

UNIVERSITY OF MISSOURI COLLEGE OF AGRICULTURE
AGRICULTURAL EXPERIMENT STATION

J. H. LONGWELL, *Director*

Environmental Physiology and Shelter Engineering

With Special Reference to Domestic Animals

XLVII. The Influence of Constant Ambient Temperature on the
Thyroid Activity and Iodide Metabolism of Shorthorn, Santa
Gertrudis, and Brahman Calves during Growth

CLIFTON BLINCOE



(Publication authorized January 17, 1958)

COLUMBIA, MISSOURI

SUMMARY AND CONCLUSIONS

Data are presented on the influence of two ambient temperatures, 50° and 80° F (10° and 27° C), and growth on the thyroid activity and extrathyroidal iodide metabolism of Shorthorn, Santa Gertrudis, and Brahman heifers. Data are also presented on the effect of increasing ambient temperature on these heifers at about 18 months of age.

The rate constants for thyroid hormone release and thyroid uptake of I^{131} by the thyroid gland were used as parameters of thyroid function. The iodide space was measured and a few measurements of blood volume (determined by the initial dilution of iodide and the rate constant for transcapillary diffusion of iodide) are also reported. The following conclusions are drawn from these data.

1. Heifers grown at 50° F exhibited a decline in thyroid secretory activity to about seven months of age. At 50° F the thyroid secretory activity of Shorthorn, Santa Gertrudis, and Brahman heifers was the same.

2. The 80° F environmental temperature depressed the thyroid secretory activity of Shorthorn heifers by 45 percent and that of Santa Gertrudis, slightly; the Brahman heifers were unaffected.

3. The uptake of I^{131} by the thyroid gland was constant to about seven months of age and then decreased, again becoming constant at about one year of age. The rate of amount of I^{131} uptake decreased only after the thyroid secretory rate had become essentially constant.

4. Increasing the ambient temperature to 100° F (38° C) decreased the thyroid secretory activity of Shorthorn heifers raised at 50° F by 60 percent. Thyroid activity of the Shorthorn heifers raised at 80° F was not depressed by 90° F environmental temperature; this was probably due to their disproportionately large surface area. The thyroid secretory activity of Santa Gertrudis raised in the 50° and 80° F environments was depressed 30 percent by 100° F. Brahman heifers were unaffected by 90° F.

5. The iodide space (volume into which iodide diffuses) is not a function of breed or temperature during growth. The iodide space varies as the 0.73 power of body weight.

6. The rate constant for transcapillary diffusion of iodide tended to increase with increasing ambient temperature, probably as a result of increased body temperature.

7. The initial dilution of radioiodide may be used to measure total blood volume. Results are comparable to those obtained with Evans blue dye.

TABLE OF CONTENTS

Introduction	4
Review of Literature on Thyroid Activity in Relation to Growth	4
Methods	6
Experimental Animals and Schedules	6
Radioiodine Methods	8
Calculations and Graphical Methods	10
Data and Discussion	11
Effect of Constant Ambient Temperature During Growth	11
Effect of Thermal Stress of Heifers Grown at 50° and 80° F	15
Blood Volume	16
Transcapillary Diffusion of Iodide	18
Iodide Space	20
Bibliography	22
Appendix (Figures 10-13)	23

ACKNOWLEDGEMENTS

This is a part of a broad cooperative investigation between the Departments of Dairy Husbandry and Agricultural Engineering of the Missouri Agricultural Experiment Station, University of Missouri, and the Agricultural Engineering Research Division, Agricultural Research Service, U. S. Department of Agriculture. This bulletin reports on Department of Dairy Husbandry Research Project No. 125, "Climatic Factors".

Grateful acknowledgements are made to A. C. Ragsdale for selection and management of the animals, to R. G. Yeck and M. M. Jones for cooperation on the engineering aspects, to H. E. Dale, D.V.M. for the injections and blood samplings, and to the U. S. Atomic Energy Commission for financial assistance (Contract No. AT(11-1)-73).

Acknowledgements are also due to Mr. Robert J. Kleberg, owner of the Santa Gertrudis cattle, King Ranch, Kingsville, Texas; James W. Box, Sand Springs Farm, Sand Springs, Oklahoma, owner of the Shorthorn cattle; and to the owners of the Brahman cattle: Southern Rice Farms, Carlisle, Arkansas; Burke Brothers, Corsicana, Texas; Whitcombe's Clear Creek Farms, Houston, Texas; W. S. Gibbs, Huntsville, Texas; C. Y. Jacobs, Yoakum, Texas; V. W. Frost, Pecan Acres Ranch, Simonton, Texas; and R. C. Parker, V-8 Ranch, Center, Texas.

Environmental Physiology and Shelter Engineering

With Special Reference to Domestic Animals

XLVII. THE INFLUENCE OF CONSTANT AMBIENT TEMPERATURE ON THE THYROID ACTIVITY AND IODIDE METABOLISM OF SHORTHORN, SANTA GERTRUDIS, AND BRAHMAN CALVES DURING GROWTH*

CLIFTON BLINCOE**

INTRODUCTION

Previous studies of thyroid function and iodide metabolism in this series have been concerned with the influence of temperature on mature dairy cows.^{1,2} This report is concerned (1) with the effect of two constant temperatures, 50° and 80° F, during growth, on beef heifer calves and (2) with the effect of thermal stress on animals raised for 14 months at these temperatures.

Preceding bulletins reported that high environmental temperature (95° F or 35° C) decreased the thyroid activity of Jersey, Holstein, and Brahman cows by 30 to 65 percent.¹ Also, a diurnal temperature cycle of 70° to 100° F (21° to 38° C) decreased the thyroid activity of Jersey and Holstein cows by about 30 percent.² It was indicated that these data roughly paralleled the changes in resting heat production. These data have been summarized in detail elsewhere.³

Definitions of terms peculiar to this work are given in Missouri Research Bulletin 576.

REVIEW OF THE LITERATURE ON THYROID ACTIVITY IN RELATION TO GROWTH

The literature on thyroid activity in relation to temperature has been reviewed in a previous report.¹

Recently, Stevens *et al.*⁴ found that exposure to cold (7° C) greatly increased the thyrotropic hormone content of the pituitary gland and the blood in adult female guinea pigs. This increase in thyrotrophic hormone content of the pituitary gland occurred gradually. After one week exposure no change had occurred, and after 9-12 weeks the gland content was four times that of control animals at 23° C. They also found that exposure to cold did not increase the 24-hour up-

*This research was conducted under the leadership of the late Dr. Samuel Brody to whom the author is grateful for his inspiration, encouragement, and suggestions.

**Present address: Department of Agricultural Chemistry, University of Nevada, Reno, Nevada.

take of I^{131} but significantly increased the turnover of I^{131} by the thyroid gland. Using their data, the present authors computed the rate constant for hormone release and found it doubled by exposure to cold (0.028 at 23° C and 0.056 at 7° C).

Brown-Grant,⁵ using adult male albino rats, studied the thyroid turnover of I^{131} on short (72-hour) exposure to cold. He found that if the rats were exposed to cold *after* the maximum uptake of I^{131} by the thyroid gland had occurred, 16° C had no effect, 11.5° and 6.5° C increased the thyroid turnover of I^{131} and that 2.0° and 0° C decreased the turnover. These data indicate a stimulation of the secretory activity of the thyroid gland by 6.5° and 11.5° C and a depression of it by temperatures near the freezing point. Adrenalectomized rats exposed to 11.1° C experienced a depression of thyroid function. These data indicate an interrelation between the thyroid and the adrenal glands in the response of the rat to cold.

Hurst and Turner,⁶ using the thyroxine-thiouracil method proposed by Dempsey and Astwood,⁷ found that the thyroxine secretion rate per unit body weight decreased with growth in mice. They found no difference between the thyroxine secretion rates of growing white and yellow mice. This is of particular interest because the yellow mice have an inherited ability to deposit large amounts of body fat before reaching maturity.

Monroe and Turner,⁸ also using the thyroxine-thiouracil method, found that thyroxine secretion rate per unit body weight decreased with age in growing white rats. Male rats showed a small decrease but for female rats the thyroxine secretion rate per unit body weight decreased approximately 50 percent as body weight increased from 83 to 276 g.

Schultz and Turner⁹ observed a decrease in the thyroxine secretion rate per unit body weight during growth in chickens as did Biellier and Turner¹⁰ in turkey poults. A difference between sexes was not apparent. Smyth and Fox¹¹ believed that the thyroxine secretion rate of turkey poults was related to their rate of growth.

The blood plasma concentration of protein-bound iodine (PBI) has been taken as indicative of thyroid function. Long *et al.*¹² observed a decrease of PBI with advancing age in dairy cattle. They found 4.8 percent in calves, 3.1 percent in three to four-year old cows and 2.6 percent in seven to eight-year old cows. Reece and Mann¹³ also reported lower PBI in calves than in mature cows. Lewis and Ralson¹⁴ found the following average PBI levels in dairy cows: 48 hours old, 13.7 percent; two days to 12 months old, 7.2 percent; one to two-years old, 6.2 percent; and older cows 4.6 percent.

In beef animals Kunkel, Colby, and Lyman¹⁵ and Gawienowski and Mayer¹⁶ observed a negative correlation between blood PBI concentration and rate of gain. This indicates an adverse effect of high thyroid function on rate of gain. Stokes, Futrell, and Kunkel,¹⁷ however, found that the optimum level of blood plasma PBI for good feedlot gain was 5.0 to 6.8 percent. Reineke and Henne-
man¹⁸ found that the thyroid secretion rate as determined by a radioiodine technique was significantly correlated with the rate of gain of ewe lambs.

In Rhesis monkeys, Pickering *et al.*¹⁹ found that the 24-hour uptake of I¹³¹ was higher (35 to 45 percent) in two-month old animals than in one-year old animals (20 to 30 percent). In mature man, Quimby, Werner, and Schmidt²⁰ found a statistically significant decline in the 24-hour uptake of I¹³¹ with advancing age.

In summary, in all species studied one finds a decrease of the relative (per unit weight, per unit of blood, etc.) thyroid secretory activity with increasing age, in both growing and mature animals.

METHODS

Experimental Animals and Schedules.

These studies were made under the controlled environmental conditions of the Psychroenergetic Laboratory.²¹ This laboratory consists of two independently

TABLE 1--SCHEDULE OF ENVIRONMENTAL CONDITIONS
Psychroenergetic Laboratory
12/28/55 to 3/31/56

Test Room I				Test Room II			
50°F calves (all breeds)*				80°F calves (all breeds)			
12/28 - 2/2	65°F	70% r.h.		1/4 - 2/9	65°F	70% r.h.	
2/3 - 2/26	80°F	42% r.h.		2/10 - 2/19	80°F	42% r.h.	
2/27 - 3/2	90°F	31% r.h.		2/20 - 3/2	90°F	31% r.h.	

