THE RELATIONSHIP OF THYROID ACTIVITY TO LACTATION, GROWTH, AND SEX IN SHEEP

BY

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INTRODUCTION

Reported research indicates that the thyroid gland is associated with almost every organ and tissue in the body. Therefore, a change in its functional level, such as hypo- or hyper-thyroidism, reflects demonstrable changes in many functional processes of an individual. One of the most notable effects of its varying activity is the accompanying change in the basal metabolic rate. However, other processes in the body, viz. growth, lactation, sexual activity etc., are found to be related with it, directly or indirectly, to a varying extent.

Growth is one of the most important characteristics of a living organism. It is either the basis of or closely associated with many productive processes in livestock. Meat, milk and wool production are dependent upon or closely related to growth. The relationship of thyroid activity and growth rate has received very little attention and therefore it was made a part of this study.

In all farm animals where the newly born animal is not artificially reared, the young depends upon the milk of its dam for adequate nourishment during the early growth period. Though the hereditary growth potentialities of the individual are predetermined at conception, the expression of it is subject to the influence exerted by environmental factors. The most important of these factors during the early stages after birth is the dam's milk. Therefore, the quantity of milk produced by the ewe is of fundamental economic importance for the success of fat-lamb production. In this study an attempt has been made to correlate thyroid activity with the milk production of the ewe as measured by lamb gains up to 3 weeks of age.

The classical methods of thyroid research, designed to produce a deficiency state by removal of the thyroid or by thiouracil administration, and to produce a hyper-functioning state by administration of glandular extract or synthetic products have not shed any light on the normal function of the thyroid in relation to the existing variation in the various economic characters of farm animals. Moreover, the results of the studies with added thyroactive substances and its effect on growth and other characters have been found to be contradictory. Some of the conflicting reports may be partly due to the large amount of variation in the hyperthyroidism induced. It seems, therefore, of utmost importance to obtain the actual thyroid hormone secretion rate of animals under normal conditions. It is obvious that the most desirable and practical technique for determining thyroid secretion rate will be the one that can be used on live animals.

There is some indication that thyroid activity is related to the problem of summer sterility in rams and also may have an effect on the seasonal breeding habit of the ewe. Before additional studies can be conducted on the addition of thyroactive substances, a basic knowledge of thyroxine secretion rate in the different sexes would be helpful. If we learn the differences occuring under normal conditions in the hormone secretion rate, we may be able to breed more consistently the type of animal capable of high producing ability. This study has been designed to obtain such basic information on the thyroid hormone secretion rate in relation to certain characters in sheep.

OBJECTIVES

1. To refine an extrapolation technique for determining the thyroid secretion rates in life sheep which would be practical for other livestock.
2. To determine the relationship between the thyroid activity of lactating ewes and growth of their suckling lambs during the early stages of life.
3. To determine the relationship of thyroid secretion rate to growth and sex in sheep.

REVIEW OF LITERATURE

Studies of the thyroid gland have shown that it exercises a profound influence on the growth and development of all the higher vertebrates.

Curling (1850) observed an absence or atrophy of the thyroid in two typical cases of cretinism in the human. Pfaundler (1924) also observed marked dwarfism in the human resulting from a non-functional thyroid gland.

Schiff (1856) studied the effect of thyroidectomy in dogs and observed a stasis of growth in all cases. Similar results of thyroidectomy in dogs were reported by Dott (1923), and Binswanger (1936).

The effects of thyroidectomy in laboratory animals are analogous to those observed in the human. Kojimi (1917) thyroidectomised growing rats and observed retarded growth, reduced calcium and nitrogen retention, and decreased feed intake. Salmon (1938) observed the characteristics of cretinism in rats due to the effect of thyro-parathyroidectomy in new-born individuals. Hughes (1944) studied the effect of thiouracil administration to rats from the time of birth and reported that it resulted in a marked retardation of growth, arrested development and other changes similar to cretinism. Similar effects of thyroidectomy have been observed for many other laboratory animals, such as, the mouse (Davenport and Swingle, 1927), guinea pig (Silberberg and Silberberg, 1940; Williams et. al. 1941), rabbit (Basinger 1916, Kunde 1926), and monkey Fleischmann, Schumaker and Straus 1943).

Numerous investigations have also demonstrated that thyroidectomy has greatly depressed growth in farm animals. Simpson (1924) reported the effect of thyroidectomy on triplet female goats. Two of them were thyroidectomised at the age of 22 days while the third was kept as a control. About three months following the operation, he observed marked cretinism of the two kids compared to the normal growth of the control. Moreover, he (1913 and 1924) observed similar results after thyroid ablation in sheep, and found that the age at thyroidectomy had a marked influence on its effect on the individual. He reported that the lambs thyroidectomised at one to two months of age exhibited marked stunted growth, whereas practically no ill effect on growth was found in those thyroidectomised at 6 to 8 months of age. Subsequently, Mangold (1932), Marston and Peirce (1932), Todd and Wharton (1934), and Todd, Wharton and Todd (1938) experimenting with sheep; and Reineke and Turner (1941), Reineke, Bergman and Turner (1941) using goats; confirmed the reported cretin condition as observed by Simpson (1913 and 1924).

Only a few experimental reports are available regarding the effects of thyroidectomy on the growth of cattle. Brody and Frankenbach (1942) reported that thyroidectomy of a Jersey heifer at 54 days of age reduced the mature body weight by over 50 percent. The characteristic symptoms of hypothyroidism began to appear about a month after the thyroidectomy.

The observations of Spielman et al (1954) were similar to those of Brody and Frankenbach (1942). They stated that thyroidectomy of the immature bovine was followed by a serious impairment of the normal growth processes. There was complete stasis of gain in height and severe retardation of gain in body weight.

Marked differential response in the pattern of growth depression due to thyroidectomy has been observed by various workers. Todd and Wharton (1934) studied the disturbed growth patterns of the skull in thyroidectomised lambs and reported a delayed eruption of the teeth, defective growth of the frontal bones, nasal bones and of the upper jaw. Demonstrable defects in the growth of the brain case proper and mandibles were not observed. Deficient growth of the epiphysis, defective development of age characters in the epiphysis and shaft, and diminished velocity of the growth of shaft were also observed in the early thyroidectomised sheep by Todd, Wharton and Todd (1938). Marston and Peirce (1932) reported their findings on the growth of wool in Merino sheep following thyroidectomy. They observed a considerable decrease in the wool production and the degree of greasiness of the fleece. No appreciable difference was found in the fibre diameter.

The reports reviewed indicate the analogous effects of thyroidectomy in all mammals and in general the results are more severe if the function is impaired in early life.

Pathological conditions resulting from thyroid removal in human patients led workers to attempt replacement therapy. The first reported attempt was made by Schiff (1884) in the dog. He stated that part of the effects of thyroidectomy could be relieved by transplanting the thyroid from another dog. Murray (1891) reported that myxedema in humans was relieved by the injection of sheep thyroid extract. Resumption of growth of young, thyroidectomised animals has been observed by the replacement therapy with thyroxin or thyroprotein by Brody and Frankenbach (1942), Reineke and Turner (1941), and Spielman et al (1945).

An increase in the thyroid functional level in the initially normal animal, as a result of thyroid administration, may result in either acceleration (Cameron and Carmichael, 1920) or retardation of growth (Hammett, 1924). Variability of the effect was mainly due to the size of the dose administered and its relation to the physiologically optimal thyroid functional level. If the amount administered did not increase total metabolism to the extent where catabolism predominated or was not above the optimum level, growth in weight was hastened. If the amount administered was large enough, that is above the optimum level, growth was retarded.

Some evidence indicates that mild hyperthyroidism may be conducive to rapid growth. Irwin, Reineke and Turner (1943) fed several levels of thyroprotein to White Plymouth Rock and Rhode Island Red chicks for 3 months and reported that 36 grams per cwt. of feed was the best dose for feathering and growth.

Wheeler, Hoffman and Graham (1948) reported a significant increase in body weight of male Rhode Island Red chicks at 12 weeks of age that were fed 10 grams of thyroprotein per hundred pounds of feed but observed no significant difference in weight of the females. There was a marked stimulation of early feather growth in the treated birds.

Quisenberry and Krueger (1948) studied the effect of feeding protamone (iodinated casein) up to 6 weeks of age on 800 chicks of New Hampshire and White Plymouth Rock breeds, and reported that the rate of gain and feed utilisation were improved.

Distortion of body proportions produced by increased thyroid activity has been observed by various workers. Cameron (1922) reported that thyroid feeding in rats and rabbits resulted in hypertrophy of the internal organs which tended to recover following the discontinuance. Silberberg and Silberberg (1938) found that the feeding of thyroid substance stimulated the growth of the epiphyseal cartilage and accelerated its further development into hypertrophic cartilage in immature guinea pigs. In fowl also, definite structural alterations have been reported from feeding thyroid materials (Nevalonnyi 1927, Horning and Torrey 1927).

The interrelationship between the thyroid and the gonads has been indicated by much research, but its nature is not very clearly understood.

The early studies of Marine and Kendall (1917), Levin (1921), and others showed that the incidence of thyroid disturbance was greater in girls and women than in boys and men.

Evans and Long (1921a, 1921b) observed no effect of thyroidectomy in rats on the onset of puberty or the length of the estrous cycle. Moreover, no marked effect on the estrous cycle was found as a result of feeding fresh thyroid gland. Lee (1925) reported that thyroidectomy in rats did not affect materially the age of puberty but lengthened the estrous cycle. Hammett (1929) also observed no relationship between thyroid activity and the development of the reproductive system. He suggested that the reported disturbed sex conditions were secondary to the disturbance in general growth.

The work of Brody et al (1942) suggested that the reported absence of a relationship may be due to the differences in age at thyroidectomy. Brody and Frankenbach (1942) studied the effect of thyroidectomy on a Jersey heifer and reported that at the age of 40 months, the heifer was completely undeveloped sexually. Moreover, the administration of thyrolactin (iodinised milk protein) after 40 months of age stimulated the sexual development.

Da Costa and Carlson (1933) reported that the administration of large doses of desiccated thyroid to white rats resulted in the retardation of the sexual maturation of both sexes, while small doses of thyroid tended to accelerate it. Schockart (1931) observed a greater hypertrophy of the male accessory sex glands after thyroidectomy than before when anterior pituitary emulsions were fed.

Marine (1937) observed the enlargement of the thyroid gland during puberty and pregnancy. However, he (1935) suggested that such an effect on the thyroid was perhaps caused by thyrotropic hormone stimulation.

The effect of estrogenic hormone on thyroid activity in animals has been studied by many workers. Laqueur, Hart and de Jongh (1926) reported that the injection of estrogenic hormone increased the basal metabolism of both normal and ovariectomised rats from 15 to 20 percent two or three days after administration. Tagliaferro (1933) observed hyperactivity of the thyroid after 5 to 10 days of estrin administration. He further reported that continued administration of estrin for 20 days or more resulted in the opposite effect. Kunde et al (1930) found marked hyperplasia of the thyroid in the dog as a result of estrogen administration. Aron and Benoit (1932) reported that hyperthyroidism produced by thyrotropic hormone injection was prevented by the administration of large doses of estrin. Their observation was later confirmed by Spence (1936), and Elmer, Giedosz and Scheps (1938). Farbman (1944) reported that the administration of large doses of estrogenic hormone seemed to have some inhibitory effect on the thyroid of humans. Epstein (1950) studied the effect of exogenous estrogen administration on the thyroid of immature chicks. He stated that the administration of estrogen caused no effect on the size of the thyroid gland but depressed the iodine turnover rate in normal animals.

Thyroid has been reported to influence the fertility of farm animals and fowls. During summer months, rams of some breeds have been observed to produce low quality semen as indicated by decreased sperm concentration and volume of semen, with an increased number of abnormal spermatozoa (McKenzie and Berliner 1937 , Bogart and Mayer 1946, and Gunn et al 1942). Berliner and Warbritton (1937) reported that thyroidectomised rams produced semen of low quality and administration of thyroxine to such animals resulted in increased spermatogenesis. Moreover, rams with low fertility also showed marked improvement in semen quality when treated with thyroxine. They, therefore, suggested that the summer sterility might be indirect and due to a thyroid deficiency. Bogart and Mayer (1946) observed similar results with thyroprotein feeding. But the results obtained by Warwick et al (1948) did not support the observations of Berliner and Warbritton (1937) and Bogart and Mayer (1946).

