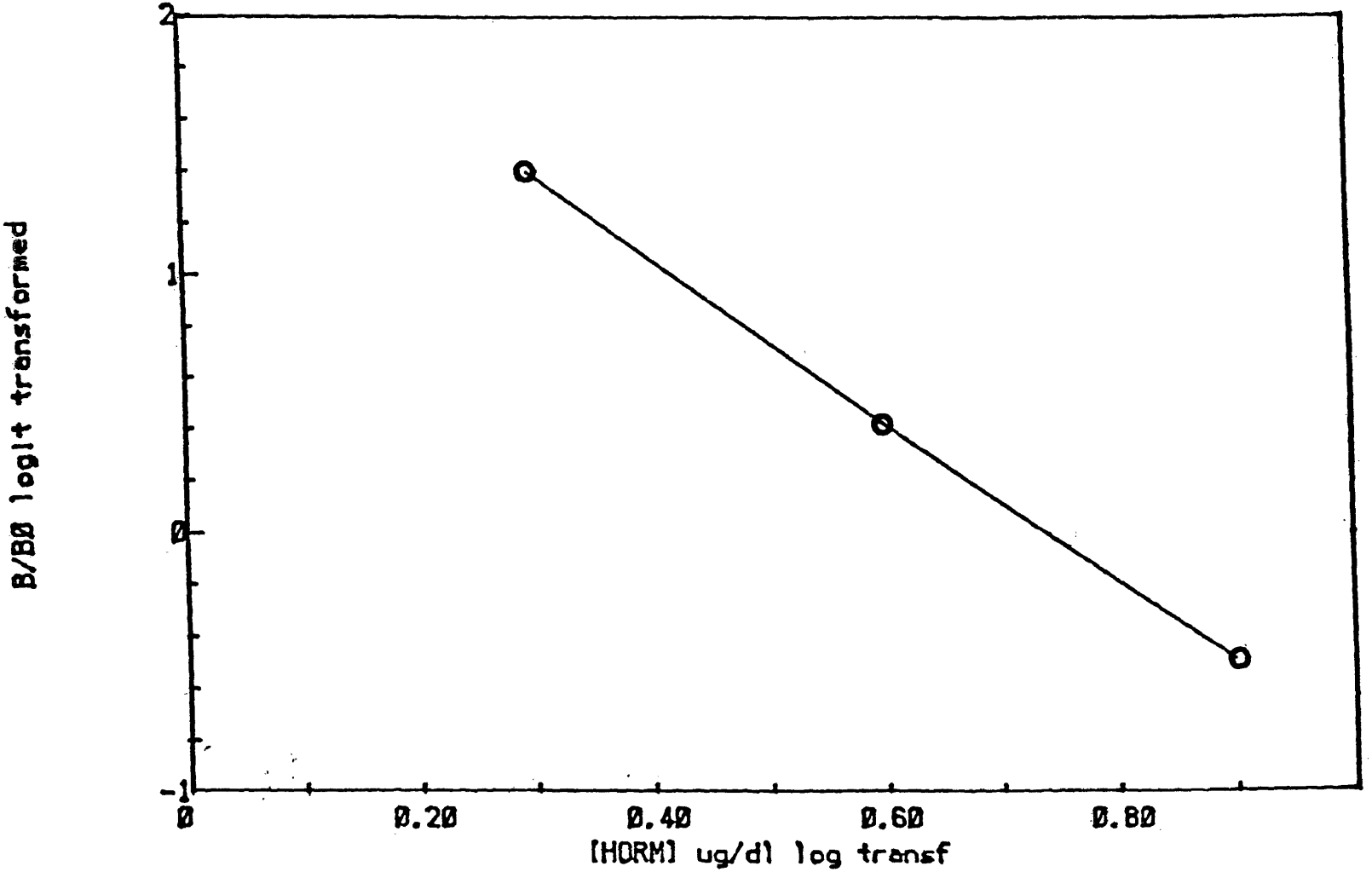

FIGURE 1

FIGURE 2: The mean standard curve for the free thyroxine radioimmunoassay. The single curve is derived from three different assays each run with standards in triplicate.