50 and 80°F calves were interchanged 3/2/56 and primary attention given to the calves in Test Room II.

*50°F calves represent those raised at 50°F in Test Room I from 11/17/54 to 12/28/55.

50°F calves (all breeds)	Test Room II			Test Room II	
	Day			Night	
3/2 - 3/9	90°F	31% r.h.	90°F	31% r.h.	
3/10 - 3/11	82°F	33% r.h.	82°F	33% r.h.	
3/12 - 3/16	100°F	23% r.h.	94°F	30% r.h.	
50° and 80°F Santa Gertrudis and 50°F Brahman					
3/17 - 3/18	94°F	28% r.h.	94°F	28% r.h.	
3/19 - 3/21	110°F	23% r.h.	104°F	26% r.h.	
3/22 - 3/23	106°F	26% r.h.	93°F	28% r.h.	
3/24 - 3/25	80°F	35% r.h.	80°F	35% r.h.	
50° and 80°F Brahman					
3/26 - 3/27	105°F	25% r.h.	100°F	27% r.h.	
3/27	Dropped to 65°F at night				
3/28 - 3/30	105°F	52% r.h.	95°F	26% r.h.	

Test Room I

80°F calves	
3/2 - 3/16	Variable 70 - 80°F and about 50% r.h.
50° and 80°F Shorthorn - 80°F Brahman	
3/16 - 3/24	Variable 65 - 80°F and 45 to 75% r.h.
50° and 80°F Santa Gertrudis - 50°F Shorthorn (80°F Shorthorn moved out of laboratory)	
3/24 - 4/1	Variable 65 - 80°F and 45 to 80% r.h.

Two major differences may be observed between this schedule and previous test schedules. One, the dew point was held approximately constant at 55°F in the above tests instead of the relative humidity as in previous tests. At 110°F air temperatures the dew point was slightly elevated to about 65°F. Of course with 52% humidity at 105°F air temperatures, it was about 85°F.

controlled chambers, each modified to contain three calves in each of three pens. Temperature, humidity, air velocity and radiation (light) were controlled.

This experiment was divided into two phases. First, the influence of two constant temperatures, 50° and 80° F (10° and 27° C) on growing heifer calves and second, the influence of increasing ambient temperature on these animals at approximately 17 months of age. The temperature and relative humidity schedule is in Table 1. During the experiment the mean air velocity through the chambers was 0.5 mile per hour (0.8 Km per hour).

Shorthorn, Brahman, and Santa Gertrudis heifer calves were used in these studies. Three calves of each breed were placed in each chamber of the Psychroenergetic Laboratory. In addition, a group of six calves, two of each breed, were kept under conditions normally used in raising dairy calves. Other calves in this outside group were available for replacements if needed. The vital statistics concerning these animals are given in Table 2.

TABLE 2--EXPERIMENTAL ANIMALS

Breed	Calf No.	Birth date, 1954	Age, days as of Nov. 8, 1954
<u>Chamber 1 - 50°F</u>			
Brahman	301	Sept. 20*	49
	309	Sept. 18	51
	319	Oct. 3	36
Santa Gertrudis	387	Oct. 1*	38
	366	Sept. 22	47
	368	Oct. 2	37
Shorthorn	332	Aug. 15	85
	342	Sept. 28	41
	349	Aug. 7	93
<u>Chamber 2 - 80°F</u>			
Brahman	302	Sept. 20	49
	315	Sept. 21	48
	321	Sept. 29	40
Santa Gertrudis	384	Oct. 1*	38
	393	Sept. 19*	50
	396	Sept. 22*	47
Shorthorn	338	Aug. 7	93
	354	Aug. 28	72
	355	Sept. 30	39
<u>Open Shed</u>			
Brahman	313	Sept. 26*	43
	361	Sept. 25*	44
Santa Gertrudis	371	Oct. 17	22
	385	Oct. 22*	17
Shorthorn	334	Aug. 22	78
	344	Oct. 1	38

*Estimated.

The Santa Gertrudis represent a new breed of beef cattle developed at the King Ranch, Kingsville, Tex. They are said to be $\frac{5}{8}$ Shorthorn and $\frac{3}{8}$ Brahman, inbred to the high degree of uniformity characteristic of a breed. They are re-

ported to be highly resistant to temperature and to give good beef production under adverse environmental conditions.²² This experiment offered the opportunity to compare this new breed with purebred representatives of its parent breeds. Such a comparison offers some insight into the mechanisms of heat tolerance in cattle.

Radioiodine Methods.

Three methods of assaying thyroid activity with the aid of radioactive iodine were used in this study. The rate constant for uptake of I^{131} by the thyroid gland (k_1)*** and the maximum uptake of I^{131} by the thyroid gland (U) were used as measures of the iodide uptake and iodide fixation phases of thyroid function. The rate constant for thyroid hormone release (k_4) was used as a measure of thyroid secretory function. These rate constants are the instantaneous relative rates of the processes—they are the speeds of the processes if the materials entering into them were always present at unit concentrations. A rate constant has the units (dimensions) of a frequency—i.e. reciprocal time. It is a number per unit of time. For example, if k_1 has a value of 0.01 hr^{-1} , the thyroid is acquiring iodide at a rate of 1 percent (of that available in the blood) per hour. Also, if k_4 has a value of 0.003 hr^{-1} , the thyroid is secreting the thyroid hormone at a rate of 0.1 percent (of that available in the gland) per hour.

The mathematical approach to thyroid function was reviewed in previous bulletins which also detailed the techniques of measuring these quantities.^{1,2} It suffices to say here that the maximum uptake of I^{131} by the thyroid gland is measured with an externally placed Geiger counter.²³ The rate constant for hormone release (k_4) is ascertained by measuring the rate at which the thyroid gland loses I^{131} after its maximum uptake and correcting for the recycling of I^{131} . In this study all data taken after 100 hours post-injection were used in computing this rate constant. Figure 1 gives representative data of this type. The rate constant for thyroid uptake (k_1) is measured by the rate of decrease of I^{131} in the blood for the six hours immediately after intravenous injection of I^{131} . The iodide space, rate constant for transcapillary diffusion of radioiodide, and the blood volume were measured. Details of the methods used will be given subsequently.

For a single assay of thyroid activity, carrier-free NaI^{131} was injected through an indwelling polyethylene venous catheter. Blood samples were also taken through this catheter. Dosages of I^{131} used in this study are given in Table 3. The I^{131} solution was injected through the polyethylene tube with the aid of an

TABLE 3--DOSE OF RADIOIODINE

Body weight kg.	Dose mc. I^{131}
50-100	0.08
100-200	0.1
200-300	0.2
300-500	0.3

***Terminology and notation of Brownell²⁴ used throughout.

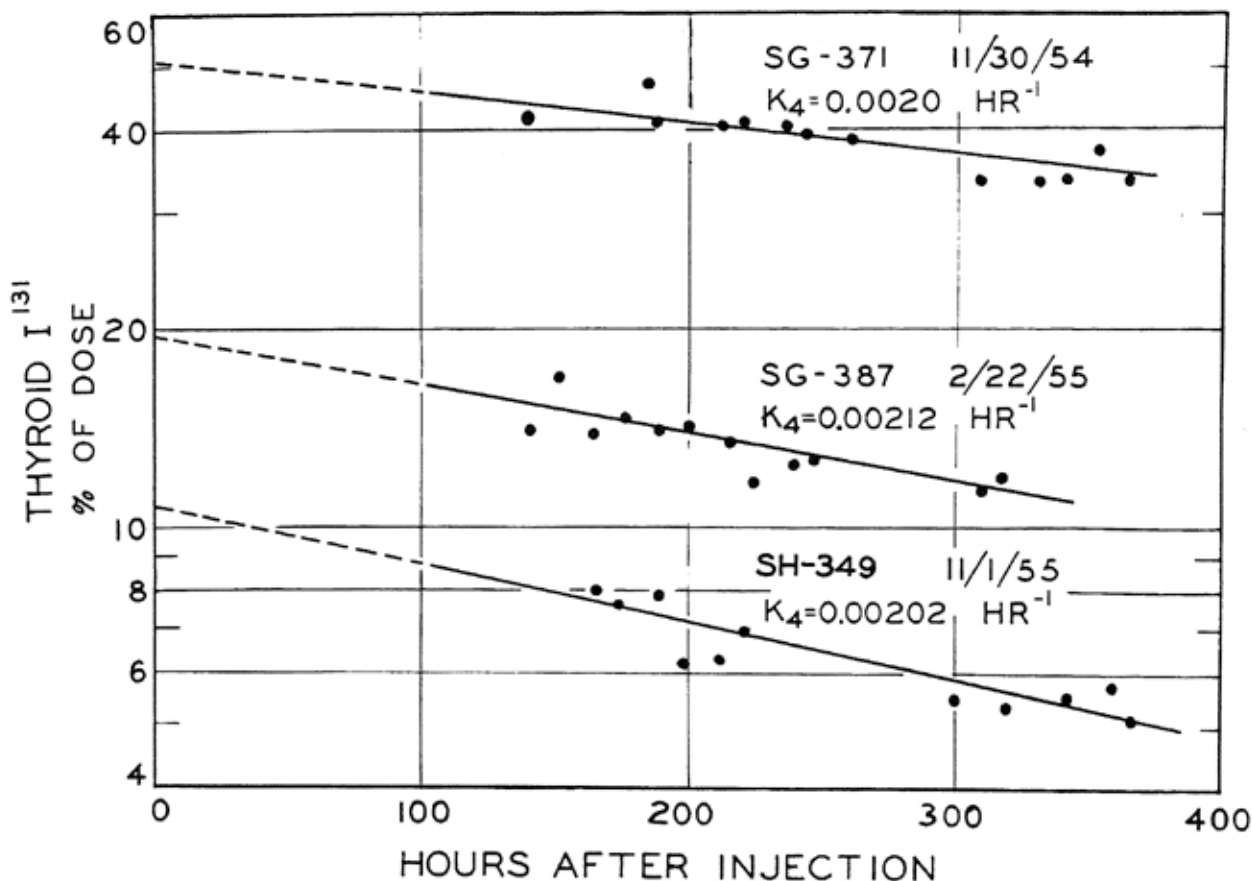


Figure 1. Representative data used to compute the rate constant for thyroid hormone secretion (k_4). The individual measurements of the I^{131} content of the thyroid gland are plotted on semilogarithmic paper against time after injection. The extrapolated intercept is the theoretical maximum uptake of I^{131} by the thyroid gland (U).