Schultze and Davis (1946), and Reineke (1946) treated dairy bulls with varying amounts of thyroprotein for different lengths of time and reported that improvement was observed in the quality of semen and to some extent in the conception rate.

Winchester (1939), and Taylor and Burmester (1940), working with chickens, observed a marked decline in egg production following thyroidectomy which was found to be increased after replacement therapy. Shaffner and Andrews (1948) found reduced semen quality in fowls as a result of hypothyroidism. They concluded that thiouracil impaired the ability of the gonads to produce viable sperms which were capable of surviving normal lengths of time in the oviduct of hen.

Both qualitative and quantitative methods have been used to determine the secretory activity of the thyroid gland. The qualitative methods are based upon the changes which occur in the thyroid gland in conjunction with the changes in its secretory activity. By these methods, the thyroid function is determined by: (i) observation of the changes in mitotic activity, (ii) measurement of the diameter of the thyroid follicles, (iii) measurement of the follicular epithelium, and (iv) determination of increased or decreased amounts of protein bound iodine in the thyroid and/or in the blood.

Until recently, the quantitative determination of thyroid activity was based on replacement therapy. By this method, the amount of thyroactive material required to maintain thyroidectomised animals in a normal state was determined. In 1943, Dempsey and Astwood proposed a new method, the goitrogenic method, for the determination of the thyroid secretion rate. For this, a goitrogenic drug, e.g., thiouracil, was administered simultaneously with graded doses of thyroxine for a period of time, and the amount of thyroxine required to maintain the normal weight of the thyroid was considered to be the normal secretion rate. Though this method is in general use today in the study of thyroid function of laboratory animals, its application for the determination of the normal thyroid secretion rate of large animals is not practical. Therefore, studies have been directed towards developing a technique suitable for large animal research.

The use of radioiodine (I^{131}) for thyroid studies is based on the principle that the thyroid has a great affinity for iodine, and its hormone (thyroxine) contains about 65 percent of iodine. Hertz and coworkers were the first to employ radioiodine in 1938 as an indicator of the thyroid function. Their works (1938-1941) on rabbits demonstrated the selective concentration of iodine by the thyroid, which was greatly increased by stimulation of the thyroid through thyrotropin administration.

Henneman (1953) developed an extrapolation technique for measuring the thyroid secretion rate. Sheep were used as the experimental animal and they were injected with one microcurie of I^{131} per pound of body weight. A base count was taken over the thyroid gland 7 days after injection of I^{131}. After this period, different levels of l-thyroxine were injected subcutaneously daily for 3 consecutive days, so that the thyroid might adjust its secretion to that dose. Another count was taken after this period, and expressed in terms of the percent of previous count. The estimated thyroid secretion rate was the level of l-thyroxine which gave 100 percent of previous count, and was predicted by the regression equation. When the technique was used for the determination of individual l-thyroxine secretion, consistent results were obtained, but due to the smaller number of observations on each individual sheep, statistically significant values were not consistently obtained.

To obtain a significant value of l-thyroxine secretion for an individual animal, it was realized that more observations were necessary in response to varying doses of l-thyroxine administration on the radioactivity of the thyroid. With this in view, an attempt was made to refine the technique.

EXPERIMENTAL PROCEDURE

There are mainly two ways to study the accumulation of radioiodine in the thyroid: (i) direct, and (ii) indirect. The direct method is the measure of gamma radiation by applying the Geiger-Mueller or scintillation counter externally at the thyroid. Indirect measurement is the estimation of thyroid uptake by the determination of total urinary excretion of iodine in a specified period. For this, it is assumed that the thyroid uptake is equal to the difference between the dose administered and the amount excreted (Keating et al 1949, Shipley et al 1950, and Fields and Le Roy 1952). In general, direct measurement is preferred over the indirect or excretory one.

The method used in this study for the determination of thyroid activity in sheep was the direct one. The animals were injected with I^{131} subcutaneously at the rate of 1 uc. per pound of body weight. The amount of radioactivity of I^{131} at the time of administration was computed by the formula:

$$N = N_o e^{-\lambda t}$$

where N = the activity at time, t
No = the activity when t = 0

e = base of natural logrithm

λ = decay constant of I^{131}

t = time

A Geiger-Mueller or scintillation counter, shown in figure 1, was used for measuring the radioactivity in sheep. Several counts were taken over the thyroid gland, which was presumed to be in the area of the neck where the highest count was obtained, at regular time intervals by the external application of the Geiger-Mueller or scintillation tube (figure 2). The body background was taken on the outside of the foreleg of the sheep as shown in figure 3. A shield was used on the Geiger-Mueller or scintillation tube when taking counts so that only gamma rays were measured. Moreover, the scintillation tube was wrapped with cloth to facillitate its handling. Throughout the experiment the same amount of pressure was used on holding the tube against the neck and foreleg as far as possible. The wool was clipped from the thyroid region of the neck and foreleg of all the sheep before the administration of I^{131}. A standard source of Co^{60} was counted at the time counts were taken on the sheep to check the monitor. The readings obtained on the sheep were corrected to the standard to eliminate any error due to the variable efficiency of the counter. The counts obtained on the thyroid of the sheep were further corrected for the body background and physical decay and plotted on a semi-log scale.

There are various ways to compare the individuals regarding their thyroid activity from the curves obtained. They may be compared with respect to the rapidity of uptake or the rapidity of output. In either case, they can be compared by the computed values for k. b, or biological $t_{\frac{1}{2}}$. For this

Figure 1. A Monitor with a Scintillation and Geiger-Mueller Tube.

Figure 2. External Thyroid Count.

Figure 3. External Foreleg Count.

study, the regression coefficient (b) of the thyroid counts on different time intervals for each sheep was used and obtained by the formula:

$$b_{YX} = \frac{S(X - \bar{X})(Y - \bar{Y})}{S\ (X - \bar{X})}$$

where S = sum

X = time

Y = counts per minute

A straight line was fitted to the output portion of the plotted curve of thyroid activity, by solving the regression equation: $Y = a + bX$; where $a = \bar{Y} - b\bar{X}$.

The thyroid output half-time of I^{131} for each sheep was obtained from the turnover portion of the curve.

Though the individuals are compared for their thyroid activity by the obtained values of $t_{\frac{1}{2}}$ of radioiodine, the estimate of actual amount of thyroid hormone secretion cannot be made. For a quantitative estimate of the daily secretion rate of the thyroid, the method used was the one developed by Henneman (1953) and modified in this study.

Quantitative determination of the thyroid secretion has been made in terms of either d,l-thyroxine or l-thyroxine. These two estimates are interchangeable, since Reineke and Turner (1945) have reported that l-thyroxine is twice as active physiologically as d,l-thyroxine. Harington and Salter (1930) have shown that l-thyroxine is the form of thyroxine produced by the thyroid gland. In this study, l-thyroxine was used to determine the thyroid secretion rate. It was supplied by

Glaxo Laboratories, Greenford, Middlesex, England, and was further purified by Dr. E. F. Reineke. The dry thyroxine was weighed on an analytical balance and dissolved in distilled water. This solution was first made slightly alkaline with NaOH, and then enough acid (HCl) was added to make it slightly cloudy. It was then stored in the refrigerator and used within a two week period.

RESULTS AND DISCUSSION

A. Refinement of a Technique for Measuring Thyroid Secretion Rate

To refine the technique, developed by Henneman (1953), for measuring the thyroid secretion rate of live sheep, four experiments were conducted. In three experiments rats were used because they were inexpensive and easy to handle and the results obtained may be applicable in other species. The fourth experiment was conducted on the wether lambs of the Shropshire breed.

Experiment I and II

The first and second experiments were conducted on four and six female rats respectively, maintained on an ordinary laboratory diet at a room temperature of 74° F. They were injected intraperitoneally with 40 micro curies of I^{131} and the base count was taken at 73 hours after the injection of I^{131}. Following this, l-thyroxine was injected once daily for two consecutive days and the effect of different levels of l-thyroxine administration on the radioactivity of the gland was determined by the application of a Geiger-Mueller gamma-ray tube. In calculation of the results, each day's count was first corrected to a cobalt standard. The thyroid count was further corrected by one-half the body background (Wolff 1951), and the background. The counts were also corrected for physical decay and expressed as a percent of previous count.

Data from experiments I and II are graphically presented in figures 4 and 5. An increase in the dose of l-thyroxine administration was associated with the increase in percent of previous count to a certain level, after which it leveled off. The coefficients of correlation and regression between the l-thyroxine injected and percent of previous count for the ascending portion of the curve were 0.843 and 8.435 for the first experiment, and 0.749 and 7.250 for the second one, respectively. These values are statistically significant at the 1 percent level.

The average daily secretion rate of l-thyroxine for the group was estimated from the regression equation and was found to be 2.565 ug. per 100 grams body weight for the first and 2.702 ug. for the second experiment. In the first experiment, the estimated daily l-thyroxine secretion rate per 100 gm. of body weight for each individual rat was 2.515, 2.412, 2.290, and 3.048 ug. In the second experiment, the individual secretion rates were 4.017, 2.865, 1.772, 2.561, 2.597, and 2.794 ug. The average daily secretion rate of rats in the first and second experiments was found to be 2.566 ± 0.145 ug., and 2.768 ± 0.271 ug., respectively. These average values are very close to those obtained by a regression line for the respective group previously.

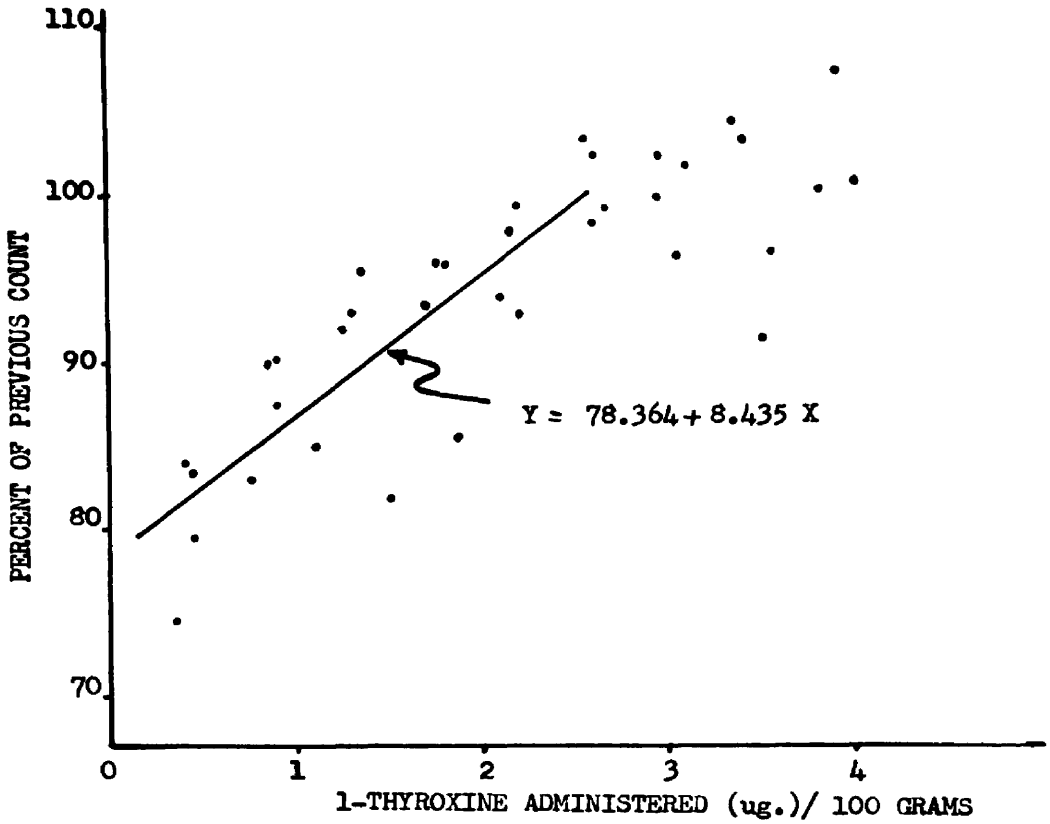

Fig. 4. Effect of 1-Thyroxine Injections on Percent of Previous External Thyroid Counts.