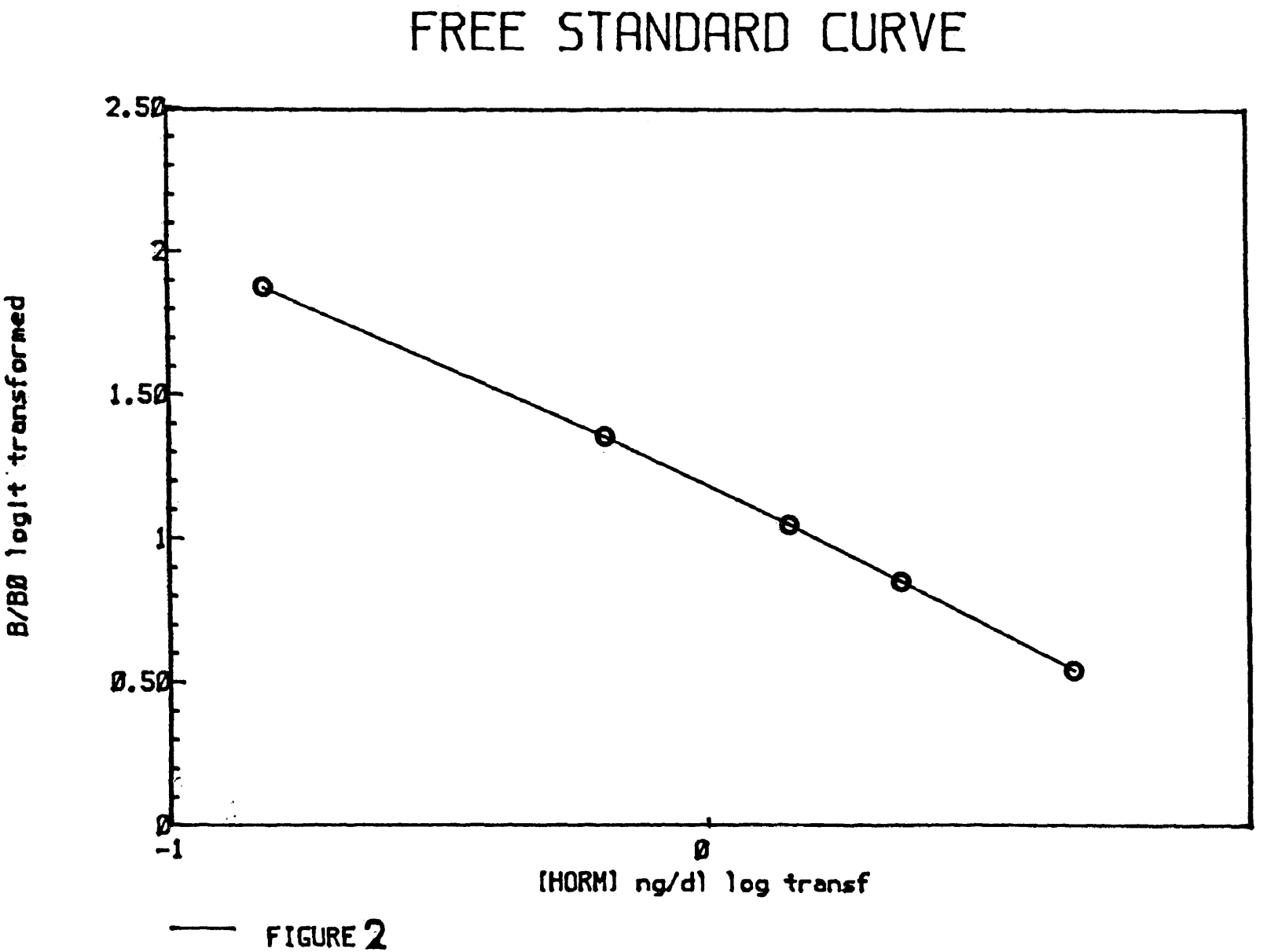
FREE STANDARD CURVE
2.50
2
1.50
1
0.50
0
-1
0
B/B0 logit transformed
[HORM] ng/dl log transf

FIGURE 2

STATISTICS

Basic arithmetic operations on the data were accomplished using MINITAB. Analysis and comparisons of the slopes of radioimmunoassay curves for different groups were evaluated using Biomedical Computer Programs' (BMDP) BMDP1R Multiple-Regression Program (University of California, Berkley, CA--see APPENDIX B). Linear regression analysis on SPSSX was used to fit standard curves to a line and fit unknown hormone concentrations to the computed line. A one-way model one ANOVA was utilized to analyze hormonal concentrations between groups as well as for differences between groups regarding body and organ weights. Because of a significant heterogeneity of variance, a square-root transformation was performed to allow parametric analysis of free serum thyroxine concentrations using ANOVA. The pelage evaluation procedure was statistically evaluated by a non-parametric Kruskall-Wallace test on SPSSX. This statistic allowed for an analysis of where in each evaluator's color scheme experimental groups occured, detected outliers, and tested for significant differences between groups.

In addition, Pearson product moment correlation coefficients were utilized to ascertain if there were any correlations between body weight, gonadal weights, mean serum concentration of hormone, and pelage coloration of

individuals and/or groups. All Pearson statistics reported were positive correlations.

All statistics are reported as the mean $\pm$ the standard error of the mean (SEM) and were considered significant at the $P<0.05$ level.

RESULTS

The mean body weights of both male and female population animals were significantly ($P<0.001$) lower than their control groups (TABLE 1). In addition, population females as a group had body weights that were significantly less than population males as a group ($P<0.05$).

Mean paired testes weight of population males was significantly ($P<0.001$) lighter when compared with control males (TABLE 2). Likewise, population male mean seminal vesicle weights were significantly ($P<0.001$) lower with respect to their corresponding control male values.

The mean paired ovaries weights of population females were significantly ($P<0.001$) lower in weight than their respective controls (TABLE 3). Population females also showed a significantly ($P<0.001$) lowered uterine weight than reproductively capable control females.

Total serum thyroxine concentrations were significantly ($P<0.004$) lower in population males compared with the corresponding values from control animals. Population females tended ($P<0.1$) to be lower in total serum thyroxine concentration compared with female controls (TABLE 4).

TABLE 1

A comparison of body weight between control and selected population males and females. Values are expressed as the mean ± SEM.

Group	Sex	n	Body weight (g)
Control	Male	23	21.5 ± 3.85
Population	Male	10	17.2 ± 1.98***
Control	Female	25	19.5 ± 1.89
Population	Female	10	16.4 ± 1.55***

*** $P<0.001$

TABLE 2

A comparison of paired reproductive organ weights between control and population males. Values are expressed as the mean ± SEM.

Group	n	Paired Testes Weight(mg)	Paired Seminal Vesicles Weight(mg)
Control	23	288.1 ± 13.50	117.3 ± 2.92
Population	10	44.1 ± 2.07***	3.5 ± 0.04***

*** $P<0.001$

TABLE 3

A comparison of paired ovaries and uterus weights between control and population females. Values are expressed as the mean ± SEM.

