AT(11-1)-COO-1758-26

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From: The Department of Dairy Husbandry, College of Agriculture
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Subject: Technical Progress Report for 1970

Contract No. AT(11-1)-1758-Anderson

Project Title: "Factors Affecting Thyroid Hormone Secretion Rates
and Utilization Rates in Mammals Using Iodine-131
as a Tracer."

Technical Progress Report. During the year a total of
7 articles, including papers presented at scientific meetings,
have been published or submitted for publication. These
include the following:

1. Bauman, T. R. and R. R. Anderson. 1970. Thyroid Activity of
the Ground Squirrel (Citellus tridecemlineatus) Using a Cannula
Technique. Gen. and Comp. Endocrinol. (accepted) (AEC-AT(11-1)
COO-1758-19).

SUMMARY

Chronically implanted aortic and jugular cannulae were used
to study thyroid status in the ground squirrel by a body pool-
turnover technique. Thyroid secretion rates (TSR) increased after
cold exposure, and then began to decline with time in the cold
until hibernation. PBI values were unchanged from controls through
cold exposure and into hibernation. Binding of L-T₃-125I by serum
thyroxine binding proteins increased after cold exposure and was
2X the control values during hibernation. It is believed that
alterations in thyroxine metabolism begin before hibernation is
entered, hence reduction of body temperature is not the only
factor involved in reduced thyroid activity.

2. Anderson, R. R. and C. W. Turner. 1970. Thyroid Hormone
Secretion Rates in Rats Following Changes in Dietary Bulk and Energy
Intake. Submitted to Proc. Soc. Exptl. Biol. Med. (AEC-AT(11-1)
COO-1758-20).

SUMMARY

Thyroid hormone secretion rates (TSR) were determined by the
substitution method in mature female rats of the Sprague-Dawley

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Rolfsmeyer strain after two weeks on (a) control diet (22.4% protein), (b) 50% control-50% cellulose flour diet ad libitum and (c) idem restricted to 15 g per day. The TSR of 24 rats was 1.30 ug L-thyroxine (L-T₄)/100 g bw/day during the period the rats were receiving the control diet. It rose to 1.44 ug L-T₄ after 2 weeks on diet (b) a nonsignificant increase of 11%, and decreased significantly ($P < .01$) to 0.62 ug L-T₄ on diet (c). Food consumption was 15.0 g/day on (a), 25.8 g/day on (b) and 13.3 g/day on (c). Fecal bulk produced per day averaged over a 3-week period was 6.9 g on diet (a), 20.8 g on diet (b), and 11.3 g on diet (c) ($P < .05$). The daily urine volume changed from 10.6 ml on diet (a) to 4.1 ml on diet (b) to 7.0 ml on diet (c) ($P < .05$). Energy intake appears to be more important in TSR control than is dietary bulk.

3. Singh, D. V. and C. W. Turner. 1970. Effect of Melatonin on Thyroid Hormone Secretion Rate (TSR) in Female Hamsters. Submitted to Experientia. (AEC-AT(11-1)COO-1758-21).

SUMMARY

The TSR of 43 hamsters was determined as 0.75 ug L-thyroxine (T₄)/100 g bw at 25 days of age. The animals were divided into 3 groups and at 55 days of age given normal saline (I), 50 ug melatonin/100 g bw (II), or 100 ug melatonin/100 g bw (III) for 7 days prior to the start of and during the TSR determination. TSR in groups II and III was reduced 20% below group I. Daily food consumption of groups II was 8% below control group I and group III was 16% below group I.

4. Singh, D. V. and C. W. Turner. 1970. Melatonin on Endocrine DNA Changes in Female Rats at Increasing Ages. Submitted in Proc. Soc. Exptl. Biol. Med. (AEC-AT(11-1)COO-1758-22).

SUMMARY

Eighty female rats were divided into four equal groups at 25 days of age. One half of each group, serving as controls, received saline. The other half received 100 ug melatonin/100 g bw/day at 25, 35, 45, or 55 days of age for 10 days. They were killed 24 hours after the last injection. In general, pituitary, ovary, and uterine weights decreased; thyroid weights increased at increasing age by melatonin treatments. Ovarian total DNA and DNA/100 g bw increased significantly at 35 days of age, but the total DNA and DNA/100 g bw were significantly decreased at 45 and 55 days of age and nonsignificantly decreased at 65 days of age in melatonin-treated groups as compared to their corresponding controls. There was no significant decrease in adrenal DNA/100 g bw at any age. Uterine DNA/100 g bw increased significantly at 55 and 65 days of age after melatonin treatment.

5. Anderson, R. R. and T. R. Bauman. 1970. Thyroid hormone secretion and utilization rates in the guinea pig. Submitted to Endocrinology (AEC-AT(11-1)COO-1758-23).