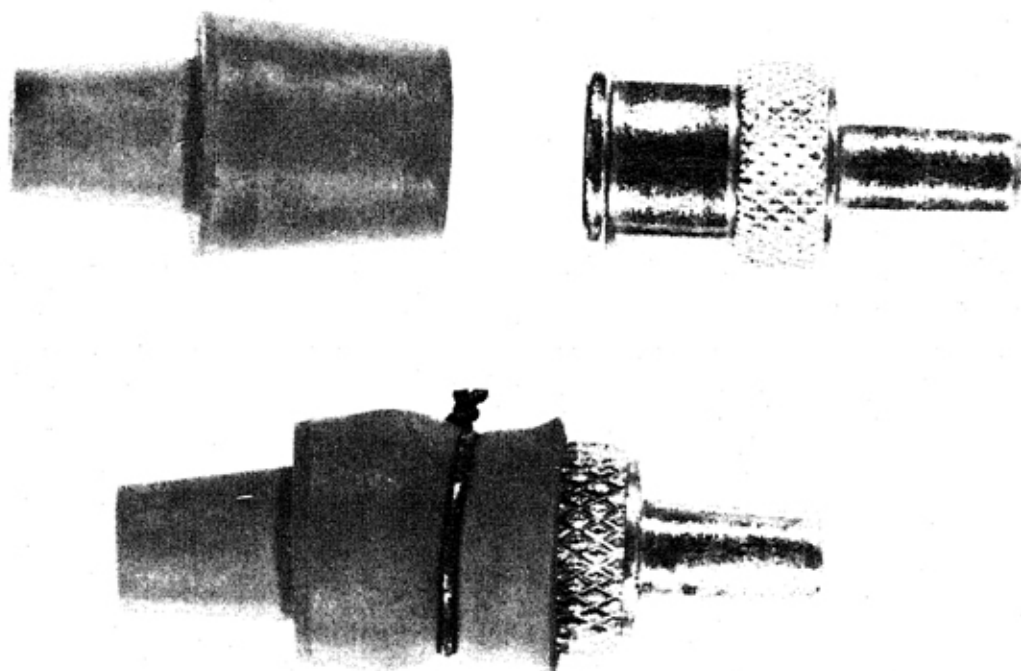


Figure 2. Adapter used for injection of I^{131} . This is fitted to a polyethylene venous catheter and injections made through the rubber serum vial cap.

adapter fitted to one end. This adapter was composed of a rubber serum vial cap and an adapter designed to fit leur taper hyperdermic needles to large taper syringes (Fig. 2). The adapter permitted injection of the I^{131} and a saline wash through the rubber cap into the polyethylene tube. It was found unsatisfactory to attempt to inject the I^{131} through the wall of the polyethylene tubing. No difficulty was encountered in using the same polyethylene catheter for both injection and bleeding.

Calculation and Graphical Methods.

Details of computation of the radioiodine data are given in previous bulletins.^{1,2} In all cases where it was desired to determine the slope of a curve as in the calculation of k_1 and k_4 , a regression equation was fitted to the data. Figure 1 gives examples of the data used in computation of the rate constant for hormone release (k_4). All data collected were used in computing the regression equation unless they were in disagreement with the body of the data by at least 50 percent and it could be clearly demonstrated that an equipment failure was involved or that the calf was ill at that time. All data inadvertently collected during the reaction of the animals to vaccination and dehorning were rejected because of their atypical character and because of the obvious reactions of the animals to the procedure.

In constructing graphs of the rate constant for thyroid uptake of I^{131} (k_1) and the maximum uptake of I^{131} by the thyroid gland (U), the age at the time of injection of I^{131} was used. These phenomena occur quickly. Hence they represent the animal at essentially the time of injection. The rate constant for thyroid hormone secretion (k_4) is measured over a two to three-week time interval after injection and represents an age older than the age at injection. In plotting this variable the age of the calf at the midpoint of data collection was used. This correction was relatively small, being only nine days in the early part of the experiment and 12 days in the latter part.

A non-statistical technique was used in constructing graphs showing the average thyroid activity. This is illustrated in Figure 3. A graph of the data was constructed and the points for each animal were connected by straight lines. The values represented by these lines at intervals of 25 days were noted and averaged. For example, in Figure 3, at 200 days, we have values of .00282, .00245, and .00230 or an average of .00252. These averages were plotted and a smooth curve passed through them by inspection. This technique was necessitated by the fact that the ages of the animals were not identical at the time of thyroid assay.

Data are presented in two forms. Figures 4, 5, and 6 were prepared as described above. These figures provide a convenient method of presenting the general trends of the data without the confusion of the original data points and are so used in the discussion. The complete data are presented in the Appendix as Figures 10, 11, and 12. These will enable you to study the variability of the data and the validity of the averaged figures. In all references to the averaged curves,

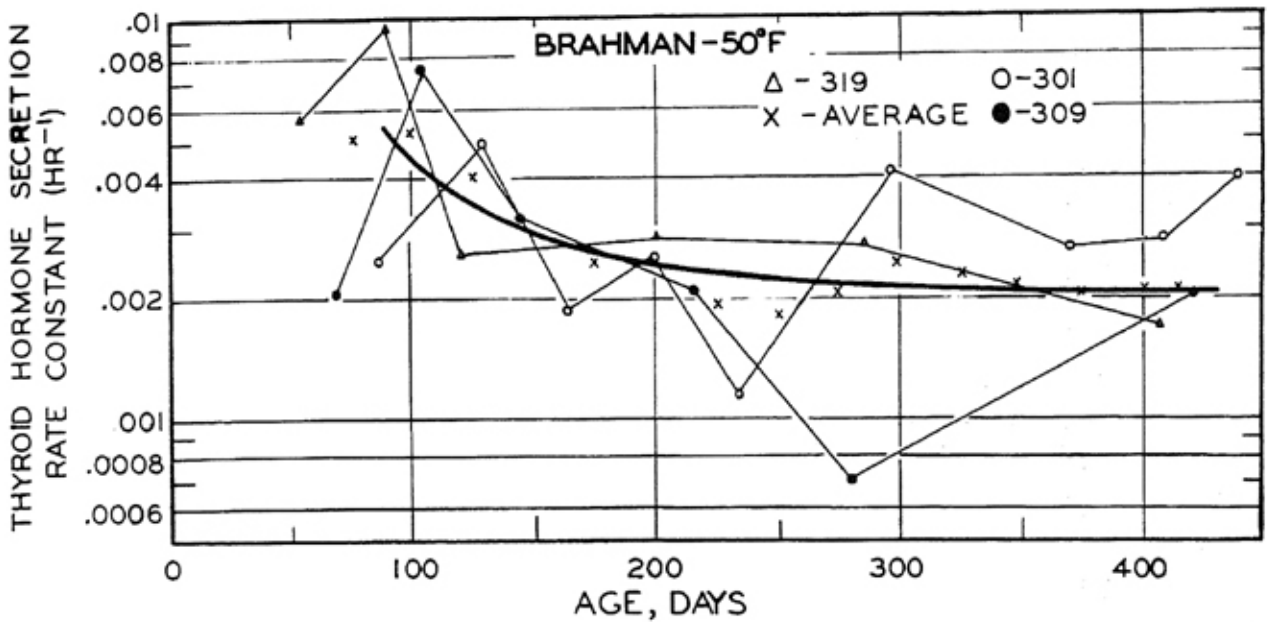


Figure 3. Example of the procedure used for average graphs. See text for explanation.

reference is also made to the appropriate figure showing the complete data.

Data on thyroid function are presented in semilogarithmic form as were the data in previous bulletins in this series.^{1,2} In semilogarithmic plots, equal percentage changes are represented by parallel lines. This presentation has the concurrent disadvantage of accentuating deviations below the average in relation to those above the average. The advantages of this form of data presentation have been discussed elsewhere.²⁶

DATA AND DISCUSSION

Effect of Constant Ambient Temperature During Growth.

Figures 4 and 5 give the thyroid activity as expressed by the rate constant for thyroid hormone release (k_4). Figure 6 gives a comparison of the rate constants for hormone release (k_4) and iodide uptake (k_1), and the maximum thyroid uptake of I^{131} (U). Complete data are given in Figures 10, 11, 12, and 13 in the Appendix.

As indicated in Figure 4 (also in Figures 10-12) the rate constant for hormone release decreases in all breeds at 50° F until about six months of age. This is in agreement with the previous data on growing animals. At 50° F all three breeds had essentially the same thyroid secretory activity. After about six months of age there was no observable change in thyroid function with age to 400 days. At 80° F (27° C) the thyroid activity was essentially unchanged by age. Percentage-wise this would indicate a greater depression of thyroid activity by temperature in young (100 day) calves than in older heifers. Perhaps this indicates