Group	n	Uterus Weight(mg)	Paired Ovaries Weight(mg)
Control	25	54.8 ± 8.01	139.1 ± 3.20
Population	10	7.7 ± 0.09***	73.9 ± 5.80***

*** $P<0.001$

TABLE 4

A comparison of free and total serum thyroxine concentrations between control and population males and females. Thyroxine concentrations are expressed as the mean ± SEM in ug/dl for the total assay, and ng/dl for the free assay.

Group (n)	Sex	Serum Total Thyroxine(ug/dl)	Serum Free Thyroxine(ng/dl)
Control (23)	Males	3.72 ± 0.675	2.75 ± 0.051
Population (10)	Males	2.91 ± 0.866**	2.48 ± 0.101**
Control (25)	Females	2.96 ± 0.573	2.71 ± 0.049
Population (10)	Females	2.81 ± 0.666*	2.17 ± 0.096***

* $P=0.1$
** $0.001<P<0.05$
*** $P<0.001$

However, free serum thyroxine concentrations of population females were highly significantly ($P<0.001$) below those of corresponding control females. Population males showed a significantly ($P<0.009$) reduced free serum thyroxine concentration compared to controls.

Analysis of pelt evaluations showed that at no time was a pelt from a population animal given a score greater than two, and no control pelts were scored with values less than three. Mean scores based on an evaluator's subjective color scheme differed significantly between population versus control groups (TABLE 5). High values were representative of what evaluators termed: "darker, richer, or blacker" tones, while lower numbers on the scale refered to "lighter, golden, or redder" pelts. Population animals as a group (both males and females) had significantly lower (lighter) pelt scores than controls taken as a group. There were no statistically significant differences between population males and population females, nor between control males and control females. Interestingly, there was no significant difference between the two methods of evaluation (see APPENDIX A).

Pearson product moment correlations not reported here were determined not to be significant. For a table of all comparisons analyzed, see Appendix C. When control plus population males were taken as a group, correlation

TABLE 5

A comparison of pelt scores based on two independent methods (see text) between population and control animals. Values reported are the mean pelt score ± SEM for a group after evaluation by 10 evaluators. No significant differences between the mean values for the two methods were observed.

Group (n)	Mean Score Using Method 1	Mean Score Using Method 2
Control (48)	3.2 ± 0.06	3.2 ± 0.04
Population (20)	1.2 ± 0.02***	1.1 ± 0.02***

*** $P<0.001$

statistics showed a significant correlation between body weight and paired testis weight ($P<0.001$); body weight and paired seminal vesicle weight ($P<0.005$); free serum thyroxine concentration and paired testis weight ($P<0.001$); free serum thyroxine concentration and paired seminal vesicle weight ($P<0.006$); and paired testis weight and paired seminal vesicle weight ($P<0.001$).

In addition, significant correlations were shown between free serum thyroxine concentration and paired testis weight ($P<0.02$); free serum thyroxine concentration and paired seminal vesicle weight ($P<0.009$); and paired testis weight and paired seminal vesicle weight ($P<0.01$) in population males when taken as a group.

When control males were considered alone, significant correlations were seen between body weight and paired testis weight ($P<0.05$) and between paired testis weight and paired seminal vesicle weight ($P<0.009$). Free serum thyroxine concentration tended to be correlated with both paired testis weight and paired seminal vesicle weight ($P<0.1$; and $P<0.1$; respectively).

In females taken as a group (controls and population animals together) a significant correlation existed between total serum thyroxine concentration and free serum thyroxine concentration ($P<0.02$); as well as between free serum thyroxine concentration and both uterine weight ($P<0.005$)

and paired ovary weight ($P<0.01$). In this group, body weight tended to be correlated with reproductive organ weights (uterus $P<0.1$; paired ovaries: $P<0.1$), as well as to total serum thyroxine concentration ($P<0.1$).

In population females taken alone, a significant correlation existed between free serum thyroxine concentrations and uterine weight ($P<0.001$); free serum thyroxine concentration and paired ovary weight ($P<0.03$); free serum thyroxine concentration and body weight ($P<0.05$); and free serum thyroxine concentration and total serum thyroxine concentration ($P<0.04$).

A significant correlation between free serum thyroxine concentration and paired ovarian weight ($P<0.008$) as well as with uterine weight ($P<0.009$) was noted when control females were taken as a single group; other-wise, no significant correlations were evident in this group.

A highly significant positive correlation between total thyroxine concentration and pelt score ($P<0.001$) was present when all males were considered as one group, as well as when considering females as a single group ($P<0.001$). Due to the lack of variation around the mean pelt score, comparisons between the sexes were not significantly correlated with any parameters investigated in this study.

DISCUSSION

The drastic degree of reproductive inhibition observed in white-footed mice selected from populations was similar to that reported in studies on the prairie deermouse (Terman 1965, 1969, 1973a, 1980, 1987; Bradley and Terman 1981a,b,c; Sung et al. 1977; Albertson et al. 1971; Coppes and Bradley 1980; Peebles et al. 1984; Pitman and Bradley 1984; Kirkland and Bradley 1980). In these earlier studies it was shown that at least 90% of the deermice born into the laboratory population fail to mature reproductively, both during the growth phase of the population and when numerical growth has ceased (Terman 1965, 1969, 1973a, 1980, 1987). These present data indicate a highly significant reduction in reproductive capability in both sexes selected during the growth phase from laboratory populations of Peromyscus leucopus noveboracensis. In fact, none of the young born into the three, growing populations ever produced young.