SUMMARY

Thyroid hormone secretion rates (TSR) of L-thyroxine (L-T₄) and L-triiodothyronine (L-T₃) were determined by the substitution method in albino guinea pigs of both sexes and of various ages. The mean TSR of L-T₄ for 30 animals was 0.57 ± 0.02 ug L-T₄/100 g bw/day. No significant difference between the sexes was found; the TSR of 13 females was 0.55 ± 0.04 and the TSR of 17 males averaged 0.58 ± 0.02 . The mean TSR of L-T₃ in 36 guinea pigs was 0.18 ± 0.01 ug L-T₃/100 g bw/day with no significant difference between the sexes. Thus, L-T₃ was found to be 3.2 times as potent as L-T₄ based on the substitution method for TSR determination. TSR's of L-T₄ and L-T₃ were also determined by the thyroid hormone pool-turnover method. In 11 animals the TSR of L-T₄ was found to be 0.59 ± 0.07 . The TSR of L-T₃ as measured in 36 guinea pigs averaged 0.143 ± 0.03 . The disappearance rate of L-T₄-¹³¹I from the blood in terms of the half-life of L-T₃-¹³¹I was 14.5 ± 0.6 hours.

6. Anderson, R. R., J. Clark and T. R. Bauman. 1970. Potassium (⁴⁰K) Measurements of Dairy Cattle. Published as abstract in J. Animal Sci. 31:158. (AEC-AT(11-1)COO-1758-24).

SUMMARY

Measurement of whole body potassium by the K⁴⁰ counting technique was carried out in a number of dairy animals of the Jersey breed to develop average values for growth curves. These values will then be used as a base for endocrine experiments relating to K changes in the body. Two Jersey bulls were counted once a month from 2 weeks of age to 29 months, when they were slaughtered and the carcasses counted. Total K in the whole body ranged from 75 g at 2 weeks of age to 1168 g at 29 months. The concentration of K ranged from 1.5 g to 2.0 g/kg body weight in the whole body. Parts of the body had the following K concentrations: gut, 0.96 g/kg; pluck, 2.15; head and hide, 1.09; rumen contents, 1.25; and remainder (muscle and skeleton), 2.36. Recovery of K in the parts was 1163 g in relation to 1168 g K in the whole animal count of one bull, while the parts totaled 1025 g K and the whole animal count was 1069 g K in the second bull. The difference was due to the loss of blood at the time of slaughter. Total K in females ranged from 28 g at 1 day of age to 975 g in a 4 year old cow. The concentration of K varied from 1.3 to 2.4 g/kg. Mean K concentration in 132 observations from 15 females was 1.66 while in 103 observations from 8 males it was 1.76.

7. Friedlander, R. C. and R. R. Anderson. 1970. The Clearance of ¹³¹I into Milk of Dairy Cows. Published as abstract in J. Dairy Sci. 53:663. (AEC-AT(11-1)COO-1758-25).

SUMMARY

Lactating Jersey and Guernsey cows were injected subcutaneously with 150 uCi of ¹³¹I, or L-thyroxine (T₄)-¹³¹I, or L-triiodothyronine (T₃)-¹³¹I. Milk samples were taken eight hours after injection for 12 consecutive milkings. Thyroid counts were also taken. The

^{131}I disappeared exponentially from the milk in the six day period. Three to 8% of the injected ^{131}I was recovered in milk. The rate of passage of ^{131}I was directly proportional to the milk yield. A delay was observed in the L- T_4 - ^{131}I (60 hr) and L- T_3 - ^{131}I (40 hr) experiments in the passage of ^{131}I into the milk. The % dose of ^{131}I uptake by the thyroid was 1.6--4.7% and 2.2--5.3%, respectively, with T_4 - ^{131}I and T_3 - ^{131}I , while the % uptake by the thyroid of ^{131}I alone was 12%. It seemed that the ^{131}I was separated from the T_4 and T_3 molecules and only the ^{131}I was trapped by the mammary gland.

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Summary of Papers in Preparation and Research Underway

Thyroid Hormone Secretion Rates (TSR) in the Gerbil (*Meriones unguiculatus*).

Using the substitution method, the TSR in normal mature gerbils is 0.5 to 0.6 ug L-thyroxine/100 g bw/day. This is similar to the TSR of guinea pigs, rabbits, hamsters and ground squirrels. The second method being used to measure TSR is the thyroxine pool-turnover method. Since this method requires considerable blood for PBI determination and ^{131}I measurements, a procedure for blood sampling is being developed. The heart puncturing technique has resulted in high mortality. A second method entails the removal of small quantities of blood from the ophthalmic venus plexus by capillary tubes and is being accomplished with some success.

Release rates of ^{131}I from the thyroid of ground squirrels (*Citellus tridecemlineatus*).