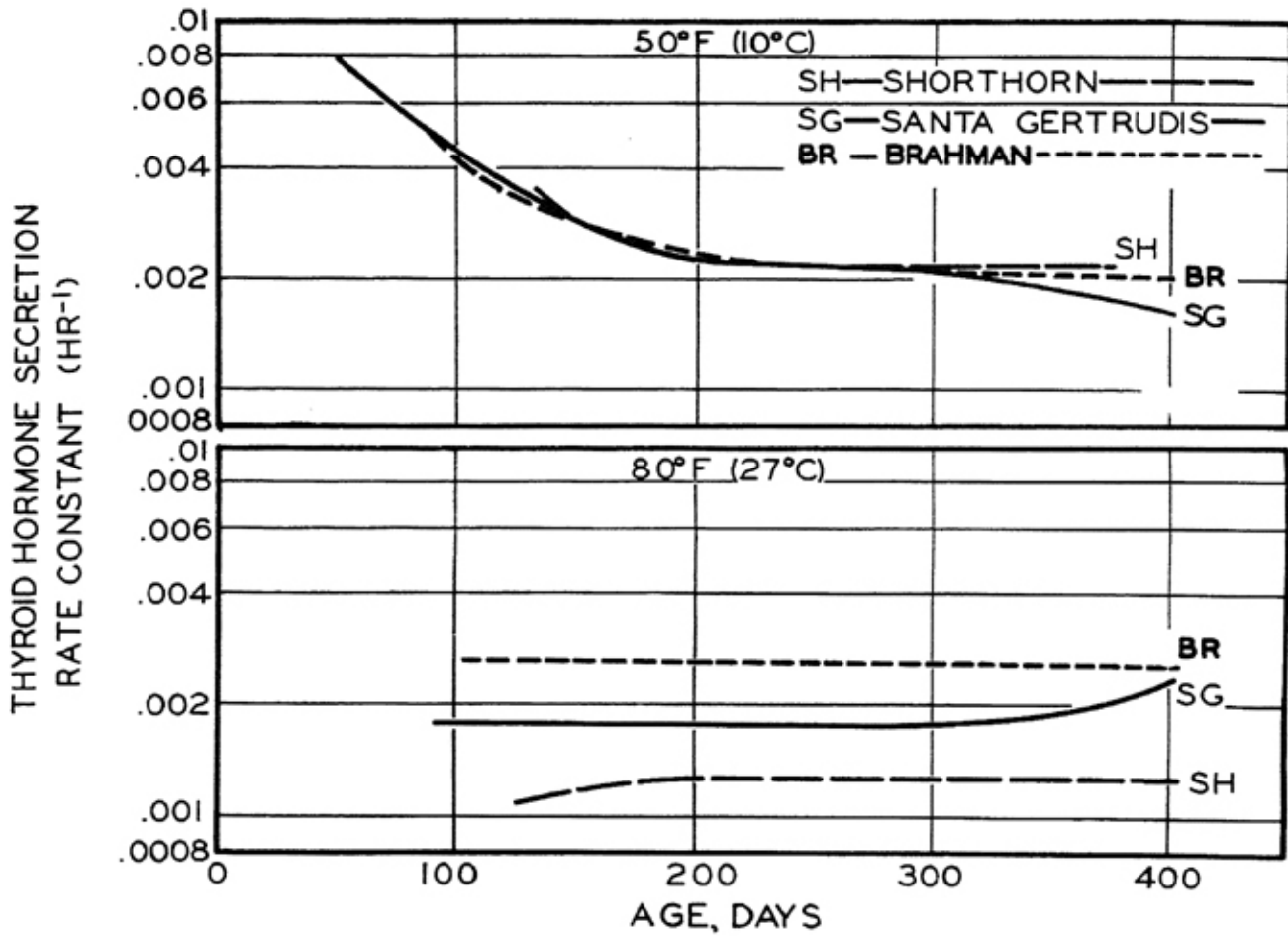


Figure 4. Effect of temperature on the thyroid secretory activity of growing heifers. All three breeds have essentially the same thyroid secretory activity at activity 50° F. The decline in thyroid activity before puberty is not present in heifers raised at 80° F. (See figures 10, 11, and 12 for complete data.)

acclimatization. In any event, an ambient temperature of 80° F prevented the normal decrease of thyroid secretory activity with age.

Comparing the breeds in their response to these two temperatures (Figs. 5, and 10-12), the rate constant for hormone release of the Shorthorn heifers was severely depressed (45 percent) at 80° F. The Brahman heifers showed no depression and the Santa Gertrudis were slightly depressed. The Shorthorn heifers exhibited marked elevation of their rectal temperature at 80° F, but the Brahman and Santa Gertrudis heifers showed no rise in rectal temperature.²⁷ The depressing effect of high ambient temperature on thyroid activity was associated with a rise in body temperature. In other words, the thyroid secretory activity responds not to ambient but to body (cellular) temperature.

During this study one Shorthorn heifer (338) differed markedly in thyroid secretory activity from the other two Shorthorn heifers (see Fig. 10 in the Appendix) at 80° F. The early (about 100 day) measurement was in agreement with the other heifers. At all other times, however, her thyroid secretory activity was

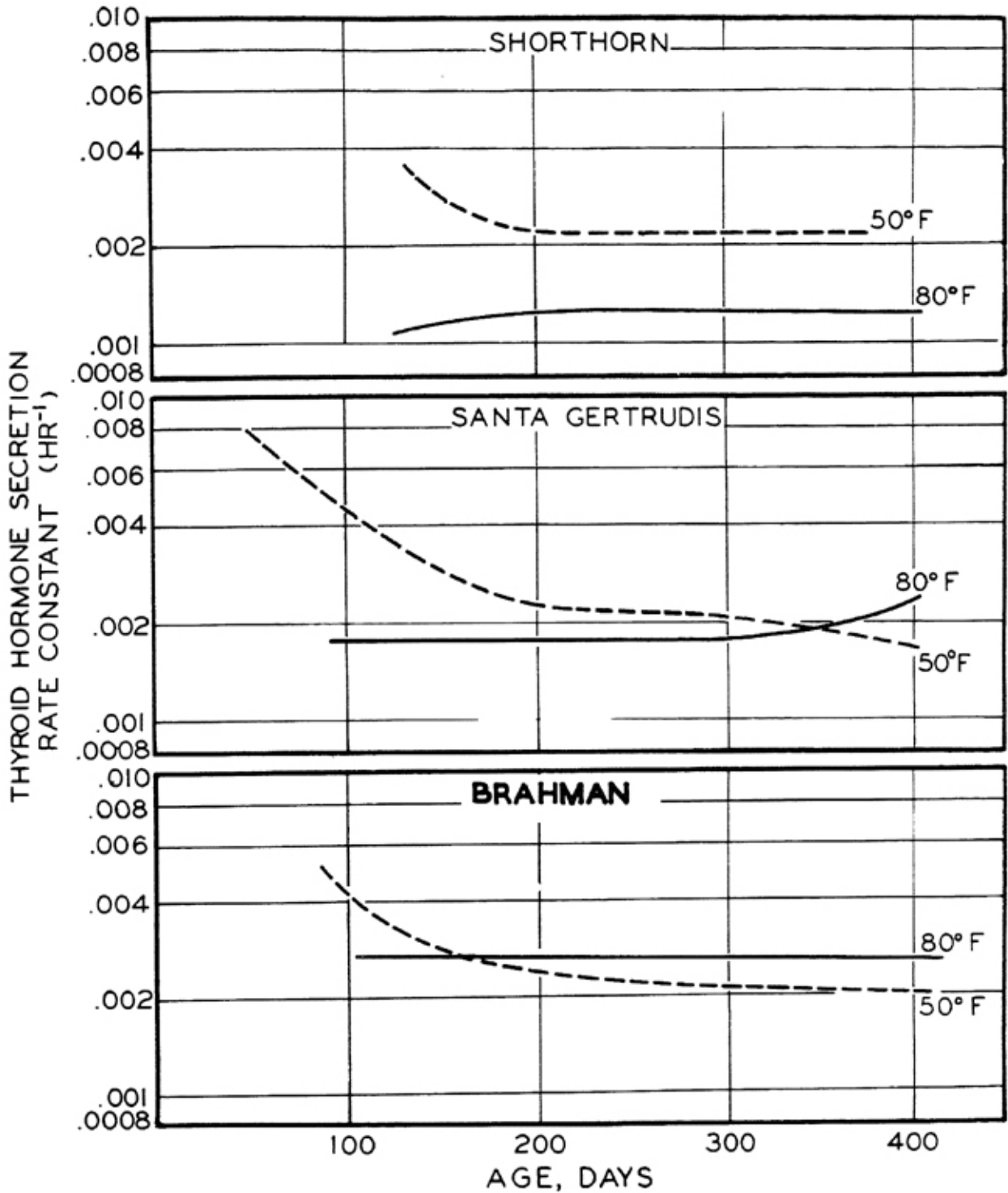


Figure 5. Effect of temperature on the thyroid secretory activity of growing heifers. The 80° F temperature depressed the thyroid secretory activity of Short-horn heifers by 45 percent, of Santa Gertrudis slightly, and does not reduce that of the Brahman heifers. (See figures 10, 11, and 12 for complete data.)

three to four times greater. This atypical behavior was not apparent in the rate constant for thyroid uptake of I^{131} or the maximum thyroid uptake of I^{131} (Fig. 10). Other measurements taken during this time, to be published in other bul-

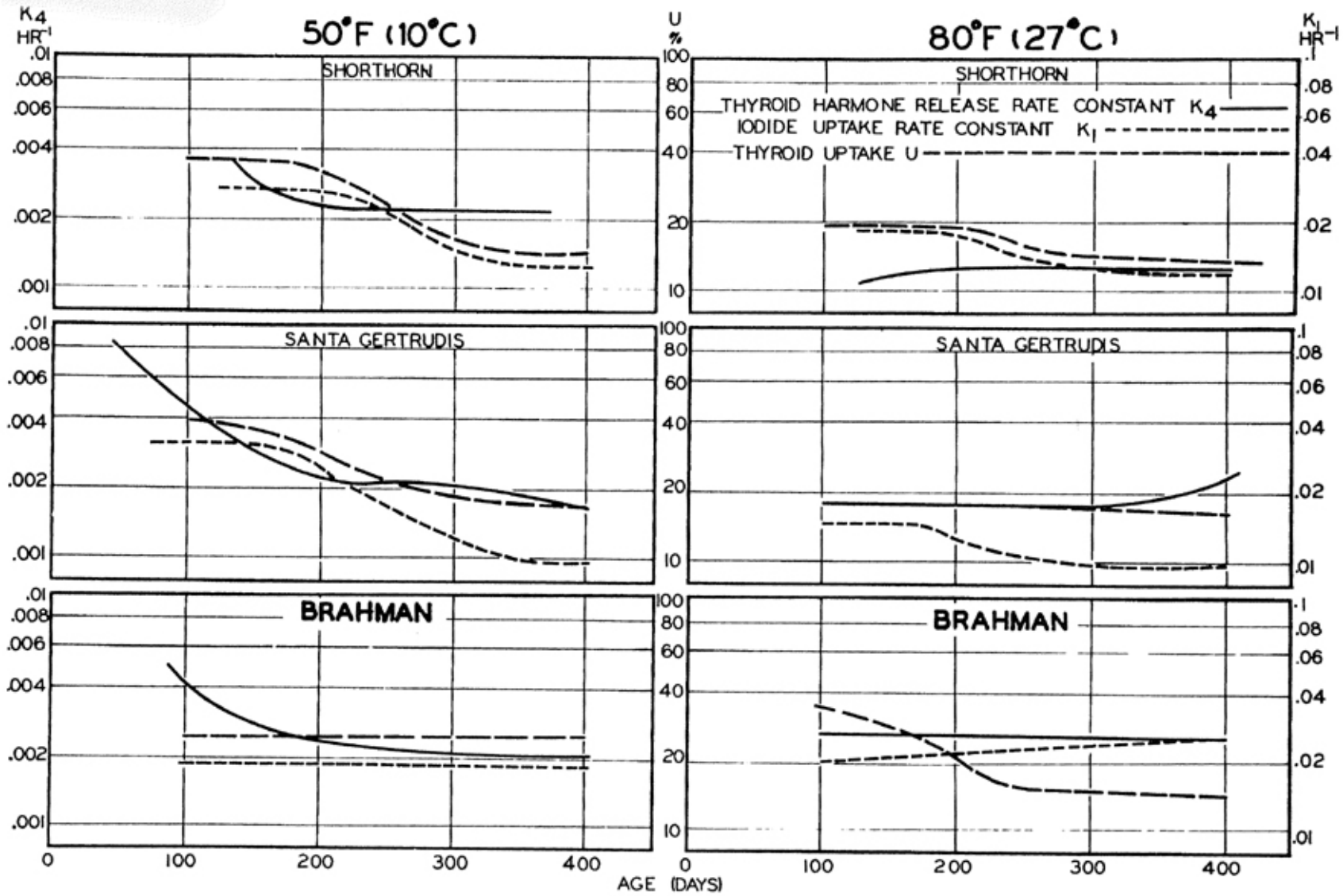


Figure 6. Effect of temperature on thyroid iodide uptake and secretory activity of growing heifers. Note that the rate constant for thyroid uptake and the maximum thyroid uptake of I^{131} decreases after the decrease in the rate constant for thyroid hormone secretion. (See figures 10, 11, and 12 for complete data.)

letins in this series, were also atypical.²⁷ For example, her surface area was greater at a given weight, her rectal temperature was lower, and her weight gain was better. In short, she appeared to be an unusually heat tolerant Shorthorn. Because of these differences, thyroid secretory rate constant data from this heifer were *not* included in constructing the average curves.