Comparisons of the body weights of animals maintained in populations were lower than those of controls. This differs from the report of Wolfe (1981), who found no significant difference between body weights in population versus control groups of P. leucopus with a mean age of 317

days (range 152 to 564 days). The correlations seen between body weight versus testis weight and body weight versus seminal vesicle weight in males as well as correlations between body weight versus uterine weight and body weight versus paired ovarian weight in females, suggest that body weight and gonad weight are affected similarly, and independently of functional reproductive ability.

Weights of reproductive organs of population animals were markedly below those of their respective controls. The degree of significance in this study is greater than that reported by Wolfe (1981) in his study on older animals. These weight differences are assumed to reflect decreased secretion of gonadotropins and androgens suggesting a significant inhibition of the development of these organs in population animals (Bradley and Terman 1981b, c). In addition, correlations between paired testis weight and seminal vesicle weight in males may be suggestive of a direct effect of lowered testis function on seminal vesicle function (Bradley and Terman 1981c).

The primary goal of this study was to evaluate if thyroid function in reproductively inhibited animals selected from populations was below that of controls, and to determine if this species was reproductively inhibited in the same manner that has been demonstrated in P. maniculatus. The measurement of both free and total

thyroxine is thought to be sufficient to estimate the presumed reduction in thyroid function (Chopra 1986). Measurement of tri-iodothyronine (T3) in assessing thyroid function is valuable only if T3 thyrotoxicosis is expected (Larsen 1986). Pitman and Bradley (1984) suggest that in P. maniculatus, serum thyroxine concentration varies over a 24-hour period. They determined that the time of day when thyroxine concentration was relatively constant for both male and female deermice occurs two to three hours before the light-to-dark transition. Therefore, serum samples for this study were collected during that time period.

In this experiment, total serum thyroxine concentration in population males was significantly below that of corresponding control males, while females showed a similar trend. Even more suggestive of a hypothyroid condition in male and female population animals is the observation that free serum thyroxine concentrations were significantly lower than their respective control groups. Because the free thyroxine concentration is an indicator of T4 disposal and secretion rates, a low free T4 implies deficient secretion of thyroid hormone (Kaptein, et al. 1981). To date, the direct radioimmunoassay of thyroid-stimulating-hormone (TSH) has not been possible because there are no commercially available antibodies that are reactive to Peromyscus TSH (Martineau 1988). Without serum

TSH concentration information, an accurate determination of primary versus secondary hypothyroidism is difficult. Nevertheless, it can be stated unequivocally that for P. leucopus, serum levels of thyroxine for reproductively inhibited animals maintained in laboratory populations are markedly below those of their reproductively capable controls.

In hypothyroidism, it is not unusual to see total thyroxine concentrations on the normal to low side with corresponding free thyroxine concentrations that are significantly lowered (such as those observed in population females). Probable causes for this relate to the fact that an endocrine feedback mechanism alleviates low free hormone levels by either increasing the output of hormone, or by releasing bound hormone from binding proteins causing an increase in the free thyroxine pool. It is well known that the free hormone is considered to be the entity capable of entering a cell to effect its actions, while the remaining amount of hormone acts as a reserve (Chopra 1986 and Ingbar 1981).

The levels of thyroxine determined for P. leucopus population animals may be directly responsible for low body weight. The positive correlations between both free and total serum concentrations of the hormone versus body weight that were observed in females, support this idea. Thyroxine

is not only necessary for proper growth hormone (GH) secretion by the pituitary, but it also has a synergistic role that, along with GH, promotes normal growth and development. Kikayuma et al. (1974) have shown that thyroidectomy in rats negatively affects GH concentrations of the anterior pituitary and serum. Human studies in both children (Katz et al. 1969) and adults (Wilkinson et al. 1972) have indicated that with hypothyroidism there is impaired GH release as tested with arginine infusion or induction of hypogylcemia.

Still, it is quite possible that other factors--either alone or in conjunction with a decreased thyroid activity--contribute to the lower body weights of population animals. GH release is inhibited by adrenocortical stimulation and also by glucocorticoids acting alone (Christian 1978). In addition, Cronin and Bradley (1988) have recently shown that a reduced food intake by population animals (P. maniculatus) may be partly responsible for a diminished body weight. Therefore, density-related stress among population white-footed mice could be inhibitory to growth through the interactions of the pituitary, thyroid, adrenals, and social behaviors that reduce food intake.

Hypothyroidism that is induced or occurs soon after birth is associated with a marked delay in sexual maturation and development in rabbits and mice (Maqsood 1950, 1951). A

significant reduction in the weights of the testes in male animals of these species is associated with arrested spermatogenesis and degenerative and atrophic changes in the seminiferous tubules (Maqsood et al. 1950). If hypothyroidism persists untreated in humans, there is an arrest of sexual maturity with absent libido and ejaculate (Longcope 1986). Maqsood (1951) also suggested that the arrested growth of accessory male sex organs indicated a decrease in the production of testosterone.

Likewise, following thyroidectomy of the day-old female rat, there was delayed vaginal opening, the ovaries were smaller and contained only a few small follicles compared with controls, and the uterus and vagina were not developed (Leathem 1972). When female mice were rendered hypothyroid, their ovaries showed degenerative changes and the estrous cycle was altered (Morris et al. 1945). There has been shown a suppression in the number of ova in thyroidectomized rats (Hagino 1971), and reductions in body weight and number of young brought to term have been studied (Hendrich et al. 1976).