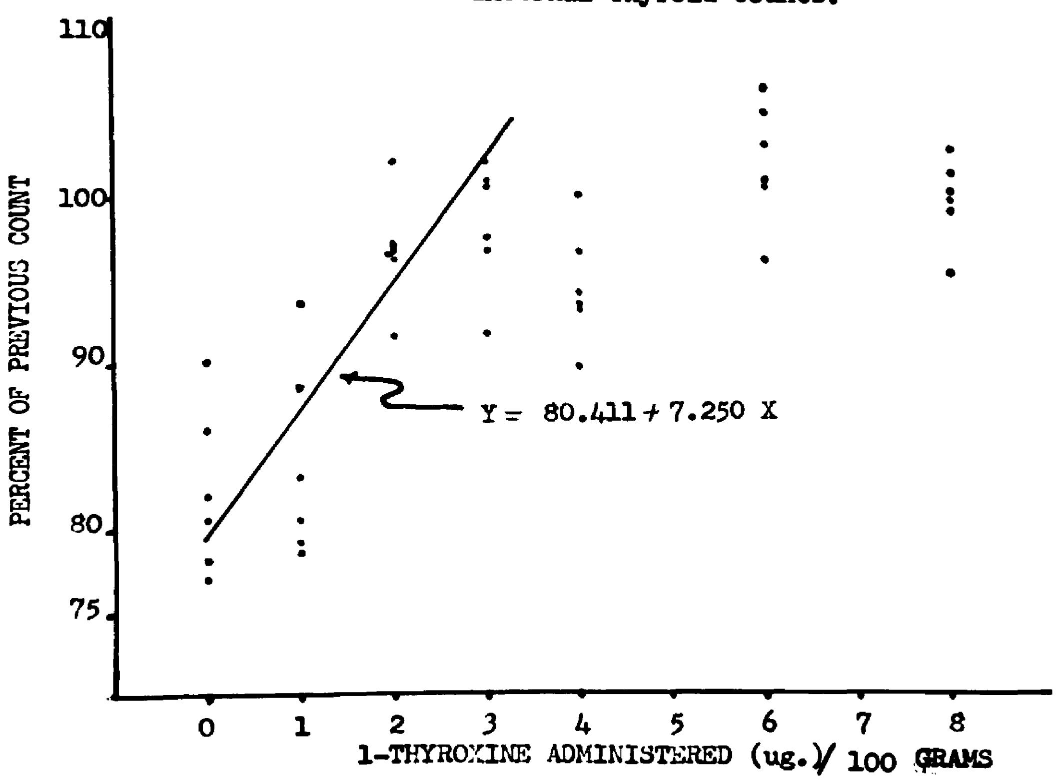

Fig. 5. Effect of 1-Thyroxine Injections on Percent of Previous External Thyroid Counts.

Experiment III

To check the secretion rate estimated by the method used in the first two experiments, a third experiment was conducted on 24 female rats. All the rats were injected with 40 uc. of I^{131} and the base count was taken 120 hours after injection. A scintillation counter was used in this experiment. The rats were divided into 5 groups of 5 each, except for the control which included 4 rats. All five groups had approximately the same average weight. Each of the four groups under treatment was injected subcutaneously with a different level of l-thyroxine once daily for 7 days. The doses used were 1.0, 1.5, 2.0, and 2.5 ug. per 100 gm. body weight. The second or final count was taken 7 days after the base count. The data were corrected for physical decay and body background as in the other two experiments.

The data are presented in figure 6. The coefficients of correlation and regression obtained between the levels of l-thyroxine administration and percent of previous count were 0.942 and 23.8, respectively. These values are statistically significant at the 1 percent level. The average daily secretion rate of l-thyroxine, as estimated by the regression equation $Y = 44.3 - 23.8X$, was 2.340 ug. per 100 gms. of body weight.

With any new method and in the absence of similar determinations for comparison, there is always the possibility of some error being introduced by misunderstood factors involved in the method. The results obtained by this method were

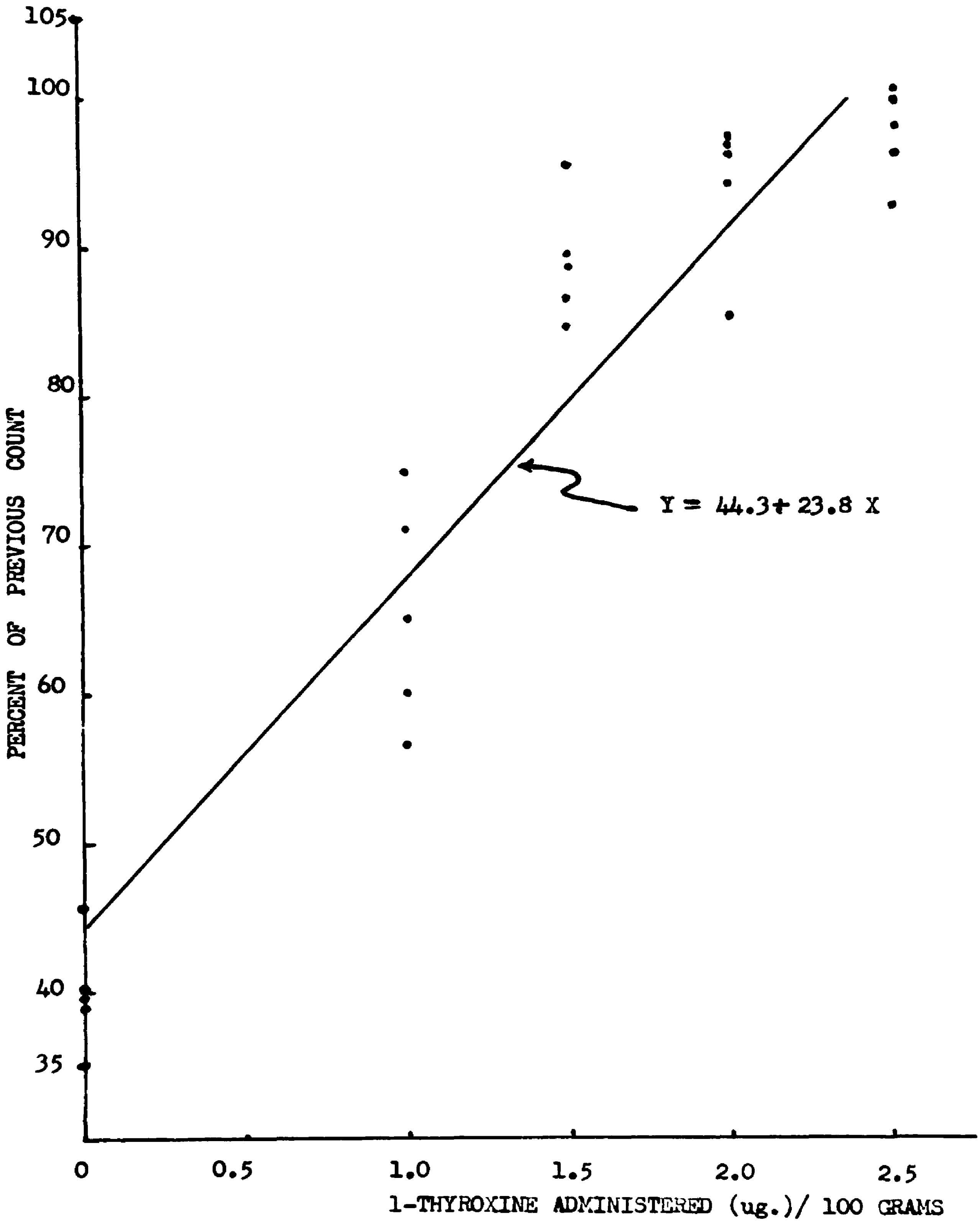

Fig. 6. Effect of 1-Thyroxine Injections on Percent of Previous External Thyroid Counts.

fairly repeatable as found in the determination of l-thyroxine secretion rates of different groups of rats, maintained under similar environmental conditions, at different periods. However, the estimated secretion rate was markedly lower than the one reported by Perry (1951) which may be attributed to the probable difference in the quality of l-thyroxine administered. The estimated l-thyroxine secretion rate in this study was close to the one determined by the goitrogen technique. Monroe and Turner (1946) reported that the thyroid secretion rate of growing female rats ranged from 2.82 to 4.63 micrograms of d,l-thyroxine per hundred grams body weight.

EXPERIMENT IV

In this experiment, 5 wether lambs of the Shropshire breed were used. They were injected subcutaneously with I^{131} at the rate of 1 uc. per pound of body weight, and the radioactivity of the thyroid was measured by a Geiger-Mueller tube between the 7th and the 22nd day after the injection. The wethers were divided into two groups with three animals in the first group (A) and two in the second group (B). On the output portion of the curve of thyroid radioactivity, the wethers in group A were injected daily for two consecutive days with a quantity of l-thyroxine, whereas those in group B were injected daily for three days. The level of l-thyroxine administration was changed after this period. In group A, the thyroid radioactivity was determined daily, while in group B, it was determined every third day prior to the administration of a different level of l-thyroxine.

The data obtained are presented in tables 1, 2, 3, and 4. As in the other experiment, it was assumed that the level of l-thyroxine administration, which held the count at one hundred percent of previous count, was the amount to replace the normal thyroid secretion. Hence, the regression equation was computed for each individual lamb and was used to estimate the rate of l-thyroxine secretion. The daily l-thyroxine secretion rates of 3 wether lambs were estimated to be 0.107, 0.095, and 0.106 mg. per 100 pounds of body weight based on the daily measurement of thyroid radioactivity. For the same lambs, they were 0.108, 0.096, and 0.106 mg. when the radioactivity was measured on alternate days. The secretion rate of the other two lambs were 0.110 and 0.118 mg. when the counts were taken every third day.

Tables 5, 6, and 7 show the correlation and regression coefficients between the level of l-thyroxine administration and the percent of previous count, when the counts were taken daily, alternate days and every third day. None of the coefficients, except 0.646 and 1.002, obtained for the counts taken daily on individual wether, is statistically significant. The obtained high but insignificant correlation values on the individual animals suggest the necessity of more observations because by using the intra-wether statistical treatment the coefficients are highly significant for the counts taken every day and also for counts taken on alternate days, and significant when taken every day.