Figure 6 compares the rate constants for hormone release and iodide uptake and the maximum thyroid uptake of I^{131} (See also Figs. 10-12). Note that the two parameters characteristic of the uptake of iodide by the thyroid gland—the rate constant for thyroid uptake (k_1) and the maximum uptake of I^{131} (U)—parallel each other closely in all cases except for the Brahmans at 80° F. There was a wide dispersion of the data for these animals (see Fig. 12).

Comparing the parameters of iodide metabolism (k_1 and U) with the rate constant for hormone release (k_4) for the 50° F group, iodide metabolism is essentially constant as the hormone secretion rate decreases. As the hormone secretion rate becomes constant, the iodide metabolism decreases and again becomes constant at 300-400 days of age. In the Brahman animals at 50° F iodide metabolism was invariant with time. At 80° F we again see this same pattern of iodide metabolism but with the magnitude of the change greatly reduced.

The heifers raised outside the Climatic Laboratory exhibited a declining trend in thyroid secretory activity and thyroid iodide uptake with age. These changes are not as clearcut as in the 50° F group because the age changes are confounded by variable temperature. The data are given in Figure 13 in the Appendix.

In this experiment the rate of iodide clearance (k_1) and the overall efficiency (U) of iodide uptake by the thyroid gland decrease only after the rate of hormone release (k_4) has reached its minimum value. This could possibly indicate that reduced secretion of hormone "causes" reduced uptake of iodide rather than the converse.

Effect of Thermal Stress on Heifers Grown at 50° and 80° F.

Due to the nature of this study, and the short time interval at 100° F (38° C) (see Table 1), a special technique was necessary for assaying thyroid activity at this high temperature:

If the heifers were at a given temperature for two weeks or more or at 50°, 65°, 80° F, the technique described earlier was used. At 100° F, a short, 5 day, exposure was used. This was insufficient for measuring the slope of the curve for the release of I^{131} after injection. The following technique was used. At 90° F (a two week temperature period), 0.3 mc NaI^{131} was injected and the measurements conducted as described earlier. Approximately two weeks after injection the temperature was raised to 100° F. Measurements of the thyroid I^{131} were continued three times daily for the five days the animals were at 100° F. The slope of the thyroid I^{131} curve decreased when the temperature increased. The slopes of the two segments were calculated separately.

To obtain k_4 , the rate constant for hormone release, it is necessary to correct the slope for reutilization of I^{131} by the thyroid gland. As explained elsewhere,²⁴ this is done by dividing the slope (of the natural logarithm thyroid I^{131} vs. time curve) by $1-U$ where U (maximum thyroid uptake) is expressed as a fraction rather than as a percent. For the 100° F portion of the curve we have no measured U . Since the curve is very flat at 100° F and since the measured U at 90° F was of the order of 10 percent, the extrapolation of the 100° F curve to the time of injection was taken as U . These values were somewhat less than the U at 90° F being about 8 percent. This procedure is approximately valid only because the maximum uptake values are low and hence the correction factor $1-U$ was near unity. In this case if the assumed uptake is in error by 50 percent the correction factor would be in error by only 5 percent. This is not a generally valid procedure and is approximately valid only for calculations where the slope of the curve is nearly flat and its absolute magnitude is low.

The average data for the rate constant for hormone release are given in Figure 7. The temperature during growth did not affect the thyroid response of the heat tolerant Santa Gertrudis and Brahman heifers. Shorthorn heifers raised at 80° F showed markedly greater thyroid activity at 90° F than those raised at 50° F. The Shorthorns raised at 80° F were stunted and had a disproportionately large surface area per unit body weight.† Thus, probably because they were abnormal, they were able to maintain their thyroid secretion in the face of rising ambient temperature. In this study, Shorthorn 338, which had reacted atypically in the previous study, reacted similarly to the other two Shorthorn heifers and was included in preparing Figure 7.

The Shorthorn calves raised at 50° F were most affected by high temperature. At 100° F their thyroid secretory activity was reduced 60 percent compared to that at 50° to 65° F. The Santa Gertrudis were less affected and the Brahmans practically unaffected. Again we see the superior heat tolerance of Santa Gertrudis and Brahman animals.

Blood Volume.

Brownell²⁴ pointed out that the initial dilution of injected radioiodide could be used as a measure of blood volume. Immediately after injection, radioiodide is mixed with the blood and undergoes transcapillary diffusion. Serial blood samples taken immediately after injection reflect this transcapillary transfer and if plotted will give an extrapolated value at zero time of the initial dilution of the iodide. From this the blood volume is computed. Details of the method are given below:

Radioiodide was quickly injected into the jugular vein through an indwelling polyethylene tube, and the tube flushed with isotonic saline. After allowing 1 to 1.5 minutes for mixing, two 5-ml blood samples were drawn in quick succession and rejected. Two minutes after injection and every two minutes thereafter for 10 minutes, a 10-ml blood sample was drawn for determination of the plasma radioiodide concentration. Care was taken to draw a few milliliters of blood from the tube and reject it before each sample was taken.

†Data on surface area will be presented in a later bulletin.

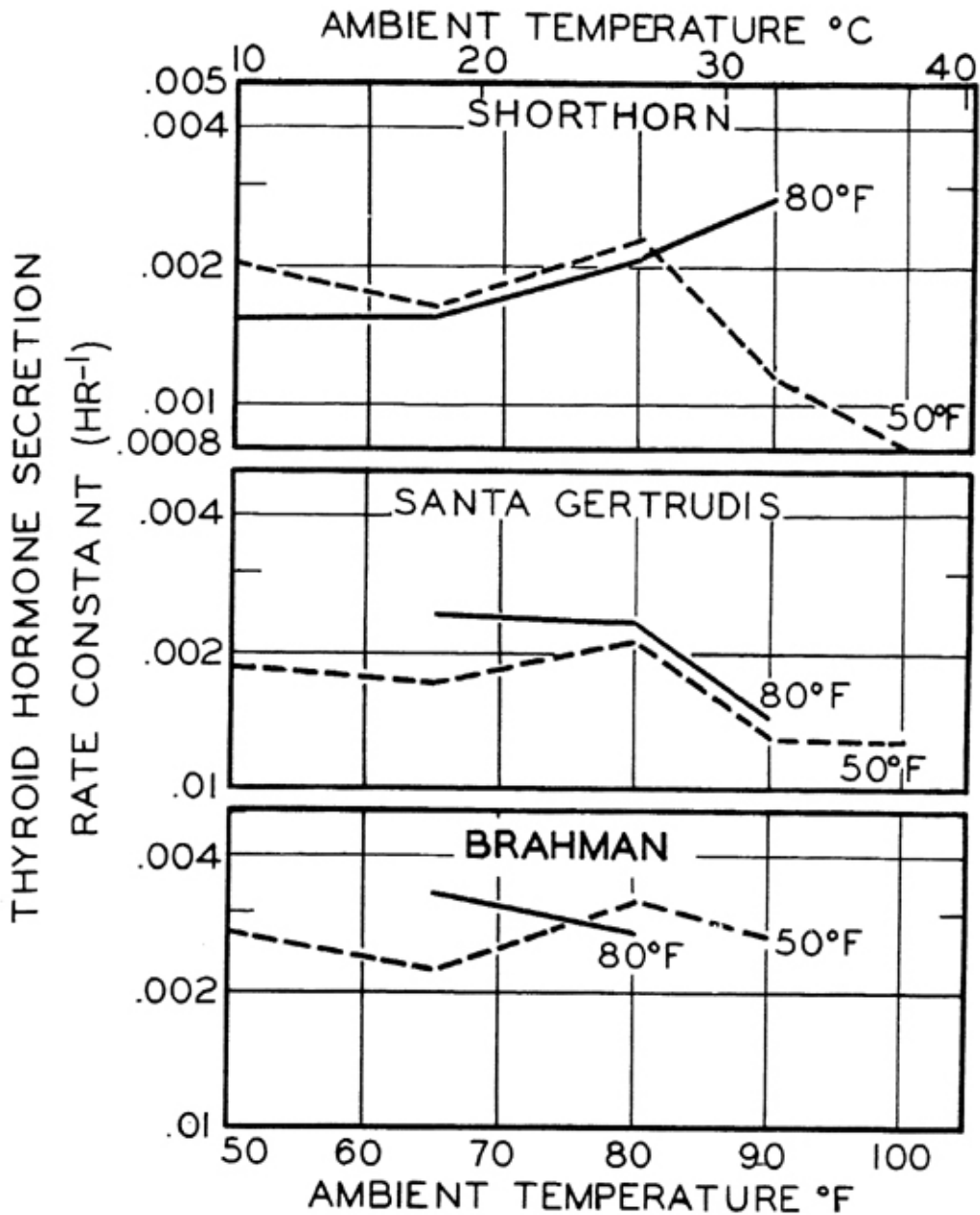


Figure 7. Effect of increasing ambient temperature on the thyroid secretory activity of heifers raised at 50° and 80° F. Each data point is the average of three animals.

The plasma radioiodide concentration in percent of dose per liter was plotted against time after injection on semilogarithmic paper. The straight line was extrapolated to the zero time axis. The blood volume in liters is 100 divided by the extrapolated initial concentration of I^{131} in percent of dose per liter. The slope of the line times 0.303 is the rate constant for transcapillary diffusion of I^{131} .