Exactly how hypothyroidism negatively affects reproductive maturation is not completely understood. There is the possibility that the direct effects of thyroid hormones on protein synthesis could be altered to produce reductions in body and gonadal weights. Work suggests that

a major role of thyroid hormones in mammals is an interaction with the cell nucleus during development. It is believed that such an interaction brings about the induction of specific messenger-RNA synthesis, which in turn codes for specific enzymes directing the normal orderly sequence of development (Oppenheimer et al. 1972, and Samuels and Tsai 1973). The low titers of thyroid hormone observed in this species may act in this way to limit proper development of reproductive tissues. Indeed, the positive correlations observed in this study between both free and total thyroxine concentrations and lowered reproductive organ weights are suggestive that this may be the case.

Alternatively, it has long been established that the thyroid is indirectly involved in maintaining normal reproductive function, and that thyroid dysfuction may adversely affect reproduction. Thyroid hormones are permissive to the actions of the gonadotropins, and in hypothyroidism, a reduction in normal circulating levels of thyroid hormones is associated with a reduction in the secretion and plasma levels of pituitary gonadotropins (Ingbar 1986). It is in this way that reduced thyroid hormones play an indirect role in altering the maturation, differentiation and development of reproductive tissues.

In this study of seventy day-old animals, significant positive correlations were observed between free serum

thyroxine concentrations in males and females of both population and control animals taken singly and together, versus weights of reproductive organs. This may demonstrate the role (direct or permissive) that thyroid hormones play in regard to reproductive development.

Color changes in the feathers of birds, as well as in the skin of mammals, have been associated with thyroid function (Gorbman and Bern 1962). According to molting patterns characteristic of P. leucopus (Gottshang 1956), animals from reproductively inhibited laboratory populations show a pre- or peri-pubertal pelage coloration. This fact suggests one additional physiologic parameter associated with reproductive inhibition. Whether the thyroid hormones have any role in this phenomenon, either directly through changes in differentiation and development of the hair follicle, or indirectly through synergy with the sex steroids, cannot be determined from the available data. However, the distinct difference in pelage color may serve as an indicator of reproductive status in future studies on P. leucopus.

Based on many reports that thyroid deficiency is disruptive of reproductive function and development, it can be suggested that lowered serum thyroxine concentrations (both total and free) in reproductively inhibited population P. leucopus may be a factor contributing to their

reproductive inhibition. In addition, the extent of reproductive inhibtion seen in P. leucopus in this study is comparable to that seen previously in similarly selected and aged (90 versus 70 days-old) P. maniculatus (Peebles et al. 1984, and Pitman and Bradley 1984).

The depression of thyroid activity manifest in reproductively inhibited deermice and white-footed mice from laboratory populations could suggest the possibility of a thyroid based mechanism of population control. Indeed, data from other reports indicate that other physiological parameters such as a 60% reduction in food intake in reproductively inhibited populations (Cronin and Bradley 1988), could be explained by a reduction in thyroid function. Also, Bradley (1988) has reported the patterns of circadiel body temperature variation in P. maniculatus. He found that the internal temperatures of deermice housed either singly or in groups of two, five, and ten are not statistically different from each other over a twenty-four hour period. The observation that huddled deermice can control their internal body temperature despite the differences in heat production and the insulative effects of variable numbers of cage-mates, suggests a sensitive body temperature regulation mechanism in this species (Bradley 1988). Because thyroid hormones have been shown to control thermogenesis in such divergent species as mice and humans

(Edelman, 1974), it is tempting to speculate that in relatively dense huddles thyroid hormone is reduced to compensate for increased exogenous heat and insulation. If this is true, it may account for the reduction of thyroid hormone levels in population animals in this study. On the basis of the data presented here, it is possible that a thyroid based mechanism of population control exists in P. leucopus. However, further studies will potentiate the contribution of thyroid activity to the endocrine regulation of reproductive inhibition in laboratory populations of the white-footed mouse.

APPENDIX A

A comparison of pelt scores based on two independent methods between population and control males and females. Values are reported as the mean pelt score for each group by each evaluator ± SEM. No significant differences between the values for each method were observed.

Evaluator	Group	Score by Method 1	Score by Method 2
1	Control	3.7 ± 0.08	3.4 ± 0.03
	Population	1.5 ± 0.04	1.8 ± 0.06
2	Control	3.4 ± 0.06	3.1 ± 0.09
	Population	1.0 ± 0.00	1.2 ± 0.01
3	Control	2.9 ± 0.08	3.0 ± 0.09
	Population	1.0 ± 0.00	1.0 ± 0.00
4	Control	2.8 ± 0.06	3.1 ± 0.09
	Population	1.2 ± 0.02	1.1 ± 0.01
5	Control	3.0 ± 0.07	3.2 ± 0.08
	Population	1.2 ± 0.02	1.2 ± 0.02
6	Control	3.3 ± 0.09	3.0 ± 0.07
	Population	1.0 ± 0.00	1.2 ± 0.02
7	Control	2.9 ± 0.09	3.4 ± 0.07
	Population	1.1 ± 0.01	1.5 ± 0.04
8	Control	3.4 ± 0.06	3.3 ± 0.07
	Population	1.2 ± 0.02	1.2 ± 0.02
9	Control	3.0 ± 0.05	2.9 ± 0.08
	Population	1.1 ± 0.01	1.2 ± 0.02
10	Control	3.3 ± 0.06	3.0 ± 0.09
	Population	1.2 ± 0.03	1.2 ± 0.01
MEAN	Control	3.2 ± 0.06	3.2 ± 0.04
	Population	1.2 ± 0.02***	1.1 ± 0.02***