TABLE 1

EFFECT OF 1-THYROXINE ADMINISTRATION ON THE EXTERNAL THYROID COUNTS OF SHROPSHIRE WETHER 380

Days Following I^{131} Administration	Mg. of 1-Thyroxine Administered per 100 Lbs. Body Weight	Thyroid* Counts per Minute	Percent of Previous Count	Percent of Previous Day Before Count
7 (Zero time)		968		
8		1022		
9		1196		
10		1255		
11		1133	90.3	
12	0.025	1052	92.9	83.8
13	0.025	988	92.6	
14	0.050	908	91.9	86.3
15	0.050	876	96.5	
16	0.075	731	83.4	80.5
17	0.075	707	96.5	
18	0.100	671	94.9	91.8
19	0.100	668	99.6	
20		702	105.1	104.6

*Corrected for background and physical decay

TABLE 2

EFFECT OF l-THYROXINE ADMINISTRATION ON THE EXTERNAL THYROID COUNTS OF SHROPSHIRE WETHER 302

Days Following I^{131} Administration	Mg. of l-Thyroxine Administered per 100 Lbs. Body Weight	Thyroid* Counts per Minute	Percent of Previous Count	Percent of Previous Day Before Count
7 (Zero time)		2631		
8		3343		
9		3588		
10		3816		
11		3572	93.6	
12	0.025	3394	95.0	88.9
13	0.025	3300	97.2	
14	0.050	3107	94.2	91.5
15	0.050	2932	94.4	
16	0.075	2602	88.7	83.7
17	0.075	2542	97.7	
18	0.100	2538	99.8	97.5
19	0.100	2453	96.7	
20		2584	105.3	101.8

*Corrected for background and physical decay

TABLE 3

EFFECT OF 1-THYROXINE ADMINISTRATION ON THE EXTERNAL THYROID COUNTS OF SHROPSHIRE WETHER 371

Days Following I^{131} Administration	Mg. of 1-Thyroxine Administered per 100 Lbs. Body Weight	Thyroid* Counts per Minute	Percent of Previous Count	Percent of Previous Day Before Count
7 (Zero time)		2240		
8		2293		
9		2362		
10		2503		
11		2310	92.3	
12	0.025	2247	97.2	89.8
13	0.025	2105	93.7	
14	0.050	1993	94.7	88.7
15	0.050	1902	95.4	
16	0.075	1771	93.1	88.9
17	0.075	1706	97.4	
18	0.100	1755	102.9	100.2
19	0.100	1672	95.3	
20		1774	106.1	101.1

*Corrected for background and physical decay

TABLE 4

EFFECT OF 1-THYROXINE ADMINISTRATION ON THE EXTERNAL THYROID COUNTS OF SHROPSHIRE WETHERS

Days Following I^{131} Adminis-tration	Mg. of 1-Thyroxine Administered per 100 Lbs. Body Weight	Wether 325		Wether 0	
		Thyroid* Counts per Minute	Percent of Previous Count	Thyroid* Counts per Minute	Percent of Previous Count
7 (Zero time)		3291		2127	
10		4225		2171	
13	0.025	3790	89.7	1564	72.0
14	0.025				
15	0.025				
16	0.050	3129	82.6	1200	76.7
17	0.050				
18	0.050				
19	0.100	2662	85.1	1103	91.9
20	0.100				
21	0.100				
22		2697	101.3	1047	94.9

*Corrected for background and physical decay

TABLE 5

CORRELATION AND REGRESSION COEFFICIENTS BETWEEN 1-THYROXINE ADMINISTRATION AND PERCENT OF PREVIOUS COUNT OF THYROID RADIOACTIVITY TAKEN DAILY

Wether Number	D.F.	Sum of Squares & Products			r	b
		Sx^2	Sxy	Sy^2		
380	9	0.01250	0.01253	0.03010	0.646*	1.002*
302	9	0.01250	0.00823	0.01709	0.563	0.658
371	9	0.01250	0.00893	0.01764	0.601	0.714
Intra-wether	27	0.03750	0.02969	0.06483	0.602**	0.792**

*Significant at 5 percent level
**Significant at 1 percent level

TABLE 6

CORRELATION AND REGRESSION COEFFICIENTS BETWEEN 1-THYROXINE ADMINISTRATION AND PERCENT OF PREVIOUS COUNT OF THYROID RADIOACTIVITY TAKEN ALTERNATE DAY

Wether Number	D.F.	Sum of Squares & Products			r	b
		Sx^2	Sxy	Sy^2		
380	4	0.00625	0.01178	0.03570	0.788	1.884
302	4	0.00625	0.00795	0.02027	0.706	1.272
371	4	0.00625	0.00853	0.01603	0.852	1.364
Intra-wether	12	0.01875	0.02826	0.07200	0.769**	1.507**

**Significant at 1 percent level

TABLE 7

CORRELATION AND REGRESSION COEFFICIENTS BETWEEN 1-THYROXINE ADMINISTRATION AND PERCENT OF PREVIOUS COUNT OF THYROID RADIOACTIVITY TAKEN EVERY THIRD DAY

Wether Number	D.F.	Sum of Squares & Products			r	b
		Sx^2	Sxy	Sy^2		
325	3	0.00547	0.00757	0.02061	0.713	1.384
No tag	3	0.00547	0.01324	0.03785	0.921	2.422
Intra-wether	6	0.01094	0.02081	0.05846	0.823*	1.902*

*Significant at 5 percent level.

As there was not much difference between the uncorrected count when radioactivity was measured every day, the effect of errors in the readings could be a high percentage of the difference between the counts. There was a much greater difference between the counts taken on alternate days and therefore the percentage effect of normal errors in obtaining the thyroid counts was materially reduced. Hence, on the basis of such general observation as well as the results obtained from the statistical treatment, it was decided to administer the same level of l-thyroxine for four consecutive days and measure the thyroid radioactivity on alternate days which would provide two counts for each level of l-thyroxine administration. From the data to be presented in other sections, it is apparent that this technique gave a good estimate of the thyroid hormone secretion. However, the observation of the last experiment of the studies indicates that more than two counts may be obtained for each level of l-thyroxine administration by the use of a scintillation tube. The scintillation tube was much more sensitive than the G.M. tube to gamma radiation. Therefore thyroid counts significantly greater than the background count could be obtained for a much greater length of time after I^{131} injection when the scintillation tube was substituted for the G.M. tube.

B. The Relationship of Thyroid Output Rate to Lactation in Ewes as Measured by Growth Rate of the Lambs

Eleven Shropshire ewes were used to determine the relationship between the thyroid output rate ($t_{\frac{1}{2}}$) of I^{131} and milk production as measured by the growth rate of the nursing lambs up to three weeks of age.

The data on the external thyroid counts of the ewes are graphically shown in figures 7, 8, 9, 10, 11 and 12. The output half-time was computed for each individual ewe and they are presented in table 8 along with the lamb gains. The thyroid output rate varied between 144.7 hours to 358.3 hours. These values of output half-time are much lower than those obtained by Terry (1951) for non-lactating adult ewes which was 32 days. This difference may be due to increased thyroid activity during lactation. Rough (1951) reported that the process of lactation protected the thyroid of the mouse from radiation damage indicating a higher output of radioiodine from the thyroid. Henneman (1953) reported a significantly greater thyroid activity in lactating ewes than in non-lactating ewes. However, Monroe and Turner (1946) observed no significant difference in the thyroid activity of rats due to lactation.

The coefficient of correlation between the output $t_{\frac{1}{2}}$ of seven lactating ewes and the gain of their suckling twin lambs was -0.552. This is statistically significant at the 5 percent level, indicating a relationship between the thyroid activity of the dam and the growth and development of lambs during the first three weeks following birth.

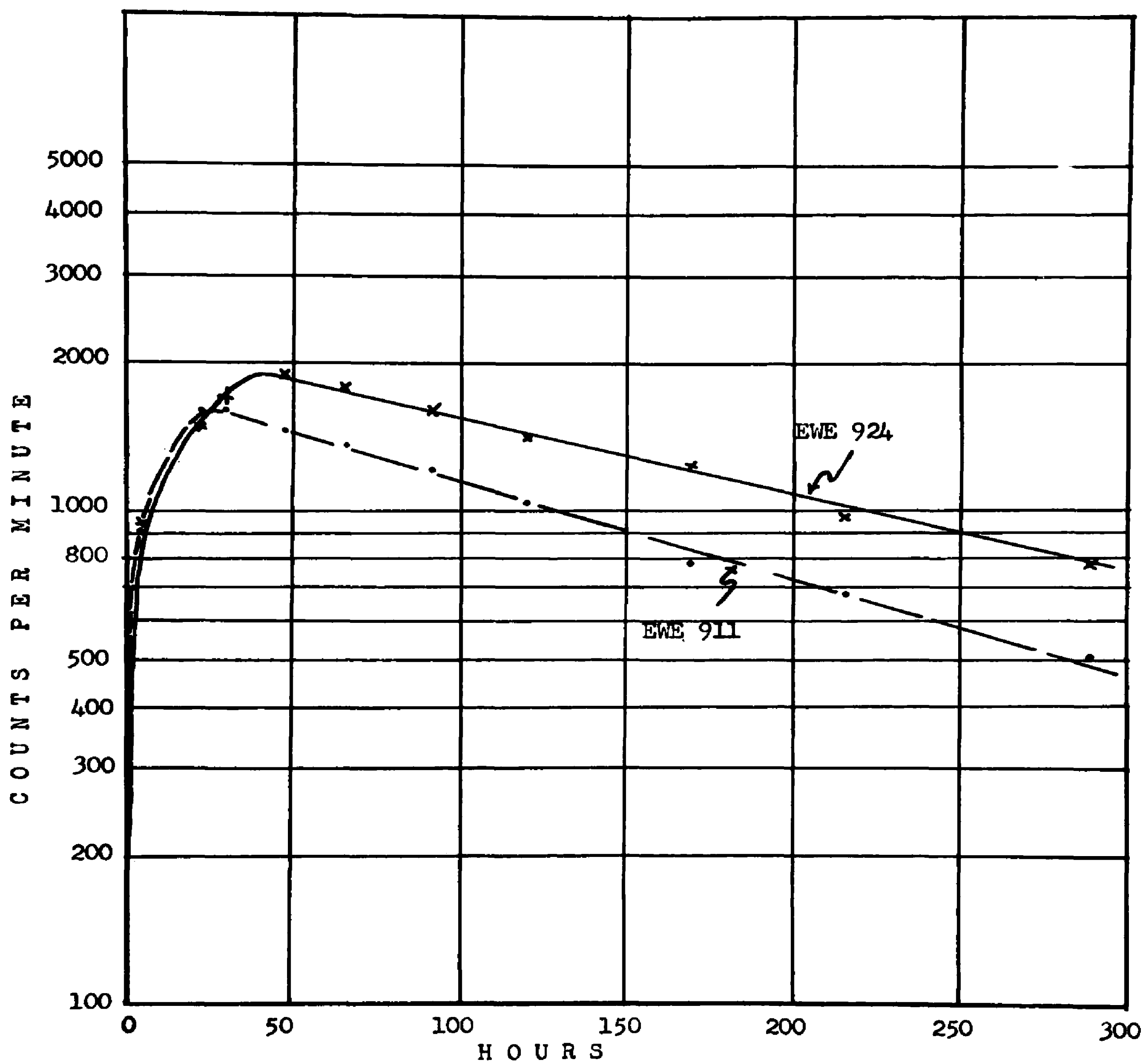

Fig. 7. External Thyroid Counts on Shropshire Ewes

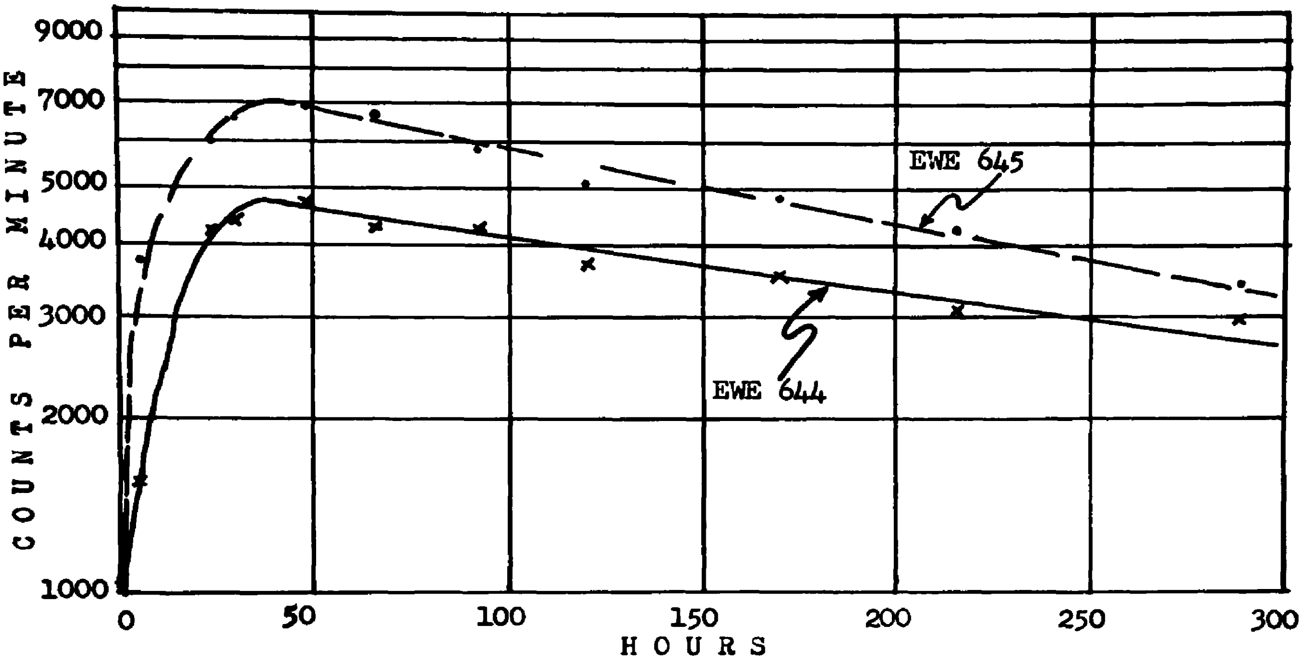

Fig. 8. External Thyroid Counts on Shropshire Ewes.