Table 4 compares this *experimental* radioiodide method for measuring blood volume with the standard method using the dilution of Evans blue dye (T-1824).

TABLE 4--COMPARISON OF METHODS OF DETERMINING BLOOD VOLUME

Calf no.	Date	Blood volume (liters)		Difference		
		Iodide ¹³¹	Evans blue*	Lite	%	
S-332	3/1/56	31	22	+ 9	+22	
S-338	12/6/55	22	18	+ 4	+22	
	1/24/56	32	30	+ 2	+ 7	
	2/22/56	36	27	+ 9	+33	
	12/13/56	33	26	+ 7	+27	
S-342	1/17/56	34	29	+ 5	+17	
	2/7/56	28	25	+ 3	+12	
	12/13/55	25	34	- 9	-27	
SG-366	12/13/55	25	34	- 9	-27	
SG-384	12/6/55	26	27	- 1	- 4	
	2/22/56	25	30	- 5	-17	
	1/17/56	50	33	+ 7	+21	
SG-387	2/7/56	30	34	- 4	-12	
	3/1/56	19	26	- 7	-27	
	1/24/56	29	28	+ 1	+ 4	
SG-393	1/24/56	29	28	+ 1	+ 4	
B-301	1/17/56	23	33	-10	-30	
	2/7/56	26	22	+ 4	+18	
	12/13/55	21	16	+ 5	+31	
B-309	1/17/56	15	15	0	0	
	3/1/56	22	17	+ 5	+29	
	1/24/56	36	31	+ 5	+16	
	2/22/56	21	24	- 3	-13	
				Average	+ 1.3	+ 7
				Average difference	+ 5.0	+19

*Data from: Dale, H.E. and Brody, S., Unpublished data.

Over the 21 comparisons given in Table 4, the mean difference appears insignificant. The two methods thus may measure the same blood volume. Data are not available for comparison of the relative accuracy of the two procedures.

Both techniques are dilution techniques. However, the radioiodide method measures the blood volume directly, whereas the Evans blue dye method measures the plasma volume directly, and the blood volume may be computed by using the hematocrit. Furthermore, the radioiodide method requires very rapid sampling over a short (10 to 15 minutes) time period, whereas the Evans blue dye method requires the same number of samples over a longer (60 to 90 minutes) period. The rate of disappearance of iodide from the blood represents the transcapillary diffusion of an ion and the rate of disappearance of Evans blue dye is the rate of metabolism of a very complex synthetic dye. The blood volume may be determined by the iodide dilution technique as a by-product of a thyroid activity study by using the same injection of I^{131} .

Transcapillary Diffusion of Iodide.

The rate of transfer of I^{131} across the capillary barrier can be measured by taking serial blood samples immediately after radioiodide injection. The detailed method is given in the previous section and elsewhere.²

The data were taken in connection with the blood volume study. For the blood volume study a random sample was desired of the heifer in the Psychro-energetic Laboratory. Data at more than one ambient temperature were obtained

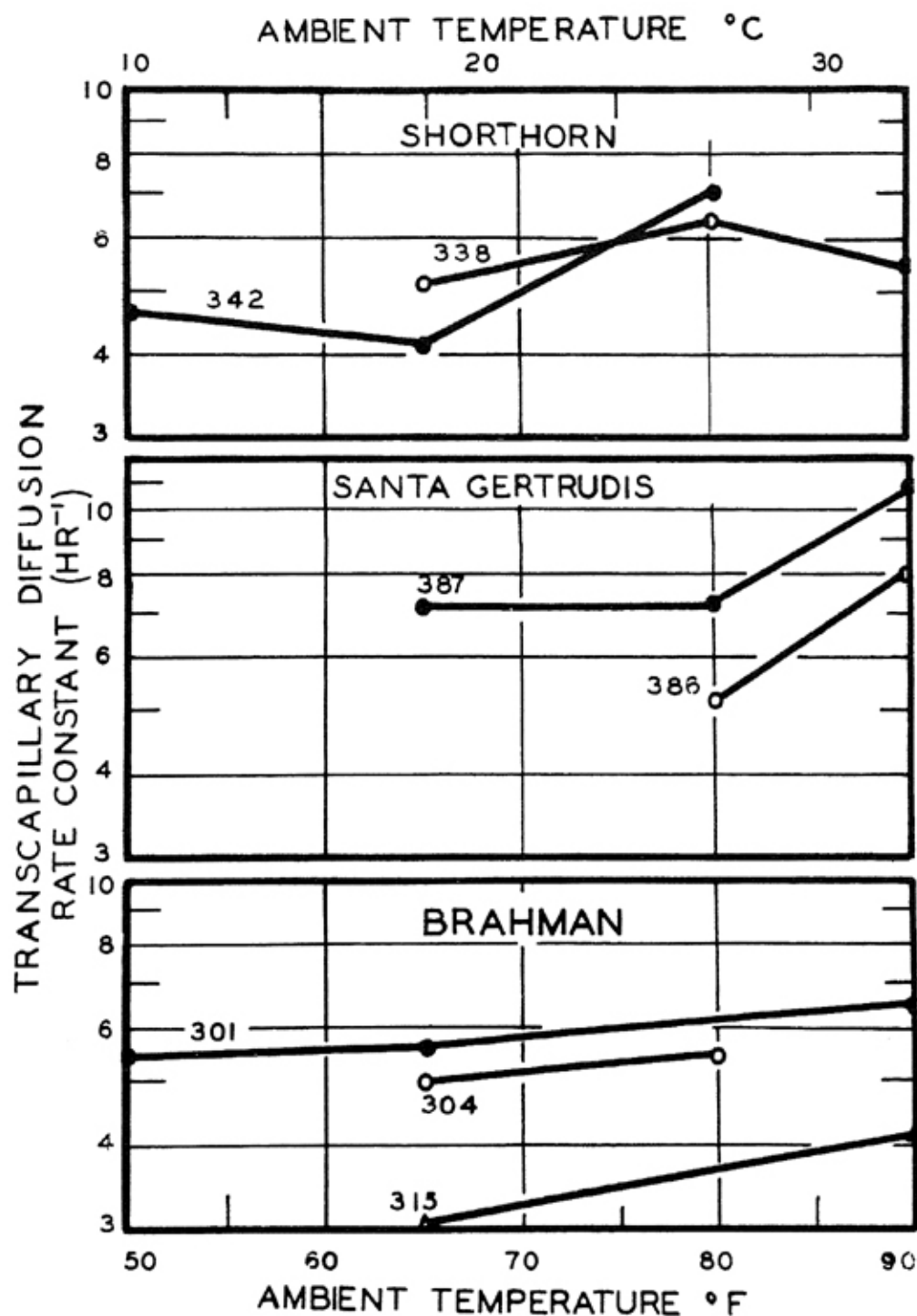


Figure 8. Effect of increasing ambient temperature on the rate of transcapillary diffusion of I^{131} . As the ambient temperature increased, the rate constant for transcapillary diffusion increased. The heifer numbers are indicated on the graph. (Individual data points shown).

on seven heifers. These data are given in Figure 8. As ambient temperature increased, the rate constant for transcapillary diffusion of I^{131} tended to increase slightly. This increased diffusion rate was probably the result of increased tem-

perature of the capillary bed and due to purely physical rather than biological phenomena.

Iodide Space.

The iodide space is the total volume of body fluids into which the iodide ion can diffuse.²⁴ This includes the blood volume, the thyroid gland, the extracellular fluids and perhaps other smaller volumes. The diffusion of radioiodide from the blood and into the extrablood fluids occurs rather rapidly. After approximately one-half hour the concentration of radioiodide in the blood is representative of that in the entire iodide space.¹ It is lost slowly from the iodide space by excretion and by uptake by the thyroid gland. For measurement,^{1,2,24} serial blood samples were taken hourly after injection of radioiodide. The concentration of I^{131} is plotted against time and the exponential curve extrapolated to zero time to give the dilution of I^{131} as if it diffused instantaneously into the entire iodide space. The detailed method and calculations are analogous to those given above for blood volume, the only difference being that samples were taken hourly.

Iodide space was measured in all animals each time thyroid function was assayed. It was found to be independent of breed and temperature.

The equation relating body weight and iodide space (Fig. 9) had an exponent of 0.73. This is precisely the exponent found in equations relating body weight with surface area, resting metabolism, endocrine gland weight (except the thyroid gland) and many other physiological variables.²⁶ Why? Blood volume is known to vary as the first power of body weight.²⁶ The weight of the thyroid gland, and hence, presumably, that part of the thyroid gland included in the iodide space, varies as the first power of body weight.²⁶ Thus the extracellular fluid space probably varies as something less than the first power of body weight.