*** $P<0.001$

APPENDIX B

A printout of the format of the BIMED, BMDP1R Multiple Regression Analysis Program.

```
//#REGR JOB (0000,WBIG,1,4),SNR,NOTIFY=WBIGSNR
/*ROUTE    PRINT U4
//     EXEC BIMED,PROG=BMDP1R
//FT08F001 DD DSN=WBIGSNR.REG.DATA,DISP=SHR
PROBLEM TITLE='DOSE RESPONSE EXAMPLE'./
INPUT UNIT = 8.
      VARIABLE = 3.
      FORMAT = '(F1.0,1X,F5.4,1X,F7.5)'./
VARIABLE BLANKS = MISSING.
         NAMES = GROUP,DOSE,RESPONSE.
         GROUPING = GROUP./
TRANSF DOSE = LOG(DOSE)./
GROUP CODE(1) = 1,2,3. NAME(1) = CURVE1,CURVE2,CURVE3./
PLOT RESIDUALS./
REGRESSION TITLE = 'DOSE RESPONSE'.
           DEPEND = 3.
           INDEPEND = 2./
END/
FINISH/
/*
//
```

APPENDIX C

A list of all comparisons determined by Pearson product moment correlation statistics.

MALES	POP	CONTROL	COMBINED
T vs. F	n.s.	n.s.	n.s.
vs. BW	n.s.	n.s.	n.s.
vs. PT	n.s.	n.s.	n.s.
vs. SV	n.s.	n.s.	n.s.
F vs. BW	n.s.	n.s.	n.s.
vs. PT	r=0.70136**	r=0.3464*	r=0.54812***
vs. SV	r=0.59507**	r=0.3173*	r=0.46571**
BW vs. PT	n.s.	r=0.40113**	r=0.59130***
vs. SV	n.s.	n.s.	r=0.48031**
PT vs. SV	r=0.57624**	r=0.53070**	r=0.84795***
FEMALES	POP	CONTROL	COMBINED
$\overline{T}$ vs. F	r=0.6148**	n.s.	r=0.6158**
vs. BW	n.s.	n.s.	r=0.3876*
vs. O	n.s.	n.s.	n.s.
vs. U	n.s	n.s.	n.s.
F vs. BW	r=0.5599**	n.s.	n.s.
vs. O	r=0.6987**	r=0.4157**	r=0.5549**
vs. U	r=0.7549***	r=0.5511**	r=0.7154**
BW vs. O	n.s.	n.s.	r=0.3397*
vs. U	n.s.	n.s	r=0.3187*
O vs. U	n.s.	n.s.	n.s.

$\overline{T}$ = Total serum thyroxine concentration(ug/dl)
F = Free serum thyroxine concentration(ng/dl)
BW = Body weight(g)
PT = Paired testes weight(mg)
SV = Paired seminal vesicles weight(mg)
O = Paired ovaries weight(mg)
U = Uterus weight(mg)

* $\underline{P}$=0.1
** $\underline{P}$<0.05
*** $\underline{P}$<0.001

LITERATURE CITED

Albertson, B.D., Bradley, E.L. and Terman, C.R. (1975). Plasma progesterone concentrations in prairie deermice (Peromyscus maniculatus bairdi) from experimental laboratory populations. J. Reprod. Fertil. 42:407-414.

Andrews, R.V., Keil, L.C., and Keil, N.N. (1968). Future observations on the adrenal secretory rhythm of the brown lemming. Acta Endocrinol. 59:36.

Andrews, R.V., Belknap, J., Southard, J., Lorincz, M. and Hess, S. (1972). Physiological, demographic and pathological changes in wild Norway rat populations over an annual cycle. Comp. Biochem. Physiol. 41A:149.

Bradley, E.L. (1988). Core-body temperature in prairie deermice at various times of day and at four cage densities. Eastern Regional Conference on Comparative Endocrinology. (abstract).

Bradley, E.L. and Terman, C.R. (1981a). A comparison of the adrenal histology, reproductive condition, and serum corticosterone concentrations of prairie deermice (Peromyscus maniculatus bairdi) in captivity. J. Mammal. 62:353-361.

Bradley, E.L. and Terman, C.R. (1981b). Serum testosterone concentrations in male prairie deermice (Peromyscus maniculatus bairdi) from laboratory populations. J. Mammal. 62:811-814.

Bradley, E.L. and Terman, C.R. (1981c). Studies on the nature of reproductive inhibition in animals from laboratory populations of prairie deermice (Peromyscus maniculatus bairdi): serum LH and FSH concentrations. Comp. Biochem. and Physiol. 68A:563-570.

Chopra, I.J. (1986). Nature, sources, and relative biological significance of thyroid circulating hormones. In: The Thyroid. 5th edition. (Ingbar, S.H. and Braverman, L.E., eds.). J.B. Lippincott Company, Philadelphia, PA. pp.136-153.

Christian, J.J. (1950). The adreno-pituitary system and population cycles in animals. J. Mammal. 31:247-259.

Christian, J.J. (1956). Adrenal and reproductive responses to population size in mice from freely growing populations. Ecology 37:258-273.

Christian, J.J. (1964). Effect of chronic ACTH treatment on maturation of intact female mice. Endocrinology 74:669-679.