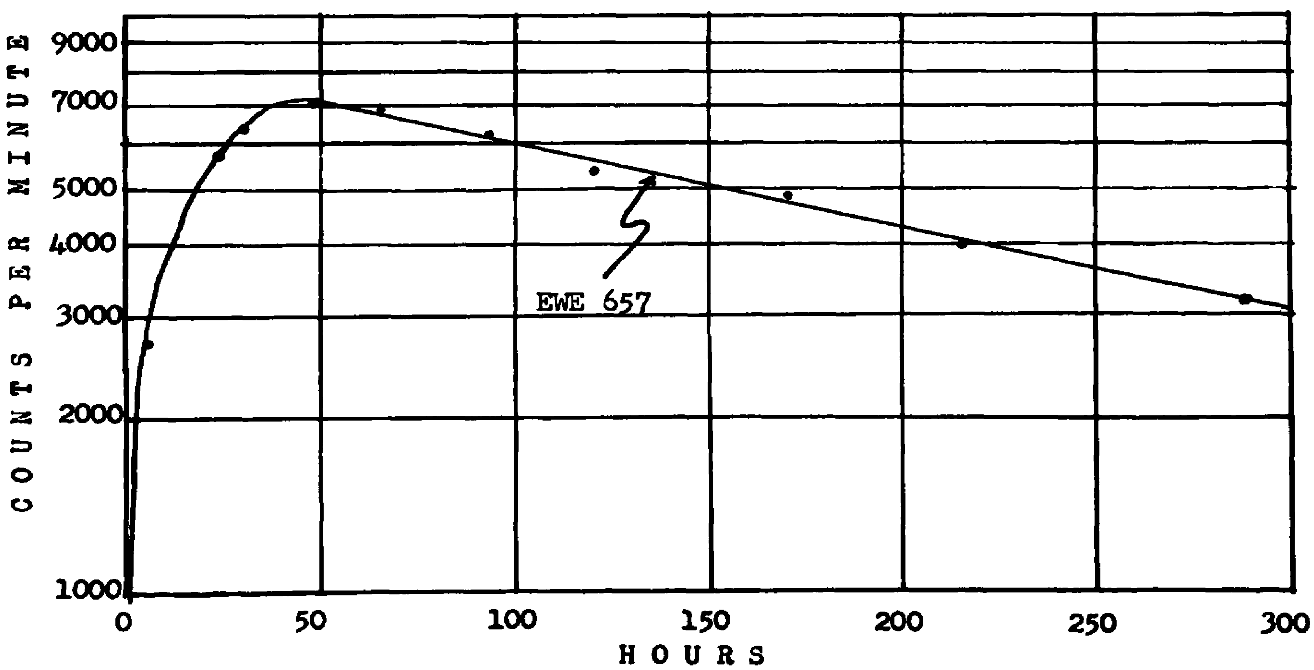

Fig. 9. External Thyroid Counts on Shropshire Ewe.

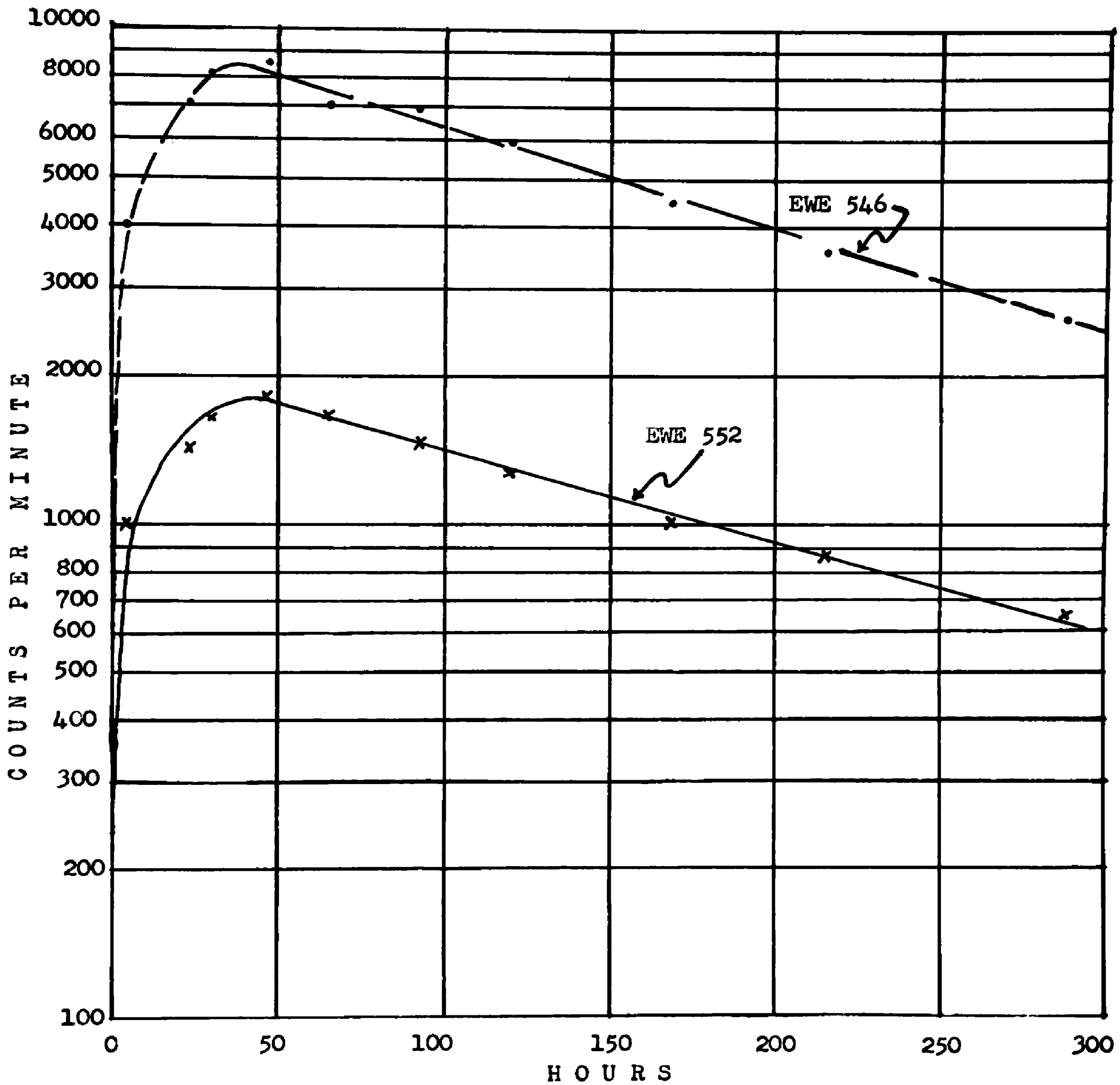

Fig. 10. External Thyroid Counts on Shropshire Ewes.

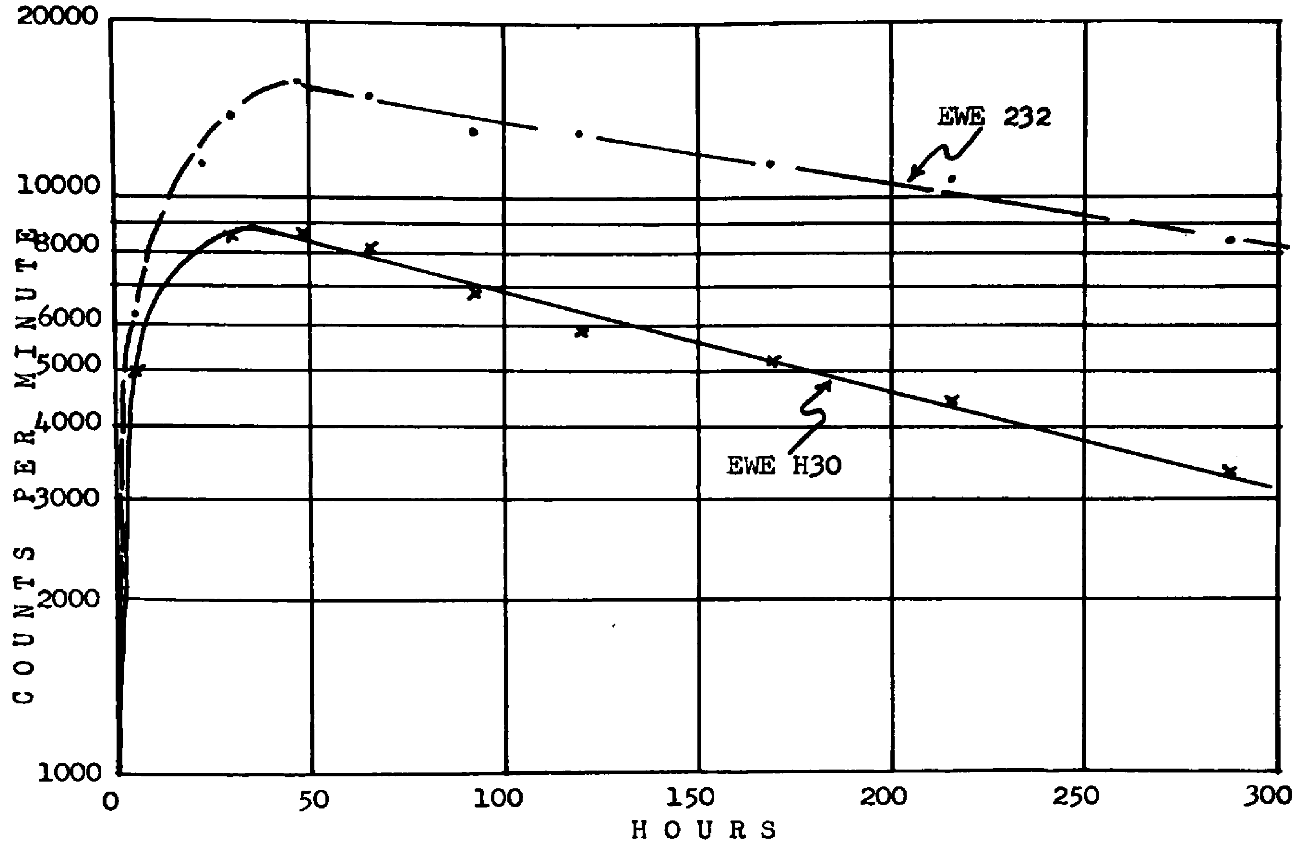

Fig. 11. External Thyroid Counts on Shropshire Ewes.