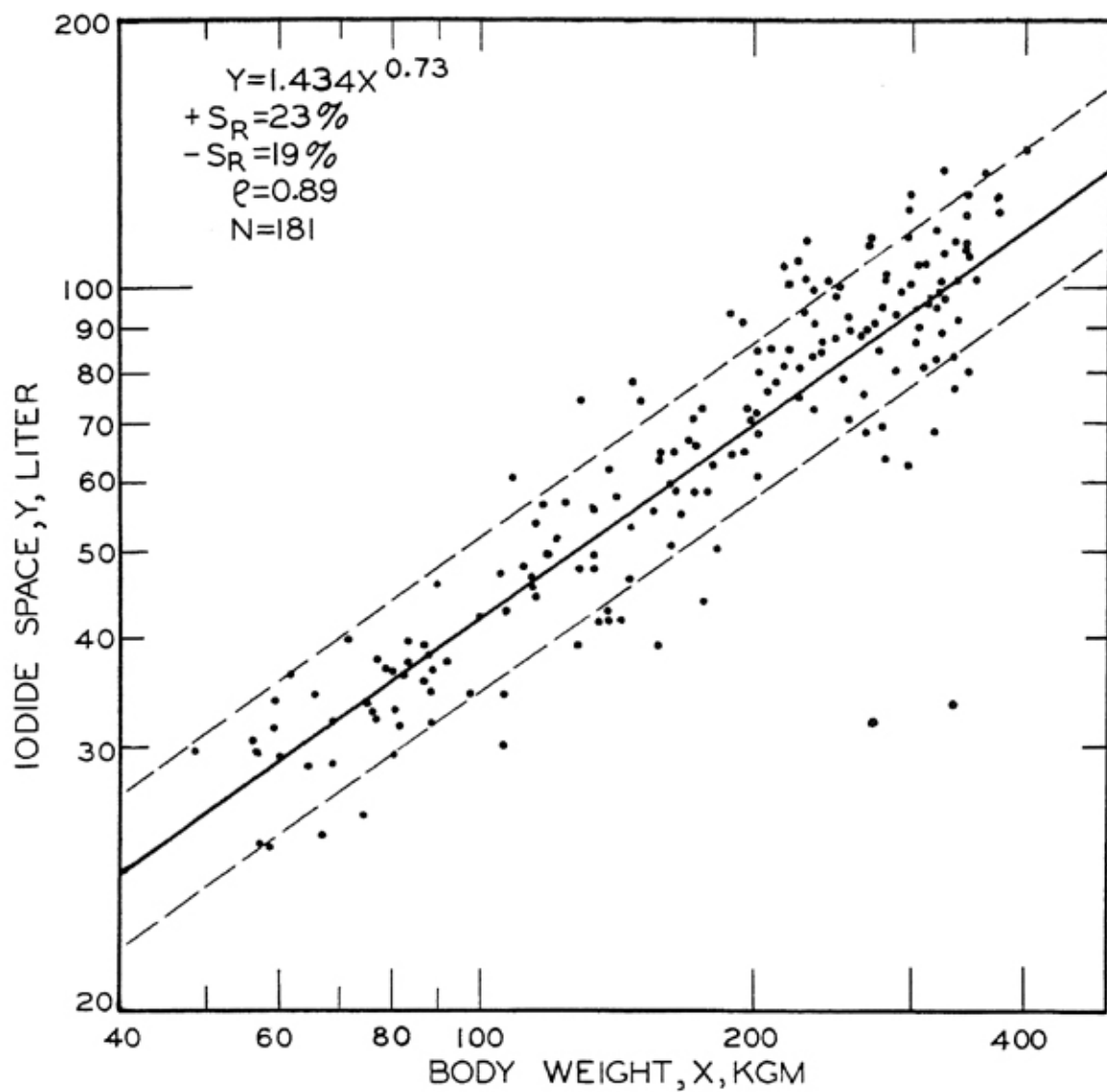


Figure 9. Iodide space as a function of body weight. The correlation coefficient of 0.89 is highly significant.

BIBLIOGRAPHY

1. Blincoe, C., and Brody, S., Univ. Mo. Agr. Exp. Sta. Res. Bul. 576, 1955.
2. *Ibid.*, 579, 1955.
3. Blincoe, C., and Brody, S., Proceedings of the International Conference on the Peaceful Uses of Atomic Energy. Vol. 12, p. 266, 1956.
4. Stevens, C. E., D'Angelo, S. A., Paschkis, K. E., Cantarow, A., and Sunderman, F. William, *Endocrinology*, 56:143, 1955.
5. Brown-Grant, K., *J. Physiol.*, 131:52, 1956.
6. Hurst, V., and Turner, C. W., Univ. Mo. Agr. Exp. Sta. Res. Bul. 417, 1948.
7. Dempsev, E. Q., and Astwood, E. B., *Endocrinology*, 32:509, 1943.
8. Monroe, M. A., and Turner, C. W., Univ. Mo. Agr. Exp. Sta. Res. Bul. 403, 1946.
9. Schultz, A. B., and Turner, C. W., *Ibid.*, 392, 1945.
10. Biellier, H. V., and Turner, C. W., *Poultry Sci.*, 34:1158, 1955.
11. Smyth, J. R., and Fox, T. W., *Poultry Sci.*, 30:607, 1951.
12. Long, J. F., Gilmore, C. O., Curtis, G. M., and Rife, D. C., *J. Animal Sci.*, 10:1027, 1951, and *J. Dairy Sci.*, 35:603, 1952.
13. Reese, R. P., and Mann, E. B., *Proc. Soc. Exptl. Biol. Med.*, 79:208, 1952.
14. Lewis, R. C., and Ralston, N. O., *J. Dairy Sci.*, 36:33, 1953.
15. Kunkel, H. O., Colby, R. W., and Lyman, C. M., *J. Animal Sci.*, 12:3, 1953.
16. Gawienowski, A., Mayer, D. T., and Lasley, J. F., *J. Animal Sci.*, 12:946, 1953 (abstract).
17. Stokes, D. K., Jr., Futrell, M. F., and Kunkel, H. D., *J. Animal Sci.*, 12:897, 1953 (abstract).
18. Reineke, E. P., and Henneman, H. A., Proceedings of the International Conference on the Peaceful Uses of Atomic Energy. Vol. 12, p. 397, 1956.
19. Pickering, O. E., Fisher, D. A., Scott, K. G., Wagener, G. Van, and Smyth, F. S., *Am. J. Diseases of Children*, 86:574, 1953.
20. Quimby, E. H., Werner, S. C., and Schmidt, C., *Proc. Soc. Exptl. Biol. Med.*, 75:537, 1950.
21. Thompson, H. J., and Stewart, R., *Agr. Eng.*, 33:201, 1952; and Thompson, H. J., *Mo. Agr. Exp. Sta. Res. Bul.* 542, 1954.
22. Rhoad, A. O., *J. Heredity*, 40:115, 1949.
23. Blincoe, A., *Nucleonics*, 11(#11):70, 1953.
24. Brownell, G. L., *J. Clin. Endo.*, 11:1095, 1951.
25. Dale, H. E., and Brody, S., Unpublished data.
26. Brody, S., *Bioenergetics and Growth*, Reinhold Publishing Corp., New York, 1945.
27. Ragsdale, A. C., Cheng, Chu Shan, and Johnson, H. D., *Univ. Mo. Agr. Exp. Sta. Res. Bul.* 642, 1957.

APPENDIX

SHORT HORN

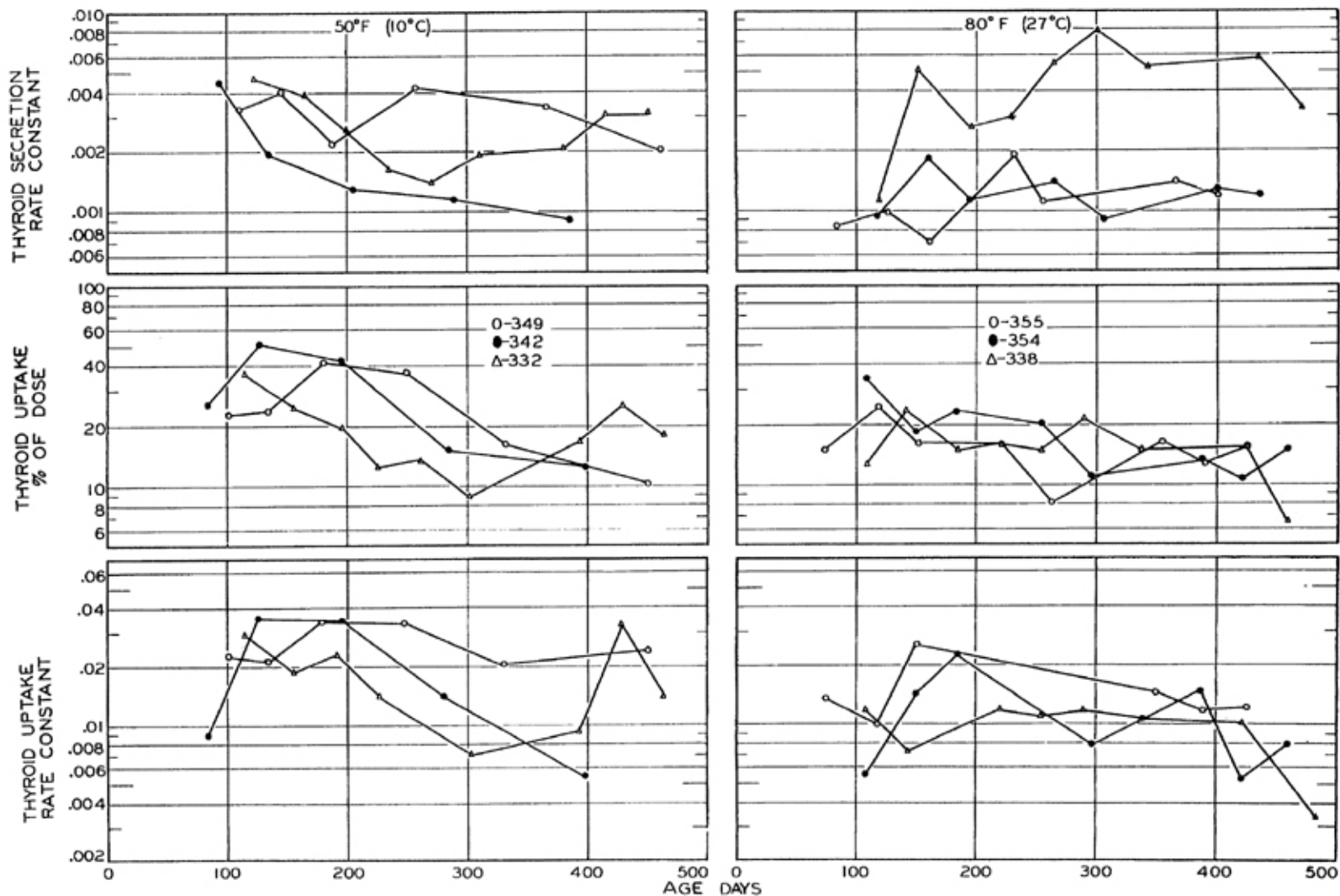


Figure 10. Detailed graph of the effect of ambient temperature on the thyroid function of growing heifers. See figures 4, 5, and 6 for the average graphs.