Ground squirrels were given 10 uCi ^{131}I and thyroid counts were taken. Release rates were very slow. The goitrogen tapazole was given at varying levels to increase the release rate of ^{131}I from the thyroid by preventing recycling of ^{131}I . The release rates were not increased after the goitrogen. During a 19-day counting period in mid-December a release of only 2% of thyroid uptake was observed. In February the release rate over 19 days was less than 10% of initial uptake. The data suggested that the ground squirrels, although awake, were able to slow their thyroid function in anticipation of hibernation, which would have occurred had the animals been in their natural environs.

Utilization rates of L-thyroxine- ^{131}I by various tissues in gerbils (*Meriones unguiculatus*).

Thyroid hormone, L-T₄- ^{131}I , is injected into groups of gerbils and at periods of one-half, 1, 2, 4, 6 and 8 days following injection, the animals are counted for ^{131}I in the whole body counter. They are then sacrificed and divided into twelve different tissues and organs. These parts are counted and the counts are expressed as percent of dose injected. The elimination rate of L-T₄- ^{131}I from the whole body and parts is then calculated. Results to date indicate that the half-life of L-T₄ in the gerbil is approximately 24 hours, slightly longer than for the rat. A disappearance of ^{131}I at an exponential rate of the first order is seen between days 1 and 6. Between days 6 and 8 there is a delay in the elimination of ^{131}I from the whole body and each individual organ or tissue. The delay is most pronounced in the skin and hair. This phenomenon is also prominent in the rat and suggests that the gerbil, like the rat, can store iodine in the integument and hair as a reserve supply to compensate for shortages in the diet.

Relation of hypothyroidism and hyperthyroidism to reproductive performance in the rat.

A previous study (Lu, Mayan and Anderson, AT(11-1)COO-1758-12) indicated that total thyroidectomy resulted in termination of reproductive performance due to irregular estrous cycling. The

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administration of L-T₄ to 12 ug/100 g bw/day had no deleterious effects on pregnancy and lactation. However, levels of L-T₄ at 24, 48, and 96 ug/100 g bw/day resulted in no effect on pregnancy but a diminution of lactation and loss of pups. The design of this experiment is being repeated using L-triiodothyronine from 1 ug to 32 ug/100 g bw/day.

Thyroid hormone secretion rates in cattle.

TSR in dairy cattle as determined by the substitution method had been accomplished in several growing animals. It has been noted that the TSR is 0.5 to 0.6 ug L-T₄/100 lbs bw/day in calves from 1 week to 1 month of age. The TSR then drops gradually to 12 months of age when it is essentially the same as the adult, that is, 0.1 to 0.3 ug L-T₄/100 lb bw/day. These data are being expanded with more animals to make the study more meaningful.

Thyroid hormone utilization rates in cattle.

The TSR in cattle may be determined by the thyroxine pool-turnover method which measures the utilization rate of the hormone. Studies are being continued to compare the TSR of the substitution method with that of the pool-turnover method. Since only a small number of dairy cattle is available for this study, data in significant numbers are accumulated very slowly.

Clearance of ¹³¹I from milk after intravenous injection of L-T₄ and L-T₃-¹³¹I.

A study was reported on the appearance of ¹³¹I in milk after injection of L-T₄ or L-T₃-¹³¹I via the subcutaneous route. The experiment is now being repeated using the same materials by intravenous injection and following the course of ¹³¹I elimination into milk.

Relation of whole body ⁴⁰K and ⁴⁰K in various parts at slaughter to TSR in Jersey cattle.

A limited number of dairy cattle of the Jersey breed are available for study of TSR and counting ⁴⁰K in the whole body of the animal. The TSR is made at least twice per year and the animals are counted once each month. Five male and five female animals are presently on experiment.

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Percentage of time or effort devoted to the project.

The principal investigator has devoted approximately 33% of his time or effort on the project concerned with "Factors affecting thyroid hormone secretion rates and utilization rates in mammals using iodine-131 as a tracer." He has actively directed the research efforts of 2 doctoral candidates who have completed the Ph. D. and are currently active in thyroid research at other institutions. He is presently directing the research programs of 2 M.S. degree candidates and 3 Ph.D. candidates who are directly involved in the research efforts which are being undertaken in conjunction with fulfillment of the proposals outlined in the Atomic Energy Commission, Contract AT(11-1)-1758-Anderson.

Acknowledgement.

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Bibliography of papers published or submitted for publication

- Anderson, R. R. and T. R. Bauman. 1970. Thyroid hormone secretion and utilization rates in the guinea pig. *Endocrinology*. (submitted) (AEC-AT(11-1)COO-1758-23).
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- Bauman, T. R. and R. R. Anderson. 1970. Thyroid activity of the ground squirrel (*Citellus tridecemlineatus*) using a cannula technique. *Gen. and Comp. Endocrinol.* (accepted) (AEC-AT(11-1)COO-1758-19).
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- Technical Progress Report. 1970. Factors affecting thyroid hormone secretion rates and utilization rates in mammals using iodine-131 as a tracer. Submitted to Chicago Operations Office, Division of Biology and Medicine, United States Atomic Energy Commission. (AEC-AT(11-1)COO-1758-26).