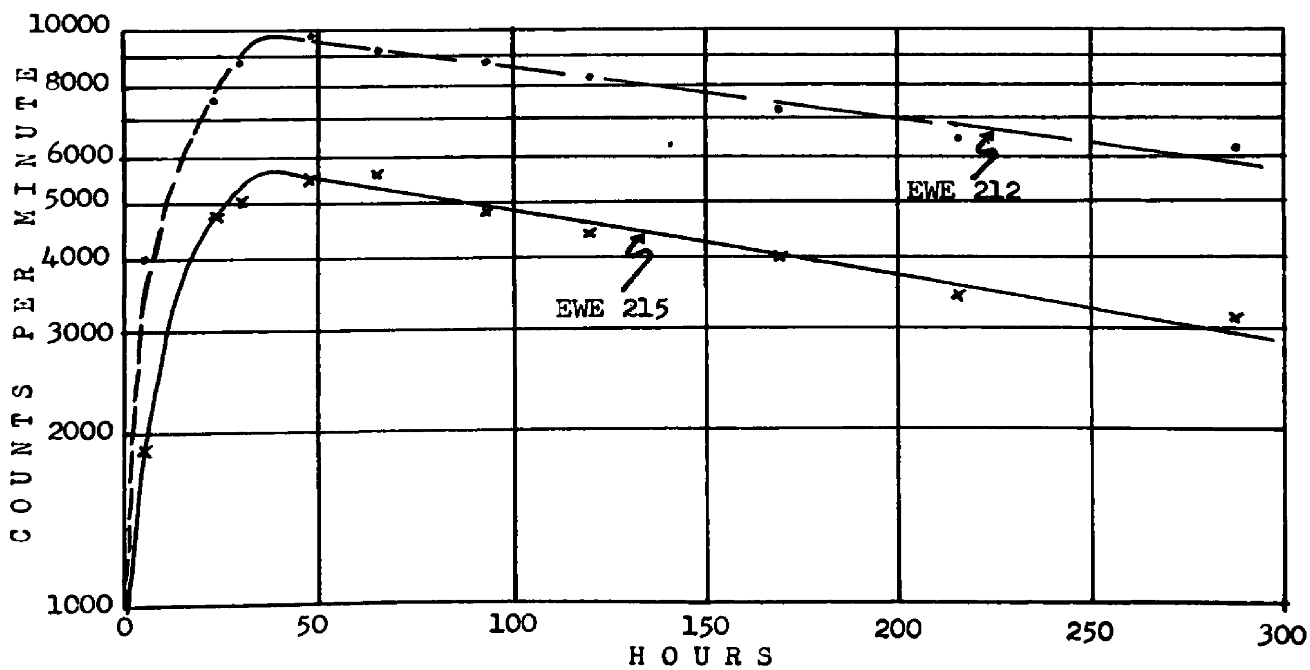

Fig. 12. External Thyroid Counts on Shropshire Ewes.

TABLE 8

THE THYROID OUTPUT RATE ($t_{\frac{1}{2}}$) of I^{131} IN LACTATING SHROPSHIRE EWES AND GAIN IN WEIGHT OF THEIR LAMBS UP TO THREE WEEKS OF AGE

Ewe No. and Year of Birth	Thyroid Output $t_{\frac{1}{2}}$ (hrs.)	Lamb Number and Sex	Birth Weight (lbs.)	21-Day Weight (lbs.)	Gain in Weight (lbs.)	Correction for Sex	Corrected Gain in Weight (lbs.)
911-50	152.0	734 E	8.0	20	12		12
		735 E	9.0	18	9		9
924-50	184.7	739 R	8.0	16.5	8.5	-2	6.5
		740 E	7.0	14.5	7.5		7.5
657-49	212.0	676 E	7.5	16.25	8.75		8.75
		677 E	8.0	16.0	8.0		8.0
644-49	358.3	678 E	8.5	16.0	7.5		7.5
		679 R	8.5	17.75	9.25	-2	7.25
645-49	235.2	743 E	7.0	14.25	7.25		7.25
		744 E	6.5	15.0	8.5		8.5
552-48	161.8	741 R	7.5	21.0	13.5	-2	11.5
		742 E	7.0	15.0	8.0		8.0
546-48	144.7	682 E	8.0	18.5	10.5		10.5
		683 E	8.0	18.0	10.0		10.0
215-47	271.3	738 E	8.5	22.25	13.75		13.75
212-47	338.2	746 E	8.0	17.5	9.5		9.5
232-47	281.3	674 R	9.0	23.5	14.5	-1	13.5
H30-47	178.1	685 E	9.5	23.25	13.75		13.75

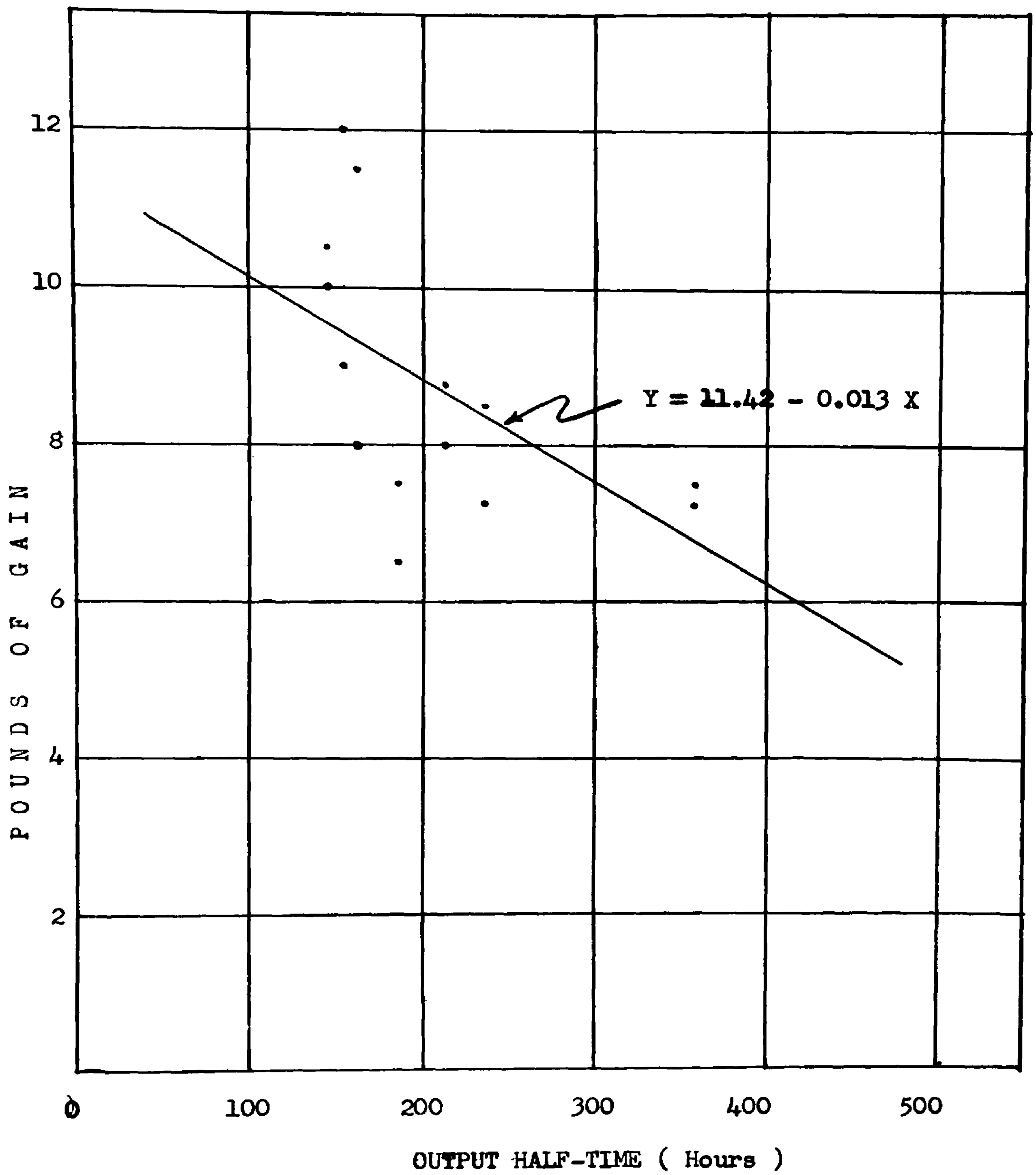

Fig. 13. Regression Line of Gain in Weight of Suckling Twin Lambs up to Three Weeks of Age on the Output $t_{\frac{1}{2}}$ of I^{131} in the Thyroid of Lactating Dams.

The regression coefficient of the gain of suckling twin lambs on the turnover $t\frac{1}{2}$ of I^{131} in the thyroid of lactating ewes was found to be -0.013. The regression line was fitted to the data and is shown in figure 13.

Schultze and Turner (1945) studied the effect of lactation on thyroid secretion in goats. They reported that 6 lactating goats, producing an average of 2.6 pounds of milk per day had a daily d,l-thyroxine secretion rate of 1425 ug., whereas the same goats in advanced lactation, producing an average of 1.8 pounds of milk per day, secreted 1000 ug.

Various workers have reported the effect of feeding thyroid materials on lactation and of lactation on the rate of early post-natal growth. The literature on the response to thyroid feeding on lactation has been reviewed by Blaxter et al (1949). Graham (1934a, 1934b), Reineke (1943), and Archibald (1945) observed an increase in milk yield of dairy cows by thyroid feeding or thyroxine injection. Bonsma (1944) reported that differences in the level of milk production of ewes has a marked influence on the early post-natal growth rate of lambs, mainly up to six weeks of age. These reports give support to the observation of this study that the lactating ewe with greater thyroid activity secretes a larger quantity of milk resulting in increased growth of suckling lambs.

The data on the thyroid activity of four lactating ewes and growth of their single lambs in the first three-week period are presented in table 8. Inspection of these data shows that there is no apparent relationship between the two variables. It may be due to the small amount of data or that the ewe with a low thyroid activity was producing enough milk for the rearing of a single lamb.

Out of eleven ewes used in this study, four were 6 years old, two were 5, three were 4, and two were 3. Table 8 shows no significant influence of the age of ewes on the thyroid activity during lactation. It may be due to the small amount of data or lactation probably has a greater effect on the function of the thyroid than age.

C. Thyroid Secretion Rate and Growth

For the study on the growth of lambs in relation to the thyroid activity, twelve Shropshire ewe lambs were used. They were fed in the barn for three weeks after weaning (approximately 120 days of age) to accustom them to barn feeding. At the end of this period, an initial weight was taken and the lambs remained on feed for one month (August 24 to September 23, 1953). The final weight was taken at the end of the month. The daily l-thyroxine secretion rate of individual lambs was estimated during this period. For this, different levels of l-thyroxine were injected, each for 4 days and counts were obtained on the alternate days. A scintillation counter was used to measure the thyroid radioactivity. A regression line was fitted to the ascending portion of the curve, and the dose of l-thyroxine holding 100 percent radio-iodine in the thyroid was predicted and considered to be the daily thyroid secretion rate of the individual. The estimated thyroid secretion rate of individual lambs and their growth during a one-month period are presented in table 9.

The degree of relationship between the two variables--thyroid secretion rate and growth of ewe lambs--was measured by the correlation and regression coefficients. A correlation of 0.792 was obtained between the daily l-thyroxine secretion rate and the growth of ewe lambs. This is statistically significant at the 1 percent level, and indicates that the lambs with a higher thyroid activity gained faster than those with a lower thyroid activity.

TABLE 9

DAILY 1-THYROXINE SECRETION RATE OF LAMBS AND THEIR GAIN IN WEIGHT DURING ONE MONTH PERIOD

Ewe Lamb No.	Daily 1-Thyroxine Secretion per 100 lbs. Body Weight (mg.)	Initial Weight (lbs.)	Final Weight (lbs.)	Total Gain (lbs.)
735	0.058	53.0	57.0	4.0
720	0.088	67.0	78.0	11.0
678	0.059	67.0	71.0	4.0
738	0.083	88.5	94.5	6.0
719	0.084	75.0	82.0	7.0
718	0.040	78.5	81.0	2.5
740	0.105	52.5	66.0	13.5
682	0.086	67.5	76.5	9.0
684	0.134	76.5	87.5	11.0
743	0.058	64.0	70.5	6.5
744	0.080	63.5	69.0	5.5
746	0.112	77.5	86.0	8.5

The regression of growth of lambs on the daily secretion rate of l-thyroxine was 97.25. The regression line was fitted to the data, by solving the equation: $Y = a + bX$, as shown in figure 14. Hence, the pounds of gain of ewe lambs (Y) for the period would be estimated by multiphying the mg. of daily l-thyroxine secretion rate of an individual (X) with the regression coefficient (b) and adding the product to 'a' which is -0.59.