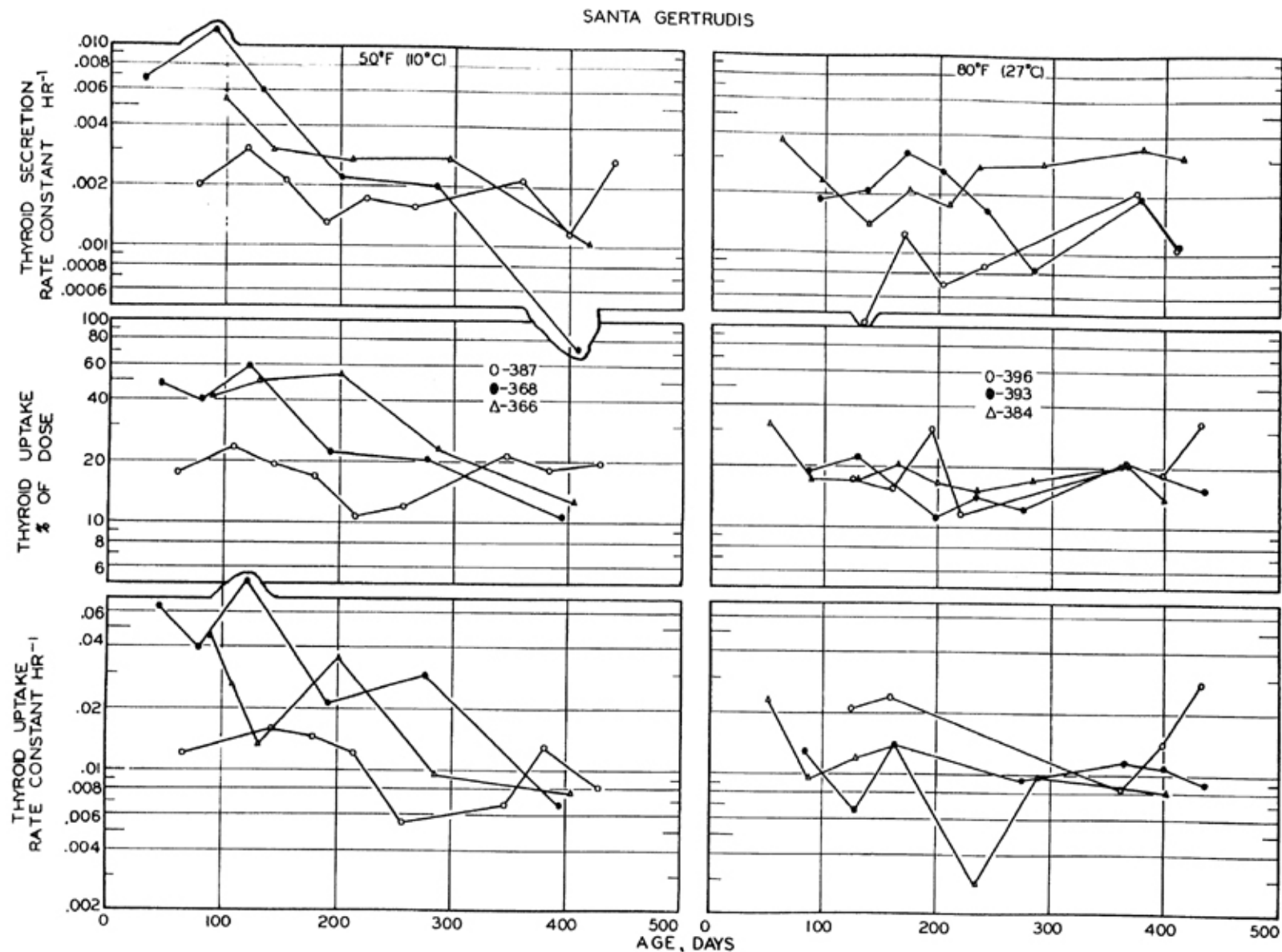


Figure 11. Detailed graph of the effect of ambient temperature on the thyroid function of growing heifers. See figures 4, 5, and 6 for the average graphs.

BRAHMAN

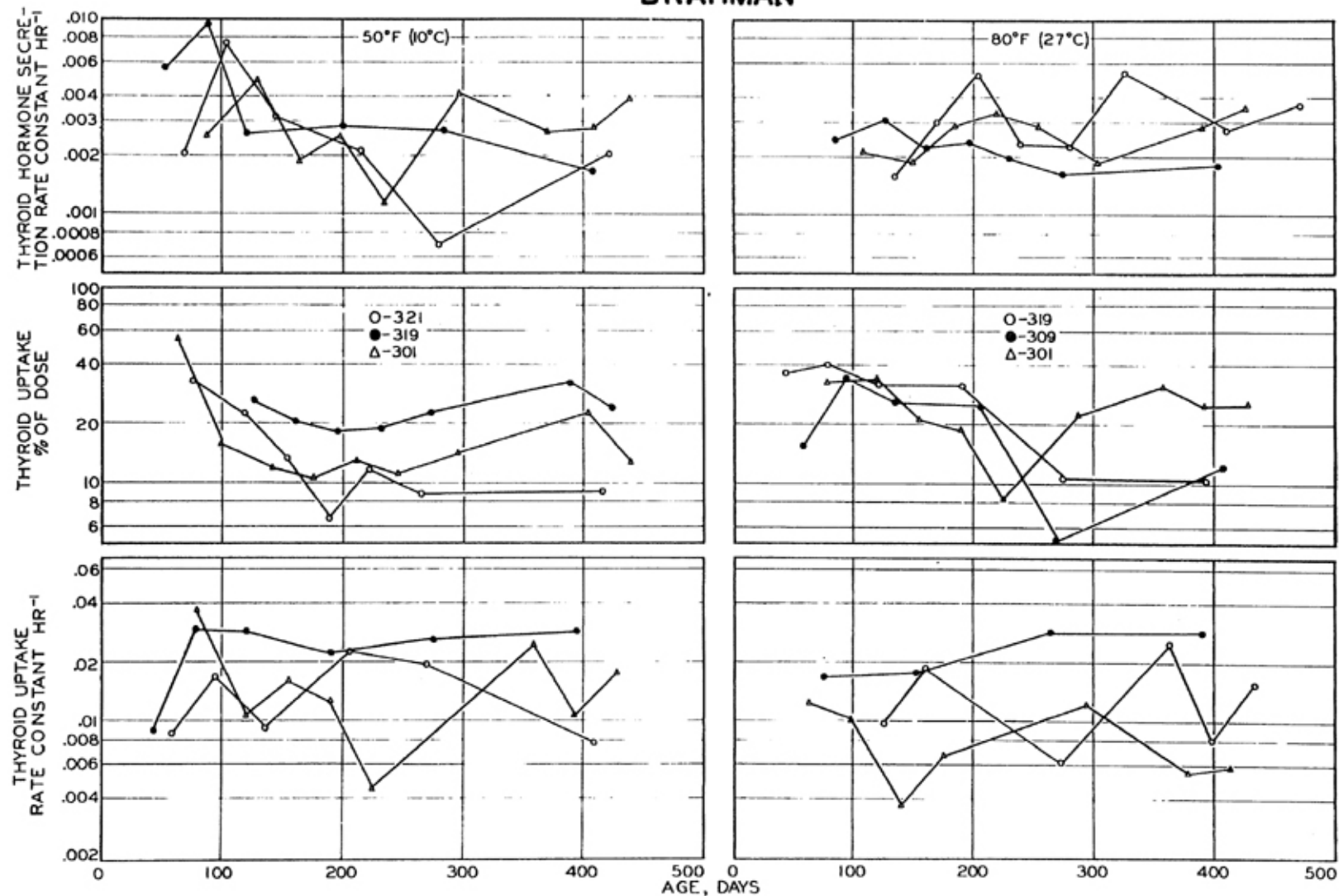


Figure 12. Detailed graph of the effect of ambient temperature on the thyroid function of growing heifers. See figures 4, 5, and 6 for the average graphs.

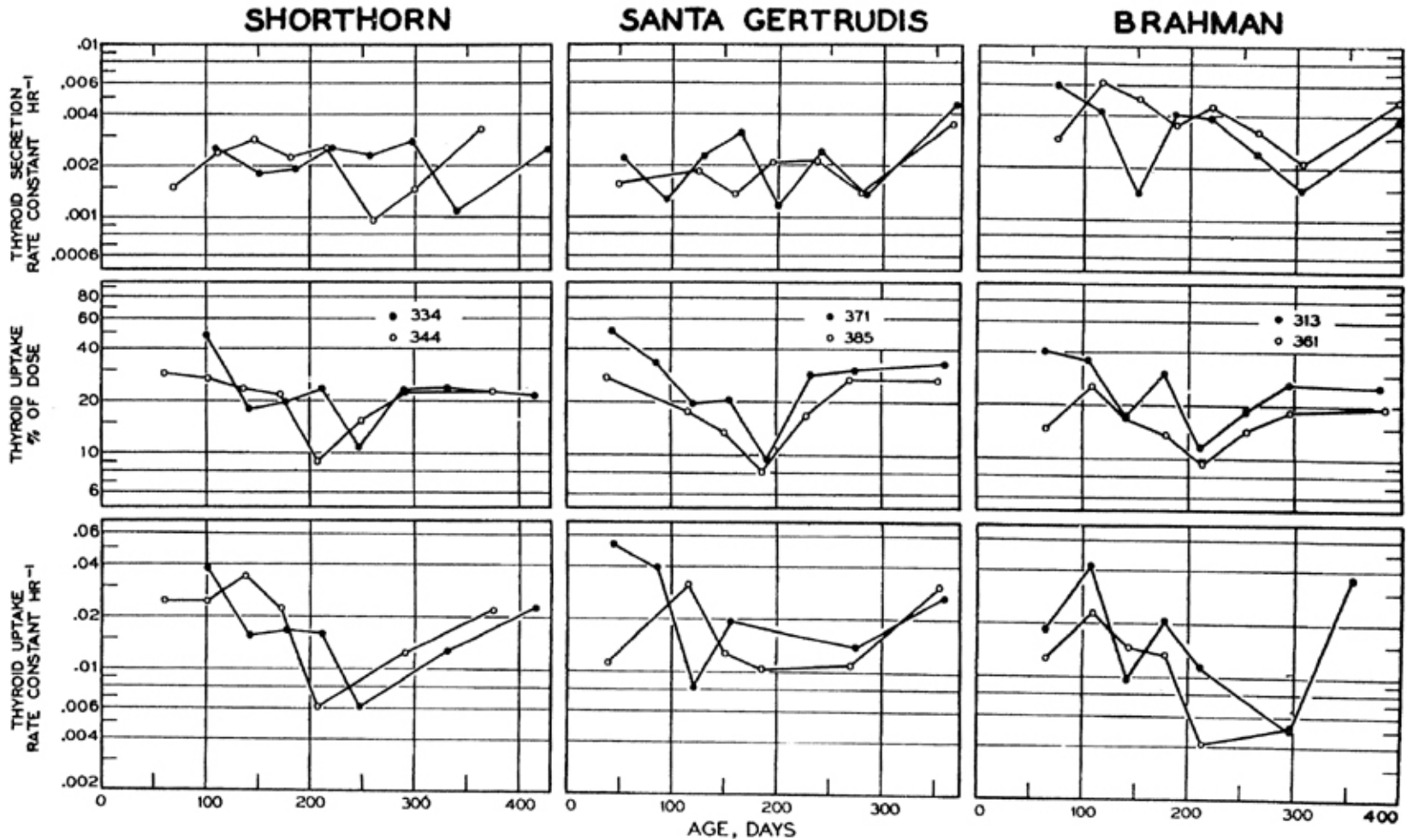


Figure 13. Detailed graph of the thyroid function of growing heifers raised under normal (outdoor) conditions.