Christian, J.J. (1975). Hormonal control of population growth. In: Hormonal Correlates of Behavior, vol I

(B.E. Eleftheriou and R.L. Sprott, eds.). Plenum Publ., New York, pp. 205-274.

Christian, J.J. (1978). Neurobehavioral endocrine regulation of small mammal populations. In: Population of Small Mammals Under Natural Conditions (D.P. Snyder, ed.). Pymatuning Laboratory of Ecology Special Publication No. 5, pp. 143-158.

Christian, J.J. (1980). Endocrine factors in population regulation. In: Biosocial Mechanisms of Population Regulation (M.N. Cohen, R.S. Malpass and H. G. Klein, eds.). Yale University Press, New Haven, pp. 55-115.

Coppes, J.C. and Bradley, E.L. (1984). Serum ACTH and adrenal histology in reproductively inhibited male prairie deermice (Peromyscus maniculatus bairdi). Comp. Biochem. Physiol. 78A:197-206.

Cronin, K.L. and Bradley, E.L. (1988). The relationship between food intake, body fat and reproductive inhibition in prairie deermice (Peromyscus maniculatus bairdi). Comp. Biochem. Physiol. 89A:669-673.

Dawson, W.D. (1967). Comparative thyroid activity in two species of Peromyscus. Gen. Comp. Endocrinol. 8:267-272.

Dice, L.R. (1937). Fertility relationships in the Peromyscus leucopus group of mice. Contrib. Lab Vertebrate

Genetics. University of Michigan, Ann Arbor, MI. No. 4, pp. 1-3.

DiStefano, J.J., III and Stear, E.B. (1968). On identification of hypothalamo-hypophysial control and feedback relationships with the thyroid gland. J. Theoret. Biol. 19:29-50.

Dixit, V.P., Arya, M. and Lohiya, N.K. (1976). The effect of hypothyroidism on the female genital tract of gerbils (Meriones hurrianae Jerdon). Acta Biol. Med. Germ. 35:205-217.

Edelman, I.S. (1974). Thyroid thermogenesis. New Engl. J. Med. 290:1303-1308.

Fukuda, H., Greer, M.A., Roberts, L., Allen, C.F., Critchlow, V. and Wilson, M. (1975). Nyctohemeral and sex-related variations in plasma thyrotropin, thyroxine, and triiodothyronine. Endocrinology 97:1424-1431.

Gorbman, A. and Bern, H.A. (1962). Thyroid gland. In: A textbook of comparative endocrinology. John Wiley and Sons, Inc., New York. pp155-159.

Gottschang, J.L. (1956). Juvenile molt in Peromyscus leucopus noveboracensis. J. Mammal. 37:516-520.

Hagino, N. (1971). Influence of hypothyroid state on ovulation in rats. Endocrinology 88:1332-1336.

Hendrich, C.E., Porterfield, S.P., Henderson, J. and Galton, V.A. (1976). A comparison of the effects of altered thyroid and parathyroid function on reproduction in the rat. Horm. Metab. Res. 8:220-226.

Humason, G.L. (1972). PAS and Feulgen techniques, and related reactions. In: Animal Tissue Techniques. W.H. Freeman and Co. San Francisco, CA. pp. 325-335.

Ingbar, S.H. and Woeber, K.A. (1981). The thyroid gland. In: Texbook of Endocrinology, 7th edition (R.H. Williams, ed.). W.B. Saunders, Philadelphia, pp. 117-247.

Johansson, H., and Jonsson, L.E. (1971). Relationship between thyroid and adrenal glands in hypothyroidism. Acta Chir. Scand. 137:59-66.

Kalland, G.A., Vera, A., Peterson, M. and Swerdloff, R. (1978). Reproductive hormonal axis of the male rat in experimental hypothyroidism. Endocrinology 102:476-484.

Kaptein, E.M., MacIntyre, S.S., Weiner, J.M., et al. (1981). Free thyroxine estimates in nonthyroidal illnesses: comparisons of eight methods. J. Clin. Endocrinol. Metab. 53:1073-1080.

Katz, H.P., Yaltun, R., Kaplan, S.L. and Grumbach, M.M. (1969). Growth and growth hormone III growth hormone release in children with hypothyroidism and

thyrotoxicosis. J. Clin. Endocrinol. Metab. 29:346-351.

Kieffer, J.D., Mover, H., Federico, P. and Maloof, F. (1976). Pituitary-thyroid axis in neonatal and adult rats: comparison of the sexes. Endocrinology 98:295-304.

Kikuyama, S., Nagasawa, H., Yanai, R and Yamanouchi, K. (1974). Effect of perinatal hypothyroidism on pituitary secretion of growth hormone and prolactin in rats. J. Endocrinol. 62:213-223.

King, J.A., Price, E.O. and Weber, P.L. (1968). Behavioral comparisons within the genus Peromyscus. Papers of the Michigan Academy of Science, Arts and Letter. 53:113-136.

Kirkland, L.E. and Bradley, E.L. (1986). Reproductive inhibition and serum prolactin concentrations in laboratory populations of the prairie deermouse. Biol. of Reprod. 35:579-586.

Koh, H.S. and Peterson, R. L. (1983). Systematic studies of deermice, Peromyscus maniculatus Wagner (Cricetidae, Rodentia): analysis of age and secondary sexual variation in morphometric charaters. Can. J. Zool. 61:2618-2628.

Kuhl, W.J., Jr. and Ziff, M. (1952). Alteration of thyroid function by ACTH and cortisone. J. Clin. Endocrinol. Metab. 12:554-559.