The results obtained are in line with some reported research. Glazener and Shaffner (1948) observed rapid growing strains of Barred Plymouth Rock and New Hampshire Red chickens to have higher thyroid activity than slow growing strains. Conversely, the slow growing Plymouth Rocks showed a greater growth response to iodinated casein than the rapid growing strain. However, no differences were found between fast and slow feathering strains of Rhode Island Red chicks by Boone, Davidson and Reineke (1950). More recently, Kunkel et al (1953) studied the relationship of the level of serum protein-bound iodine to the rates of gain in beef calves, and reported that there was an optimum level of protein-bound iodine associated with fast gaining rate of the animals. In the light of their observations the result of this study indicates that the optimum level of thyroid secretion rate was not passed or reached in this study. Moreover, the protein-bound iodine level and the thyroid secretion as determined in the present study are not necessarily directly comparable. The P.B.I. represents the balance between the rate of hormone secretion

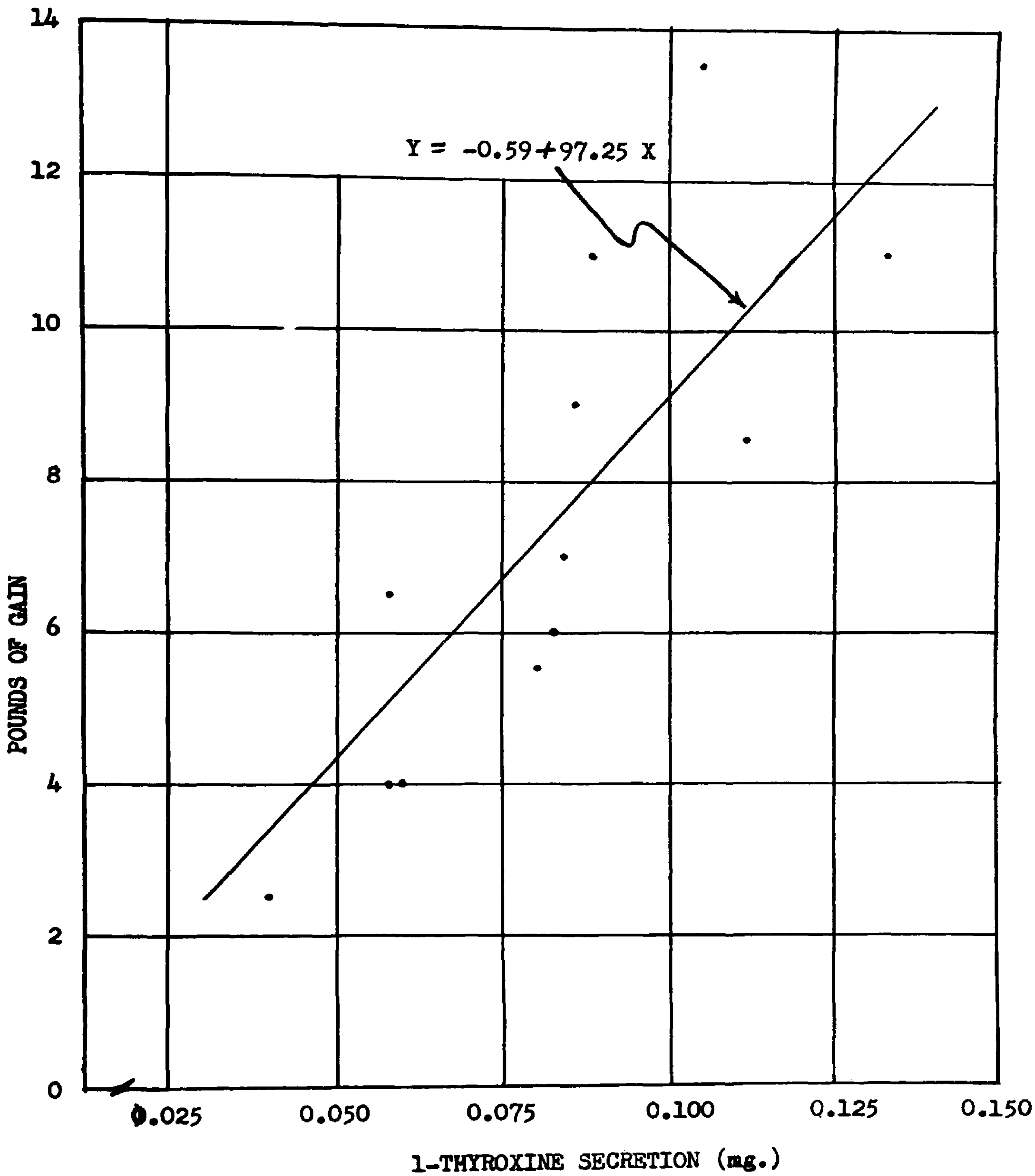

Fig. 14. Regression Line of One Month Gain in Weight on Daily 1-Thyroxine Secretion of Ewe Lambs.

by the thyroid and the rate of its metabolism and excretion. The direct estimate of thyroid secretion gives a measure of the total daily output by the thyroid.

D. Thyroid Secretion Rate and Sex

In studying differences in the thyroid secretion rate of sheep due to the effect of sex, the group of 20 Shropshire lambs, consisting of 12 ewes, 5 rams, and 4 wethers, was used. While selecting the lambs for this study, age was considered an important factor and held as nearly equal as possible. This study was conducted along with the one on the thyroid secretion rate and growth of ewe lambs under similar feeding and management.

The estimated thyroid secretion rates of lambs are presented in table 10. On the average, the daily 1-thyroxine secretion rate per 100 pounds of body weight in different sexes of lambs was found to be: ewe 0.082 mg., ram 0.066 mg., and wether 0.048 mg. To study the difference in thyroid secretion rate between sexes, the analysis of variance was used as shown in table 11. The 'F' value indicates a significant difference between at least two of the means at the five percent level. By 't' test, the difference between the mean secretion rate of ewe and wether lambs was found to be significant at the five percent level, which indicates that the ewe lambs on the average secrete more 1-thyroxine than the wether lambs. The differences between the average secretion rate of ewe and ram lambs, and ram and wether lambs were not significant.

Studies on the effect of sex on thyroid function has been made for several animal species. In the pigeon, Riddle (1929) reported that the thyroid of the female was larger than that of the male. Marza and Blinov (1936) made histological

TABLE 10

DAILY 1-THYROXINE SECRETED PER 100 POUNDS OF BODY WEIGHT BY EWE, RAM, AND WETHER LAMBS

EWE		RAM		WETHER	
No.	1-Thyroxine Secretion (mg.)	No.	1-Thyroxine Secretion (mg.)	No.	1-Thyroxine Secretion (mg.)
735	0.058	731	0.065	737	0.068
720	0.088	739	0.051	733	0.042
678	0.059	732	0.052	680	0.031
738	0.083	686	0.076	741	0.052
719	0.084	688	0.085		
718	0.040				
740	0.105				
682	0.086				
684	0.134				
743	0.058				
744	0.080				
746	0.112				
Average:	0.082		0.066		0.048

examinations of the thyroid of the two sexes in the pigeon, and stated that the female pigeon had a higher secretory activity than the male. Schultze and Turner (1945) studied the thyroid secretion rate of males and females of the White Plymouth Rock breed of chickens, and reported that the thyroid of the female was more active than that of the male. In the female, the rate ranged from 1.5 ug. to 2.01 ug. of d, l-thyroxine per 100 grams body weight while in the male, it was from 1.44 ug. to 1.98 ug. Monroe and Turner (1946) studied the daily thyroid secretion rate for growing rats and reported that it varied from 2.82 to 4.63 micrograms of d,l-thyroxine in females and 3.29 to 3.64 micrograms of d,l-thyroxine in males per hundred grams body weight.

TABLE 11

ANALYSIS OF VARIANCE

Source of Variation	D.F.	S.S.	M.S.	F.
Total	20	0.01297		
Between sex	2	0.00371	0.00186	
Error	18	0.00926	0.00051	3.647*

*Significant at the 5 percent level.

Results obtained on the effects of castration on thyroid function are somewhat controversial. Chouke, Friedman and Loeb (1930), working with guinea pigs, observed no significant difference in the mitotic activity of the thyroid as a result of castration. Zalesky (1935) also did not find any gross or microscopic effect of castration on the thyroid in the 13-

lined ground squirrel. Schultze and Turner (1945) reported that the thyroid secretion rate of the castrated male fowl was about 16 percent less than that of the normal. Sherwood, Savage and Hall (1933) stated that the metabolism rate in rats was decreased after castration.

As the activity of the thyroid gland is governed by the thyrotropic hormone secretion of the anterior pituitary, studies have been made on the effect of castration in this regard. In cattle, thyrotropic hormone content of the pituitary was found to be lowered due to castration (Bates el al 1935, Reece and Turner 1937). Turner and Cupps (1940) also observed a similar result in rats.

SUMMARY AND CONCLUSIONS

1. A study was made to determine the relationship of thyroid activity to lactation, growth and sex in sheep. Experiments were conducted to refine an extrapolation technique for measuring the thyroid secretion rate of live sheep.

2. The thyroid adjusted its secretion to the administration of a certain level of l-thyroxine within two days.

3. The sensitivity of the scintillation tube was found to be greater than the Geiger-Mueller in this study.

4. Using this technique, the estimated daily l-thyroxine secretion rate of female rats per 100 gms. body weight in two experiments was 2.566 $\pm$ 0.145 ug. and 2.768 $\pm$ 0.271 ug. These values are in agreement with the secretion rate obtained by the goitrogen technique.

5. The turnover rate ($t_{\frac{1}{2}}$) of I^{131} in the thyroid of eleven lactating Shropshire ewes was found to vary from 144.7 hours to 358.3 hours.

6. The coefficients of correlation and regression obtained between biological $t_{\frac{1}{2}}$ of seven lactating ewes and gain of suckling twin lambs for the first three-week period were -0.552 and -0.013 respectively, which are significant at the 5 percent level. These values indicate that the lactating ewe with a greater thyroid activity probably secretes a larger quantity of milk, resulting in an increased growth of suckling lambs.

7. There was no apparent relationship between biological $t_{\frac{1}{2}}$ of four lactating ewes and gain of their suckling single lambs during the first three weeks of lactation. This may be due either to the limited amount of data or to the fact that ewes with low thyroid activity were producing enough milk for the rearing of a single lamb.

8. The effect of thyroid secretion rate on the growth of sheep was studied on twelve ewe lambs, about five months old. The correlation coefficient between daily l-thyroxine secretion rate and growth of ewe lambs was 0.792, and the regression coefficient was 97.25, both significant at the 1 percent level. This indicates that lambs with higher thyroid activity gained faster than those with lower secretion rate.

9. The relationship of sex in sheep to thyroid activity was studied on 12 ewe lambs, 5 ram lambs, and 4 wether lambs of the Shropshire breed. On the average, the daily secretion rate per 100 pounds of body weight in different sexes of lambs was: ewe 0.082 mgm., ram 0.066 mgm., and wether 0.048 mgm. Only the difference in secretion rate between ewe and wether lambs is significant at the 5 percent level.