Krebs, C.J., Gaines, M.S., Keller, B.L., Myers, J.H., Tamarin, R.H. (1973). Population cylces in small rodents. Science 179:34-41.

Larsen, P.R. (1986). Thyroid hormone concentrations. In: The Thyroid. 5th edition. (Ingbar, S.H. and Braverman, L.E., eds.). J.B. Lippincott Company, Philadelphia, PA. pp. 479-501.

Leathem, J.H. (1972). Role of the thyroid. In: Reproductive biology (Balin, H. and Glasser, S. eds.). Amsterdam, Exerpta Medica. p. 23.

Louch, C.D. (1958). Adrenocortical activity in two meadow vole populations. J. Mammal. 39:109.

Maqsood, M. (1950). Role of the thyroid in sexual development in the male. Nature 166:692.

Maqsood, M. (1951). Influence of thyroid status on spermatogenesis. Science 114:693-694.

Maqsood M. and Reineke, E.P. (1950). Influence of environmental temperatures and thyroid status on sexual development in the male mouse. Am. J. Physiol. 162:24-30.

Martineau, Sheila. (1988). Investigations into the measurement of serum thyrotrpin in Peromyscus

maniculatus bairdi using radioimmunoassay. Unpublished Honors Thesis, College of William and Mary, Williamsburg, Va.

Morley, J.E. (1981). Neuroendocrine control of thyrotropin secretion. Endocrine Rev. 2:396-340.

Morris, H.P., Dubnik, C. and Dalton, A.J. (1947). Action of thiouracil on C3H mice. Proc. 4th Int Concer Res. Congr. p. 152.

Oppenheimer. J.H., Koener, D. and Schwartz, H.L. (1972). Specific nuclear triiodothyronine binding sites in rat liver and kidney. J. Clin. Endocrinol. Metab. 35:330.

Pamenter, R.W. and Hedge, G.A. (1980). Inhibition of thyrotropin secretion by physiological levels of corticosterone. Endocrinology 106:162-166.

Peebles, E.D., Painter, J.A. and Bradley, E.L. (1984). A possible role for the thyroid in reproductive inhibition in laboratory populations of the prairie deermouse (Peromyscus maniculatus bairdi). Comp. Biochem. Physiol. 77A:293-298.

Peterson, R.E. (1958). The influence of the thyroid on adrenal cortical function. J. Clin. Invest. 37:736-743.

Pitman, J.M. III, and Bradley, E.L. (1984). Hypothyroidism in reproductively inhibited prairie deermice

(Peromyscus maniculatus bairdi) from laboratory populations. Bio. of Reprod. 31:895-904.

Samel, M. (1968). Thyroid function during postnatal development in the rat. Gen. Comp. Endocrinol. 10:229-234.

Samuels, H.H. and Tsai, J.S. (1973). Thyroid hormone action in cell culture: demonstration of nuclear receptors in intact cells and isolated nuclei. Proc. Natl. Acad. Sci. USA 70:3488.

Sung, Kuo-Li P., Bradley, E.L. and Terman, C.R. (1977). Serum corticosterone concentrations in reproductively mature and inhibited deermice (Peromyscus maniculatus bairdi). J. Reprod Fertil. 49:201-206.

Terman, C.R. (1965). A study of population growth and control exhibited in the laboratory by prairie deermice. Ecology. 46:860-895.

Terman, C.R. (1966). Population fluctuations of Peromyscus maniculatus and other small mammals as revealed by the North American Census of Small Mammals. Am. Midland Naturalist. 76:419-426.

Terman, C.R. (1968). Population dynamics of Peromyscus. In: The Biology of Peromyscus (Rodentia). (J.A. King, ed.). Special Publ. No. 2, The American Society of Mammal. pp. 412-451.

Terman, C.R. (1969). Weights of selected organs of deermice (Peromyscus maniculatus bairdii) from asymptotic laboratory populations. J. Mammal. 50:311-320.

Terman, C.R. (1973a). Reproductive inhibition in asymptotic populations of prairie deermice. J. Reprod. Fertil. Suppl. 19:457-463.

Terman, C.R. (1973b). Recovery of reproductive function by prairie deermice (Peromyscus maniculatus bairdi) from asymptotic populations. Anim. Behav. 21:443-448.

Terman, C.R.(1980). Social factors influencing delayed reproductive maturation in prairie deermice (Peromyscus maniculatus bairdi) in laboratory populations. J. Mammal. 61:(2):219-223.

Terman, C.R. (1987). Intrinsic behavioral and physiological differences among laboratory populations of prairie deermice. Amer. Zool. 27:853-866.

Vigouroux, E. (1976). Dynamic study of post-natal thyroid function in the rat. Acta Endocrinol. 83:752-762.

Wilkinson, R., Anderson, M. and Smart, G.A. (1972). Growth hormone deficiency in iatrogenic hypothyroidism. Br. Med. J. 2:87-88.

Wolfe, C.C. (1981). Population growth, social behavior and selected organ weights in laboratory populations of Peromyscus leucopus noveboracensis. Master's thesis, College of William and Mary, Williamsburg, VA.

Wong, C.C., Dohler, K.D. and von zur Muhlen, A. (1980) Effects of tri-iodothyronine, thyroxine and isopropyl-di-iodothyronine on thryoid-stimulating-hormone in serum and pituitary gland and on pituitary concentrations of prolactin, growth hormone, lutenizing hormone, and follicle-stimulating-hormone in hypothyroid rats. J. Endocrinol. 87:255-263.

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