APPENDIX I

TABLE 1

DATA ON THE THYROID RADIOACTIVITY OF RATS IN RESPONSE TO DIFFERENT LEVELS OF 1-THYROXINE ADMINISTRATION
EXPERIMENT I

Day	Rat 1			Rat 2		
	1-Thyroxine per 100 Gm. Body Weight (ug.)	Thyroid* Count per Minute	Percent of Previous Count	1-Thyroxine per 100 Gm. Body Weight (ug.)	Thyroid* Count per Minute	Percent of Previous Count
0		4799			2432	
2	0.42	4034	84.1	0.44	2029	83.4
4	0.85	3621	89.8	0.89	1774	87.4
6	1.27	3340	92.2	1.33	1697	95.7
8	1.69	3116	93.3	1.78	1628	95.9
10	2.12	2927	93.9	2.22	1618	99.4
12	2.54	3023	103.3	2.67	1613	99.7
13		2874			1518	
15	2.97	2880	100.2	3.11	1545	101.8
17	3.39	2987	103.7	3.56	1495	96.8
19	3.81	2995	100.3	4.00	1513	101.2
21	4.24	2810	93.8	4.44	1275	84.3
23	8.47	2558	91.0	8.89	1216	95.3

TABLE 1 - continued

Day	Rat 3			Rat 4		
	l-Thyroxine per 100 Gm. Body Weight (ug.)	Thyroid* Count per Minute	Percent of Previous Count	l-Thyroxine per 100 Gm. Body Weight (ug.)	Thyroid* Count per Minute	Percent of Previous Count
0		4400			4781	
2	0.43	3499	79.5	0.37	3552	74.3
4	0.87	3154	90.1	0.74	2941	82.8
6	1.30	2927	92.8	1.11	2493	84.8
8	1.74	2810	96.0	1.48	2036	81.7
10	2.17	2749	97.8	1.85	1737	85.3
12	2.61	2812	102.3	2.22	1613	92.9
13		2566			1565	
15	3.04	2474	96.4	2.59	1545	98.7
17	3.48	2263	91.5	2.96	1583	102.4
19	3.91	2434	107.5	3.33	1654	104.5
21	4.35	1894	77.8	3.70	1367	82.7
23	8.70	1789	94.5	7.41	1121	82.0

*Corrected for background and physical decay

TABLE 2

DATA ON THE THYROID RADIOACTIVITY OF RATS IN RESPONSE TO DIFFERENT LEVELS OF 1-THYROXINE ADMINISTRATION EXPERIMENT II

Day	1-Thyroxine per 100 Gm. Body Weight (ug.)	Rat 1		Rat 2	
		Thyroid* Count per Min.	Percent of Previous Count	Thyroid* Count per Min.	Percent of Previous Count
0	0	5610		4000	
1	0	4613	82.2	3223	80.6
3	1	3832	83.1	2540	78.8
5	2	3514	91.7	2449	96.4
7	3	3223	91.7	2467	100.7
9	4	3216	99.8	2300	93.2
11	6	3081	95.8	2444	106.3
13	8	3043	98.8	2473	101.2

TABLE 2 - continued

Day	l-Thyroxine per 100 Gm. Body Weight (ug.)	Rat 3		Rat 4	
		Thyroid* Count per Min.	Percent of Previous Count	Thyroid* Count per Min.	Percent of Previous Count
0	0	5130		2822	
1	0	4624	90.1	2171	76.9
3	1	4332	93.7	1708	78.7
5	2	4427	102.2	1655	97.1
7	3	4474	101.1	1601	96.7
9	4	4318	96.5	1489	93.0
11	6	4347	100.7	1537	103.2
13	8	4457	102.5	1540	100.2
		Rat 5		Rat 6	
0	0	4540		6022	
1	0	3545	78.1	5172	85.9
3	1	2847	80.3	4585	88.7
5	2	2757	96.8	4431	96.6
7	3	2683	97.3	4515	101.9
9	4	2404	89.6	4251	94.2
11	6	2415	100.5	4464	105.0
13	8	2298	95.2	4444	99.6

*Corrected for background and physical decay

TABLE 3

DATA ON THE THYROID RADIOACTIVITY OF RATS IN RESPONSE TO DIFFERENT LEVELS OF 1-THYROXINE ADMINISTRATION
EXPERIMENT III

Rat No.	1-Thyroxine Administered Daily/100 Gm. (ug.)	0 Day* Thyroid Count/Min.	7th Day* Thyroid Count/Min.	Percent of Previous Count
1	0	10987	4363	39.7
2	0	8987	3486	38.8
3	0	10000	4548	45.5
4	0	6395	2549	39.9
5	1.0	9582	5748	60.0
6	1.0	6095	4220	71.2
7	1.0	7464	6090	56.5
8	1.0	9372	4341	65.0
9	1.0	15799	11842	74.9
10	1.5	10145	8808	86.8
11	1.5	9645	8647	89.7
12	1.5	9777	8288	84.8
13	1.5	8927	7922	88.7
14	1.5	8095	7743	95.7
15	2.0	8074	6895	85.4
16	2.0	13827	13447	97.3
17	2.0	7671	7252	94.5
18	2.0	22709	21859	96.3
19	2.0	8084	7832	96.9
20	2.5	9429	8762	92.9
21	2.5	8503	8581	100.9
22	2.5	7022	6897	98.2
23	2.5	10073	10069	100.0
24	2.5	5981	5765	96.4

*Corrected for background and physical decay

TABLE 4

DATA ON THE THYROID RADIOACTIVITY IN RESPONSE TO DIFFERENT LEVELS OF 1-THYROXINE ADMINISTRATION TO EWE LAMBS

Day	1-Thyroxine per 100 lbs. Body Weight (mg.)	Ewe 735	
		Thyroid Count per Minute	Percent of Previous Count
0	0	22090	
2	0	20448	92.6
4	0.05	18962	92.7
6	0.05	18547	97.8
8	0.10	17760	95.8
10	0.10	19516	109.9
12	0.15	21237	108.8
14	0.15	18655	87.8
16		18800	100.8

TABLE 4 - continued

Day	l-Thyroxine per 100 lbs. Body Weight (mg.)	Ewe 720	
		Thyroid* Count per minute	Percent of Previous Count
0	0	24217	
2	0	21679	89.5
4	0.05	19318	89.1
6	0.05	17741	91.8
8	0.10	16840	94.9
10	0.10	18088	107.4
12	0.15	17574	97.2
14	0.15	17563	99.9
16	0.20	18680	106.4
18	0.20	16898	90.5
20		16187	95.8

TABLE 4- continued

Day	l-Thyroxine per 100 lbs. Body Weight (mg.)	Ewe 678		Ewe 738	
		Thyroid* Count per Min.	Percent of Previous Count	Thyroid* Count per Min.	Percent of Previous Count
0	0	22182		25242	
2	0	21135	95.3	23551	93.3
4	0.05	20393	96.5	22825	96.9
6	0.05	20110	98.6	22764	99.7
8	0.10	19440	96.7	21240	93.3
10	0.10	20516	105.5	21111	99.4
12	0.15	21150	103.1	21894	103.7
14	0.15	18655	88.2	22781	104.1
16	0.20	18280	98.0	20320	89.2
18	0.20	17965	98.3	20856	102.6
20		18476	102.8	21809	104.6

TABLE 4 - continued

Day	1-Thyroxine per 100 lbs. Body Weight (mg.)	Ewe 719		Ewe 718	
		Thyroid* Count per Min.	Percent of Previous Count	Thyroid* Count per Min.	Percent of Previous Count
0	0	23249		18102	
2	0	22367	96.2	16885	93.3
4	0.05	19648	87.8	14454	85.6
6	0.05	19454	99.0	15204	105.2
8	0.10	18200	93.6	14900	98.0
10	0.10	19326	106.2	15232	102.2
12	0.15	18747	97.0	14768	97.0
14	0.15	17664	94.2	15312	103.7
16	0.25	18680	105.8	13480	88.0
18	0.25	18533	99.2	12964	96.2
20		17120	92.4	13221	102.0

TABLE 4 - continued

Day	l-Thyroxine per 100 Lbs. Body Weight (mg.)	Ewe 740		Ewe 682	
		Thyroid* Count per Min.	Percent of Previous Count	Thyroid* Count per Min.	Percent of Previous Count
0	0	20668		26273	
2	0	18177	87.9	25121	95.6
4	0.05	15283	84.1	23183	92.3
6	0.05	14398	94.2	22142	95.5
8	0.10	13360	92.8	21300	96.2
10	0.10	13447	100.7	21039	98.8
12	0.15	13107	97.5	21866	103.9
14	0.15	12617	96.3	22404	102.5
16	0.25	11680	92.6	22080	98.6
18	0.25	11471	98.2	20453	92.6
20		11498	100.2	22205	108.6

TABLE 4- continued

Day	1-Thyroxine per 100 Lbs. Body Weight (mg.)	Ewe 684		Ewe 743	
		Thyroid* Count per Min.	Percent of Previous Count	Thyroid* Count per Min.	Percent of Previous Count
0	0	19514		18082	
2	0	16993	87.1	16993	94.0
4	0.05	15885	93.5	15197	89.4
6	0.05	14112	88.8	14734	97.0
8	0.10	13320	94.4	14700	99.8
10	0.10	13376	100.4	14875	101.2
12	0.15	12794	95.6	15112	101.6
14	0.15	11595	90.6	16027	106.1
16	0.30	11120	95.9	13280	82.9
18	0.30	11421	102.7	14125	106.4
20		10283	90.0	13504	95.6

TABLE 4 - continued

Day	1-Thyroxine per 100 Lbs. Body Weight (mg.)	Ewe 744		Ewe 746	
		Thyroid* Count per Min.	Percent of Previous Count	Thyroid* Count per Min.	Percent of Previous Count
0	0	27736		26839	
2	0	24808	89.4	24156	90.0
4	0.05	22997	92.7	21580	89.3
6	0.05	22848	99.4	19488	90.3
8	0.10	20720	90.7	18300	93.9
10	0.10	20563	99.2	18207	99.5
12	0.15	21982	106.9	18144	99.7
14	0.15	20120	91.5	17734	97.7
16	0.30	20480	101.8	18120	102.2
18	0.30	20998	102.5	15761	87.0
20		22261	106.0	16611	105.4

*Corrected for background and physical decay

TABLE 5

DATA ON THE THYROID RADIOACTIVITY IN RESPONSE TO DIFFERENT LEVELS OF 1-THYROXINE ADMINISTRATION TO WETHER LAMBS

Day	1-Thyroxine per 100 Lbs. Body Weight (mg.)	Wether 737		Wether 733	
		Thyroid* Count per Min.	Percent of Previous Count	Thyroid* Count per Min.	Percent of Previous Count
0	0	13118		28783	
2	0	12077	92.1	27754	96.4
4	0.05	10984	90.9	25352	91.3
6	0.05	9744	88.7	27754	109.5
8	0.10	10200	104.7	26120	94.1
10	0.10	11160	109.4	22284	85.3
12	0.15	11167	100.1	23830	106.9
14		10114	90.6	20563	86.3

TABLE 5 - continued

Day	l-Thyroxine per 100 Lbs. Body Weight (mg.)	Wether 680		Wether 741	
		Thyroid* Count per Min.	Percent of Previous Count	Thyroid* Count per Min.	Percent of Previous Count
0	0	29819		16158	
2	0	28925	97.0	15127	93.6
4	0.05	26085	90.2	13141	86.9
6	0.05	28241	108.3	12768	97.2
8	0.10	29160	103.3	12800	100.3
10	0.10	28020	96.1	13528	105.7
12	0.15	24929	89.0	13705	101.3
14		25872	103.8	12768	93.2

*Corrected for background and physical decay

TABLE 6

DATA ON THE THYROID RADIOACTIVITY IN RESPONSE TO DIFFERENT LEVELS OF 1-THYROXINE ADMINISTRATION TO RAM LAMBS

Day	1-Thyroxine per 100 Lbs. Body Weight (mg.)	Ram 731		Ram 739	
		Thyroid* Count per Min.	Percent of Previous Count	Thyroid* Count per Min.	Percent of Previous Count
0	0	12585		21719	
2	0	12174	96.7	20592	94.8
4	0.05	10998	90.3	17343	84.2
6	0.05	10668	97.0	17430	100.5
8	0.10	10480	98.2	17200	98.7
10	0.10	10677	101.9	17936	104.3
12	0.15	9503	89.0	16074	89.6
14		9106	95.8	16531	102.8

TABLE 6 - continued

Day	l-Thyroxine per 100 Lbs. Body Weight (mg.)	Ram 732		Ram 686	
		Thyroid* Count per Min.	Percent of Previous Count	Thyroid* Count per Min.	Percent of Previous Count
0	0	12108		20725	
2	0	10363	85.6	19445	93.8
4	0.05	9842	95.0	17766	91.4
6	0.05	10248	104.1	17421	98.1
8	0.10	9640	94.1	16800	96.4
10	0.10	8744	90.7	16003	95.3
12	0.15	8122	92.9	16074	100.4
14		8198	100.9	15926	99.1

TABLE 6 - continued

Day	l-Thyroxine per 100 Lbs. Body Weight (mg.)	Ram 688	
		Thyroid* Count per minute	Percent of Previous Count
0	0	14716	
2	0	12766	86.7
4	0.05	11393	89.2
6	0.05	10248	89.9
8	0.10	10280	100.3
10	0.10	10434	101.5
12	0.15	9588	91.9
14		8837	92.2

*Corrected for background and physical decay

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